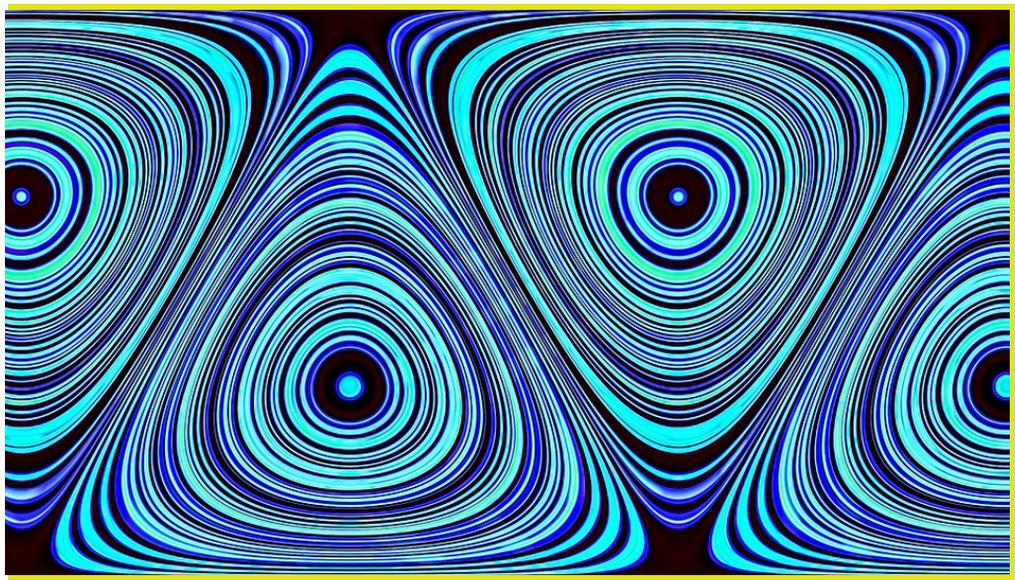
E-ISSN 2564-7288

JBACHS

Journal of Basic and Clinical Health Sciences



Volume 8 • Issue 2 • May 2024

https://dergipark.org.tr/en/pub/jbachs

DOKUZ EYLÜL UNIVERSITY INSTITUTE OF HEALTH SCIENCES

Journal of Basic and Clinical Health Sciences

Journal Boards

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 226
RETRACTION- RESEARCH ARTICLE

RETRACTION: EFFECTS OF MOTHERS PERCEIVED SOCIAL SUPPORT DURING POSTNATAL PERIOD ON THEIR PERCEIVED BREASTFEEDING SELF-EFFICACY

Tuba Giynas[1], Nurdan Akcay Didisen[1]

[1] Ege University, Nursing Faculty, Pediatric Nursing Department, Izmir, Turkey

ORCID: T.G. 0000-0002-4738-0421; N.A.D. 0000-0002-4371-6020

Corresponding author: Nurdan Akcay Didisen, **E-mail:** nurdan.akcay@ege.edu.tr

NOTICE OF RETRACTION:

Related Article: Giynas T, Akcay-Didisen N. Effects of Mothers Perceived Social Support During Postnatal Period on Their Perceived Breastfeeding Self-Efficacy. J Basic Clin Health Sci 2022; 6: 81-88 (https://doi.org/10.30621/jbachs.978506).

The article given details above and published in the Journal of Basic and Clinical Health Sciences (2022; 6: 81-88), has been retracted based on the decision of (Decision No:3) Health Sciences-Scientific Research and Publication Ethics Committee of Dokuz Eylul University on 25 April 2024.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 227-235
https://doi.org/10.30621/jbachs.1070068
RESEARCH ARTICLE

INVESTIGATION OF EMOTIONAL EATING, UNCONTROLLED EATING AND MINDFUL EATING BEHAVIORS IN FEMALE NURSING STUDENTS: A CROSS-SECTIONAL STUDY

Gülsüm Zekiye Tuncer[1], Zekiye Çetinkaya Duman[2]

[1] Dokuz Eylul University, Faculty of Nursing, Department of Psychiatric Nursing, Izmir, Turkey
[2] Dokuz Eylul University, Faculty of Nursing, Department of Psychiatric Nursing, Izmir, Turkey

ORCID: G.Z.T. 0000-0001-8969-7139; Z.Ç.D. 0000-0002-7447-874X

Corresponding author: Gülsüm Zekiye Tuncer, **E-mail:** gulsumdamlarkaya@gmail.com
Received: 08.02.2022; **Accepted:** 19.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Tuncer GZ, Çetinkaya-Duman Z. Investigation of Emotional Eating, Uncontrolled Eating and Mindful Eating Behaviors in Female Nursing Students: A Cross-sectional Study. J Basic Clin Health Sci 2024; 8: 227-235.

ABSTRACT

Purpose: In this study, it was aimed to investigate female nursing students' emotional eating, uncontrolled eating and mindful eating behaviors, perceived stress levels and the relationship between these variables.
Material and Methods: The sample of the study consisted of 106 3rd and 4th grade female nursing students aged 20-28 years studying in a nursing faculty in the 2020-2021 academic year. Data were collected using Three-Factor Eating Questionnaire (TFEQ), Mindful Eating Questionnaire (MEQ), and Perceived Stress Scale (PSS).
Results: While the mean score the participants who did not eat regularly obtained from the uncontrolled eating subscale was significantly higher, the mean scores the participants who were on a diet obtained from the MEQ, and cognitive restriction, emotional eating subscales and their mean BMI values were significantly higher ($p<.05$). It was determined that while the change in the participants' BMI could explain their emotional eating behaviors ($B = 1.35$, $p <.05$), the change in their mindful eating could explain both their emotional eating and uncontrolled eating ($p <.05$).
Conclusion: In this study, it was determined that during the online education period, the participants suffered eating behaviors-related problems, that they did not develop mindful eating behaviors, and that there was a relationship between their eating behavior-related problems.

Keywords: Emotional eating, female nursing students, mindful eating, uncontrolled eating,perceived stress

INTRODUCTION

Eating behavior is an important requirement for individuals to maintain their survival. This requirement is a complex process in which not only physiological factors but also psychological factors play an important role (1). In general, eating behavior problems are defined as binge eating, undereating and compensatory behaviors (2). Emotional eating triggered by emotional stimulation constitutes an important dimension of binge eating behavior and may urge an individual to overeat (1). Emotional eating is an eating problem that refers to the tendency to overeat, which occurs in response to stress and negative emotions (3). Emotional eaters use their eating behavior as a coping method to get rid of negative emotions or stress, which as a result, turns into a problematic behavior (1,4). Another binge eating behavior is uncontrolled eating. Uncontrolled

eating is defined as a tendency to lose control over food consumption when a person feels hungry, and he or she is exposed to an external stimulus (5). In several studies, eating problems have been reported to increase weight gain, and to cause problems such as low self-esteem, lack of emotion management and eating disorders (3). In addition, eating problems can be a potential factor of obesity (6). One of the appropriate eating behaviors that prevent these problems from occurring is an individual's developing mindful eating behavior (7). Mindful eating is defined as an eating behavior through which a person internalizes the symptoms of physical hunger and satiety and becomes aware of his or her feelings and thoughts by focusing on the food to be consumed at that moment without judging the environmental factors and food choices (8,9). In the literature, it is reported that individuals with a high level of mindful eating behavior have emotional eating behaviors less and experience less stress (10).

Among the groups suffering from eating problems frequently are children, adolescents, women, and obese individuals (11-13). Eating problems are common not only in obese people, but, in particular, also in normal weight young women (14). Therefore, it is very important for young women to maintain appropriate eating behaviors to protect their health (15). The review of the literature has revealed that nursing students who are in one of these risk groups including young women suffer from eating problems (16). In several studies, it has been determined that students' eating habits worsen as their stress level increases (17-20). Students' emotional and uncontrolled eating behaviors are also affected by their perception of stress. In addition, in studies, presence of a relationship between these students' emotional eating behaviors and their perceived stress levels is reported (14,21). Therefore, high levels of perceived stress adversely affect students' eating behaviors (22,23). Especially female nursing students are exposed to stress at high levels during their education, a transition period of their lives (21). Nursing students may face academic, clinical and psychosocial stressors from the first moments of their education life (20). Especially during the online education period, life changes such as fear of illness, health anxiety, social isolation, online education, and disruption of nursing education processes are also among the factors leading to stress (23,24).

Female nursing students' being in the educational process and in a transition period due to the Covid-19 Pandemic causes them to perceive stress at a higher level, which may cause female nursing students to have eating behaviors-related problems (23-25). In the literature, the relationship between nursing students' emotional eating, uncontrolled eating and mindful eating behaviors, and their perceived stress levels has not been fully illuminated and the number of studies investigating this issue from the aspect of women is very few. In addition, determining the emotional eating and uncontrolled eating behaviors of students in a stressful period such as the Covid-19 Pandemic and the variables that affect this eating behavior will contribute to the content of the interventions that can affect the impaired eating behaviors (25,26). Therefore, this study was conducted to investigate female nursing students' emotional eating, uncontrolled eating and mindful eating behaviors, perceived stress levels during the online education period and the relationship between these variables.

Study questions are listed below:

- What are the emotional eating, uncontrolled eating and mindful eating behaviors of female nursing students like?
- What are the variables that affect female nursing students' emotional eating, uncontrolled eating and mindful eating behaviors and perceived stress?
- Is there a relationship between emotional eating, uncontrolled eating and mindful eating behaviors and perceived stress levels of female nursing students?
- What are the predictive variables for female nursing students' emotional eating, uncontrolled eating and mindful eating behaviors?

MATERIAL AND METHODS

Research Design: This descriptive and cross-sectional study was conducted with 3rd and 4th year female nursing students studying at a Faculty of Nursing between May 2020 and December 2020. In the spring semester, it is aimed to give one-third of the education online and the rest in clinics.

Participants and Sample: The study population included 334 3rd and 4th grade female nursing students studying in the Faculty of Nursing in the 2020-2021 Education and Training year. In this study, 3rd and 4th grade students were purposively selected. In the education program of the faculty where the study was conducted, there is a Nutrition

course in the 2nd semester of the 2nd grade. In order to ensure that students have similar knowledge about eating and nutrition, it was planned that students who had taken the basic nutrition course would constitute the sample. The inclusion criteria of this study were, "3rd and 4th year female students of the nursing faculty", 18-28 years of age" and "taking the Nutrition course in the second year". The students were in the age group of 20-28 years. Of these 334 nursing students, 106 who volunteered to participate in the study comprised the sample of the study. In the Post-hoc Power Analysis performed after the volunteer students included in the sample, the effect size and the power of the study were determined as 0.3 and 94% respectively.

Instruments: The Personal Data Form, Three-Factor Eating Questionnaire (TFEQ), Mindful Eating Scale (MEQ), and Perceived Stress Scale (PSS) were used as data collection tools.

1. Personal Data Form: The Personal Data Form was developed by the researchers based on the pertinent literature (14) in order to obtain information about the sociodemographic, and health- and diet-related characteristics of the participants. The form includes items questioning variables such as the participating nurses' age, body mass index (BMI), eating regularly, doing physical activities regularly and previous dieting status, and the number of meals they have.

2. Three Factor Eating Questionnaire (TFEQ): The Three-Factor Eating Questionnaire (TFEQ) was first developed by Stunkard and Messick in 1985 to measure the behavioral and cognitive components of eating. In 2016, Karakuş et al. studied the psychometric properties of the 21-item TFEQ adapted it into Turkish (5). The items of the TFEQ are rated on a 4-point Likert-type scale feature. The TFEQ measures eating behavior with three sub-dimensions: cognitive restriction (CR), uncontrolled eating (UE) and emotional eating (EE). In Karakuş et al.'s study, the Cronbach's α coefficient values of the subscales were as follows: .80 for the cognitive restriction (CR), .87 for the emotional eating (EE), and.78 for the uncontrolled eating (UE) (5). In this study, the Cronbach's α coefficient values of the subscales were as follows: .89 for the CR, .93 for the EE, and .86 for the UE.

3. Mindful Eating Questionnaire (MEQ): The Mindful Eating Questionnaire (MEQ) was first developed by Framson et al. in 2009 to measure mindful eating. In 2016, Köse et al. studied the psychometric properties of the MEQ adapted it into Turkish (8). The MEQ includes 7 sub-dimensions and 30 items whose responses are rated on a 5-point Likert type scale. Of the 30 items, 20 are reverse scored. The arithmetic mean of the scores obtained from the overall MEQ and its subscales is used for the assessment. The scale also gives a total mindful eating score. The Cronbach's α coefficient value of the scale was .78 in Köse et al.'s study (8) and .67 in the present study.

4. Perceived Stress Scale (PSS): Perceived Stress Scale (PSS-14) was developed by Cohen, Kamarck and Mermelstein (1983) to measure how stressful an individual perceives situations in his or her life. The validity and reliability study of the Turkish version of the PSS was conducted by Eskin et al. (27). The scale consists of 14 items whose responses are rated on a 5-point Likert-type scale. Of the 14 items, seven are reverse scored. While 10 of the items are in the Perceived Helplessness subscale (PSS-10), 4 of the items are in the Perceived Self-Efficacy subscale (PSS-4). The higher the score the person obtains from the scale is, the higher his or her perception of stress is. The Cronbach's α coefficient value of the scale was .84 in Eskin et al.'s study (27) and .88 in the present study.

Procedure: The data collection tools were transferred to the Google Survey forms and the data was collected by sending the forms to the participants' e-mail addresses with ".edu" domain. The forms were sent to the students through their e-mail addresses twice with announcements and three times with reminders. Of the participants, 107 filled in the data collection tool on the dates when the data of the study were collected, and of the forms, 106 which were completely filled out were evaluated. The average time for the participants to answer the tools administered in the study was 9.56 minutes.

Analysis: The mean scores obtained from the TFEQ and MEQ and their subscales were the dependent variables of the study whereas the participants' characteristics were the independent variables of the study. The SPSS 22.0 was used to analyze the data. The descriptive findings were calculated over the number, percentage and mean. Before calculating the data of the study, the Shapiro Wilk test was applied; data showed normal distribution. To perform the analysis of the scores obtained from the Emotional Eating, Uncontrolled Eating, and Mindful Eating subscales, the multiple regression analysis

Table 1. Sociodemographic Characteristics of Female Nursing Students (n=106)

		n	%	X̄ ± SD	Min-Max
Age				21.45 ± 1.36	20 - 28
BMI				21.75 ± 3.51	15.57 - 38.75
The number of meals they have daily				2.86 ± .82	2 - 6
Doing physical activities	**No**	27	25.5		
	Yes	**79**	**74.5**		
Eating regularly	**No**	**74**	**69.8**		
	Yes	32	30.2		
Dieting	**No**	45	42.5		
	Yes	**61**	**57.5**		
Total		106	100		

Table 2. The Mean Scores the Female Nursing Students Obtained from the TFEQ, MEQ and PSS (n=106)

Variables	Sub-dimensions	X̄ ± SD	Min-Max
TFEQ*	Cognitive restriction	48.58 ± 23.57	0-100
	Emotional eating	39.57 ± 28.50	0-100
	Uncontrolled eating	41.12 ± 19.64	0-92
MEQ**	Total score	2.86 ± .33	2.13-3.70
PSS***	Total score	47.06 ± 3.67	37-55
	PSS-4	12.85 ± 1.29	9-15
	PSS-10	33.15 ± 2.94	26-39

*TFEQ = Three-Factor Eating Questionnaire ** MEQ = Mindful Eating Questionnaire *** PSS =Perceived Stress Scale

was used. Pearson Correlation analysis was used to examine the relationship between the variables such as BMI and age, and the mean scores obtained from the TFEQ and its sub-dimensions, from the MEQ and its sub-dimensions and from the PSS and its sub-dimensions. Independent-group t-test analyzes were used to calculate the differences between variables the TFEQ and its sub-dimensions, the MEQ and its sub-dimensions, and the PSS and its sub-dimensions.

Ethical considerations: In order to conduct the study, an institutional permission was obtained from the Faculty of Nursing of a university (decision number: 153, date: May 27, 2020) and the ethics committee approval was obtained from the relevant university's Non-interventional Clinical Research Ethics Committee (date: August 04, 2020, decision number: 2020 / 17-33, 5552-GOA). To administer the TFEQ, MEQ and PSS, permission was obtained from the authors who performed the validity and reliability studies of the scales. In addition, from the participants, informed consent indicating that they volunteered to participate in the study was obtained.

RESULTS

In Table 1, mean values related to the female nursing students' age and BMI, and the number of meals they have daily are given. The analysis of the sociodemographic characteristics of the participants indicated that their mean age and BMI value were 21.45 and 21.75 respectively, that the average number of meals they had daily was 2.86, that 74.5% of them did physical activities, that 69.8% of them did not eat regularly and skipped meals and that 57.5% went on a diet at least once. In Table 2, the mean scores the participants obtained from the TFEQ, MEQ and PSS are given. The mean scores the participants obtained from the cognitive restriction, emotional eating and uncontrolled eating sub-dimensions of the TFEQ were 48.58 ± 23.57, 39.57 ± 28.50 and 41.12 ± 19.64 respectively. The mean score the participants obtained from the MEQ was 2.86 ± .33. The mean scores the participants obtained from the overall PSS, and its PSS-4 and PSS-10 sub-dimensions were 47.06 ± 3.67, 12.85 ± 1.29 and 33.15 ± 2.94 respectively.

In Table 3, the comparison of the mean TFEQ, MEQ, PSS scores with BMI values in terms of the female nursing students' regular eating behavior and physical activity levels are given. The mean score obtained from the uncontrolled eating behavior subscale by the participants who did not eat regularly was significantly higher than was that obtained by the participants who ate regularly ($t = -4.172$, $p < .05$). The mean scores obtained from the mindful eating, cognitive restriction and emotional eating

Table 3. Comparison of TFEQ, MEQ, PSS Scores with BMI in Terms of the Female Nursing Students' Regular Eating Behavior and Physical Activity Levels (n=106)

			MEQ Total		TFEQ cognitive restriction		TFEQ emotional eating		TFEQ uncontrolled eating		PSS		BMI	
			t	p	t	p	t	p	t	p	t	p	t	p
Doing physical activities	**No**	27	-.082	.93	-1.432	.15	.160	.87	.008	.99	-.168	.86	.735	.46
	Yes	**79**												
Eating regularly	**No**	**74**	-1.888	.06	-.191	.84	-1.792	.07	**-4.172***	**.00**	-1.042	.30	.329	.74
	Yes	32												
Dieting	**No**	**61**	**-3.878***	**.00**	**-6.025***	**.00**	**-3.001***	**.00**	-1.213	.22	.055	.95	**-5.338***	**.00**
	Yes	45												

*p < 0.05 **Independent-group t-test analyzes

Table 4. Distribution of the Relationship between the Mean Scores obtained from the TFEQ, MEQ and PSS by the Female Nursing Students (n=106)

		MEQ Total	TFEQ cognitive restriction	TFEQ emotional eating	TFEQ uncontrolled eating	PSS
MEQ Total	r**	1				
	p					
TFEQ cognitive restriction	r	.352*	1			
	p	.000				
TFEQ emotional eating	r	.642*	.250*	1		
	p	.000	.010			
TFEQ uncontrolled eating	r	.583*	.220*	.713*	1	
	p	.000	.024	.000		
PSS	r	.126	.154	.003	.075	1
	p	.199	.116	.975	.446	
BMI	r	.300*	.227*	.353*	.307*	.088
	p	.002	.020	.000	.001	.369

* p < 0.05 **Pearson correlation analyzes

subscales by the participants who dieted and their BMI values were significantly higher than were those of the participants who did not diet (t = -3.878, p <.05; t = -6.025, p <.05; t = -3.001, p <.05; t = -5.338, p <.05).

As is seen in Table 4, there was a low, positive, significant correlation between the mean score for the overall MEQ and that for the cognitive restriction subscale of the TFEQ (r = .35, p <.001), a moderate, positive, significant correlation between the mean score for the overall MEQ and that for the emotional eating subscale of the TFEQ (r = .64, p <.001), a moderate, positive, significant correlation between the mean score for the overall MEQ and that for the uncontrolled eating of the TFEQ (r = .58, p <.001), and a low, positive, significant correlation between the mean score for the overall MEQ and BMI (r = .30, p <.05).

In Table 5, how independent variables explained the female nursing students' emotional eating, uncontrolled eating and mindful eating behaviors was investigated through the multiple regression analysis. It was found that the change in the participants' mindful eating behaviors and BMI values could explain emotional eating behavior (B = 1.35, p <.05; B = 47.75, p <.05), that change in their mindful eating behaviors could explain their uncontrolled eating behaviors (B = 29.43, p <.05), and that the change in their cognitive restriction, emotional eating and uncontrolled eating behaviors could explain their mindful eating behaviors (p <.05).

DISCUSSION

In the present study, female nursing students' eating behaviors and their perceived stress levels, and the relationship between them were examined. The mean value of BMI of the participating students, whose mean age was 21.75, years was 21.45 and the mean number of the meals they had daily was 2.86. In addition, the majority of the participants did physical activities, more than half of them did not eat regularly and skipped meals and more than half of them went on a diet at least once in lifetime (Table 1). In Costarelli and Patsai's study, the mean BMI values of female nursing students in the age group of 18-25 years was 21.38 (28). Similarly, in Salma et al.'s study, the mean BMI values of 67% of female nursing students aged between 22 and 24 years was normal

(19). In a study conducted during the Covid-19 Pandemic, the number of meals nursing students had daily was insufficient (21). In Constant et al.'s study, 68% of the female university students did physical activities moderately (29). In another study, 72% of the female nursing students did not eat regularly (19). In a study conducted during the Covid-19 Pandemic, regular dietary habits of young adults worsened (30). The results of the present study and those of the studies in the literature demonstrate that female nursing students' diet and regular eating behaviors were impaired during the online education period.

In the present study, the scores the participants obtained from the sub-dimensions of the TFEQ suggest that they had eating behavior-related problems (Table 2). In a similar study, the mean scores the young adult students obtained from the cognitive restriction, emotional eating and uncontrolled eating subscales of the TFEQ were 39.3, 37.3 and 40.9 respectively (31). In the present study, the mean score the participants obtained from the mindful eating questionnaire was low. In a study conducted in Australia, the mean score the participating students obtained from the overall MEQ was 2.92 (7). In the present study, the mean score the participants obtained from the Perceived Stress Scale (PSS) was quite high. In another study, 63% of the participating nursing students' perceived stress levels were high (32). In Kalkan Uğurlu et al.'s study conducted with female nursing students during the Covid-19 Pandemic, the participating students' stress levels were high (24). These results suggest that female nursing students perceive high levels of stress and that their eating behaviors are impaired especially during stressful periods such as the Covid-19 Pandemic and the learning process.

In the present study, of the participants, those who did not eat regularly obtained significantly higher mean scores from the uncontrolled eating subscale than did those who ate regularly. In addition, of the participants, those who were on a diet obtained significantly higher mean scores from the emotional eating subscale than did those who did not diet (Table 3). Our search for studies in which the correlation between uncontrolled eating behavior and regular eating habits during the COVID-19 Pandemic was investigated revealed a gap in the literature. However, in a study conducted during the COVID-19 Pandemic, the correlation between the dietary compliance behaviors and uncontrolled eating scores of young individuals was investigated. In that study, the participants' intra-pandemic uncontrolled eating and emotional eating subscale scores were higher than were their pre-pandemic scores, and their intra-pandemic dietary compliance behaviors were worse than their pre-pandemic dietary compliance behaviors (30). In another study, college students with high sweet craving obtained high scores from the uncontrolled eating and emotional eating subscales (31). These results indicate that there may be an association between the disruption in eating patterns and uncontrolled eating behavior in young individuals.

In the present study, the mean cognitive restriction subscale scores and BMI values of the participants who were on a diet were significantly higher than were those of the participants who were not on a diet. In a similar study, BMI levels of female nursing students who were not on a diet were normal (19). These results indicate that an increase in female nursing students' BMI values causes them to display restricted eating and dieting behaviors more.

In the present study, a positive and significant relationship was determined between the participants' total MEQ scores and their BMI values and the mean scores they obtained from the Cognitive Restriction, Emotional Eating and Uncontrolled Eating subscales of the TFEQ (Table 4). In another study, no significant relationship was determined between university students' TFEQ scores and their BMI levels and mindful eating behaviors, thought to stem from the fact that the sample included both male and female students (33). In the study, no relationship was found between perceived stress level and eating behaviors. It is thought that this may be due to the difference in coping strategies with perceived stress. It is thought that the difference in coping strategies may affect the emergence of eating behaviors. In the present study, the change in BMI values and mindful eating behaviors of the participating female nursing students could predict their emotional eating behaviors (Table 5). Our search for studies in which variables that predict the emotional eating behavior of nursing students were studied revealed a gap in the literature. However, in a study conducted with obese women, a decrease in the mindful eating behavior explained their emotional eating behavior (13). In the present study, it was concluded that a decrease in the mindful eating behavior increased the BMI level, which can predict emotional eating behavior. In the present study, the change in the participants' mindful eating behaviors predicted their uncontrolled eating

Table 5. Results of the Multiple Regression Analysis of the Variables that Predict Emotional Eating, Uncontrolled Eating and Mindful Eating Behaviors of the Female Nursing Students (n = 106)

		t	p	B (%95 Confidence Interval)**	ANOVA(F)	Model(p)	R^2
TFEQ Emotional Eating	**Age**	.06	.51	1.03(-2.13-4.20)	17.512	.00*	.44
	BMI	2.13*	.03	1.35(.09-2.61)			
	The number of meals	1.78	.07	4.71 (.53-9.95)			
	MEQ total	7.00*	.00	47.75 (34.23-61.27)			
	PSS total	-1.11	.26	-.64 (1.80-.50)			
TFEQ Uncontrolled Eating	**Age**	1.10	.27	1.30(-1.04-3.66)	12.410	.00*	.352
	BMI	1.45	.15	.68(-.25-1.61)			
	The number of meals	1.63	.10	3.20 (-.69-7.09)			
	MEQ total	5.82*	.00	29.43(19.40-39.45)			
	PSS total	-.09	.92	-.04(-.89-.81)			
Mindful Eating	**Age**	.15	.87	.003(-.01-.01)	13.425	.00*	.453
	BMI	.39	.69	.003(-.03-.04)			
	The number of meals	.83	.40	.02 (-.03-.08)			
	PSS total	1.06	.29	.007(-.00-.02)			
	TFEQ Cognitive Restriction	2.27*	.02	.003(.000-.005)			
	Emotional Eating	3.82*	.00	.005(.002-.005)			
	Uncontrolled Eating	2.04*	.04	.004(.002-.007)			

*p < .05 **The multiple regression analyzes

behaviors. Similarly, in a study, the change in the mindful eating behaviors and BMI levels of university students explained their uncontrolled eating behaviors (34). In the present study, the change in the participants' cognitive restriction, emotional eating and uncontrolled eating behaviors explained their mindful eating behaviors. In the literature, there is a gap related to studies in which variables predicting nursing students' mindful eating behaviors were investigated. Unlike the present study, in a study conducted with university students, their cognitive restriction, emotional eating and uncontrolled eating behaviors did not predict their mindful eating behaviors (13). However, in another study, emotional eating and cognitive restriction behaviors of obese women predicted their mindful eating behaviors (33). These results indicate that the results of studies conducted to find out whether the increase in women's mindful eating behaviors would explain their emotional eating behaviors varied from one study to another. In addition, in the literature, the number of studies in which whether the change in female nursing students' mindful eating behaviors would predict their emotional eating behaviors was investigated is few.

Limitations: One of the limitations of the present study is that it was conducted only with female nursing students studying at a nursing faculty of a university. Therefore, the results obtained from this study are applicable only to the female nursing students surveyed during the Covid-19 Pandemic and they cannot be generalized to all female nursing students. Another limitation of the present study is that the data were collected by e-mails. Therefore, some of the students may not have received or accessed the e-mail sent to them. Another limitation of this study is that the faculty where the study was conducted had a nutrition course in the fall semester of the 2nd grade, which caused the sample of the study to consist of only 3rd and 4th grade students. This situation caused that the eating behaviors of all nursing students could not be measured.

CONCLUSION

In the present study, it was determined that the female nursing students suffered eating behaviors-

related problems during the online education period, that they displayed poor mindful eating behaviors, and that there was a relationship between their eating behavior-related problems and unconscious eating behaviors. The increase in the time spent by the participants at home due to the Covid-19 pandemic caused them to have eating behavior-related problems, which reveals the importance of interventions aimed at establishing correct eating behaviors in the 3rd and 4th grade female nursing students who are the candidates of the nursing profession. Because it is uncertain when the pandemic process will end, it is recommended to implement online interventions aimed at improving female nursing students' mindful eating behaviors and encouraging them to establish correct eating behaviors when they stay at home. In the present study, although no relationship was determined between the perceived stress level and eating behaviors, it was observed that the participants perceived high levels of stress during the online education process. Therefore, it is recommended to conduct online intervention studies aimed at enabling students to cope with stressors. It is also recommended that descriptive qualitative studies in which the stressors of female nursing students and the effects of these stressors on eating behaviors are investigated should be conducted. It is recommended to conduct a study in which eating behaviors, perceived stress and coping patterns are examined together.

Acknowledgement: None.
Author contributions: Conception: GZT, ZÇD. Design: GZT, ZÇD. Supervision: ZÇD. Funding: GZT. Materials: GZT. Data Collection: GZT. Analysis: GZT. Literature Search: GZT, ZÇD. Writing: GZT, ZÇD. Critical Review: GZT, ZÇD.
Conflict of interests: There was no conflict of interest.
Ethical approval: In order to conduct the study, an institutional permission was obtained from the Faculty of Nursing of a university (decision number: 153, date: May 27, 2020) and the ethics committee approval was obtained from the relevant university's Non-interventional Clinical Research Ethics Committee (date: August 04, 2020, decision number: 2020 / 17-33, 5552-GOA). The document is attached.
Funding: No financial support was received for this study.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Altheimer G, Urry HL. Do emotions cause eating? The role of previous experiences and social context in emotional eating. Current Directions in Psychological Science 2019;28(3):234–240.
2. Konttinen H, Van Strien T, Männistö S, et al. Depression, emotional eating and long-term weight changes: a population-based prospective study. International Journal of Behavioral Nutrition and Physical Activity 2019;16(1):28.
3. Tan CC, Chow CM. Stress and emotional eating: The mediating role of eating dysregulation. Personality and Individual Differences 2014;66:1-4.
4. Araiza AM, Lobel M. Stress and eating: Definitions, findings, explanations, and implications. Social and Personality Psychology Compass 2018;12(4):e12378.
5. Karakuş SŞ, Yıldırım H, Büyüköztürk Ş. Üç faktörlü yeme ölçeğinin Türk kültürüne uyarlanması: geçerlik ve güvenirlik çalışması. TAF Preventive Medicine Bulletin 2016;15(3):229-237.
6. Lazarevich I, Camacho I., del Consuelo Velázquez-Alva M, et al. Relationship among obesity, depression, and emotional eating in young adults. Appetite 2016;107:639-644.
7. Beshara M, Hutchinson AD, Wilson C. Does mindfulness matter? Everyday mindfulness, mindful eating and self-reported serving size of energy dense foods among a sample of South Australian adults. Appetite 2013;67:25-29.
8. Köse G, Tayfur M, Birincioğlu İ, et al. Adaptation study of the Mindful Eating Questionnare (MEQ) into Turkish, Journal of Cognitive-Behavioral Psychotherapy and Research 2016;5(3):125-134.
9. Barışkan H, Karakoç Kumsar A. Sağlık bilimleri fakültesi öğrencilerinde abdominal obezite sıklığı ve yeme farkındalık düzeyleri. Koç Üniversitesi Hemşirelikte Eğitim ve Araştırma Dergisi 2020;17(2):162-169.
10. Lofgren IE. Mindful eating: an emerging approach for healthy weight management. American Journal of Lifestyle Medicine. 2015;9(3):212-216.
11. Richardson AS, Arsenault JE, Cates SC, et al. Perceived stress, unhealthy eating behaviors, and severe obesity in low-income women. Nutrition Journal 2015;14(1):122-132.
12. Bourdier L, Morvan Y, Kotbagi G, et al. Examination of emotion-induced changes in eating: A latent profile analysis of the Emotional Appetite Questionnaire. Appetite 2018;123:72-81.
13. Czepczor-Bernat K, Brytek-Matera A, Gramaglia C, et al. The moderating effects of mindful eating

on the relationship between emotional functioning and eating styles in overweight and obese women. Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity 2020;25:841–849.
14. Ohara K, Mase T, Kouda K, et al. Association of anthropometric status, perceived stress, and personality traits with eating behavior in university students. Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity 2019;24(3):521-531.
15. Bilici S, Ayhan B, Karabudak E, et al. Factors affecting emotional eating and eating palatable food in adults. Nutrition Research and Practice 2020;14(1):70-75.
16. Evagelou E, Vlachou E, Polikandrioti M, et al. Exploration of Nursing students' dietary habits. Health Science Journal 2014;8(4):452-468.
17. Balhara YPS, Mathur S, Kataria DK. Body shape and eating attitudes among female nursing students in India. East Asian Archives of Psychiatr. 2012;22(2):70-74.
18. Çelik S, Ugur BA, Aykurt FA, et al. Eating attitudes and related factors in Turkish nursing students. Nursing and Midwifery Studies. 20154(2);e25479.
19. Salma KJ, Wafaa AA, Zainab A. A study of eating habits among female nursing students in the university of Babylon/Iraq. Journal of Contemporary Medical Sciences. 2016;2(8):141-147.
20. Sarini IL, Afifah E, Gayatri D. Relationship between stress level and eating behaviour of nursing student during clinical practice in hospital. In AIP Conference Proceedings. 2019;2092(1):040011.
21. Yönder Ertem M, Karakaş M. Relationship between emotional eating and coping with stress of nursing students. Perspectives in Psychiatric Care 2020;1–10.
22. Kato Y, Greimel E, Hu C, et al. The Relationship between Sense of Coherence, Stress, Body Image Satisfaction and Eating Behavior in Japanese and Austrian Students. Psych 2019;1(1):504-514.
23. Al-Musharaf S. Prevalence and Predictors of Emotional Eating among Healthy Young Saudi Women during the Covid-19 Pandemic. Nutrients 2020;12(10):2923.
24. Kalkan Uğurlu Y, Mataracı Değirmenci D, Durgun H, et al. The examination of the relationship between nursing students' depression, anxiety and stress levels and restrictive, emotional, and external eating behaviors in COVID-19 social isolation process. Perspectives in Psychiatric Care 2020;1-10
25. Flaudias V, Iceta S, Zerhouni O, et al. COVID-19 pandemic lockdown and problematic eating behaviors in a student population. Journal of Behavioral Addictions 2020;9(3):826-835.
26. Işik K, Cengi ZZ. The effect of sociodemographic characteristics of university students on emotional eating behavior. Perspectives in Psychiatric Care. 2020;57(1):214-218.
27. Eskin M, Harlak H, Demirkıran F, et al. Algılanan stres ölçeğinin Türkçeye uyarlanması: güvenirlik ve geçerlik analizi. In New/Yeni Symposium Journal 2013;51(3):132-140.
28. Costarelli V, Patsai A. Academic examination stress increases disordered eating symptomatology in female university students. Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity 2012;17(3):e164-e169.
29. Constant A, Gautier Y, Coquery N, et al. Emotional overeating is common and negatively associated with alcohol use in normal-weight female university students. Appetite 2018;129:186-191.
30. Elmacioğlu F, Emiroğlu E, Ülker MT, et al. Evaluation of nutritional behavior related to Covid-19. Public Health Nutrition 2020;1-20.
31. de Oliveira Penaforte FR, Minelli MCS, Anastácio LR, et al. Anxiety symptoms and emotional eating are independently associated with sweet craving in young adults. Psychiatry Res 2019;271:715-720.
32. Kaur MK, Sharma CP. The Relatıonshıp Between Stress And Eatıng Habıts In Nursıng Students. IDC International Journal 2020;6(4):2395.
33. Anderson LM, Reilly EE, Schaumberg K, et al. Contributions of mindful eating, intuitive eating, and restraint to BMI, disordered eating, and meal consumption in college students. Eating and Weight Disorders-Studies on Anorexia, Bulimia and Obesity, 2016;21(1):83-90.
34. Pintado-Cucarella S, Rodríguez-Salgado P. Mindful eating and its relationship with body mass index, binge eating, anxiety and negative affect. Journal of Behavior, Health & Social Issues 2016;8(2):19-24.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 236-243
https://doi.org/10.30621/jbachs.1075229
RESEARCH ARTICLE

EVALUATION OF CMV DNA ANTIGENEMIA STATUS IN PATIENTS WITH ALLOGENEIC BONE MARROW TRANSPLANT

Merve Keskinkilic[1], Serife Solmaz[2], Ahmet Seyhanli[3], Ozgur Appak[4], Ayca Arzu Sayiner[4], Guner Hayri Ozsan[5], Inci Alacacioglu[5]

[1] Dokuz Eylul University Faculty of Medicine Hospital, Department of Medical Oncology, Izmir
[2] Izmir Katip Celebi Atatürk Training and Research Hospital, Department of Hematology, Izmir
[3] Sivas Numune Hospital, Department of Hematology, Sivas
[4] Dokuz Eylul University Faculty of Medicine Hospital, Department of Microbiology, Izmir
[5] Dokuz Eylul University Faculty of Medicine Hospital, Department of Hematology, Izmir

ORCID: M.K. 0000-0002-3342-3144; S.S. 0000-0001-7180-3423; A.S. 0000-0001-6082-2995; O.A. 0000-0003-1810-8346; A.S. 0000-0001-6750-2353; G.H.O. 0000-0002-0930-6300; I.A. 0000-0002-8187-7159

Corresponding author: Merve Keskinkilic, **E-mail:** mervekeskinkilic90@gmail.com
Received: 18.07.2022; **Accepted:** 19.03.2024; **Available Online Date:** 31.05.2024

Cite this article as: Keskinkilic M, Solmaz S, Seyhanli A, Appak O, Sayiner AA, Ozsan GH, Alacacioglu I. Evaluation of CMV DNA Antigenemia Status in Patients with Allogeneic Bone Marrow Transplant. J Basic Clin Health Sci 2024; 8: 236-243.

ABSTRACT

Purpose: The risk of cytomegalovirus (CMV) reactivation following allogeneic hematopoietic stem cell transplantation (ASCT) reaches 30-50%, and there are numerous diagnostic tests to detect CMV replication. The most common tests used in this group of patients include 65kDa phosphoprotein (pp65) antigenemia immunofluorescence assay and nucleic-acid-based quantitative CMV-DNA polymerase chain reaction (qPCR).
Material and Methods: In this study, patients who underwent ASCT and developed CMV positivity from 2009 to 2016 in our hospital were evaluated retrospectively. The study included samples of the same patient with antigenemia and CMV-DNA qPCR test for up to 48 hours. The study aimed to determine the factors affecting CMV DNA antigenemia and compare CMV DNA PCR and pp65 antigenemia immunofluorescence assay.
Results: The results of 138 specimens of 39 patients who underwent ASCT were evaluated. The mean value of CMV PCR, which was positive for both tests, was 57.887 copies/ml (70- 1.213.633 copies/ml) and a significant correlation was found between the two tests and the positive samples ($p = 0.018$). The ROC analysis showed that 322 copies/ml CMV viral load in plasma corresponds to ≥1 antigen-positive cells/200 thousand leukocytes (Sensitivity: 68.5%; Specificity: 31.5%). CMV infection was observed in 32 samples; CMV DNA cut-off values of the reference according to CMV DNA PCR and antigenemia results, compared to the development of CMV infection, presented a significant correlation ($p=0.004$).
Conclusion: Although there is a common agreement between antigenemia and CMV DNA PCR tests, one should keep in mind that the sensitivity of antigenemia test is low especially in the neutropenic period.

Keywords: Allogeneic Hematopoietic Stem Cell Transplantation (ASCT), CMV Antigenemia (pp65), CMV DNA qPCR, CMV Infection

INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is the process of collecting stem cells from individuals or tissue-compatible individuals and transferring them to the recipient under appropriate conditions in order to restore the hematopoietic system. Hematopoietic

stem cell transplantation (HSCT) can be performed in various ways depending on the diagnosis and stage of the patient. It is mainly divided into two: allogeneic and autologous HSCT. Autologous stem cell transplantation (autologous SCT) is the infusion of healthy hematopoietic stem and progenitor cells taken from the patient's own cells into the patient. Allogeneic SCT, on the other hand, uses hematopoietic progenitor cells collected from a healthy person (not the patients themselves). There are several possible sources for the origin of these cells: 1-An identical twin (syngeneic, human leukocyte antigen [HLA] identical), 2-A sibling, relative, or unrelated donor (whose HLA may be identical, haploidentical, or incompatible), and finally 3-Umbilical cord blood (may be the same as HLA, haploidentical or incompatible) (1). ASCT is the transfer of HLA tissue from the compatible donor to the recipient after the preparation of stem cells (2). CMV reactivation or primary infection after ASCT is observed in 15-80% of patients and CMV infections are the most important cause of viral disease morbidity and mortality in this patient group (3,4). CMV seropositivity or post-transplant CMV reactivation adversely affects the ASCT results. In the past, most of the CMV reactivations and cases of pneumonia were seen in the early post-transplant period, but this rate was significantly decreased with preemptive therapies following routine ganciclovir prophylaxis or viral reactivation. However, recent years have seen an increased rate of late CMV reactivation and diseases. Late CMV disease is observed in between 4% and 15% of the cases and usually after 4 to 12 months (4). If the recipient and donor are seronegative, CMV disease occurs in less than 3% after transplantation, whereas if both are seropositive, CMV disease occurs in up to 30% of cases (5).

CMV pp65 antigenemia immunofluorescence test (CMV antigenemia), CMV DNA quantitative real-time PCR test (CMV DNA qPCR), cell culture, histopathology, and serological tests are used for detection of CMV infection. The two tests most commonly used in the diagnosis and follow-up of CMV infection are CMV antigenemia test and CMV-DNA qPCR. The viral pp65 antigen is a structural late protein expressed in blood leukocytes at an early stage of the CMV replication cycle. Antigenemia is measured by the quantification of the positive leukocyte nucleus in an immunofluorescence assay for CMV matrix phosphoprotein pp65 in a cytospin preparation of 2x105 peripheral blood leukocytes. In neutropenic patients, false-negative results may occur; antigenemia test result depends on the presence of a sufficient number of polymorphonuclear leukocytes (6). For optimal results, samples should be studied within 6 hours (6). The other nucleic acid-based test is the detection of CMV DNA by PCR method, which quantitatively realizes the CMV DNA by the quantitative real-time PCR method in a more sensitive and quantitative manner (4). PCR generally targets a number of early and late antigen genes in large, well-conserved regions to detect CMV DNA. DNA can be removed from whole blood, leukocytes, plasma or any other tissue (tissue biopsy samples) or body fluids (urine, cerebrospinal fluid (CSF), bronchoalveolar lavage (BAL)) (7). Live cell presence is not required for measurement. In the presence of a mutation in the regions where the primers bind, false negative results may be obtained. The situation can be illuminated by using a primer suitable for another region in the virus genome. In such cases, CMV antigenemia is positive and CMV DNA PCR may be negative. Sequence analysis is the most accurate method to determine mutation (5). The sensitivity and specificity of the test were 55.4% and 95.5%, respectively, when the standard CMV DNA qPCR assay was used to detect antigenemia (8). PCR-based assays are more sensitive than antigenemia; however, high sensitivity leads to the detection of controversial low viral replications with clinical implications. Although the international CMV-DNA standard has been developed, differences between the qPCR tests employed make it difficult to achieve inter-laboratory standardization and also complicates decision making on clinically significant thresholds. In this study, the results of CMV antigenemia and plasma CMV-DNA qPCR in plasma leukocytes were compared in the patients who had ASCT at the Hematology Unit of Dokuz Eylul University Hospital. The correlation between the two methods was evaluated, and the viral load level corresponding to the antigenemia positivity was determined.

MATERIAL AND METHODS

This study included all patients with CMV pp65 antigenemia positivity in the Stem Cell Transplantation Unit of Dokuz Eylul University Hospital between June 2009 and October 2016. All patients with hematological malignancies who had a

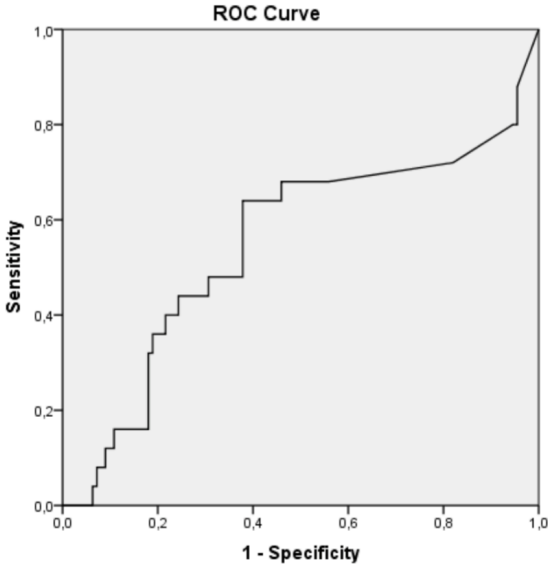


Figure 1. ROC Curve for CMV pp65 antigenemia assay

fully compatible relative donor and underwent ASCT were included in the study. Patients under 18 years of age, who had undergone autologous stem cell transplantation and without fully accessible medical data were excluded from the study. We noted the results of the antigenemia test and CMV DNA PCR test of the same patient. The laboratory values of the patients with CMV positivity were determined by any test. This value was taken as >1 positive cell/200,000 cells for pp65 antigenemia test and as >80 x 108 copies/ml and above for CMV DNA PCR test.

In total, 138 specimens of 39 patients with CMV positivity were retrospectively reviewed. Demographic characteristics, clinical status, diagnosis, laboratory values of transplantation, time of engraftment, amount of CD34 infused product, transplant preparation regimens, GVHD development status, CMV infection status, pp65 at the time of CMV infection and concurrent CMV DNA levels, CMV immunization, the immunosuppressive therapy of the donor, GM data of the recipient's CMV infection, BK virus status, white blood cell, neutrophil, lymphocyte and CRP values were evaluated retrospectively and all data were recorded in the SPSS Statistics V22.0 program. The data about the patients were obtained by scanning the patient's ID and patient numbers from the electronic medical record system (HEMCIS) of the hematology department.

CINAKit Argene® (France) Rapid Antigenemia test was used as a method of detection of CMV Antigenemia, and the internal matrix phosphoprotein (protein kinase) of peripheral blood leukocytes from cytomegalovirus (CMV) was determined by indirect immunofluorescence method of 65-68 kD (pp65). Artus® CMV QS-RGQ KIT - QIAGEN (Germany) PCR method was used to determine the CMV DNA level.

Statistical Analysis

In our study, descriptive statistics were used to interpret the available data. The data were evaluated with the package program Statistical Package for the Social Sciences (SPSS) (version 22.0 SPSS Inc, Chicago, IL, USA). The variables yielded by counting were summarized by means of percentage distribution as well as mean and standard deviation. Pearson and Spearman correlation tests were used for dependent group analysis of the variables. ROC analysis was also performed to determine the viral load corresponding to CMV antigenemia positivity. The level of significance was set at $p < 0.05$.

Ethical considerations

The study was approved by Dokuz Eylul University Faculty of Medicine Ethics Committee for Non-Invasive Clinical Studies on 18/01/2018 with the decision number 2018/02-38.

RESULTS

In our study, 138 of the 39 patients with CMV antigenemia and concomitant CMV DNA qPCR positivity were evaluated retrospectively. The female/male ratio of cases was 1.05/1 and the median age was 38 years (range: 18-64). CMV infection developed in 23.2% of the patients and survival rate was 28.2% during follow up period.

Of the 39 patients examined, 20 (51%) had acute myeloid leukemia (AML), 12 (30%) had acute lymphoid leukemia (ALL), 4 (10%) had myelodysplastic syndrome (MDS), 1 (3%) had biphenotypic leukemia, 1 (3%) had lymphoblastic lymphoma, 1 (3%) had non-Hodgkin's lymphoma (NHL). Evaluated according to the diagnostic CMV episodes, there were 50 episodes with AML (36.2%), 45 episodes with ALL (32.6%), 21 episodes with MDS (15.2%), 9 episodes with biphenotypic leukemia (6.5%), 7 episodes with lymphoblastic lymphoma (5.1%) and 6 episodes with NHL (4.3%).

The conditioning regimens of patients before AHSCT included Busulfan plus cyclophosphamide in 35 patients (90%), Busulfan plus Fludarabin in 1 patient (2.5%), RIC (Reduced intensity conditioning, Fludarabin plus Melfalan) in 1 patient (2.5%), TBI plus

Table 1. Patient and donor CMV conditions at the transplantation

Patient / donor CMV status in transplant	Samples	
	N	%
Positive / Positive	98	%71
Positive / Negative	3	%2,2
Negative / Positive	16	%11,6
Negative / Negative	16	%11,6
Not Reached	5	%3,6

Table 2. Distribution of pp65 and CMV DNA PCR results

	Pp 65 positive N (%)	Pp 65 negative N (%)	Total N (%)
CMV DNA			
Positive ≥80 copies / ml	42 (30.4%)	62 (45%)	112 (75.4%)
Positive < 80 copies / ml	7 (5.1%)	19 (13.9%)	26 (19%)
CMV DNA negative	0	8 (5.6%)	8 (5.6 %)
Total N (%)	49 (35.5%)	89 (64.5%)	138 (100%)

ATG plus Fludarabin in 1 patient (2.5%), in 1 patient (2.5%) TBI plus Etoposide, and preparatory regimens of the 138 CMV samples examined included 116 samples (84.1%) of Busulfan plus Cyclophosphamide, 12 samples (8.8%) of Busulfan plus Fludarabine, 6 samples of (4.4%) RIC, 3 samples of (2.2%) TBI plus ATG plus Fludarabin, and 1 sample (0.8%) of TBI plus Etoposide was built. (While the first sentence expresses the preparation regimens through the patient, the second sentence describes the ratio of the preparation regimens through examples.).

The average amount of CD34+ cells infused was 5.9 x106/kg (2-12x106/kg) and the mean neutrophil engraftment period was 12 days (10-22 days), whereas the mean platelet engraftment period was 15.7 days (10-30 days). CMV antigenemia positivity was more common in patients with early neutrophil engraftment (p=0.028).

When CMV Ig M and Ig G status of the patients at the time of transplantation were examined, CMV Ig G was found to be positive in 68% and negative in 23%, whereas the CMV status could not be reached in 9% of cases. The donor CMV status was Ig G negative in 17% and Ig G positive in 83%. Patient and donor CMV conditions during transplantation are presented in Table 1.

All patients received prophylaxis for the treatment of viral infections, including prophylaxis for the treatment of bacterial, fungal and pneumocystis carini infections. CMV infection was detected in 23.2% (n: 32) of all CMV positive samples. Of the 7 patients with clinically diagnosed CMV infection, 6 had gastrointestinal tract (GIS) involvement and 1 had CMV pneumonia. All the patients were treated with antiviral treatment with IV ganciclovir and three patients were treated with oral valganciclovir. Seven patients had undergone preemptive antiviral treatment due to CMV infection. Cidofovir treatment was started for 1 patient because of resistance to ganciclovir.

While acute graft versus host disease (GVHD) cases were detected in 42.8 % of the patients with CMV infection, skin GVHD, skin and lung GVHD were found in 19.5%, skin and lung GVHD were present in 10.2%, skin and hepatic GVHD were present in 7.2%, and in 20.3% of patients with CMV infection there was no GVHD. As immunosuppressive treatment, 54.4% of the patients received prednisolone and cyclosporine, 19.2% received cyclosporine, 10.3% received prednisolone, 9.5% received combination with prednisolone, cyclosporine and MMF, and 6.6% received combination with prednisolone and tacrolimus. One patient was treated with photophoresis and 2 had mesenchymal stem cell therapy. Of the patients with GVHD, 46.2% had GVHD grade 2 (n: 48), 31.8% had grade 3 (n: 33), 20% had grade 4 (n: 21), and 2% had grade 1 (n: 2). In addition, there was no correlation between the grade of GVHD and CMV infection (p = 0.12).

Regarding the CMV status, cases were positive after transplantation median on the 112th day (10-720 days). White blood cell count, neutrophil and lymphocyte levels were examined in this period).

Table 3. Comparison of CMV DNA PCR results and Antigenemia results with respect to CMV DNA cut-off values in the references.

	CMV DNA copy / ml < 2x 10^2 (n:75)	CMV DNA copy / ml ≥ 2x 10^2 (n:63)
CMV Antigenemia Positive	15 (20 %)	34 (54%)
CMV Antigenemia Negative	44 (58.6 %)	9 (14.3%)
Insufficient cell	6 (8%)	2 (3.2%)
Unseen	10 (13.4%)	18 (28.5%)
	Sensivity 97.7 % and Specificity 94 %	

There was no statistically significant difference between the post-transplant lymphocyte value and the CMV DNA titers (p = 0.07). However, when the lymphocyte count was grouped as <500/mm3 and >500/mm3, the difference was significant in the patient group with a lymphocyte value <500/mm3 and positivity was found to be higher (p = 0.017). It was found that this situation was due to the lack of cell counts in patients with lymphopenia and in the absence of a sufficient number of cells for measure pp65 antigenemia test. As the lymphocyte count increased, antigenemia positivity was found to be higher and there was a statistically significant difference between the values of lymphocytes and CMV antigenemia (p = 0.038).

White blood cell count and neutrophil values were correlated with CMV DNA (p = 0.003, p = 0.002). Neutrophil values <1000/mm3, 1000-2000/mm3, >2000/mm3 were also correlated with CMV DNA qPCR, and as the neutrophil value increased, the CMV DNA qPCR titres increased as well (p = 0.027). There was also a statistical relationship between neutrophil value and CMV antigen (p = 0.034). Again, when the neutrophil values were examined with <1000mm3 and >1000/ mm3 as CMV antigenemia, the statistical relationship was found significant (p = 0.005). CMV antigenemia positivity was high in patients with neutrophil values >1000/ mm3.

Significance was determined between neutrophil engraftment and CMV antigenemia, and it was observed that those with late neutrophil engraftment were more positive, while those with CMV clinical infection were observed to be in the late neutrophil engraftment group (p = 0.028, p = 0.0001).

There was a significant difference between the platelet engraftment and CMV antigenemia and CMV DNA qPCR positivity; a higher positivity was detected in those with late platelet engraftment, and late platelet engraftment was observed in patients with CMV clinical infection (p = 0.025, p = 0.001).

The stem cell source used in all of our patients was peripheral CD 34 positive stem cells and no significant difference was found between the amount of infused CD34-positive stem cells and CMV antigenemia and CMV DNA positivity (p = 0.07, p= 0.2).

CMV antigenemia values ranged from 0 to 20 in 37 samples (26.8%) and 20 to 100 in 8 samples (5.8%), CMV antigenemia result was >100 in 4 samples (3%), and in 65 samples (47.1%) CMV antigenemia was negative although CMV DNA result was positive. A cell deficiency was observed in 31 samples (22.5%).

It was observed that 38 of the 49 samples with positive CMV antigenemia were detected within the first 100 days after transplantation.

In eight of the samples (5.8%), CMV pp65 antigenemia and CMV DNA qPCR were negative, while in 49 (35.5 %) both tests were positive. The number of CMV antigenemia negative/ CMV DNA qPCR positive samples was 81 (58.7%), whereas there was no positive antigenemia/ CMV DNA qPCR negative sample. The mean value of the CMV DNA was 49.887 copies/ml (70-1.213.633 p/ml). A significant correlation was found between the two tests and positive samples (p= 0.018). ROC analysis showed that 322 copies/ml CMV viral load in plasma corresponded to ≥1 antigen-positive cell/200 thousand leukocytes (Sensitivity: 68.5 %, Specificity: 31.5%) (Table 2, Figure-1). The samples with CMV DNA qPCR positive and pp65 antigenemia negative were attributed to false negative results of the CMV antigenemia test due to the patients being leukopenic. Again, the absence of CMV DNA negative and antigenemia positive samples can be explained by the fact that the CMV DNA qPCR test is more sensitive.

The highest CMV DNA value was found to be 1.213.633 copies/ml. This sample belongs to a patient with GIS CMV infection. The CMV DNA level was found to be > 80 copies/ml in 10^4 samples. ROC curve analysis was performed on CMV DNA levels of 138 samples according to the CMV infection development status, and as a result, when CMV DNA was <2x10^2 cut-off, the sensitivity was found to be

97.7% and the specificity was 94%, and in 75 of the samples, the CMV DNA copy was < $2x10^2$ copies/ml., in 63 of the samples, the result was >$2x10^2$ copies/ml. CMV infection was observed in 32 samples, CMV DNA cutoff values were compared with CMV DNA qPCR results, and antigenemia results were compared with respect to CMV infection (p = 0.004) (Table 3).

DISCUSSION

In stem cell transplant recipients, approximately 50-90% of them develop CMV infection in the post-transplant period in relation to recipient and donor's CMV status before transplantation, and 30%- 50% of them are symptomatic (9, 10, 11). CMV infection is an important cause of mortality and morbidity in ASCT patients in hematology stem cell transplantation clinics. CMV positivity may progress CMV disease with organ involvement such as pneumonia, gastroenteritis, retinitis, and central nervous system involvement. CMV seropositivity and CMV infection are more common in the first 100 days of post-transplantation period. In these patients, CMV pp65 antigenemia assay and CMV DNA qPCR tests can be used in the diagnosis of CMV infection. Currently, CMV DNA qPCR is preferred to a higher extent for pre-emptive treatment. In the study of Landolfo et al., post-ASCT CMV infection was found to be around 32-70% (12). CMV infection was detected in 23.2% (n: 32) of 138 samples from 39 patients who underwent ASCT with CMV positivity in our clinic, and it was found to be slightly lower compared to the literature (13).

In the literature, CMV positivity was shown to be more frequent in the first 3-4 months after transplantation, and CMV positivity was found in 112 days after transplantation in our study. It was observed that 38 of the 49 samples with positive CMV antigenemia were detected within the first 100 days after transplantation.

In a study conducted to determine the frequency of CMV infections and risk factors after day 100 (14), CMV disease was detected in 17.8% of patients and on median 169 (96-784) days, while mortality was 46% in this group. In the study, it was found that the risk increased in cases of antigen positivity, GVHD presence, low CD4 positive lymphocyte count, lymphocyte count <100/mm3 and CMV positivity before the 100th day. In our results, CMV positivity was detected on the median 112th day after the transplant, 80% of our patients had GVHD, and 51.3% had grade 3-4 GVHD. However, there was no correlation between GVHD degree and CMV detection. CMV DNA positivity rate was found to be significantly higher in the patient group with lymphocyte value <500/mm3.

Immunosuppression is important in the pathogenesis of CMV infection in patients with ASCT and the factors that affect it include age, HLA compliance, stem cell source, administered conditioning regimen (ATG, history of RT) as well as steroid treatment (12). In addition, the serological status of the recipient is an important risk factor, too (13). In our study, no relation was found between the preparation regimes and CMV status; however, there was a statistically significant correlation between age and CMV DNA qPCR positivity (p = 0.029), yet no correlation was found between CMV antigenemia and age. CMV copy positivity was more common in patients under 40 years of age (p = 0.014).

The donor serology is one of the most important criteria for CMV risk. According to the risk ratio,, those with Donor (D) positivity (+) and Recipient (A) negativity (-) have the highest risk, while D+ A+, D-A+ indicates a decreasing risk level. The presence of viremia has been demonstrated to be a risk factor for CMV disease. It has been shown that high viral load constitutes the greatest risk for CMV considering the donor and recipient serological status, high viral load and viremia (15). When the CMV status of our patients was examined at the time of transplant, 71% was D + A +, 11.6% had DA-, 11.6% had D-A + and 2.2% had D + A. In the study conducted by Schulenburg et al., D + A +, 24.3% DA and D-A + 19% were detected in 42% of the donor and donor CMV cases (16).

We know that CMV DNA qPCR positivity is considered to be a more sensitive test than CMV antigenemia in neutropenic patients. In our study, the neutrophil value <1000/ mm3, 1000 – 2000/ mm3, >2000/ mm3 were also correlated with CMV DNA, CMV DNA titres increased as the neutrophil value increased. There was also a statistical relationship between the neutrophil value and the CMV antigen. Also, CMV antigenemia positivity was high in the patient group with a neutrophil value >1000/ mm3.

Einsele et al. found an unfavorable prognostic factor for CMV infection in lymphopenia after bone marrow transplantation (17). There was no significant difference between post-engraftment lymphocyte and CMV DNA titres in our study, but CMV DNA positivity

rate was found higher in patients with a lymphocyte value <500/mm3.

In our patient population, CMV infections were observed more frequently in patients with late neutrophil and platelet engraftment. The reason for this can be the delay of engraftment in our patients due to CMV infection.

Gökahmetoğlu et al. investigated the presence of CMV in 450 samples from 54 bone marrow recipients with CMV antigenemia test and CMV DNA qPCR methods. The researchers found positive results in 5.2% of the samples, the antigenemia test alone in 6%, and the CMV DNA qPCR test alone in 9.3% (18). In our study, both tests were positive in 35.5% of the samples, the CMV antigenemia test alone was found in 5.7% and CMV DNA qPCR test alone was found in 38.4% of the samples.

In another study in which 415 peripheral blood samples were obtained from 42 patients with AHSCT every week until the 100th day after transplantation, the presence of CMV DNA was investigated by the real-time PCR method. It was stated that 51% of the patients had viral reactivation. It was also reported that the CMV DNA qPCR testing may be useful in monitoring CMV reactivation and response to the antiviral therapy in BMT receptors (19). In our study, it was observed that 38 of the 49 samples with positive CMV antigenemia were detected within the first 100 days after transplantation.

In a study by Schulenburg et al. (16), the CMV DNA qPCR method was employed to determine the CMV infection and CMV antigenemia. In our cases, CMV DNA qPCR results and antigenemia results were compared in terms of CMV DNA cutoff values according to the CMV DNA cutoff values. In our study, there was a significant correlation between CMV DNA qPCR and CMV antigenemia in CMV detection.

In a study conducted on the stem cell transplant receivers in Turkey, which compared the results of CMV pp65 antigenemia test with two different PCR test results, the value of viremia corresponding to antigenemia positivity (≥1 positive cell/200,000 cells) was found 1543.5 copies/ml in one test and 423 copies/ml in the other (18). A cutoff value of 423 copies/ml was determined in the study of Çolak et al., and sensitivity and specificity were found to be 70.7% and 79.5%, respectively (20). In a study conducted in solid organ transplant patients in our university, ROC analysis was performed based on pp65 antigenemia positive (≥1 positive cell/200.000 cell), and the CMV DNA threshold value corresponding to antigenemia positivity in solid organ transplant recipients was found to be 205 copies/ml (sensitivity: 91.7%, specificity: 90.3%) (21). In a study by Breda et al., the cutoff value in which CMV antigenemia could be separated as positive and negative was 1067.5 copies/ml, which was reported with 100% sensitivity and 71% specificity (22). In our study, the mean value of CMV DNA qPCR of 49 samples in both tests was 57.887 copies/ml (70- 1.213.633 copies/ml) and a significant correlation was found between the two tests and positive samples ($p = 0.018$). In ROC analysis, 322 copies/ml CMV viral load in plasma corresponds to ≥1 antigen-positive cell/200 thousand leukocytes (sensitivity: 68.5%, specificity: 31.5%).

CONCLUSION

As a result, in this study, in the group that received stem cell transplantation and CMV pp65 antigenemia test, the CMV DNA qPCR test value, corresponding to 1 positive cell/200,000 cells, was determined as 322 copies/ml. Although these results may vary slightly depending on the clinic and patient population, it has been shown that there is concordance between the CMV pp65 antigenemia test and the CMV DNA qPCR test in the clinical follow-up of patients with CMV infection, and it is thought that it will be helpful in the follow-up of patients.

Acknowledgement: Professional medical writing support and editor assistance were not supported by the company.

Author contribution: Conception: SS; Design: SS, AS, OA; Supervision: IA, GHO; Materials: MK; Data Collection: MK; Analysis: SS, MK; Literature Review: MK; Writing: MK; SS; Critical Review: IA.

Conflict of interests: The author did not receive financial compensation for authoring the manuscript.

Ethical approval: The study was approved by Dokuz Eylul University Faculty of Medicine Ethics Committee for Non-Invasive Clinical Studies on 18/01/2018 with the decision number 2018/02-38.

Funding: No funding applied for or received.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Kanate AS, Perales MA, Hamadani M. Eligibility Criteria for Patients Undergoing Allogeneic Hematopoietic Cell Transplantation. J Natl Compr Canc Netw 2020;18(5):635-643.
2. Leung, AY, Kwong YL. Haematopoietic stem cell transplantation: current concepts and novel therapeutic strategies. Br Med Bull 2010;93:85-103.
3. Ljungman P, Reusser P, de la Camara R,et al. Management of CMV infections:

recommendations from the infectious diseases working party of the EBMT. Bone Marrow Transplant 2004;33(11):1075-81.
4. Zaia JA. Prevention and management of CMV-related problems after hematopoietic stem cell transplantation. Bone Marrow Transplantation 2002;29(8):633-8.
5. Özdemir E. Allojeneik Kök Hücre Nakli Sırasında Sitomegalovirüs Enfeksiyonlarının Tanı ve Tedavisindeki Gelişmeler THD, Hematolog 2011:1-1.
6. Tombuloğlu M. Ege Üniversitesi Tıp Fakültesi, Hematoloji Bilim Dalı, İzmir, Sitomegalovirus Tanı Ve Tedavisi, 2011.
7. Ross SA, Novak Z, Pati S, et al. Overview of the diagnosis of cytomegalovirus infection. Infect Disord Drug Targets. 2011;11(5):466-74.
8. Yakushiji K, Gondo H, Kamezaki K, et al. Monitoring of cytomegalovirus reactivation after allogeneic stem cell transplantation: comparison of an antigenemia assay and quantitative real-time polymerase chain reaction. Bone Marrow Transplant. 2002;29(7):599-606.
9. Sissons JGP, Bain M, Wills MR, et al. Latency and reactivation of human cytomegalovirus. J Infection 2002;44:73–77.
10. Murray PR, Baron EJ. Manual of Clinical Microbiology, 9th ed. ASM Press: Washington DC, 2007;9:1549-1563.
11. Ljungman P, Griffiths P, Paya C. Definitions of cytomegalovirus infection and disease in transplant recipients. Clin Infect Dis 2002;34: 1094-1097
12. Quamruddin AO, Oppenheim BA, Guiver M et al. Screening for cytomegalovirus (CMV) infection in allogeneic bone marrow transplantation using a quantitative whole blood polymerase chain reaction (PCR) method: analysis of potential risk factors for CMV infection. Bone Marrow Transplant 2001;27:301–306.
13. Einsele H, Hebart H, Kauffmann-Schneider C et al. Risk factors for treatment failures in patients receiving PCR-based preemptive therapy for CMV infection. Bone Marrow Transplant 2000; 25:757–763.
14. Boeckh M, Leisenring W, Riddell SR, et al. Late cytomegalovirus disease and mortality in recipients of allogeneic transplants: Importance of viral load and T cell immunity. Blood 2003;101: 407-414.
15. Schechter GP, Broudy VC, Williams ME (editors). American Society of Hematology Education Program Book. Orlando, Florida, ABD, 2001.
16. Schulenburg A, Watkins-Riedel T, Greinix HT, et al. CMV monitoring after peripheral blood stem cell and bone marrow transplantation by pp65 antigen and quantitative PCR. Bone Marrow Transplant. 2001;28(8):765-8.
17. Einsele H, Ehninger G, Steidle M et al. Lymphocytopenia as an unfavourable prognostic factor in patients with cytomegalovirus infection after bone marrow transplantation. Blood 1993; 82:1672–1678.
18. Gokahmetoglu S, Kaynar L, Altuntas F,et al. Detection and quantification of cytomegalovirus in bone marrow transplant recipients by real time PCR and pp65 antigenemia. Saudi Med J 2008; 29(11):1673– 1675.
19. Ghaffari SH, Obeidi N, Dehghan M, et al. A Monitoring of cytomegalovirus reactivation in bone marrow transplant recipients by real-time PCR. Pathol Oncol Res, 2008;14(4):399– 409.
20. Çolak D, Kazık M, Mutlu D, et al. Assessment Of Cytomegalovırus Load In Hematopoıetıc Stem Cell Transplant Recıpıents By Cmv Antıgenemıa And Two Dıfferent Real-Tıme Pcr Assays Akdeniz University, School Of Medicine, Antalya.
21. Özkarataş E, Özbek A, Oğuz V, et al. Solid Organ Nakli Alıcılarında CMV Antijenemi Testi ve CMV-DNA PCR Sonuçlarının Karşılaştırılması, Mikrobiyol Bul 50(1),44-52.
22. Breda G, Almeida B, Carstensen S, et al. Human cytomegalovirus detection by real-time PCR and pp65-antigen test in hematopoietic stem cell transplant recipients: a challenge in low and middle-income countries. Pathog Glob Health. 2013;107(6):312-9.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 244-252
https://doi.org/10.30621/jbachs.1094491
RESEARCH ARTICLE

IMPACT OF CARING FOR A CHILD WITH CANCER: PREDICTING FACTORS AFFECTING THE PHYSICAL HEALTH AND HEALTHY LIFE BEHAVIORS OF THE MOTHER

Emine Eda Baş[1], Ayfer Aydın[2], Rejin Kebudi[3], Aslı Akdeniz Kudubeş[4], Hülya Dalkılıç Bingöl[5]

[1] Istanbul Gaziosmanpaşa Education and Research Hospital, Istanbul-Turkey.
[2] Istanbul University, Faculty of Nursing, Department of Pediatric Nursing, Istanbul-Turkey.
[3] Istanbul University, Oncology Institute, Istanbul
[4] Bilecik Şeyh Edebali University, Faculty of Health Sciences, Department of Pediatric Nursing, Bilecik-Turkey
[5] Istanbul University, Oncology Institute, Pediatric Hematology-Oncology, İstanbul-Turkey.

ORCID: E.E.B. 0000-0003-1043-5289; A.A. 0000-0002-1148-7921; R.K. 0000-0003-4343-8174; A.A.K. 0000-0002-0911-8182; H.D.B. 0000-0001-7339-0490

Corresponding author: Aslı Akdeniz Kudubeş, **E-mail:** asliakdeniz@hotmail.com
Received: 13.11.2022; **Accepted:** 13.03.2024; **Available Online Date:** 31.05.2024

Cite this article as: Bas E.E, Aydın A, Kebudi R, Akdeniz-Kudubeş A, Dalkılıç-Bingöl H. Impact of Caring for A Child with Cancer: Predicting Factors Affecting The Physical Health And Healthy Life Behaviors of The Mother. J Basic Clin Health Sci 2024; 8: 244-252.

ABSTRACT

Purpose: To prevent mothers of children with cancer from developing health problems and suggest effective ways to maintain their health, it is important to accurately determine the problems they face. The aim of this study was to examine the physical health problems and healthy lifestyle behaviors of mothers whose children have cancer.
Material and Methods: This methodological, descriptive, and correlational study. The study interviewed 150 mothers whose children were receiving treatment for cancer using three forms: Sociodemographic Information Form, Mothers' Physical Health Form, and Healthy Lifestyle Behaviors Scale II. Independent samples t-test and single way variance analysis (ANOVA) tests were conducted to measure the relations between the variables.
Results: Mothers' age, number of children with cancer, age of child, educational status, income level and marital status were significantly correlated with the survey variables. A model created based on the regression analysis of the relationship among the variables showed that sociodemographic characteristics affected 24.2% of the healthy lifestyle behavior of mothers of children with cancer.
Conclusion: Our results showed that physical activity and stress management received the lowest health lifestyle behavior scores. The current findings emphasize the importance of informing mothers about stress management and physical activities during the care of their children with cancer.

Keywords: Cancer, child, healthy lifestyle, mother

INTRODUCTION

The diagnosis and treatment of cancer in children come with an array of problems and symptoms, such as nausea, vomiting, mucositis, anorexia, and pain, which are often presented with psychological problems such as anxiety, depression, and stress (1). Cancer-associated problems affect not only the child but the lives of all family members. For this reason, childhood cancers are considered a family disease (2).

Due to the long duration of treatment and the need of frequent hospitalization, families are more involved in childcare and play an important role (3). In trying to cope with their child's symptoms and treatment side effects, the physical and psychological health and lifestyle of the mothers are often negatively affected (4,5) Therefore, more attention needs to be paid to the health of those who care for children with cancer (6).

Mothers who cared for children with cancer were found to have worse physical health indicators than those who cared for healthy children (7,8). These mothers experienced physical problems such as insomnia, headache, back pain, decreased appetite, digestive and nutritional disorders, fatigue, weakness, and palpitations (9).

The burden of caring for a child with cancer can cause health problems and increase health risks. Having a child with cancer has been found to negatively affect mothers' healthy lifestyle behaviors promoting unhealthy eating, smoking, and drinking alcohol, and inability to cope with stress (3). Sleep quality was found to be lower in mothers with a child with cancer, with higher weight gain compared to those with healthy children. Maintaining physical and psychological health of parents in turn affects the outcome of child's health. Having healthy mothers will also increase the quality of life of all family members, especially the child with cancer (4).

Studies conducted in Turkey have mostly focused on the psychosocial problems of mothers having children with cancer (10,11). No study has demonstrated both physical and psychological health problems and healthy lifestyle behaviors of mothers whose children have cancer. To prevent mothers of children with cancer from developing health problems and suggest effective ways to maintain their health, it is important to accurately determine the problems they face. In this study, the effects of some characteristics of mothers with cancer children on health problems and healthy lifestyle behaviors were examined. Our findings are expected to be used to assess the health problems of the mothers, to plan for necessary counseling services in order to reduce the health problems in caregivers of children with cancer.

MATERIAL AND METHODS

Study Design

This methodological, descriptive, and correlational study examined the physical health and lifestyle behaviors characteristics of mothers whose children had cancer.

Population and Sample

In the first stage of study, according to the literature, it is stated that in scale validity and reliability studies, it is necessary to reach 5 or 10 times of the scale items (12,13). For this reason, the sampling involved 150 mothers.

In the second stage of study, the sampling calculation required for the study was performed using the G*POWER 3.1 statistical analysis software based on a 0.05 significance level, 80% power, and 0.50 effect size (medium effect size). Thus, the sample size required for independent samples t-test analysis was determined as 128 mothers. The research data were collected between May and August 2019. The sample of the study consisted of 150 mothers over 18 years of age who, for at least 3 months, have been caring for their children receiving cancer treatment. Study participants were volunteers. The research was carried out in the Division of Paediatric Haematology-Oncology of Istanbul University, Oncology Institute.

Ethical approval

The study was approved by the ethics committee on 06.03.2019 with decision number 2019.075.IRB3.050. All participants were informed about the study's aim and importance, and all subjects signed an informed consent form.

Data Collection Tools

The research data was compiled using "Sociodemographic Information Form", "Mothers' Physical Health Form" and "Health-Promoting Lifestyle Profile II (HPLP-II)". Mothers of children with cancer were asked to fill in questionnaires that took about 20–25 minutes.

Sociodemographic Information Form

The form was created by the researchers to determine the sociodemographic characteristics of mothers and children. The form consisted of questions about mother's age, child's age, child's diagnosis duration, marital status, educational status, number of children, employment status, income level, family type, and area of residence (14–17).

Mothers' Physical Health Form

This form was prepared by the researchers using

findings from the literature and clinical experience (4,6,8,14–16,18,19). The form assessed how the physical health of mothers was affected due to their caregiver role; physical health problems such as anorexia, weight gain, weight loss, headache, back pain, joint pain, and sleep problems were included. The scale consisted of 18 items. Scores obtained from the experts were analyzed with a validity review of the material. Each item in the scale was scored from 1 = Yes and 0 = No. A minimum of 0 and a maximum of 18 points were obtained from the scale. Higher scores indicated an increase in the physical health problems experienced by the mothers. The internal consistency coefficient of the scale was estimated based on the Kuder-Richardson reliability coefficient (KR-20) analysis. The KR-20 reliability coefficient of the scale is 0.81.

Health-Promoting Lifestyle Profile II (HPLP-II)

The HPLP-II, developed in 1987 by Walker, Scehnist and Pender, is a scale that measures health promoting behaviors in relation to individuals' healthy lifestyles (20). The Turkish validity and reliability study of the scale was performed in 2008 by Bahar et al. The form consisted of 52 items, in a 4-point Likert-type scale that includes choices of 'never', 'sometimes', 'often', and 'regularly' (21). The scale consisted of six subscales: 'health responsibility', 'physical activity', 'nutrition', 'spiritual development', 'interpersonal relations' and 'stress management'. Lowest score in the scale was 52 and the highest one was 208. A high score in the scale indicates that the individual has healthier lifestyle behaviors. The Cronbach Alpha value of the scale was 0.92 and the values of the sub-scale ranged from 0.64 to 0.80 (21). The Cronbach's alpha value in this study was 0.814.

Data analysis

The study data were analyzed using SPSS 21.0 statistical data analysis package program and evaluated by using frequency, arithmetical average, and percentage values.

In the first stage of study, the internal accuracy of the scale and its subscales was determined using

Table 1. Characteristics of mothers and children

Characteristics		n	%
Mother's age	19–29	54	36.0
	30 - 40	60	40.0
	41 and above	36	24.0
Child's age	0-2 years	2	14.7
	3-5 years	34	22.7
	6 years and above	94	62.6
Marital status	Married	143	95.3
	Single	7	4.7
Educational status	Literate	17	11.3
	Primary school	39	26.0
	Secondary school	38	25.4
	High school	39	26.0
	University	17	11.3
Number of children	Single	27	18.0
	More than 1	123	82.0
Employment status	Employed	13	8.7
	Unemployed	137	91.3
Income level	Well	26	17.3
	Moderate	88	58.7
	Poor	36	24.0

Table 2. Physical health problems of mothers

Physical Health Problems	n	%
Fatigue	136	90.7
Sleep Problems	114	76.0
Headache	102	68.0
Back pain	99	66.0
Lumbar pain	93	62.0
Muscle pain	92	61.3
Stomachache	88	58.7
Joint pain	84	56.0
Loss of appetite	97	64.7
Weight losses	84	56.0
Weight Gain	50	33.3
Increased hair loss	82	54.7
Irregularity in menstruation	78	52.0
Increased menstrual bleeding	32	21.3
Wound	25	16.7
Smoking (starting / increasing the number of cigarettes)	31	20.7
Chronic ailments	18	12.0
Using alcohol (starting / increasing amount of alcohol)	2	1.3

reliability analysis. The content validity index (CVI) and factor analysis were used. The relationship between item and factor was determined using EFA (exploratory factor analysis). We conducted a CFA (Confirmatory Factor Analysis) with a full estimate of the maximum likelihood using IBM SPSS Amos version 26.0. The internal consistency coefficient of the scale was estimated based on the Kuder-Richardson reliability coefficient (KR-20) analysis. For the item–total score analysis, Pearson correlation analysis was used. The margin of error was set at $p = 0.05$.

In the second stage of study, Shapiro-Wilk was used to determine compliance of the parameters with the normal distribution. Independent Samples t-test and single way variance analysis (ANOVA) tests were conducted to measure the relations between the variables. The Bonferroni test was used to determine where the difference between the variables originated. Linear regression analysis was employed to examine the extent to which the factors associated with healthy lifestyle behaviors of mothers. VIF and tolerance analysis was used to examine whether there was multicollinearity between the factors associated with healthy lifestyle behaviors of mothers. A VIF value of <10, a tolerance value of <0.2, and a condition index value of <15, which are independent variables, were included in the regression analysis (22). Level of significance was accepted as 0.05.

RESULTS

In the first part of the results, the validity and reliability findings of the Mothers' Physical Health Form used in the study are presented. This form was prepared by the researchers using findings from the literature and clinical experience (6,8,18). The form assessed how the physical health of mothers was affected due to their caregiver role; physical health problems such as anorexia, weight gain, weight loss, headache, back pain, joint pain, and sleep problems were included. The scale was evaluated by a panel of five experts in pediatric oncology (two medical doctors from the Paediatrics Department, three experts from the Department of Paediatric nursing). The scale had a Kaiser-Meyer-Olkin (KMO) value of 0.791, Bartlett's test of sphericity of 1025.744, and an explained variance of 66.19%. According to the explanatory factor analysis results, the factor loading was 0.66–0.78 for the scale. The confirmatory factor analysis

Table 3. Healthy lifestyle behaviors scale scores of mothers

HPLP II and subscales	Mean	SD	Min.	Max.	Highest and lowest obtainable score
Health responsibility	22.16	5.86	10	34	9-36
Physical activity	12.96	4.61	8	28	8-32
Nutrition	23.42	5.23	14	62	9-36
Spiritual growth	29.20	4.66	18	36	9-36
Interpersonel relationships	27.29	4.89	15	36	9-36
Stress management	19.41	5.52	8	31	8-32
Total HPLP II	134.54	25.80	80	188	52-208

SD: Standard deviation; Min: Minimum; Max: Maximum

results showed the following fit indices: X2 =399.942, df = 96, X2 / df = 4.166, RMSEA = 0.051, GFI = 0.96, CFI = 0.96, IFI = 0.96, NFI = 0.96, TLI = 0.96, and RFI = 0.95. The factor loading was 0.65–0.76 for the scale. The KR-20 reliability coefficient of the scale is 0.81. The correlation of the scale items with the scale total score was 0.56–0.68. The adapted scale was found to be a valid and reliable measurement tool for assessing the physical health problems of mothers of children with cancer.

Table 1 summarizes the demographic characteristics of mothers and children. According to the results of Shapiro-Wilks test, participants enrolled in this study were not homogeneous in terms of sociodemographic variables ($p < 0.05$).

The physical health problems experienced by the mothers are presented in Table 2. The mean score of the mothers participating in the study on the Mothers' Physical Health Problems Form was 8.71 + 3.96.

In Table 3, the mean scores of the mothers based on the HPLP-II subscale values were calculated as 29.20 ± 4.66 for “Spiritual development,” 27.29 ± 4.89 for “Interpersonal relations,” 23.42 ± 5.23 for “Nutrition,” 22.16 ± 5.86 for "Health responsibility," 19.41 ± 5.52 for "Stress management", and 12.96 ± 4.61 for "Physical activity". HPLP-II total value was found as 134.54 ± 25.80.

There was not a statistically significant difference found between mother’s age and physical activity, which is a subscale of healthy lifestyle behavior scale. There was not a statistically significant difference found between mother’s age and mothers ‘physical health problems form scores ($p > 0.05$). However, a statistically significant difference was found among healthy lifestyle behavior scale total score ($p<0.001$), nutrition ($p<0.001$), health responsibility ($p=0.007$), interpersonal relations ($p<0.001$), stress management ($p<0.001$) and spiritual development ($p<0.001$).

There was a statistically significant difference found between children age, the educational status and income level of the mothers, and health-promoting lifestyle profile scale total score and sub-scales score ($p < 0.05$), whereas no statistically significant difference was found between children age, the educational status and income level and mothers ‘physical health problems form scores ($p > 0.05$).

There was not a statistically significant difference found between number of children and health responsibility and physical activity, which are subscales of healthy lifestyle behavior scale and mothers’ physical health problems form scores ($p > 0.05$); while a statistically significant difference was found health-promoting lifestyle profile total score, nutrition, interpersonal relations, stress management and spiritual development ($p < 0.05$).

No statistically significant difference was found between marital status and employment status, and healthy lifestyle behavior scale total score and its subscales ($p > 0.05$). There was a statistically significant difference found between marital status and mothers’ physical health problems form scores ($p<0.05$), Bonferroni-corrected Mann Whitney U test determined the origin of the observed differences in mothers’ age, children age, education level, and income level. As there were three pairs of comparisons in the analysis for mothers’ age, children age and income level, the accepted significance level ($p = 0.05$) was divided by three to determine the new significance level. The new significance level was 0.05/3 = 0.016. Thus, we determined that the observed differences stemmed from mothers who were thirty years old and over, children aged six and over, and participants with a high-income level.

Table 4. Comparison of sociodemographic characteristics and healthy lifestyle behavior scale and physical health problems form scores of mothers

Descriptive characteristics		Health responsibility	Physical activity	Nutrition	Spiritual development	Interpersonel relationships	Stress management	HPLP II Total	PHP
Mother age	19-29 years	20.26±5.89	11.92±4.29	21.36±4.32	27.32±4.96	25.30±4.94	16.78±5.64	122.98±25.78	8.38±3.41
	30-39 years	22.68±5.50	13.65±4.78	23.88±3.58	29.88±3.71	28.38±3.89	20.48±5.14	138.96±21.92	8.48±4.24
	40 years and over	24.11±5.83	13.42±4.65	25.85±7.51	30.77±5.01	28.37±5.55	21.60±4.72	144.14±26.35	9.71±4.23
	F	5.069	2.135	9.155	7.260	7.498	10.835	9.517	1.673
	p	0.007*	0.122	0.000*	0.001*	0.001*	0.000*	0.000*	0.191
Child age	0-2 years	19.00±5.45	10.59±3.44	20.00±3.57	25.90±4.33	24.18±4.66	14.40±4.05	113.68±18.25	8.09±3.35
	3-5 years	20.2 ±5.59	12.00±3.90	22.17±4.27	27.61±4.76	25.52±4.25	17.94±5.25	125.52±24.13	8.70±3.00
	6 years and above	23.57±5.58	13.87±4.79	24.28±3.81	30.55±4.14	28.62±4.67	21.11±5.07	141.92±23.50	8.86±4.39
	KW	15.290	15.784	20.553	21.800	20.770	31.499	25.886	1.250
	p	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.000*	0.535
Marital status	Married	22.34±5.77	13.06±4.61	23.27±4.18	29.29±4.58	27.38±4.91	19.54±5.51	134.77±25.09	8.54±3.96
	Single	18.28±6.39	10.85±3.53	21.28±3.77	27.42±6.13	25.00±4.32	16.71±5.58	119.57±26.11	12.14±1.67
	U	312.000	325.500	352.500	409.000	350.000	358.500	331.000	218.500
	p	0.096	0.126	0.186	0.414	0.179	0.205	0.148	0.012*
Educational status	Literate	19.70±5.68	10.88±2.47	22.70±3.56	28.64±4.76	27.00±4.96	18.23±4.91	127.17±20.53	10.00±4.04
	Primary school	19.94±4.54	11.48±3.45	21.76±4.08	27.97±4.32	25.15±4.60	17.25±5.09	123.82±22.40	8.51±3.66
	Secondary school	22.34±5.40	12.89±4.06	22.9±4.00	28.60±4.58	27.02±4.85	18.97±5.51	132.50±23.60	8.44±3.80
	High school	23.89±6.11	14.12±5.39	23.94±4.41	31.10±4.25	28.79±4.61	21.48±4.96	142.89±25.58	8.56±4.24
	University	25.23±6.67	15.94±5.57	25.70±3.60	29.58±5.44	29.47±4.62	21.76±6.34	147.70±27.96	8.82±4.43
	KW	17.003	13.096	11.567	11.206	14.765	14.784	14.803	1.952
	p	0.002*	0.011*	0.021*	0.024*	0.005*	0.005*	0.005*	0.744
Number of children	Single	20.62±5.72	13.00±5.52	21.07±3.91	27.40±4.19	25.25±4.43	16.88±6.02	124.25±25.83	8.37±3.71
	More than 1	22.48±5.84	12.95±4.37	23.64±4.09	29.60±4.68	27.71±4.89	19.96±5.27	236.2±24.71	8.78±4.02
	U	1326.500	1482.000	1065.500	1161.500	1170.000	1080.000	1153.000	1516.000
	p	0.114	0.449	0.004*	0.014*	0.016*	0.004*	0.019*	0.478
Employed status	Employed	24.23±7.38	15.15±6.21	23.76±4.88	29.84±4.77	28.00±5.49	21.84±6.36	142.84±32.57	8.61±5.39
	Unemployed	21.95±5.67	12.75±4.36	23.12±4.11	29.14±4.66	27.20±4.85	19.18±5.41	133.23±24.43	8.72±3.82
	U	684.000	736.500	798.000	810.500	813.500	664.500	704.000	887.000
	p	0.178	0.336	0.536	0.606	0.606	0.130	0.254	0.981
Income level	Well	25.15±5.55	14.50±5.93	24.96±3.96	31.65±3.76	29.50±4.67	22.23±5.79	148.00±25.75	9.07±4.50
	Moderate	22.98±5.63	13.37±4.42	23.60±4.08	29.61±4.43	27.52±4.71	20.04±5.017	139.93±23.46	8.27±4.01
	Poor	17.94±4.20	10.86±2.95	20.86±3.61	26.44±4.56	25.05±4.71	15.83±4.83	117.00±20.19	9.52±3.31
	KW	27.239	11.138	15.595	20.118	13.336	23.353	22.469	2.751
	p	0.000*	0.004*	0.000*	0.000*	0.001*	0.000*	0.000*	0.253

HPLP II: Healthy Lifestyle Behavior Scale II; PHP: Mothers'Physical Health Problems; KW: Kruskal Wallis Test; U: Mann Whitney U Test; *p<0.05

Table 5. Linear regression analysis of the factors associated with healthy lifestyle behaviors of mothers

	Healthy Lifestyle Behavior Scale II						
	Model 1						
	Unstandardized Beta	Coefficients Standart Error	Standardized Beta β	t	p	95 % Confidence Interval	
						Lower	Upper
Mothers' Age[a]	4.352	5.379	0.081	0.809	0.420	-6.282	14.986
Children' Age[b]	13.985	5.278	0.262	2.650	0.009	3.551	24.419
Education Status[c]	10.774	3.990	0.203	2.700	0.008	2.886	18.663
Number of Children[d]	5.861	5.631	0.088	1.041	0.300	-5.271	16.993
Income Level[e]	10.369	5.278	0.154	1.965	0.049	-0.065	20.803
R		**0.492**					
R^2		**0.242**					
F		**9.021**					
p		**0.000**					
Durbin Watson (1.5–2.5)		**2.166**					

[a]While coding, 30-40 years and 41 years and above was coded as 1 and 19-29 years was coded as 0; [b]While coding, 6 years and above was coded as 1 and 0-2 years and 3-5 years was coded as 0; [c]While coding, the secondary school, high school and university was coded as 1 and the literate and primary school was coded as 0; [d]While coding, more than one was coded as 1 and the single was coded as 0; [e]While coding, the weel income was coded as 1 and the moderate and poor income was coded as 0. R: correlation; R2: correlation coefficient (explained variance ratio); F: model statistics; p: level of significance

Additionally, given that there were ten pairs of comparisons in the analysis performed on the origin of the observed difference in education level, the new calculated significance level was determined as 0.005, which originated from participants who were secondary school, high school, and university graduates.

A regression model was created that included the variables that affected the level of healthy lifestyle behavior in a statistically significantly (mothers' age, children age, educational status, number of children and income level) (Table 5). Model 1 describes the effect of the sociodemographic characteristic of mothers on Health-Promoting Lifestyle Profile II, and shows that sociodemographic characteristics predicted on 24.2% of the health-promoting lifestyle behavior of mothers. Based on the analysis, for every 1 year increase in the ages of mothers of children with cancer, the healthy lifestyle behavior was 4.35 points higher, for every 1 year increase in the children's ages, the mothers' health-promoting lifestyle behavior was 13.98 points higher, and as the number of children increased by 1 per mother, the healthy lifestyle behavior of the mother was 5.86 points higher. Further, as the education level and income increased by 1 level, the healthy lifestyle behavior of the mothers was 10.77 and 10.36 points higher, respectively. Each of the factors, except for mothers' age and number of children, had a statistically significant relationship with the health-promoting lifestyle behaviors of mothers ($p < 0.05$, Table 5).

DISCUSSION

Providing care for a child with cancer, who needs intensive treatment and care, is a difficult and tiring process for family members. It is known that the health of mothers is most negatively affected during this process (6,8). In this study, we observed that, during treatment, the most common physical health problems in mothers were fatigue, sleep problems, headache, back pain, and anorexia (Table 2). The stress experienced by mothers due to physical care responsibilities, such as meeting the self-care needs of the child, as well as other responsibilities, can lead to the occurrence of such physical symptoms.

This study, the mothers' age, children age, educational status, number of children and income level that affected the level of healthy lifestyle behavior in a statistically significantly (Table 4). Healthy lifestyle behaviors are a condition that can be affected by many factors. In the literature, it is stated that the average score of healthy lifestyle behaviors

of young people is higher than that of the elderly (14,15). In addition, it is emphasized that the increase in the level of education is a positive factor in the development of healthy lifestyle behaviors of individuals (16). Studies show that income level is effective in developing healthy lifestyle behaviors of individuals. As the income level increases, the healthy lifestyle behaviors of individuals are positively affected (14–16) In addition, it is stated in the literature that the age of the children that mothers have can affect many maternal conditions (15). One of these situations is healthy lifestyle behaviors. As the child's age increases, his dependence on the mother decreases. In addition, as the age of the child increases, he/she realizes his/her self-care skills and becomes more free and independent. This may lead mothers to devote more time to themselves and to display healthy behaviors (4,17,23,24). The findings of this study support the literature.

Model 1 showed that the sociodemographic characteristic of mothers predicted on their healthy lifestyle behavior by 24.2%, based on HPLP-II. There are many factors that affect mothers' healthy lifestyle behavior, including sociodemographic characteristics, environment, chronic illness, presence of a person with a chronic or fatal disease in the family, education for a healthy lifestyle, presence of obesity, presence of addiction, stress level, social support systems, and the support of a husband (4,25). For this reason, a 24.2% influence of sociodemographic characteristic on healthy lifestyle behavior of mothers whose children were hospitalized for a long time, who had to cope with so many symptoms, and whose healthy lifestyle behavior was influenced by various variables, is consider to be good, and consistent with previous findings (25,26).

Limitations

The sample size of the study were limitations of the present study, which may affect the generalizability of the study's findings. Second limitations; one of the most important limitations of the research is using voluntary sampling.

CONCLUSION

Our results showed that physical activity and stress management received the lowest health lifestyle behavior scores. The current findings emphasize the importance of informing mothers about stress management and physical activities during the care of their children with cancer. There was an increase in the rate of smoking in mothers, indicating the need to provide these mothers with help to quit smoking. Spiritual support may help mother's wellbeing. Obstacles to health promoting behaviors should also be investigated in this population, alongside longitudinal cohort studies.

Acknowledgement: We would like to thank to all participants.

Author contribution: Conception: Emine Eda Bas, Ayfer Aydın; Design: Emine Eda Bas, Ayfer Aydın; Supervision: Aslı Akdeniz Kudubeş, Rejin Kebudi; Data Collection: Aslı Akdeniz Kudurbes, Emine Eda Bas, Ayfer Aydın; Analysis: Aslı Akdeniz Kudurbes, Emine Eda Bas, Ayfer Aydın; Literature Review: Aslı Akdeniz Kudubeş, Rejin Kebudi; Writing: Emine Eda Bas, Ayfer Aydın; Critical Review: Aslı Akdeniz Kudubeş, Ayfer Aydın.

Conflict of interests: The authors have no funding or conflicts of interest to disclose. The authors have no conflicts of interest to disclose.

Ethical approval: The study was approved by the ethics committee on 06.03.2019 with decision number 2019.075.IRB3.050.

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Pinheiro LC, McFatrich M, Lucas N, Walker JS, Withycombe JS, Hinds PS, et al. Child and adolescent self-report symptom measurement in pediatric oncology research: A systematic literature review. Quality of Life Research. 2018 Feb 1;27(2):291–319.
2. Kazak AE, Noll RB. The integration of psychology in pediatric oncology research and practice: Collaboration to improve care and outcomes for children and families. American Psychologist. 2015 Feb 1;70(2):146–58.
3. Wiener L, Viola A, Kearney J, Mullins LL, Sherman-Bien S, Zadeh S, et al. Impact of Caregiving for a Child With Cancer on Parental Health Behaviors, Relationship Quality, and Spiritual Faith: Do Lone Parents Fare Worse? Journal of Pediatric Oncology Nursing. 2016 Sep 1;33(5):378–86.
4. Bakula DM, Sharkey CM, Perez MN, Espeleta HC, Gamwell KL, Baudino M, et al. Featured Article: The Relationship between Parent and Child Distress in Pediatric Cancer: A Meta-Analysis. J Pediatr Psychol. 2019 Nov 1;44(10):1121–36.
5. Flury M, Caflisch U, Ullmann-Bremi A, Spichiger E. Experiences of Parents With Caring for Their Child After a Cancer Diagnosis. Journal of Pediatric Oncology Nursing. 2011 May 13;28(3):143–53.

6. Verstraete J, Ramma L, Jelsma J. Influence of the child's perceived general health on the primary caregiver's health status. Health Qual Life Outcomes. 2018 Jan 10;16(1):8.
7. Golfenshtein N, Srulovici E, Medoff-Cooper B. Investigating parenting stress across pediatric health conditions - A systematic review. Compr Child Adolesc Nurs. 2016 Jan 2;39(1):41–79.
8. Lee MH, Park C, Matthews AK, Hsieh K. Differences in physical health, and health behaviors between family caregivers of children with and without disabilities. Disabil Health J. 2017 Oct 1;10(4):565–70.
9. Makotore F, Dambi J. The Impact of Caregiving a Child with Cancer: A Cross Sectional Study of Experiences of Zimbabwean Caregivers. J Palliat Care Med. 2015 Aug 25;05(05):1–7.
10. Erdem E, Korkmaz Z, Tosun Ö, Avci Ö, Uslu N, Bayat M. The Burden of Care in The Mothers of The Children With Chronic Disease. Journal of Health Sciences. 2013;22(2):150–7.
11. Gülses S, Keskin Yıldırım Z, Büyükavcı M, Üniversitesi Tıp Fakültesi Yakutiye Araştırma Hastanesi A, Asistanı P, Yardımcı Doçenti P, et al. Kanserli çocukların ve anne-babalarının yaşam kalitesi diğer hastalardan farklı mı? Çocuk Sağlığı ve Hastalıkları Dergisi. 2014;57:16–23.
12. Şimşek ÖF. Yapısal eşitlik modellemesine giriş - Temel ilkeler ve LISREL (linear structural relations) uygulamaları. İstanbul: Ekinoks; 2007.
13. Şencan H. Sosyal ve davranışsal ölçümlerde güvenilirlik ve geçerlilik. Ankara: Seçkin Yayıncılık; 2005.
14. Lersilp S, Putthinoi S. Correlation Between the Well-Being of Children and Caregivers. Open Public Health J. 2018 May 28;11(1):192–200.
15. Rafii F, Oskouie F, Shoghi M. Caring for a Child with Cancer: Impact on Mother's Health. Asian Pacific Journal of Cancer Prevention. 2014;15(4):1731–8.
16. Lewandowska A, Friedman N. Influence of a Child's Cancer on the Functioning of Their Family. Children 2021, Vol 8, Page 592. 2021 Jul 13;8(7):592.
17. Klassen AF, Gulati S, Granek L, Rosenberg-Yunger ZRS, Watt L, Sung L, et al. Understanding the health impact of caregiving: a qualitative study of immigrant parents and single parents of children with cancer. Qual Life Res. 2012 Nov;21(9):1595–605.
18. Jones BL. The Challenge of Quality Care for Family Caregivers in Pediatric Cancer Care. Semin Oncol Nurs. 2012 Nov 1;28(4):213–20.
19. Smith LE, Maybach AM, Feldman A, Darling A, Akard TF, Gilmer MJ. Parent and Child Preferences and Styles of Communication About Cancer Diagnoses and Treatment. Journal of Pediatric Oncology Nursing. 2019 Nov 1;36(6):390–401.
20. Walker SN, Sechrist KR, Pender NJ. The health-promoting lifestyle profile: Development and psychometric characteristics. Nurs Res. 1987;36(2):76–81.
21. Bahar Z, Beşer A, Gördes N, Ersđn F, Kissal A. Sağlıklı Yaşam Biçimi Davranışları Ölçeği'nin Geçerlik ve Güvenirlik Çalışması. CÜ Hemşirelik Yüksekokulu Dergisi. 2008;12(1):1–13.
22. Cattaneo MD, Arbor A, Titiunik R, Vazquez-Bare G. Power calculations for regression-discontinuity designs. Stata J. 2019;19(1):210–45.
23. Ford ES, Bergmann MM, Boeing H, Li C, Capewell S. Healthy lifestyle behaviors and all-cause mortality among adults in the United States. Prev Med (Baltim). 2012 Jul 1;55(1):23–7.
24. Olsen JM, Nesbitt BJ. Health Coaching to Improve Healthy Lifestyle Behaviors: An Integrative Review. American Journal of Health Promotion. 2010 Sep 1;25(1):e1–12.
25. Beatty PC, Collins D, Kaye L, Padilla J-L, Willis GB, Wilmot A. Advances in questionnaire design, development, evaluation and testing. Beatty PC, Collins D, Kaye L, Padilla J-L, Willis GB, Wilmot A, editors. John Wiley & Sons; 2019.
26. Mozaffarian D, Hao T, Rimm EB, Willett WC, Hu FB. Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men. New England Journal of Medicine. 2011 Jun 23;364(25):2392–404.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 253-261
https://doi.org/10.30621/jbachs.1201677
RESEARCH ARTICLE

DETERMINING THE KNOWLEDGE OF NURSES WORKING IN THE TURKISH REPUBLIC OF NORTHERN CYPRUS ON PERIOPERATIVE PERIOD ENHANCED RECOVERY AFTER SURGERY (ERAS) PROTOCOLS: A QUANTITATIVE DESCRIPTIVE STUDY

Kerem Yıldız[1], Ufuk Kaya[2], Nida Aydın[3], Aynur Güzel[4], Melahat Yıldız[4], Kamil Akçalı[1], Ömer Taşargöl[4]

[1] Eastern Mediterranean University, Faculty of Health Sciences, Famagusta, Cyprus
[2] Cyprus International University, Faculty of Health Sciences, Nicosia, Cyprus
[3] Near East University, Faculty of Nursing, Nicosia, Cyprus
[4] Dr. Burhan Nalbantoğlu State Hospital, Anesthesiology and Reanimation Service, Nicosia, Cyprus

ORCID: K.Y. 0000-0001-8653-9012; U.K. 0000-0002-0911-4886; N.A. 0000-0002-3590-9092; A.G. 0000-0002-7271-0920; M.Y. 0000-0001-5391-4138; K.A. 0000-0002-7954-6799; Ö.T. 0000-0003-1408-5503

Corresponding author: Kerem Yıldız, **E-mail:** keremyldz0767@hotmail.com
Received: 10.11.2022; **Accepted:** 18.03.2024; **Available Online Date:** 31.05.2024

Cite this article as: Yildiz K, Kaya U, Aydin N, Guzel A, Yildiz M, Akcali K, Tasargol O. Determining The Knowledge of Nurses Working in The Turkish Republic of Northern Cyprus on Perioperative Period Enhanced Recovery After Surgery (ERAS) Protocols: A Quantitative Descriptive Study. J Basic Clin Health Sci 2024; 8: 253-261.

ABSTRACT

Purpose: The aim of this study is to determine the knowledge level of nurses working in surgical clinics about perioperative period (ERAS) protocols.
Material and Methods: This descriptive research design completed between March and June 2021. The population of the study consisted of 126 nurses working in the surgical clinics of a State hospital in Northern Cyprus. The study was completed with 93 nurses who volunteered to participate in the study. The data were evaluated by accepting the significance level of $p<0.05$ at the 95% confidence interval.
Results: 47.3% of the nurses who participated in the study were 38 years and older, 81.7% were women, 58.1% had undergraduate education, 72% did not receive training on ERAS, and 73.1% of the nurses reported that it was beneficial to apply the ERAS protocol. The general average score of the nurses was determined as 54.67±21.50.
Conclusion: It was determined that the majority of the nurses did not know the ERAS protocol, that the ERAS protocol applications were not included in the clinic where they worked, and they had moderate knowledge. According to these results, it can be suggested that nurses should follow current developments and evidence-based guidelines on the ERAS protocol.

Keywords: Enhanced recovery after surgery, ERAS, knowledge, nursing, perioperative care

INTRODUCTION

Enhanced Recovery After Surgery (ERAS) is a term that includes the perioperative care (pre-, intra-, and post-operative) period, used with evidence-based multidisciplinary, multimodal applications to accelerate functional recovery and optimize postoperative results (1, 2, 3, 4). This term is also called Fast Track Surgery (FTS) in the United States (USA) (5, 6). Danish Prof. Henrik Kehlet is known as a pioneer in the development of these protocols. Fearon and Ljunqvist; focused on accelerating postoperative recovery and reducing complications by modifying the metabolic response to surgical stress in 2001 with a team from Northern European countries such as the Netherlands, Scotland, Sweden, and Norway (6, 7, 8).

The ERAS team was named "ERAS Association (Enhanced Recovery After Surgery Society for Perioperative Care)" in 2010. The main philosophy of the protocol is; to reduce the metabolic stress caused by surgical trauma, to return physiological functions to normal as soon as possible, to provide early mobilization, and to accelerate the return of patients to daily life activities (9, 10). In Turkey, the first foundations were laid at the National Surgery Congress organized by surgeons and anesthesiologists in 2006, and ERAS Turkey Association started its official activities on March 15, 2017 (11). ERAS protocols were first applied for colorectal surgery. Later, protocols were developed for patients who underwent gynecology/oncology, heart/lung surgery, urology, and other gastrointestinal surgery (stomach, pancreas, hepatobiliary, bariatric, pelvic/rectal) (1, 5).

The headliners of the ERAS team are physicians, nurses, dieticians, physiotherapists, and social workers (1, 5). Surgical nurses are expected to adapt to ERAS protocols, which is an up-to-date and evidence-based approach, as they take an active role in all stages of the perioperative period. ERAS protocols are a model consisting of practices that include the dependent and independent roles of nurses (7, 12). With traditional applications, patients had to stay in the hospital long time. Due to the negative impact of this situation on the healing process, evidence-based ERAS protocols have been established that aim to reduce the problems and/or complications that may occur after surgery (13).

The main point that surgical nurses should focus on in ERAS protocols is; Due to the shortening of the hospitalization period of the patients, patient education should be included, including the discharge period. Because the protocols include applications covering the entire journey of a patient, which starts in the outpatient clinic in the preoperative period and ends at home with discharge (1). In this context, surgical nurses should closely follow current and evidence-based new developments (5, 14, 15).

The aim of the study is to determine the knowledge of perioperative period enhanced recovery after surgery (ERAS) protocols among nurses.

Research Questions

1) Is the nurses' level of knowledge about the descriptive features and perioperative period Enhanced Recovery After Surgery (ERAS) protocols sufficient?
2) What is the total knowledge score of nurses regarding the perioperative period Enhanced Recovery After Surgery (ERAS) protocols?

MATERIAL AND METHODS

The quantitative descriptive design research was conducted between March 04 / June 28 2021. The population of the study consisted of nurses working in the surgical clinics of a State Hospital affiliated with the Ministry of Health of Northern Cyprus.

The study population consisted of 126 nurses at the state hospital between 04 March and 28 June 2021. No sample selection method was used. 33 nurses who did not accept to participate in the study, who were on leave at the time of data collection, and who filled out the questionnaire incompletely were excluded from the study, so the study was completed with 93 nurses who volunteered to participate in the study.

Data Collection Tools

The data were collected with the data collection form created by the researchers in line with the literature (2, 5, 7, 11, 16). The forms consists of two parts.

Nurse Identification Form: This form was composed of 10 questions about the descriptive characteristics of nurses (age, gender, educational status, duration of clinical experience, educational status about ERAS protocols, information resources on ERAS Protocols, usefulness of ERAS Protocols, etc.).

Knowledge Level Form of ERAS Protocols: This form was composed of 20 questions to determine the nurses level of knowledge about ERAS protocols. The Knowledge Level Form of ERAS Protocols consists of three sub-dimensions covering

Table 1. The mean knowledge level of nurses working in surgical clinics about ERAS protocols (N=93)

Sub-Dimensions	Mean±SD	Minimum	Maximum
Preoperative period	25.75±9.38	0	45
Intraoperative period	13.54±7.82	0	25
Postoperative period	15.37±10.00	0	30
General total	54.67±21.50	0	100

SD: *Standard Deviation*

preoperative, intraoperative and postoperative period. Questions from 1 to 9 are about the Preoperative period, from 10 to 14 about Intraoperative, and questions from 15 to 20 are about the Postoperative period. In the Knowledge Level Form of ERAS Protocols, each question answered correctly was evaluated with 5 points, a total of 100 points, and wrong answers and no idea answers were evaluated over 0 points. Each correct answer indicates that the knowledge level of nurses increases. The sub-dimensions of the Knowledge Level Form of ERAS Protocols constitute the lowest and highest scores within themselves. Nurses in the preoperative period will be able to get the highest score of 45, the highest score of 25 in the intraoperative period, and the highest 30 in the postoperative period. In order to evaluate the information form in terms of subject scope adequacy, expert opinion was obtained from 5 faculty members and the final form was formed.

Data Collection

The data were collected by giving verbal information about the research during the resting hours of the nurses after all necessary permissions were obtained for the research. The data collection forms filled by the nurses in the company of the researchers were given to the researcher immediately after they were completed to prevent nurses from interacting with each other. Nurses were expected to answer the knowledge level questions about ERAS by ticking one of the options "True", "False" or "No idea". Data collection took an average of 15 minutes.

Pilot Study

In order to determine the intelligibility of the questions in the data form, a pilot study was conducted with 12 nurses, 10% of the population. After the pilot study, no revision was necessary, and the nurses who took part in the pilot study were included in the main sample.

Ethical Approval

For the research to be implemented, written consents were obtained from the Ministry of Health of Northern Cyprus State Hospital Ethics Committee (Date: 07.05.2021, No: 27/21). Before filling out the data collection forms, the necessary explanations were made for the nurses to protect their rights, and their written and verbal consent was obtained with the "Informed Consent Form".

Statistical Analysis

Statistical analyzes were performed using the Statistical Package for the Social Sciences (SPSS) 26.0 software. Descriptive statistics, Kolmogorov Smirnov Z, Independent samples T, Mann Whitney U, and Kruskal Wallis H tests were used to evaluate the data. The data were evaluated and interpreted at the 95% confidence interval, at the $p<0.05$ significance level.

RESULTS

47.3% of the nurses participating in the research are 38 years old and above, 81.7% are women, 58.1% are undergraduate. 25.8% of the nurses gained their professional experience in the general intensive care unit. Nurses who worked for 5-9 years and 20 years or more participated in the study at the highest rate of 26.9%. Nurses working in the general intensive care unit participated in the study at the highest rate of 25.8%. 72% of the nurses reported that they did not receive training on ERAS and did not use information sources about ERAS. 35.5% of the nurses stated that they had no idea about the implementation of the ERAS protocol in the institution they work, and 73.1% of the nurses stated that ERAS protocols were beneficial.

The mean ERAS knowledge level of the nurses (N=93) who participated in the study is given in Table 1. Accordingly, the general average score of the nurses was determined as 54.67±21.50. Nurses had a general mean score of 25.75±9.35 preoperative,

Table 2. Distribution of the responses of nurses working in surgical clinics about ERAS protocols (N=93)

NO	Perioperative Period	Answers	True		False		Not Idea	
			n	%	n	%	N	%
1.	According to ERAS protocols, patient education reduces the patient's need for analgesics.	**T**	57	61.3	8	8.6	28	30.1
2.	Smoking should be stopped eight weeks before the operation.	**T**	62	66.7	16	17.2	23	24.7
3.	Before surgery, patients can be fed with solid foods for up to two hours.	**F**	5	5.4	83	89.2	5	5.4
4.	Antibiotic prophylaxis should be applied 30-60 minutes before surgery.	**T**	54	58.1	16	17.2	23	24.7
5.	Mechanical bowel cleansing should not be routinely performed in elective colon surgery.	**T**	26	28.0	58	62.4	9	9.7
6.	Informing the patient in the preoperative period increases the patient's fear and anxiety about the operation.	**F**	14	15.1	75	80.6	4	4.3
7.	To create metabolic satiety, carbohydrate-rich liquid/food should be given before the surgery.	**T**	24	25.8	39	41.9	30	32.3
8.	According to ERAS protocols, low molecular weight heparin (LMWH) should be administered to prevent deep vein thrombosis (DVT).	**T**	43	46.2	16	17.2	34	36.6
9.	According to ERAS protocols, the body temperature should be below 36°C before surgery.	**F**	17	13.8	55	59.1	21	22.6
10.	During the intraoperative period, the patient's normal body temperature should be maintained with heated intravenous infusions and external warmers.	**T**	55	59.1	10	10.8	28	30.1
11.	According to ERAS protocols, short-acting anesthetics that shorten the recovery time from anesthesia should be used.	**T**	38	40.9	17	18.3	38	40.9
12.	All patients should routinely be fitted with a drain during surgery.	**F**	8	8.6	73	78.5	12	12.9
13.	Combined antiemetics should be used to prevent vomiting during the intraoperative period.	**T**	52	55.9	18	19.4	23	24.7
14.	Vasopressor agents should be used to prevent hypotension due to intraoperative epidural anesthesia.	**T**	34	36.6	18	19.4	41	44.1
15.	With the implementation of ERAS protocols, the use of postoperative analgesics is increasing.	**F**	12	12.9	49	52.7	32	34.4
16.	With the application of ERAS protocols, gas removal occurs in the earlier period after surgery.	**T**	49	52.7	10	10.8	34	36.6
17.	With the application of ERAS protocols, postoperative wound infection is less common.	**T**	57	61.3	9	9.7	27	29.0
18.	The implementation of ERAS protocols increases the postoperative hospital stay.	**F**	8	8.6	63	67.7	22	23.7
19.	According to ERAS protocols, patients should be mobilized by keeping them out of bed for two hours on the day of surgery and six hours until discharge.	**T**	37	39.8	16	17.2	40	43.0
20.	According to ERAS protocols, opioid analgesics should be used routinely in the postoperative period.	**F**	25	26.9	31	33.3	37	39.8

Note: T: *True,* ***F:*** *False*

13.54±7.82 intraoperative, and 15.37±10.00 for the postoperative period, respectively (Table 1).

Table 2 gives the correct and incorrect response rates given by nurses to knowledge level questions about ERAS. It was found that three questions answered correctly by the nurses at the highest level are (1) 'Patients can be fed with solid foods for up to two hours before surgery (89.2%), (2) 'Informing the patient in the pre-operative period increases the patient's fear and anxiety about the surgery (80.6%), and (3) 'a drain should be routinely inserted in all patients during surgery (78.5%). It was determined that among the three questions that were answered least correctly are, (1) 'Carbohydrate-rich liquid/food

Table 3. Comparison of the descriptive characteristics of nurses working in surgical clinics and their knowledge level averages about ERAS protocols (N=93)

Descriptive Characteristics	General Total (Avg±SD)	Preoperative period (Avg±SD)	Intraoperative Period (Avg±SD)	Postoperative period (Avg±SD)
Age				
23-27	43.00±31.93	16.00±10.83	10.00±9.35	17.00±13.03
28-32	57.25±23.08	25.50±9.16	15.75±7.48	16.00±9.81
33-37	48.54±17.53	23.75±8.37	12.29±7.22	12.50±10.52
38 and above	58.18±21.02	28.06±9.16	13.63±8.09	16.47±9.49
p	.250	.115	.155	.437
Gender				
Female	53.75±21.52	25.32±9.46	13.09±7.83	15.32±10.30
Male	58.82±21.54	27.64±9.03	15.58±7.68	15.58±8.81
p	.391	.323	.230	.996
Educational status				
High school	55.00±21.32	27.08±9.40	12.91±8.10	15.00±10.66
Undergraduate	54.25±20.40	25.27±9.13	13.98±7.73	15.00±9.41
Graduate	55.37±24.37	26.11±10.12	12.96±8.11	16.29±11.14
p	.967	.733	.829	.797
Clinical experience gained				
GICU	53.54±22.13	24.37±10.76	14.58±8.83	14.58±9.43
Surgical service	53.46±20.55	27.69±8.06	12.30±7.25	13.46±9.65
Emergency	56.25±25.31	22.50±10.35	14.37±8.21	19.37±9.79
Surgery	66.17±20.57	30.88±8.88	17.05±6.85	18.23±10.44
CVSICU	54.58±22.80	24.16±6.33	13.75±8.56	16.66±11.34
Orthopedic service Cardiology service	45.62±16.13	25.62±9.42	8.75±3.53	11.25±11.57
p	46.36±21.50	22.72±9.04	10.00±7.07	13.63±8.68
Years of profession in Nursing	.300	.275	.170	.477
0-4 years	57.14±16.54	24.28±6.07	12.85±6.36	20.00±9.12
5-9 years	55.00±25.73	24.00±10.60	15.00±7.90	16.00±10.40
10-14 years	47.14±16.37	23.57±8.41	11.78±8.68	11.78±8.90
15-19 years	52.27±21.02	26.13±9.62	12.04±8.26	14.09±10.42
20 years and above	60.00±20.96	28.80±8.93	14.60±7.34	16.60±9.97
p	.403	.380	.562	.363
Currently working clinic				
Surgical service	57.00±18.43	27.00±7.88	13.50±7.83	16.50±8.51
Surgery	63.09±23.20	29.28±9.91	17.14±7.34	16.66±10.99
GICU	56.66±22.39	24.37±10.35	14.79±9.02	17.50±8.59
Orthopedic service	43.00±16.53	22.50±9.20	9.00±3.94	11.50±11.55
Urology service	51.66±15.70	29.16±5.84	12.50±6.89	10.00±8.36
Cardiology service	56.66±16.96	27.08±6.20	13.75±6.44	15.83±10.83
CIC	40.00±26.22	17.00±12.04	8.00±5.70	15.00±11.72
CVSICU	42.00±25.39	23.00±7.58	8.00±9.08	11.00±10.83
p	.177	.219	.076	.614
Educational status about ERAS protocols				
Educated	71.34±17.86	30.96±8.24	18.07±8.00	22.30±8.02
Non Educated	48.20±19.28	23.73±9.05	11.79±7.05	12.68±9.42
p	**.000***	**.001***	**.001***	**.000***
Information resources on ERAS Protocols				
In-service training Congress	70.90±12.00	30.90±7.68	20.45±6.87	19.54±6.87
etc.	77.00±14.40	30.00±7.07	19.00±6.51	28.00±4.47
Media, phone etc.	77.50±33.04	38.75±9.46	16.25±10.30	22.50±15.00
Other	63.33±18.61	26.66±7.52	14.16±9.70	22.50±5.24
Not	48.20±19.28	23.73±9.05	11.79±7.05	12.68±9.42
p	**.000***	**.009***	**.005***	**.000***
Implementation status of ERAS protocols in the institution				
Yes	58.87±18.96	25.80±7.86	14.51±8.59	18.54±7.09
No	55.34±22.71	27.41±9.96	12.75±7.62	15.17±11.29
No Idea	50.15±22.41	24.24±10.16	13.33±7.35	12.57±10.54
p	.304	.620	.699	.120
Thinking that ERAS protocols are useful				
Yes	59.55±20.29	26.83±9.05	14.19±8.13	18.52±8.51
No	0	0	0	0
No Idea	41.40±19.28	22.80±9.79	11.80±9.79	6.80±8.76
p	**.000***	.076	.197	**.000***

Avg: *Average,* ***SD:*** *Standard deviation,* ***GICU:*** *General Intensive Care Unit,* ***CVSICU:*** *Cardiovascular Surgery Intensive Care Unit,* ***CIC:*** *Coronary intensive care, *p<0.05*

metabolic satiety (25.8%), (2) 'Mechanical bowel cleansing should not be routinely applied in elective colon surgery (28.0%) and (3) 'Opioid analgesics should be used routinely in the postoperative period according to ERAS protocols (33.3%) (Table 2).

The comparison of nurses' pre-, intra-, and post-operative periods, general average score and descriptive characteristics are given in Table 3. It was determined that the groups with the highest overall score average were, 38 years and older (58.18±21.02), male (58.85±21.54), postgraduate education (55.37±24.37), experience in the operating room (66.17±20.57), years of service in the profession 20 years and over (60.00±20.96), working in the operating room (63.09±23.20), educated about ERAS (71.34±17.86), information sources such as media, telephone, etc. (77.50±33.04) (highest overall score average), who think that ERAS protocols are applied in the institution (58.87±18.96) and (59.55±20.29) nurses who thought that ERAS protocols were beneficial.

A statistically significant difference was found in the comparison of Nurses' education about ERAS ($p=0.000$, $p=0.001$, $p=0.001$, $p=0.000$, respectively) and ERAS information sources ($p=0.000$, $p=0.009$, $p=0.005$, $p=0.000$, respectively) and general, preoperative, intraoperative and postoperative mean scores ($p<0.05$). Statistical significance was also determined between thinking that ERAS protocols were beneficial and overall and postoperative score averages ($p=0.000$, $p=0.000$, respectively) ($p<0.05$) (Table 3).

DISCUSSION

In this study, it was aimed to determine the knowledge level of nurses, working in surgical clinics, about the ERAS protocol. According to the results of our research; It was determined that most of the nurses (72%) had no idea about ERAS. Studies have shown that most of the other healthcare professionals, including nurses, do not have sufficient knowledge about ERAS in perioperative care (2, 5, 17, 18, 19, 20). These results are similar to the results of our research.

It is seen that 72% of the nurses participating in the research do not use any information source about ERAS. Similar results are seen in other studies conducted in parallel with the results of our research (2, 5). Nurses (35.5%) reported that ERAS protocol applications were not included in the clinic they worked in. According to the research results 88.97% of the nurses reported that ERAS practices were not included in the clinic where they worked (5). According to these results, it is thought that namely the ERAS protocols are not implemented in their institutions or the nurses' lack of awareness about this issue has a great effect on the nurses' lack of knowledge about ERAS. According to the results of our study, 73.1% of the nurses think that ERAS protocols are beneficial.

To accelerate the post-surgical recovery process and to provide the expected benefit from ERAS, all healthcare team members should know ERAS protocols, as well as nurses' awareness and skills on the subject at a sufficient level (15, 17). Successful implementation of ERAS protocols is possible with team collaboration (21). It is reported that ERAS protocols are strong evidence-based applications, but their transition to practice in clinics is a slower process than expected (22).

ERAS protocols constitute the pre-, intra, and post-operative periods (4). These protocols are standardized with preoperative patient education and counseling, prevention of prolonged hunger associated with surgery, anesthesia management, and early postoperative mobilization (23). Education/training of the patient before the operation (deep breathing and cough, pain management, etc.) plays a major role in preventing possible complications (16, 24, 25). The education and counseling service to be given to the patient should begin during the first visit and should continue at all stages of the process (26). In this study, nurses (61.3%) reported that patient education would reduce the need for analgesics. According to the research results of previous studies nurses reported that patients should be educated in the preoperative period. The results are in agreement with our research (5, 19).

According to the 2011-2017 guideline of the American Society of Anesthesiologists (ASA), it is reported that the consumption of solid foods can be stopped six hours before the surgery and liquid foods can be stopped two hours before the surgery (16, 27, 28). According to the results of our research; It is seen that nurses do not have sufficient knowledge about the subject. The previous research results are similar to our research (5, 19, 29). It has been reported that nurses inform patients against any food and beverage consumption after midnight, which is their routine practice. Therefore, 89.2% of the nurses gave wrong answers about the subject. It can be said that this

situation is not suitable for ERAS protocols, which are evidence-based applications, and the lack of information is high.

It is reported in the literature that bowel cleansing should not be routinely performed for colon surgery (30). 62.4% of the nurses participating in the study marked the wrong option. However, it is reported in the literature that mechanical bowel cleansing should not be routinely applied in preoperative period elective colon surgery (18, 31). Few of the nurses participating in the study gave correct answers. It is thought that nurses' knowledge gaps should be eliminated by in-service training and/or literature review on the subject.

Venous thromboembolism (VTE); Among the causes of mortality and morbidity, including deep vein thrombosis (DVT) and pulmonary embolism, is a complication that can be prevented with caution (4). In this context, to prevent DVT, low molecular weight heparin (LMWH) should be administered (high level of evidence, strong recommendation level) and additionally, compression stockings should be worn (high level of evidence, strong level of recommendation) (18, 31). While the majority of the nurses participating in the research gave correct answers about the subject; It is seen that a considerable number of nurses do not have an opinion on the subject. This finding suggests that nurses stay away from current literature information.

Among the knowledge questions, the statement 'a drain should be routinely inserted in all patients during the surgery' was answered correctly with a rate of 78.5%. The presence of drain in the patient; is not routinely recommended because it restricts mobilization and does not prevent anastomotic leaks (26, 32, 33). As a result of the long immobilization process after the surgery; Insulin resistance increases, muscle atrophy develops, respiratory functions are impaired and the risk of thromboembolism increases (17, 26).

Postoperative nausea and vomiting should be prevented. Based on that, combined antiemetics that prevent vomiting should be used in the intraoperative period (11, 17). According to the results of our research, 55.9% of the nurses gave the correct answer to prevent nausea and vomiting. For this result, it is seen that a lot of nurses do not know about preventing nausea and vomiting.

According to ERAS protocols, the patient should be out of bed for two hours on the postoperative zero-day and six hours on the other days until discharge (level of evidence is moderate, level of recommendation is strong) (16, 17, 26). It is seen that 43% of the nurses participating in the research do not have an opinion on the subject. The fact that nurses working in surgical clinics do not have an idea about the subject suggests that they cannot provide effective care to patients who undergo surgery and that patients experience a delay in the wound healing process.

Limitations

This research was limited to the nurses working in the surgical clinics of the state hospital located in the capital city of the North Cyprus, Nicosia.

CONCLUSION

The importance of ERAS protocols is known all over the world by all team members in the surgical field. As stated in the results of our study, the mean level of knowledge of the nurses who received training on ERAS was found to be higher than those who did not. The level of knowledge will increase with education and awareness studies, active implementation of protocols, and/or the implementation of care obligations within the roles that the nurse performs independently on this subject, whose importance is well known.

According to these results, it can be suggested that nurses should follow current developments and evidence-based guidelines on the ERAS protocol, planning education programs for ERAS protocol applications, and increase the knowledge level of nurses by ensuring their participation.

Acknowledgement: We express our deepest gratitude to the nurses for their willingness to collaborate in this planned study. This study was presented as an oral presentation at the 2nd ERAS Congress held online on June, 11-13, 2021.

Author contribution: Conception: Yıldız K, Kaya U, Aydın N; Design: Yıldız K, Kaya U, Aydın N; Supervision: Yıldız K, Kaya U, Aydın N; Funding: Yıldız K, Kaya U, Aydın N, Güzel A, Yıldız M, Akçalı K, Taşargöl Ö; Material: Yıldız K, Güzel A, Yıldız M; Data Collection: Güzel A, Yıldız M, Akçalı K; Analysis: Yıldız K, Kaya U, Aydın N, Taşargöl Ö; Writing: Yıldız K, Kaya U, Aydın N, Akçalı K; Critical Review: Yıldız K, Kaya U, Aydın N, Güzel A, Yıldız M, Akçalı K, Taşargöl Ö.

Conflict of interests: There are no conflicts of interest.

Ethical approval: The research to be implemented, written consents were obtained from the Ministry of Health of Northern Cyprus State Hospital Ethics Committee (Date: 07.05.2021, No: 27/21). Before filling out the data collection forms, the necessary explanations were made for the nurses to protect their rights, and their written and verbal consent was obtained with the "Informed Consent Form".

Funding: No funding applied for or received.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Gündoğdu H. Current Perioperative Management Strategies for Enhanced Recovery After Surgery. Journal of Medical and Surgical Intensive Care Medicine 2018;9(2):51-59.
2. Guzel N, Yava A. The determination of knowledge and attitudes on enhanced recovery after surgery protocol of the nurses who working on surgical units. Journal of Zeugma Health Sciences 2019;1(1):15-23.
3. Ljungqvist O, Scott M, Fearon KC. Enhanced recovery after surgery: a review. JAMA surgery 2017;152(3):292-298.
4. Rollins KE, Lobo DN, Joshi GP. Enhanced recovery after surgery: Current status and future progress. Best Practice & Research Clinical Anaesthesiology 2021;35(4):479-489.
5. Ongun P, Ak ES. Assessment of knowledge levels of nurses working in surgical clinics about ERAS protocol. Med J Bakirkoy 2020;16(3):287-94.
6. Gundogdu RH. Cerrahi iyileşmenin hızlandırılması için modern teknikler. In: Eti Aslan F, editor. Cerrahi bakım vaka analizleri ile birlikte. Ankara: Akademisyen Tıp Kitabevi; 2016.p.455-70.
7. Kabatas MS, Ozbayır T. Enhanced recovery after surgery (ERAS) protocols after colorectal surgery: a systematic review. Gümüşhane University Journal of Health Sciences 2016;5(3):120-32.
8. Burch J, Fecher-Jones I, Balfour A, Fit I, Carter F. What is an enhanced recovery nurse: a literature review and audit. Gastrointestinal Nursing 2017;5(6):43–50.
9. Baldini G, Ferreira V, Carli F. Preoperative preparations for enhanced recovery after surgery programs: a role for prehabilitation. Surgical Clinics 2018;8(6):1149-1169.
10. Hübner M, Addor V, Slieker J, Griesser AC, Lécureux E, Blanc C, et al. The impact of an enhanced recovery pathway on nursing workload: a retrospective cohort study Int J Surg. 2015;24(Pt A):45-50
11. ERAS Türkiye Derneği. Available from: http://eras.org.tr/page.php?id=10&saglik calisani=true
12. Taurchini M, Del Naja C, Tancredi A. Enhanced recovery after surgery: a patient centered process. Journal of visualized surgery. 2018;4.
13. Brown D, Xhaja A. (2018). Nursing perspectives on enhanced recovery after surgery. Surg Clin North Am 2018;98(6):1211- 21.1211-1221.
14. Balfour A, Burch J, Fecher-Jones I, Carter FJ. Exploring the fundamental aspects of the Enhanced Recovery After Surgery nurse's role. Nurs Stand 2019;34:70-75.
15. Çilingir D, Candaş B. Cerrahi sonrası hızlandırılmış iyileşme protokolü ve hemşirenin rolü. [Enhanced Recovery After Surgery protocol and nurse's role]. Journal of Anatolia Nursing and Health Sciences 2017;20(2).
16. Birlikbaş S, Bölükbaş N. Cerrahi sonrası hızlandırılmış iyileşme protokolleri. [Enhanced Recovery After Surgery]. Ordu University Journal of Nursing Studies 2019;2(3):194-205.
17. Gustafsson UO, Scott MJ, Hubner M, Nygren J, Demartines N, Francis N, et al. Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS) society recommendations World J Surg. 2019;43(3):659-95.
18. Conn LG, McKenzie M, Pearsall EA, McLeod RS. Successful implementation of an enhanced recovery after surgery programme for elective colorectal surgery: a process evaluation of champions' experiences. Implement Sci 2015;10:99.
19. Celebi E, Ilce A. Determination of knowledge levels of nurses working ın surgical clinics on ERAS protocols. In: 3. International, 11. National Turkish Surgical and Operating Room Nursing Congress Book 2019.p.392-400.
20. Kırık MS. Kolorektal ameliyatlarda klinik alanda ameliyat öncesi sırası ve sonrası uygulamaların ERAS protokolüne uygunluğunun karşılaştırılması [master's thesis]. Gaziantep: Sanko Üniversitesi, Sağlık Bilimleri Enstitüsü; 2018.
21. Bozkırlı BO, Gündogdu RH, Ersoy PE, Akbaba S, Temel H, Sayın T. ERAS protokolü kolorektal cerrahi sonuçlarımızı etkiledi mi?. Turkish Journal of Surgery 2012;28(3):149-52.
22. Herbert G, Sutton E, Burden S, Lewis S, Thomas S, Ness A, et al. Healthcare professionals' views of the enhanced recovery after surgery programme: A qualitative investigation. BMC Health Serv Res 2017;17(1):617.
23. Steenhagen E. Enhanced recovery after surgery: it's time to change practice! Nutrition in Clinical Practice 2016;31(1):18-29.

24. Mendes DIA, Ferrito CRDAC, Gonçalves MIR. Nursing ınterventions in the enhanced recovery after surgery®: scoping review. Rev Bras Enferm 2018;71(suppl 6):2824-32.
25. Tezber K, Aviles C, Eller M, Cochran A, Iannitti D, Vrochides D, et al. Implementing enhanced recovery after surgery (ERAS) program on a specialty nursing unit. J Nurs Adm 2018;48(6):303-9.
26. Aksoy A, Vefikulucay Yılmaz D. A new approach to evidence based practices in gynecological surgery: ERAS protocol and nursing. Turkiye Klinikleri J Nurs Sci 2018;10(1):49-58.
27. Gök F, Yavuz Van Giersbergen M. Ameliyat öncesi aç kalma: sistematik derleme. [Preoperative fasting: a systematic review]. Pamukkale Medical Journal 2018;11(2):183-94.
28. Arslankılıç Ç, Erdem G, Çınaroğlu NS. Cerrahide hızlandırılmış iyileşme protokolü: Sistematik derleme. [Accelerated recovery protocol in surgery: Systematic review]. Cerrahi Ameliyathane Sterilizasyon Enfeksiyon Kontrol Hemşireliği Dergisi 2020;1(3):15-34.
29. Kankılıc R, Tuna A. An investigation of preoperative and postoperative nutrition, pain and early mobilisation practices in TUR-P surgery in relation to the ERAS protocol. KSU Medical Journal 2019;14(2):69-74.
30. Clifford T. Enhanced Recovery After Surgery. Journal of perianesthesia nursing: official journal of the American Society of PeriAnesthesia Nurses 2016;31(2):182-183.
31. Gustafsson UO, Scott MJ, Schwenk W, Demartines N, Roulin D, Francis N, et al. Guidelines for perioperative care in elective colonic surgery: enhanced recovery after surgery (ERAS) society recommendations. World Journal of Surgery 2013;37(2):259-284.
32. Ren L, Zhu D, Wei Y, Pan X, Liang L, Xu J. Enhanced Recovery After Surgery (ERAS) program attenuates stress and accelerates recovery in patients after radical resection for colorectal cancer: a prospective randomized controlled trial. World journal of surgery 2012;36(2):407-414.
33. Alcantara-Moral M, Serra-Aracil X, Gil-Egea MJ, Frasson M, Flor-Lorente B, Garcia-Granero E. Observational cross-sectional study of compliance with the fast track protocol in elective surgery for colon cancer in Spain. Int J Colorectal Dis 2014;29(4):477-83.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 262-270
https://doi.org/10.30621/jbachs.1223385
RESEARCH ARTICLE

INVESTIGATION OF CREATINE LEVELS IN GLIAL TUMORS USING MR SPECTROSCOPY

Nadir Moustafa[1], Berrin Cavusoglu[2], Serhat Erbayraktar[3], Emel Ada[4]

[1] Era Radiology Imaging Center, Izmir, Turkey
[2] Dokuz Eylül University, Institute of Health Sciences, Department of Medical Physics, Izmir, Turkey
[3] Dokuz Eylül University, Faculty of Medicine, Department of Neurosurgery, Izmir, Turkey
[4] Dokuz Eylül University, Faculty of Medicine, Department of Radiology, Izmir, Turkey

ORCID: N.M. 0000-0003-0432-7900; B.C. 0000-0003-1997-8861; S.E. 0000-0002-2938-578X; E.A. 0000-0002-0463-0945

Corresponding author: Berrin Cavusoglu, **E-mail:** berrncavusoglu@gmail.com
Received: 14.01.2023; **Accepted:** 03.10.2023; **Available Online Date:** 31.05.2024

Cite this article as: Moustafa N, Cavusoglu B, Erbayraktar S, Ada E. Investigation of Creatine Levels in Glial Tumors Using MR Spectroscopy.J Basic Clin Health Sci 2024; 8: 262-270.

ABSTRACT

Purpose: The present study examines the efficacy of Creatine (Cr) levels in tumor identification on single-voxel (SV) and multi-voxel (MV) magnetic resonance spectroscopy (MRS) in patients with glial tumors.
Material and Methods: A retrospective review was made of 20 SV and 20 MV MRS PDF images of patients with a pathological diagnosis of glial tumor. Cr values and metabolite ratios were measured in the tumor and compared with those in the healthy symmetrical brain parenchyma of the contralateral hemisphere.
Results: A significant difference was noted in the (Cho+Cr)/NAA and Cho/NAA ratios on SV MRS between the high-grade tumors and the healthy contralateral hemisphere. On MV MRS, Cho/NAA ratios within the minimum and maximum Cr(h) voxels ($Cho/NAA_{min\text{-}Cr(h)}$, $Cho/NAA_{max\text{-}Cr(h)}$, respectively) were higher in high-grade tumors compared to healthy tissue. ROC analysis showed that the max-Cr(h) metabolite on MV MRS was successful in distinguishing low-grade tumors from high-grade tumors.
Conclusion: Using the minimum and maximum values of Cr as a reference can improve the overall diagnostic accuracy in the diagnosis of glial tumors. Our findings showed that Cr tended to be low in high-grade tumors and further that the max-Cr(h) metabolite may help in the differentiation of glial tumors on MV MRS.

Keywords: Magnetic resonance imaging, spectroscopy, glial tumors, creatine

INTRODUCTION

Glial tumors account for 30% of primary brain tumors and originate from glial cells, which are the support cells in the brain. A positive diagnosis is established by surgery or biopsy and is used to assess prognosis and guide treatment. Depending on the location and grade of the tumor, various treatments, including surgery, radiotherapy and chemotherapy may be administered alone or in combination (1).

Since lesions may develop from regions with different malignancies, the approaches to the examination of heterogeneity in the lesion area are quite important in gliomas (2). Conventional magnetic resonance imaging (MRI) (T1, T2, and contrast-enhanced MRI) is a useful clinical tool for the identification of soft tissue contrast and morphological changes in glioma patients but remains insufficient in image-based tumor grading (2, 3). Besides, the diagnosis and grading of gliomas using conventional MRI may sometimes be unreliable due to the sensitivity of 55–83% in glioma grading (4). As such, alternative MRI approaches are needed for the investigation of tumor

Table 1. Demographic and clinical characteristics of participants

	SV	MV
Age (years / mean ± SD)	53.25 ± 14.61	54.40 ± 14.81
Gender (F/M)	9/11	10/10
Total (n)	20	20
Preop (n)	15	12
Postop (n)	5	8
Grade II	5	6
Grade III	5	2
Grade IV	10	12

F: Female, M: Male, MV: Multi-voxel, SD: Standard deviation SV: Single-voxel

metabolisms and the determination of the tumor grade, and to guide treatment planning.

Magnetic resonance spectroscopy (MRS) is an MRI approach that plays an essential role in determining the type and grade of most brain tumors. Developed for the chemical analysis of normal or pathological tissues at a molecular level, MRS can detect malignant transformations of tumor cells and metabolite concentration changes in their metabolism, thereby being useful in the prediction of tumor type and grade (5, 6). Glial tumors have some specific metabolites depending on their grade, and these metabolites vary in quantity as the tumor grade changes.

Creatine (Cr) is synthesized primarily from amino acids, and mostly in the kidneys and liver. It is transported to the peripheral organs in the blood and is referred to as an energy metabolism marker. Cr is a relatively constant element in the cellular energy metabolism of the brain and is often used as a reference metabolite in the calculation of such metabolite ratios as Cho/Cr and NAA/Cr (7).

Previous studies have identified the same Cr levels in both low-grade and high-grade gliomas (8, 9), while other studies have reported reduced Cr levels in brain tumors (10, 11). Furthermore, the amount of Cr may vary in different parts of the same tumor, with elevated Cr having been identified in hypometabolic areas and reduced Cr in hypermetabolic areas of the same tumor (12). The significance of Cr levels in the differentiation of high- and low-grade gliomas is unclear. If the Cr metabolite at the tumor site is used as an internal standard, differences in metabolite ratios may be difficult to identify, and so tumor-grade predictions may be erroneous. Cr, which provides information about the energy metabolism of glial tumor tissue on MRS, has been reported to vary according to the grade of the tumor in limited studies (7, 13), contradicting the general understanding that the Cr metabolite is stable.

In the present study, we examine the efficacy of Cr levels for tumor identification in single-voxel (SV) and multi-voxel (MV) MRS examinations in patients with glial tumors. We hypothesized that the ratios of Cr metabolite and Cr-related metabolite ratios could differentiate glial tumors from normal tissue.

MATERIAL AND METHODS

Subjects

MRS images of patients who were diagnosed pathologically with glial tumors were analyzed retrospectively. The subjects included 32 patients who had undergone MRS due to a pre-diagnosis of primary brain tumor, or in a follow-up examination following surgical treatment, who had undergone surgical resection, and who were diagnosed pathologically with glial tumors. An SV MRS examination of tumor tissue and healthy symmetrical brain parenchyma of the contralateral hemisphere was performed for comparison purposes in 20 patients, and an MV MRS examination was performed on 20 patients. The eight common patients in the two patient groups underwent both SV and MV examinations. Demographic and clinical data of the patients are presented in Table 1. All subjects provided written informed consent and the study protocol was approved by the Dokuz Eylül University

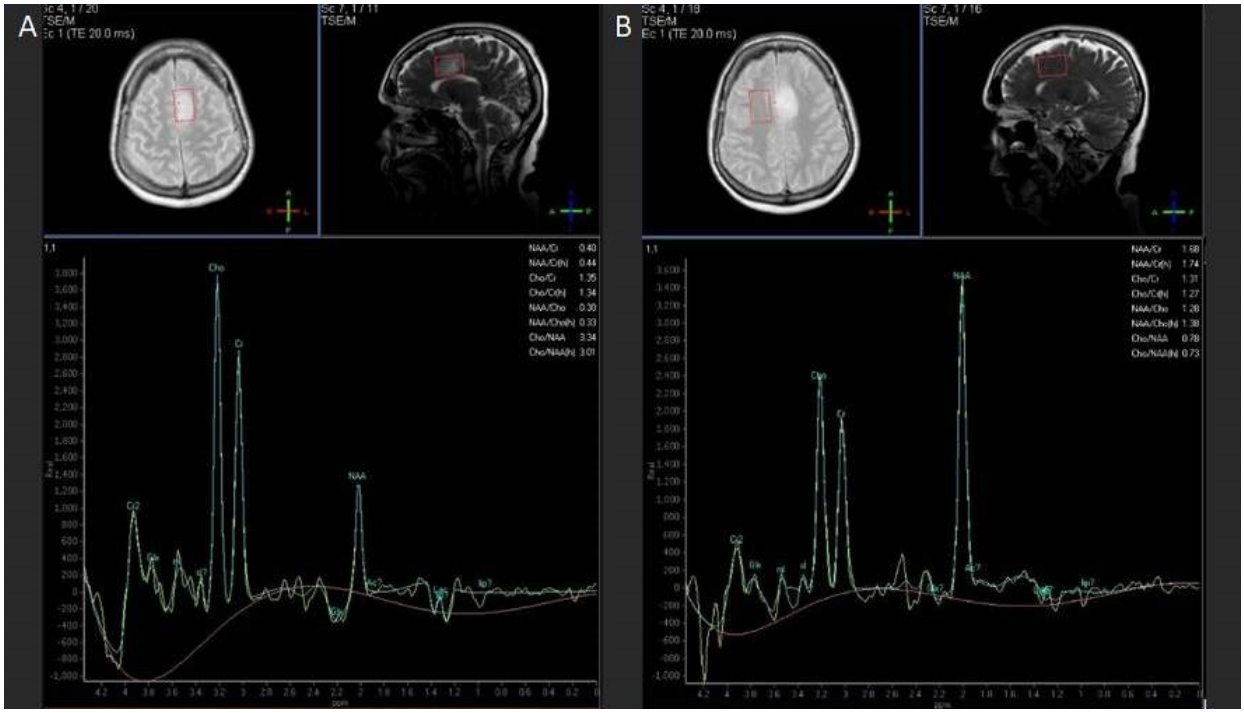


Figure 1. A 52-year-old patient with a lesion located in the right frontoparietal region. Metabolite measurements from A) tumor tissue and B) symmetric, healthy brain parenchyma for comparison with tumor tissue in MV MRS examination.

Non-invasive Research Ethical Committee (decision date: February 2, 2016, decision no: 2016/04-10).

MR Imaging Acquisition

MR imaging was performed using the 1.5 Tesla Achieva MR scanner (Philips Medical Systems, Best, The Netherlands) in the Radiology Department of Dokuz Eylül University. First, TSE T2-weighted images (TR: 6000 ms, TE: 120 ms) were acquired with a 5-mm section thickness in the axial-sagittal-coronal planes for voxel localization. Then, SV (TE: 144 ms) and 2-cm thick single-section MV (TE: 288 ms) MRS scans were acquired using the PRESS sequence. For SV MRS, voxels with the smallest size of 2 cm^3 and the largest size of 9 cm^3 were positioned within the tumor tissue and the corresponding contralateral healthy brain tissue (Figure 1). On the other hand, the voxels were positioned to include the tumor and the contralateral hemisphere for MV MRS (Figure 2).

MRS Analysis

In the SV MRS examination the Cr height (h), Cr area (a), Cho/NAA, and (Cho+Cr)/NAA values, calculated automatically by the MR unit's computer, were compared with the values in the healthy contralateral hemisphere. In the MV MRS examination, the voxels were examined in the central tumor tissue and the areas with infiltration of the surrounding tissue, and the two voxels, within which the minimum and maximum height of the Cr (Cr(h)) metabolite were measured, were compared with the reference "Cr(h)" values within the healthy contralateral parenchyma. Furthermore, the Cho/NAA ratios of the tumor tissue within the minimum and maximum Cr(h) voxels ($Cho/NAA_{min\text{-}Cr(h)}$, $Cho/NAA_{max\text{-}Cr(h)}$, respectively) were compared with the Cho/NAA ratios of the healthy contralateral side.

Statistical Analysis

The SPSS version 24.0 (Armonk, NY: IBM Corp.) was used for all statistical analyses. Non-parametric tests were used as the sample was small and the data were not normally distributed. The tumors were classified pathologically as low grade (DII) and high grade (DIII-DIV). A Mann-Whitney U test or a Wilcoxon test with Bonferroni correction were used to assess the differences in metabolites and metabolite ratios between high-grade and low-grade tumors in both groups. The optimal cut-off values for the metabolite ratios and the area under the curve (AUC) (95% confidence interval (CI)) were calculated using a receiver-operating characteristic curve (ROC) analysis to assess the ability to identify the tumor

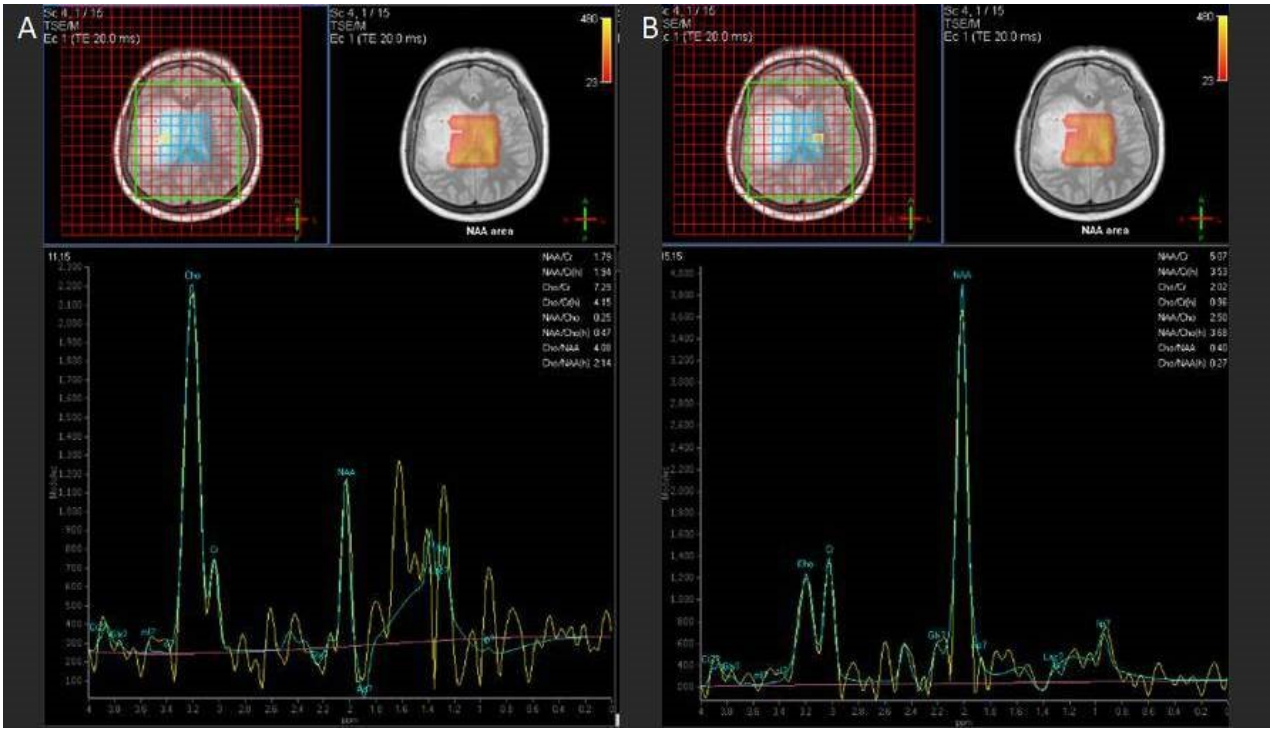


Figure 2. A 67-year-old patient with a lesion adjacent to the falx in the left frontal lobe. Metabolite measurements from A) tumor tissue and B) healthy contralateral frontal lobe for comparison with tumor tissue in SV MRS examination.

grades. A p-value of <0.05 was considered statistically significant.

RESULTS

The SV MRS examination revealed no difference between low-grade and high-grade tumors in terms of Cr levels or metabolite ratios. For the low-grade tumors, the (Cho+Cr)/NAA (p=0.043) and Cho/NAA (p=0.080) ratios were slightly higher in the low-grade group than in the normal healthy contralateral hemisphere but these differences were not statistically significant after Bonferroni correction. Also, there was no difference between low-grade tumors and normal tissue in terms of Cr(a) and Cr(h). For high-grade tumors, the (Cho+Cr)/NAA (p=0.001) and Cho/NAA (p=0.001) ratios in the tumor tissue and normal tissue differed. Although Cr(a) was lower in the high-grade group than in the normal tissue, this difference was not statistically significant after Bonferroni correction (p=0.047). The comparison of high-grade and low-grade tumors in the SV MRS examination is presented in Table 2.

The MV MRS examination revealed a difference only in max-Cr(h) (p=0.035) between low-grade and high-grade tumors, but this did not survive the Bonferroni correction (Table 3). For low-grade tumors, no statistical difference was found in the measurements of the tumor and the healthy contralateral hemisphere. For high-grade tumors, the $Cho/NAA_{min\text{-}Cr(h)}$ (p=0.001) and $Cho/NAA_{max\text{-}Cr(h)}$ (p=0.001) values between the tumor tissue and normal tissue were different (Table 4).

To assess the ability of MRS to differentiate between tumor tissue and normal healthy tissue, cut-off values for metabolites/metabolite ratios were calculated with a ROC curve analysis. On MV MRS, $Cho/NAA_{min\text{-}Cr(h)}$ ratio had the highest with an AUC value of 1.000 [95% CI: 1.000–1.000] and a cut-off value of 1.21 (sensitivity = 100%, specificity = 100%) for differentiating tumor tissue from normal tissue in high-grade tumors. The AUC, sensitivity, and specificity values of ROC curve analysis are presented in Table 5.

While the ROC curve analysis failed to differentiate between low-grade and high-grade tumors in the SV MRS examination, the MV MRS examination revealed that only max-Cr(h) had an AUC value of 0.804 [95% CI: (0.600–1.000)] and a cut-off value of 2212.5 (sensitivity = 83%, specificity = 64%).

DISCUSSION

In this study, we investigated the role of Cr metabolite in the differentiation of tumor tissue from normal tissue, and its ability to identify tumor grade in

Table 2. Comparison of measurements made from tumor and normal parenchyma in cases with low and high-grade tumors in SV MRS examination

Metabolites	Localization	Low Grade (grade II)			High Grade (grade III-IV)			Mann Whitney p-value
		Mean ± SD	Range	p-value[a]	Mean ± SD	Range	p-value[a]	
Cr(a)	Tumor	91.0 ± 68.9	55.0 – 214.0	0.893	100.3 ± 62.3	35.0 – 237.0	0.047	0.735
	Normal	88.6 ± 47.1	40.0 – 154.0		132.7 ± 70.9	56.0 – 283.0		0.168
Cr(h)	Tumor	1207.2 ± 1019.2	598.0 – 3022.0	0.893	1133.2 ± 661.2	355.0 – 2173.0	0.281	0.866
	Normal	1121.4 ± 644.3	407.0 – 1983.0		1274.3 ± 562.6	706.0 – 2839.0		0.672
(Cho+Cr)/NAA	Tumor	3.8 ± 2.0	1.7 – 6.0	0.043	6.5 ± 4.9	1.5 – 17.5	***0.001***	0.497
	Normal	1.2 ± 0.2	1.0 – 1.5		1.4 ± 0.5	0.7 – 2.5		0.395
Cho/NAA	Tumor	2.5 ± 1.6	0.6 – 4.5	0.080	4.8 ± 3.8	1.1 – 13.5	***0.001***	0.266
	Normal	0.7 ± 0.2	0.5 – 0.9		0.8 ± 0.3	0.3 – 1.4		0.445

a: Area, Cho: Choline, Cr: Creatine, h: Height, NAA: N-acetyl aspartate

A: Wilcoxon signed ranks test.

Statistically significant results that survived Bonferroni correction for multiple comparisons (p≤0.0125) are highlighted in bold and italics.

Table 3. Comparison of measurements made from tumor and normal parenchyma in cases with low and high-grade tumors in MV MRS examination

	Low Grade (grade II)		High Grade (grade III-IV)		
	Mean ± SD	**Range**	**Mean ± SD**	**Range**	**p-value**
Cr (N)	2020.7 ± 630.6	1010.0 – 2880.0	1516.2 ± 726.5	386.0 – 2530.0	0.216
Cho/NAA (N)	0.2 ± 0.1	0.1 – 0.4	0.3 ± 0.2	0.1 – 0.9	0.385
min-Cr(h) (T)	1793.5 ± 963.3	650.0 – 3062.0	1459.6 ± 649.9	260.0 – 2330.0	0.117
Cho/NAA$_{min\text{-}Cr(h)}$ (T)	2.0 ± 1.2	0.7 – 3.7	3.8 ± 2.7	1.6 – 9.9	0.099
max-Cr(h) (T)	3277.0 ± 1065.9	2040.0 – 4742.0	2046.5 ± 909.8	674.0 – 4224.0	0.035
Cho/NAA$_{max\text{-}Cr(h)}$ (T)	1.5 ± 1.2	0.3 – 3.4	2.8 ± 2.2	0.3 – 7.4	0.248

Cho: Choline, Cr: Creatine, h: height, NAA: N-acetyl aspartate, N: Measurements from normal healthy parenchyma tissue, T: Measurements from tumor tissue
Statistically significant results that survived Bonferroni correction for multiple comparisons (p≤0.0125) are highlighted in bold and italics.

Table 4. Comparison of measurements made from tumor and normal parenchyma in MV MRS examination

	Low Grade	High Grade
	p-value	**p-value**
min-Cr(h)	0.600	0.198
max-Cr(h)	0.028	0.084
Cho/NAA$_{min\text{-}Cr(h)}$	0.028	**0.001***
Cho/NAA$_{max\text{-}Cr(h)}$	0.028	**0.001***

Cho: Choline, Cr: Creatine, h: height, NAA: N-acetyl aspartate. Statistically significant results that survived Bonferroni correction for multiple comparisons (p≤0.0125) are highlighted in bold and italics.

Table 5. Sensitivity, specificity, and AUC values of metabolite ratios for differentiation tumor from normal parenchyma in high-grade tumors.

		Cutoff	Sensitivity %	Specificity %	AUC ± SE
SV	**(Cho+Cr)/NAA**	2.59	93	100	0.973 ± 0.028
	Cho/NAA	1.73	93	100	0.985 ± 0.017
MV	**Cho/NAA$_{min\text{-}Cr(h)}$**	1.21	100	100	1.000 ± 0.000
	Cho/NAA$_{max\text{-}Cr(h)}$	0.57	93	93	0.959 ± 0.035

AUC: Area under the curve, Cho: Choline, Cr: Creatine, MV: Multi-voxel, NAA: N-acetyl aspartate, SV: Single-voxel

patients with glial tumors on SV and MV MRS. In the MRS examinations of the patients, measurements were made in the tumor and the corresponding symmetrical healthy brain parenchyma of the contralateral hemisphere to compare. The Cho/NAA and (Cho+Cr)/NAA ratios were significantly higher in the high-grade tumors than in the healthy contralateral hemisphere on SV MRS. On MV MRS, Cho/NAA$_{min\text{-}Cr(h)}$ and Cho/NAA$_{max\text{-}Cr(h)}$ ratios were higher in high-grade tumors compared to healthy tissue. ROC analysis showed that only the max-Cr(h) metabolite was successful in differentiating high-grade tumors from low-grade tumors on MV MRS in accordance with our hypothesis. Moreover, the Cho/NAA$_{min\text{-}Cr(h)}$ ratio has the highest diagnostic performance to differentiate tumors from healthy tissue in high-grade tumors.

There is a lack of consensus in the literature on the level of Cr in glioma tumors. MRS studies found the amount of Cr metabolite to be low in high-grade glial tumors (14). The amount of Cr shows that its synthesis from astroglia increases as a reaction to the infiltrative growth of tumor cells (15). Xiaojuan et al. found that the Cr level changed in different areas of the same lesion, with a decrease in some areas of the tumor and an increase in others (16). Our study identified different amounts of Cr, which is used as a constant in ratios such as Cho/NAA and (Cho+Cr)/NAA, within different voxels on MV MRS in tumor tissue and healthy brain parenchyma. We found a trend for a lower Cr(h) in high-grade tumors on MV MRS. Moreover, the ROC analysis revealed the Cho/NAA ratio within the voxels containing maximum Cr(h) had higher diagnostic accuracy than those in high-grade tumors. Therefore, this finding suggests that using minimum and maximum Cr(h) as a reference may play an important role in diagnostic assessment.

It is very important to identify tumor grade before planning effective treatment. Non-invasive glioma grading is still considered challenging, despite its important role in the prognosis and management of patients (8). MRS is being used increasingly as a non-invasive method for the detection and grading of brain tumors, and the diagnostic accuracy in tumor grading can thus be further improved (8, 17). Previous studies have demonstrated the potential of MRS to differentiate between low-grade and high-grade gliomas, and have made frequent use of the Cho/NAA ratio to identify the glioma grade (3). This seems to be related to the elevated Cho, which is caused by an increase in cell membrane turnover due to tumor cell proliferation and reduced NAA values due to the tumor cells pushing and replacing the neuronal structures and damaging the neurons. Hsu et al. reported the (Cho+Cr)/NAA ratio to be the most significant predictive value for the differentiation of glial tumors of different grades when compared to other metabolites (18). Our study could not make any grade differentiation for Cho/NAA or (Cho+Cr)/NAA metabolite ratios, although the max-Cr(h) metabolite tended to be lower in high-grade glial tumors on MV MRS, but did not survive a Bonferroni correction. On the other hand, the ROC analysis revealed the max-Cr(h) to be successful in differentiating between low-grade and high-grade gliomas, with a sensitivity of 83% and a specificity of 64%. These findings suggest that Cr is increased in tumor tissue before the Cho/NAA increase and the tumor grade increase. However, given the limited data further studies are needed to confirm the efficacy of the Cr metabolite.

A potential limitation of our study is the small number of cases with low-grade tumors, thus, the results of

this study should be interpreted as preliminary. Therefore, the study findings could be improved upon with further studies involving larger patient groups.

CONCLUSION

In conclusion, in the present study, Cho/NAA metabolite ratio within the voxels containing the minimum Cr(h) on MV MRS was found to have high diagnostic performance in differentiating between tumor tissue and normal tissue in high-grade tumors. Moreover, the max-Cr(h) metabolite on MV MRS was shown to have good diagnostic performance in differentiating between high-grade and low-grade tumors. We, therefore, suggest that using minimum and maximum Cr(h) as a reference on MV MRS might improve the overall diagnostic accuracy in the diagnosis of glial tumors.

Acknowledgement: None.
Author contribution: Conception and design: NM and EA; Supervision: EA; Data collection and processing: NM, SE, EA; Analysis: NM, BÇ; Literature review: NM, BÇ; Writing: NM, BÇ; Critical review: SE, EA.
Conflict of interests: No conflict of interest was declared by the authors.
Ethical approval: Approval for the study was received from Non-Invasive Research Ethics Board of Dokuz Eylül University (decision no: 2016/04-10, date: 11.02.2016).
Funding The authors declared that this study received no financial support.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Catalaa I, Henry R, Dillon WP, et al. Perfusion, diffusion and spectroscopy values in newly diagnosed cerebral gliomas. NMR Biomed 2006;19(4):463-475.
2. Allison GT, Fujiwara T. The relationship between EMG median frequency and low frequency band amplitude changes at different levels of muscle capacity. Clin Biomech 2002;17(6):464-469.
3. Cai K, Tain RW, Zhou XJ, et al. Creatine CEST MRI for Differentiating Gliomas with Different Degrees of Aggressiveness. Mol Imaging Biol 2017;19(2):225-232.
4. Law M, Yang S, Wang H, et al. Glioma grading: sensitivity, specificity, and predictive values of perfusion MR imaging and proton MR spectroscopic imaging compared with conventional MR imaging. AJNR Am J Neuroradiol 2003;24(10):1989-1998.
5. Kleihues P, Burger PC, Scheithauer BW. The new WHO classification of brain tumours. Brain Pathol 1993;3(3):255-268.
6. Daumas-Duport C, Tucker ML, Kolles H, et al. Oligodendrogliomas. Part II: A new grading system based on morphological and imaging criteria. J Neurooncol 1997;34(1):61-78.
7. Bulik M, Jancalek R, Vanicek J, Skoch A, Mechl M. Potential of MR spectroscopy for assessment of glioma grading. Clinical Neurology and Neurosurgery 2013;115(2):146-153.
8. Stadlbauer A, Gruber S, Nimsky C, et al. Preoperative grading of gliomas by using metabolite quantification with high-spatial-resolution proton MR spectroscopic imaging. Radiology 2006;238(3):958-969.
9. Likavcanová K, Dobrota D, Liptaj T, et al. In vitro study of astrocytic tumour metabolism by proton magnetic resonance spectroscopy. Gen Physiol Biophys 2005;24(3):327-335.
10. Isobe T, Matsumura A, Anno I, et al. Quantification of cerebral metabolites in glioma patients with proton MR spectroscopy using T2 relaxation time correction. Mag Reson Imaging 2002;20(4):343-349.
11. Tong Z, Yamaki T, Harada K, Houkin K. In vivo quantification of the metabolites in normal brain and brain tumors by proton MR spectroscopy using water as an internal standard. Magn Reson Imaging 2004;22(7):1017-1024.
12. Yerli H, Ağildere AM, Ozen O, Geyik E, Atalay B, Elhan AH. Evaluation of cerebral glioma grade by using normal side creatine as an internal reference in multi-voxel 1H-MR spectroscopy. Diagn Interv Radiol 2007;13(1):3-9.
13. Hattingen E, Raab P, Franz K, et al. Prognostic value of choline and creatin in WHO grade II gliomas. Diagnostic Neuroradiology 2008;50(9):759-767.
14. Kinoshita Y, Kajiwarw H, Yokota A, Koga Y. Proton magnetic resonance spectroscopy of astrocytic tumors: an in vitro study. Neurol Med Chir (Tokyo) 1993;33(6):350-359.
15. Hattingen E, Raab P, Franz K, Zanella FE, Lanfermann H, Pilatus U. Myo-inositol: a marker of reactive astrogliosis in glial tumors. NMR Biomed 2008;21(3):233-241.
16. Xiaojuan L, Ying L, Pirzkall A, McKnight T, Nelson SJ. Analysis of the spatial characteristics of metabolic abnormalities in newly diagnosed glioma patients. Journal of magnetic resonanceimaging 2002;16(3):229-237.
17. Saraf-Lavi E, Bowen BC, Pattany PM, Sklar EM, Murdoch JB, Petito CK. Proton MR spectroscopy

of gliomatosis cerebri: case report of elevated myoinositol with normal choline levels. AJNR Am J Neuroradiol 2003;24(5):946-951.
18. Hsu YY, Chang CN, Wie KJ, Lim KE, Hsu WC, Jung SM. Proton magnetic resonance spectroscopic imaging of cerebral gliomas: correlation of metabolite ratios with histopathologic grading. Chang Gung Med J 2004;27(6):399-407.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 271-278
https://doi.org/10.30621/jbachs.1233245
RESEARCH ARTICLE

CROCIN SUPPRESSES INFLAMMATORY RESPONSE IN LPS-INDUCED ACUTE LUNG INJURY (ALI) VIA REGULATION OF HMGB1/TLR4 INFLAMMATION PATHWAY

Tayfun Ceylan[1], Ali Tugrul Akin[2], Emin Kaymak[3], Saban Varinli[4], Ayse Toluk[4]

[1] Cappadocia University, Faculty of Dentistry, Department of Basic Sciences, Nevşehir, Turkey
[2] Istinye University, Faculty of Medicine, Department of Medical Biology, Istanbul, Turkey
[3] Bozok University, Faculty of Medicine, Department of Histology and Embryology, Yozgat, Turkey
[4] Erciyes University, Faculty of Science, Department of Biology, Erciyes University, Kayseri, Turkey

ORCID: T.C. 0000-0002-0917-0378; A.T.A. 0000-0002-1408-8571; E.K. 0000-0002-3818-2693; S.V. 0000-0003-0621-5726; A.T. 0000-0003-1787-505X

Corresponding author: Tayfun Ceylan, **E-mail:** tyf.ceylan@gmail.com
Received: 12.01.2023; **Accepted:** 11.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Ceylan T, Akin A T, Kaymak E, Varinli S, Toluk A. Crocin Suppresses Inflammatory Response in LPS-Induced Acute Lung Injury (ALI) Via Regulation of HMGB1/TLR4 Inflammation Pathway. J Basic Clin Health Sci 2024; 8: 271-278.

ABSTRACT

Purpose: The most significant pathogen hypothesized to be causing the formation of Acute lung injury (ALI) in sepsis is thought to be lipopolysaccharide (LPS), a key endotoxin component of gram-negative bacteria. The main objective of this study is to determine possible anti-inflammatory effects of crocin (CRO) which has many biological properties such as anti-inflammatory, antioxidant, and anti-apoptotic in LPS-induced ALI.

Material and Methods: 40 Wistar albino rats were divided into four groups: Control (no treatment), CRO (given 50 mg/kg crocin for 9 days), LPS (given 30 mg/kg LPS at 9th day), LPS+CRO (given 50 mg/kg crocin for 9 days and 30 mg/kg LPS at 9th day). After experimental, rats were sacrificed and lungs were extracted. Histological examinations were performed in the lung tissue and the changes in the HMGB1 and TLR4 expressions were determined via immunohistochemical staining.

Results: Hemorrhage, HMGB1 and TLR4 expressions significantly increased in the LPS group. However, CRO administrations exerted a strong protective effect on the lungs in terms of these parameters in LPS+CRO group.

Conclusion: According to our results, we suggest that CRO can be considered as a protective agent against LPS induced ALI via inhibition of HMGB1/TLR4 pathway-mediated inflammatory response.

Keywords: Acute lung injury, crocin, inflammation, lipopolysaccharide

INTRODUCTION

Sepsis is an infection that causes systemic inflammatory response syndrome. It can lead to septic shock, tissue damage, multiple organ dysfunction syndrome, acute respiratory distress syndrome, and acute lung injury (ALI). Even severe sepsis can result in death (1). In sepsis, lung dysfunction is the first sign of multi-organ failure. ALI and acute respiratory distress syndrome are common complications in the intensive care unit and are

responsible for significant morbidity and mortality (2, 3). The main damage of ALI is the destruction of the pulmonary capillary endothelium and alveolar epithelium. This destruction occurs under the influence of numerous inflammatory mediators, including tumor necrosis factor-alpha (TNF-α), interleukins (ILs), and oxygen metabolites released by active neutrophils and macrophages (2). Lipopolysaccharide (LPS), a compound in the outer membrane of gram-negative bacteria, is a compound that impairs the immune function of many organs by triggering a biological inflammatory response (4). LPS-induced sepsis is a useful tool for studying the inflammatory process. Therefore, LPS is often applied to create an experimental model of inflammation (5, 6).

High mobility group box 1 (HMGB1) has been identified as a mediator in endotoxemia and sepsis. HMGB1 is secreted actively by innate immune cells (macrophages, monocytes) and passively by necrotic cells as a critical inflammatory mediator in cases of sepsis, shock, autoimmune diseases, and chronic inflammation. After HMGB1 is released into the extracellular environment, it binds to receptors such as Receptor for advanced glycation end-products (RAGE) and Toll-like Receptors (TLR), activating inflammatory responses (1, 7, 8). The overexpression of HMGB1 suggests that it may be an important therapeutic target in fatal systemic inflammatory diseases such as severe sepsis. Various studies have shown that the inflammatory reaction in the lung is significantly reduced by blocking HMGB1 (9, 10). TLR family consists of 10 members (TLR1-TLR10) (11). TLR4, a member of the TLR family, is a key receptor for innate immunity and cytokine release that mediates HMGB1-induced macrophage activation (8). Stimulation of TLR4 can activate the nuclear factor kappa B (NF-κB) protein. Activation of NF-κB leads to the induction of genes encoding proinflammatory cytokines such as IL-6 and TNF-α (12). LPS affects the TLR4/NF-κB signaling pathway by binding to cell surface receptors and also increases inflammation by activating inflammatory cascades in ALI (13). Highly effective pharmacotherapy is urgently needed for the treatment of acute inflammatory diseases such as ALI caused by sepsis caused by LPS.

Crosin (CRO), a bioactive natural product; It has anti-hypertensive, anti-depressant, anti-atherosclerotic, anti-platelet aggregation and nephron-protective properties as well as anti-oxidant activities and anti-inflammatory properties (14, 15). These properties of CRO make it interesting as a therapeutic agent. CRO is isolated from *Gardenia Jasminoides Ellis* and *Crocus sativus* (saffron). CRO, a water-soluble carotenoid, gives saffron its red color. (16). Saffron is grown in many parts of the world such as Iran, India, Greece, Spain, Turkey, Italy, Azerbaijan and China (17). The widespread cultivation of CRO shows that it can be easy to reach.

Elimination of inflammation that develops by activating TLR4 and NF-κB pathways by LPS or HMGB1 may lead to the prevention of possible ALI. For this purpose, reducing HMGB1 release from cells stimulated with LPS may prevent the activation of this pathway. Thus, TLR4 is not stimulated and the pathway does not become functional. Also, not activating NF-κB does not induce genes encoding proinflammatory cytokines such as IL-6 and TNF-α. Therefore, inflammation does not develop and the anti-inflammatory properties of CRO may inhibit the development of ALI. The aim of this study is to demonstrate the anti-inflammatory potential of CRO which has many biological properties on LPS-induced ALI'de. For this purpose, LPS-induced damage in the lung tissue were evaluated by histological methods and HMGB1 and TLR4 expressions were detected by immunohistochemical statining.

MATERIAL AND METHODS

Animals

This study was conceived and carried out at Erciyes University's Drug Application and Research Center in Turkey. The Experimental Animal and Local Ethics Committee of Erciyes University approved the experimental procedure used in this investigation on 02.06.2021 (Decision Number: 21/138) and 08.12.2022 (Decision Number: 22/270). Hakan Cetinsaya Experimental and Clinic Research Center, Erciyes University, provided a total of 40 male Wistar albino rats (8 weeks old, weighing 200-250 g). The rats were housed in cages in the typical order of the day, at 21°C and 12 hours of light/dark, with their water and nutrient needs met ad libitum.

Chemicals

Crocin (CRO) was purchased from Sigma-Aldrich (CAS: 42553-65-1). The purity of powdered CRO was approximately 90% according to the manufacturer's statement and it was dissolved in methanol and diluted in serum physiologic solution for the intraperitoneal injections to experimental animals

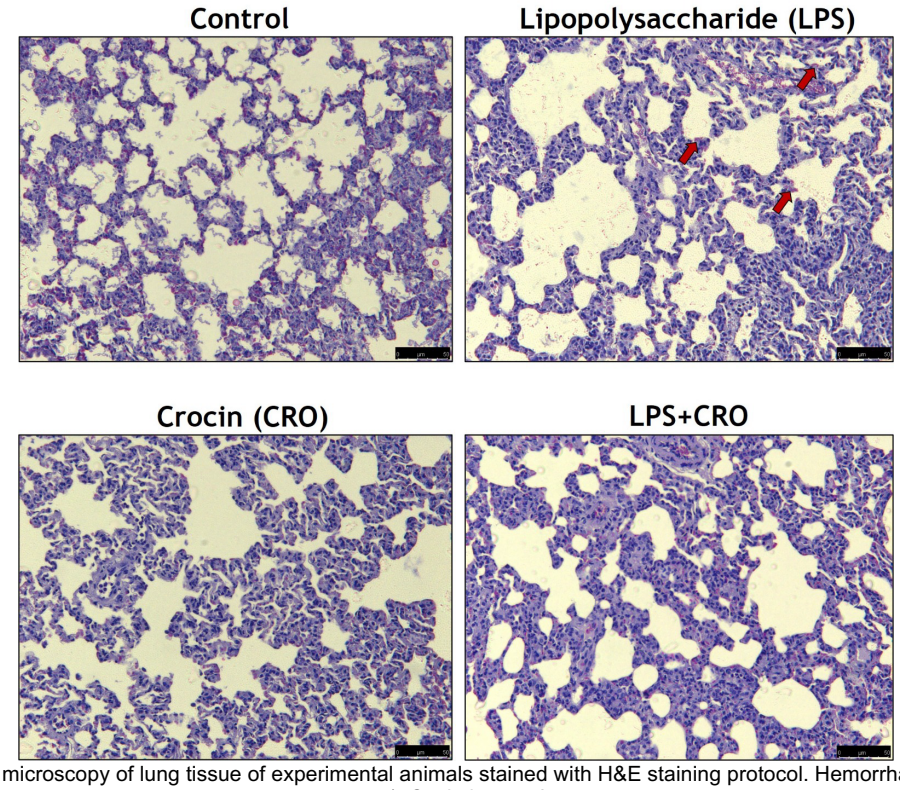


Figure 1. Light microscopy of lung tissue of experimental animals stained with H&E staining protocol. Hemorrhagic regions (red arrows). Scale bar = 50 µm

according to literatüre (18). LPS was also purchased from Sigma-Aldrich (L4130-100MG) and distilled water was used as a solvent to prepare LPS for administrations.

Experimental protocol

The sample size of this experimental study was calculated by power analysis using the G*Power v3.1 software. There was a total of 40 rats in 4 groups, 90.94% power expectation was found with 10 rats in each group. The count of animals in experimental groups was determined according to these results.

The rats were put into four groups at random, each with ten rats. The following are the groups that were formed:

1. Control group (n=10) : No treatment.
2. LPS group (n=10) : 30 mg/kg lipopolysaccharide was intraperitoneally administered to rats six hours before sacrification (18).
3. CRO group (n=10) : 50 mg/kg crocin was intraperitoneally administered to rats for 9 days (19).
4. LPS +CRO group (n=10): For 9 days, 50 mg/kg crocin was injected to rats intraperitoneally and 30 mg/kg lipopolysaccharide was administered 30 minutes after the last crocin administration.

Six hours following LPS treatment, animals were sedated with Ketamine (70 mg/bw) and Xylazine (10 mg/bw), and lung tissues were removed for histological and immunohistochemical analyses.

Histological evaluation

The lung tissues were histologically evaluated using standard histological techniques. For 24–48 hours, tissues were fixed in 10% formaldehyde, dehydrated with an alcohol series, cleared with xylene, and embedded in paraffin blocks. They were then cut into 5µm thick sections.

Hematoxylin-eosin (H&E) staining

The histological alterations in the lung tissue were determined using hematoxylin and eosin (H&E) staining (20). Images were captured and processed using a light microscope (Leica DM IL LED; Leica Microsystems, Germany). The study group looked at the structure of the lung tissue.

Immunohistochemistry

The immunohistochemistry method was applied to determine the alterations in the expression levels of HMGB1 and TLR4 antibodies as described in earlier studies of our research team. The blocks of paraffin

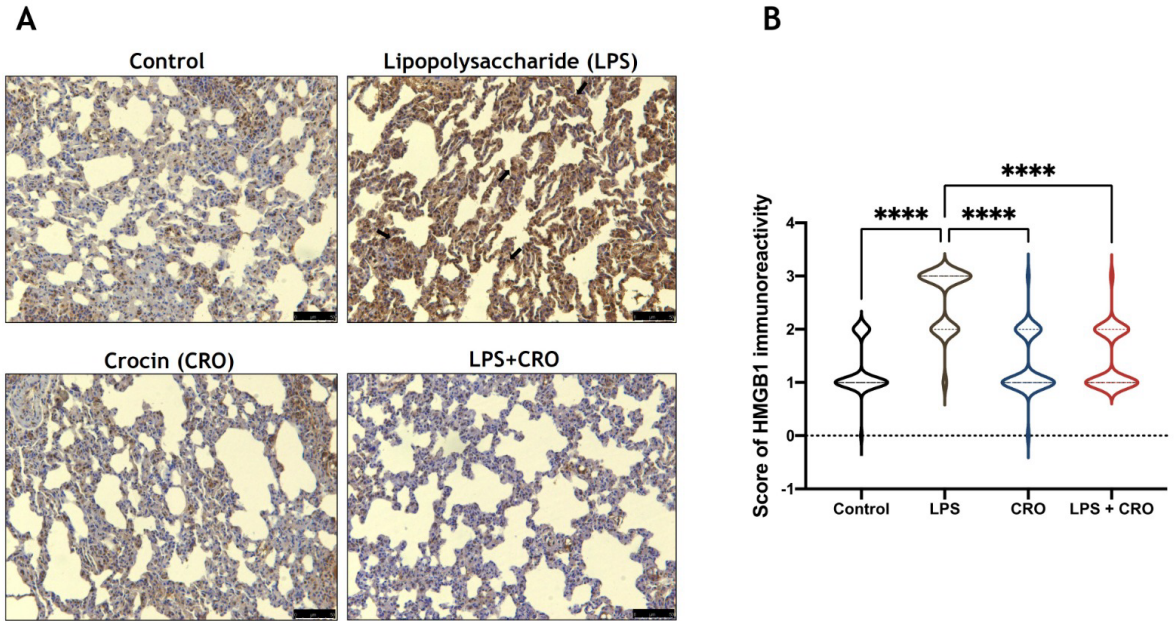


Figure 2. A. Immunohistochemical staining of HMGB1 in lung sections. Black arrows show the immunohistochemically stained areas. Scale bar: 50 µm. **B.** Statistical analysis of the immunoreactivity score among experimental groups. *= p<0.05, **= p<0.01, ***= p<0.001, ****= p<0.0001

were cut into 5 m lengths. Xylene was used for the deparaffinization of the tissues, and they hydrated with an alcohol series. Sections were put in a sterile urine cups containing 0.01 M citrate buffer and heated in a microwave oven at 350 W for antigen retrieval. Phosphate-buffered saline (PBS) was used to wash the slices three times for five minutes each time. The slices were treated with 3 percent (w/v) H_2O_2 for 10 minutes to reduce endogenous peroxidase activity. After being rewashed three times with PBS and stored in the incubation tank for five minutes, the sections were treated with Ultra V Block solution. HMGB1 (Anti HMGB1 antibody, E-AB-70044, Elabscience, USA) and TLR4 (Anti TLR4 antibody, bs-20594R, Bioss Antibodies, USA) antibodies diluted in a 1:75 ratio were then applied to the tissues overnight at 4°C. Slices were rewashed three times with PBS the next morning before being incubated with the secondary antibody for 10 minutes (TA-125-HDX, Thermo Fisher Scientific, Waltham, MA, USA). The immunoreaction was amplified using streptavidin–avidin–peroxidase solution after rewashing with PBS, and the lung sections were seen with 3,3-p-diaminobenzidine tetrahydrochloride (TA-060-HDX, Thermo Fisher Scientific, Waltham, MA, USA) (21). The photographs were taken with a light microscope. At least ten randomly chosen fields in each slide were scored at x20 magnification. Based on histological findings, the immunoreactivity was evaluated on a scale of 0 to 3, with 0 denoting no staining and 1, 2, and 3 denoting less staining, moderate staining, and high staining, respectively (22).

Statistical analysis

All quantitative data were statistically analyzed via using GraphPad Prism v9.0 for MacOS (GraphPad Software, La Jolla, California, USA). To determine the data's normal distribution, the D'Agostino Pearson omnibus test was performed. Comparison of the quantitative variables was determined using Kruskal-Wallis and Tukey's post-hoc test. p<0.05 was used to determine statistically significant differences.

RESULTS

Histopathological findings

Lung tissue sections of the control and CRO groups showed normal histological appearance. Hemorrhagic areas were observed in the lung tissue of the LPS group. Hemorrhagic areas were observed to be reduced in the LPS+CRO group. Histological images of all groups are shown in Figure 1.

Immunohistochemical findings

HMGB1 and TLR4 expressions were observed in the lung tissue. In the LPS group, HMGB1 expressions substantially raised compared to Control and CRO groups (p<0.0001). However, In the LPS+CRO

Table 1. Scoring of experimental groups.

Groups	Control	LPS	CRO	LPS+CRO	*p*
HMGB1 immunoreactivity	1 (0-2)[a]	3 (1-3)[b]	1 (0-3)[a]	1 (1-3)[a]	0.0001
TLR4 immunoreactivity	0 (0-1)[a]	1 (0-2)[b]	0 (0-1)a	0 (0-1)[q]	0.0001

Data are expressed as median (min-max). There is no significant difference between groups with the same letter. $p<0.0001$

group, HMGB1 expressions were statistically lower when compared with those in the LPS group ($p<0.0001$) and were similar to the expression levels in the Control and CRO groups. The differences in the expression levels of HMGB1 and the statistical analysis of immunoreactivity score of experimental groups are presented in the Figure 2 and Table 1.

The expression levels of TLR4 are also significantly increased in the LPS group when compared with Control and CRO groups ($p<0.0001$). Similarly, CRO administrations were significantly preserved the lung tissue against increased TLR4 expressions in the LPS+CRO group compared to LPS group ($p<0.0001$). The differences in the expression levels of TLR4 and the statistical analysis of immunoreactivity score of experimental groups are presented in the Figure 3 and Table 1.

DISCUSSION

Sepsis, one of the deadliest diseases worldwide, often leads to multi-organ failure due to an uncontrolled inflammatory response. Sepsis is often associated with organ dysfunction induced by dysregulation of the host defense against infection. The lung is the most critical and vulnerable organ to sepsis. ALI is a common inflammatory injury caused by sepsis (23). The fact that the oxygen taken by the lungs is used in many tissues and organs shows that other organs are also affected in ALI besides the lung. Therefore, this condition, in which all organs are affected, can result in death in severe sepsis. The rate of deaths due to sepsis shock is unsettling and studies on therapeutic methods are important. Herbal-derived agents are used in public health as therapeutic agents in lung injuries as well as in many diseases. CRO, one of the active compounds of saffron, has been shown in various studies to have antioxidant, anti-cancer, anti-depressant, analgesic, anti-atherosclerosis and anti-inflammatory properties (19, 24). When the literature was carefully examined, very few studies were found showing the protective effects of CRO on tissue damage caused by LPS (19, 24-26). Therefore, in this study, we aimed to investigate the protective effect of CRO on LPS-induced acute lung injury through its potential anti-inflammatory effects.

Many studies have reported that endotoxin-induced sepsis causes severe damage to the lung tissue of experimental animals. Some studies have shown that sepsis caused by LPS applications causes many histopathological changes such as decreased pulmonary alveolar number and alveolar wall thickness, cell infiltration and hemorrhagic areas in the lungs of experimental animals (4, 27, 28). In our study, LPS application caused histopathological changes in the lung tissue, similar to previous studies. Our histological evaluations showed that this damage was in the form of hemorrhagic areas. Our histopathological scoring also supports these evaluations significantly. In the lungs of the rats to which we applied CRO preventively before LPS application, these damages were reduced and histopathological scoring decreased significantly. To understand the inflammatory mechanism of this improvement, we also evaluated HMGB1 and TLR4 immunoreactivities in lung tissue. The damage mechanism of inflammation includes binding to TLR2 and TLR4, which mediates HMGB1-dependent activation of macrophage cytokine release. Extracellular HMGB1 mediates sterile inflammation. HMGB1 binds to the receptor for TLR4, causing cells to release inflammatory cytokines. Therefore, HMGB1 and TLR4 activation is an important marker in the inflammation pathway (19, 29). Several studies have reported significantly increased expressions of HMGB1 and TLR4 in lung tissue in models of LPS-induced infection (30-32).

Treatment of LPS-induced ALI showed inhibition of inflammatory reactions by suppression of the HMGB1-mediated TLR4/NF-κB pathway (33). Previous studies have reported that CRO attenuates lipopolysaccharide-induced acute lung injury (25, 26). Also, results suggested that CRO can inhibit the NF-κB and HMGB1 inflammatory pathway activation in LPS-induced acute respiratory distress syndrome mice and LPS-stimulated human umbilical vein endothelial cells (26). In this study, unlike other studies, TLR4 expression was analysed. In our study,

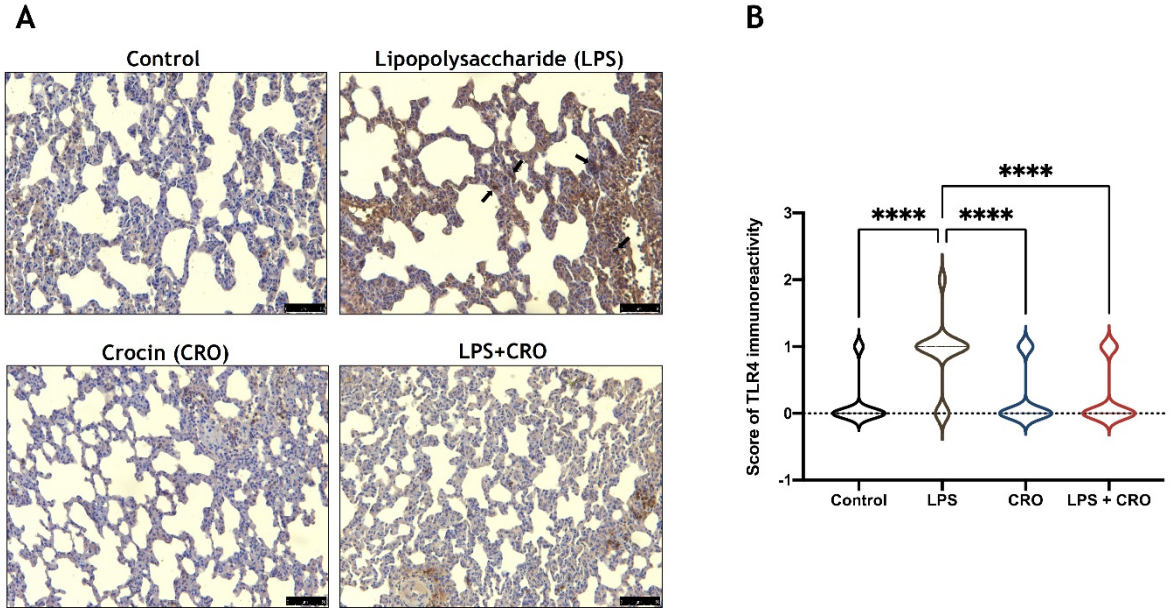


Figure 3. A. Immunohistochemical staining of TLR4 in lung sections. Black arrows show the immunohistochemically stained areas. Scale bar: 50 µm. **B.** Statistical analysis of the immunoreactivity score among experimental groups. *= $p<0.05$, **= $p<0.01$, ***= $p<0.001$, ****= $p<0.0001$

we measured HMGB1 and TLR4 immunoreactivities to understand the mechanism of histopathological changes in lung tissue. HMGB1 and TLR4 immunoreactivities were found to be significantly higher in the lungs of animals to whom we had LPS applied. This significant value indicates that cellular damage is mediated by inflammation. It is reported that the pharmacological effects of conventional drugs and inflammatory inhibitors against HMGB1 will become new therapeutic approaches for lung diseases (34). Anti-inflammatory effects of CRO in various tissues and organs have been reported (34, 35). In our study, HMGB1 and TLR4 immunoreactivities were significantly reduced in the lungs of rats to whom CRO was administered for 9 days before LPS administration. The decrease in HMGB1 and TLR4 immunoreactivity is clear evidence that CRO has a protective effect against LPS-induced inflammation.

CONCLUSION

According to our histopathological analysis and immunohistochemical results, CRO exerted a protective effect at the dose of 50 mg/kg via attenuating histopathological changes and suppressing the inflammatory response in the lung tissue. CRO administrations can be considered as a protective treatment for the elimination of the negative effects of endotoxin-induced acute lung injury and it should not be ignored in the future clinical studies. In addition, in order to better understand the protective effect of CRO, whether it is associated with different cellular mechanisms may be a subject of research for future studies.

Acknowledgement: This study was presented as a poster at the International Cappadocia Health and Life Conference (Online) in Nevşehir on 24-26.08.2022.
Author contribution: Concept/Design: TC, ATA, EK; Data acquisition: TC, ATA, EK, SV, AT; Data analysis and interpretation: TC, ATA, EK; Drafting manuscript: TC, ATA; Critical revision of manuscript: TC, ATA, EK, AT; Final approval and accountability: TC, ATA, EK, SV, AT; Technical or material support: TC, ATA, EK, SV, AT.
Conflict of interests: The authors declare no conflict of interests.
Ethical approval: The Experimental Animal and Local Ethics Committee of Erciyes University approved the experimental procedure used in this investigation on 02.06.2021 (Decision Number: 21/138) and 08.12.2022 (Decision Number: 22/270).
Funding: There is no financial support.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Cinar I, Sirin B, Aydin P, Toktay E, Cadirci E, Halici I, et al. Ameliorative effect of gossypin against acute lung injury in experimental sepsis model of rats. Life Sciences 2019;221:327-34.
2. Xiao X, Yang M, Sun D, Sun S. Curcumin protects against sepsis-induced acute lung injury in rats. Journal of Surgical Research 2012;176(1):e31-e9.

3. Ware LB, Matthay M. The acute respiratory distress syndrome. New England Journal of Medicine 2000;342(18):1334-49.
4. Cai X, Chen Y, Xie X, Yao D, Ding C, Chen M. Astaxanthin prevents against lipopolysaccharide-induced acute lung injury and sepsis via inhibiting activation of MAPK/NF-κB. American Journal of Translational Research 2019;11(3):1884.
5. Fisher BJ, Seropian IM, Kraskauskas D, Thakkar JN, Voelkel NF, Natarajan R. Ascorbic acid attenuates lipopolysaccharide-induced acute lung injury. Critical Care Medicine 2011;39(6):1454-60.
6. Mokhtari-Zaer A, Norouzi F, Askari VR, Khazdair MR, Roshan NM, Boskabady M, et al. The protective effect of Nigella sativa extract on lung inflammation and oxidative stress induced by lipopolysaccharide in rats. Journal of Ethnopharmacology 2020;253:112653.
7. Yang H, Wang H, Czura CJ, Tracey KJ. The cytokine activity of HMGB1. Journal of Leukocyte Biology 2005;78(1):1-8.
8. Zhong H, Li X, Zhou S, Jiang P, Liu X, Ouyang M, et al. Interplay between RAGE and TLR4 regulates HMGB1-induced inflammation by promoting cell surface expression of RAGE and TLR4. The Journal of Immunology 2020;205(3):767-75.
9. Ogawa EN, Ishizaka A, Tasaka S, Koh H, Ueno H, Amaya F, et al. Contribution of high-mobility group box-1 to the development of ventilator-induced lung injury. American Journal of Respiratory Critical Care Medicine 2006;174(4):400-7.
10. Ding N, Wang F, Xiao H, Xu L, She S. Mechanical ventilation enhances HMGB1 expression in an LPS-induced lung injury model. PloS One 2013;8(9):e74633.
11. Ali I, Nanchal R, Husnain F, Audi S, Konduri GG, Densmore JC, et al. Hypoxia preconditioning increases survival and decreases expression of Toll-like receptor 4 in pulmonary artery endothelial cells exposed to lipopolysaccharide. Pulmonary Circulation 2013;3(3):578-88.
12. Wu Y, Liu Y, Huang H, Zhu Y, Zhang Y, Lu F, et al. Dexmedetomidine inhibits inflammatory reaction in lung tissues of septic rats by suppressing TLR4/NF-κB pathway. Mediators of Inflammation 2013;2013.
13. Tang J, Xu L, Zeng Y, Gong F. Effect of gut microbiota on LPS-induced acute lung injury by regulating the TLR4/NF-kB signaling pathway. International Immunopharmacology 2021;91:107272.
14. Rezaei N, Avan A, Pashirzad M, Rahmani F, Moradi Marjaneh R, Behnam-Rassouli R, et al. Crocin as a novel therapeutic agent against colitis. Drug and Chemical Toxicology 2020;43(5):514-21.
15. Suh KS, Chon S, Jung W-W, Choi EM. Crocin attenuates methylglyoxal-induced osteoclast dysfunction by regulating glyoxalase, oxidative stress, and mitochondrial function. Food and Chemical Toxicology 2019;124:367-73.
16. Hashemzaei M, Mamoulakis C, Tsarouhas K, Georgiadis G, Lazopoulos G, Tsatsakis A, et al. Crocin: a fighter against inflammation and pain. Food and Chemical Toxicology 2020;143:111521.
17. Korani S, Korani M, Sathyapalan T, Sahebkar A. Therapeutic effects of Crocin in autoimmune diseases: A review. BioFactors 2019;45(6):835-43.
18. Goraca A, Józefowicz-Okonkwo G. Protective effect of an early treatment with lipoic acid in LPS-induced lung injury in rats. Journal of Physiology and Pharmacology 2007;58(3):541-9.
19. Xie Y, He Q, Chen H, Lin Z, Xu Y, Yang C. Crocin ameliorates chronic obstructive pulmonary disease-induced depression via PI3K/Akt mediated suppression of inflammation. European Journal of Pharmacology 2019;862:172640.
20. Ceylan T, Karabulut D, Öztürk E, Akin AT, Kaymak E, Yakan B. Histological evaluation of the effects of rapamycin and 3-methyladenine on cisplatin-induced epididymal injury in rats. Cukurova Medical Journal 2021;46(3):1184-90.
21. Ceylan T, Kaymak E, Akin AT, Yakan B. The ameliorative effects of caffeic acid phenethyl Ester in cisplatin-induced nephrotoxicity: Assessment of the oxidative stress an inflammation. International Journal of Morphology 2021;39(2):612-618.
22. Veale D, Ashcroft T, Marsh C, Gibson G, Harris A. Epidermal growth factor receptors in non-small cell lung cancer. British Journal of Cancer 1987;55(5):513-6.
23. Hwang J-S, Kim K-H, Park J, Kim S-M, Cho H, Lee Y, et al. Glucosamine improves survival in a mouse model of sepsis and attenuates sepsis-induced lung injury and inflammation. Journal of Biological Chemistry 2019;294(2):608-22.

24. Aslani MR, Amani M, Masrori N, Boskabady MH, Ebrahimi HA, Chodari L. Crocin attenuates inflammation of lung tissue in ovalbumin-sensitized mice by altering the expression of endoplasmic reticulum stress markers. Biofactors 2022;48(1):204-15.
25. Wang J, Kuai J, Luo Z, Wang W, Wang L, Ke C, et al. Crocin attenuates lipopolysacchride-induced acute lung injury in mice. International Journal of Clinical Experimental Pathology 2015;8(5):4844.
26. Zhang D, Qi B-y, Zhu W-w, Huang X, Wang X-z. Crocin alleviates lipopolysaccharide-induced acute respiratory distress syndrome by protecting against glycocalyx damage and suppressing inflammatory signaling pathways. Inflammation Research 2020;69:267-78.
27. Kheiry M, Dianat M, Badavi M, Mard SA, Bayati V. p-Coumaric acid attenuates lipopolysaccharide-induced lung inflammation in rats by scavenging ROS production: An in vivo and in vitro study. Inflammation 2019;42(6):1939-50.
28. Ye J, Guan M, Lu Y, Zhang D, Li C, Zhou C. Arbutin attenuates LPS-induced lung injury via Sirt1/Nrf2/NF-κBp65 pathway. Pulmonary Pharmacology & Therapeutics 2019;54:53-9.
29. Lin L, Li J, Song Q, Cheng W, Chen P. The role of HMGB1/RAGE/TLR4 signaling pathways in cigarette smoke-induced inflammation in chronic obstructive pulmonary disease. Immunity, Inflammation and Disease 2022;10(11):e711.
30. Tang J, Xu L, Zeng Y, Gong FJII. Effect of gut microbiota on LPS-induced acute lung injury by regulating the TLR4/NF-kB signaling pathway. Int Immunopharmacol 2021;91:107272.
31. Lin L, Li J, Song Q, Cheng W, Chen PJI, Inflammation, Disease. The role of HMGB1/RAGE/TLR4 signaling pathways in cigarette smoke-induced inflammation in chronic obstructive pulmonary disease. Immun Inflamm Dis 2022;10(11):e711.
32. Ge X, Meng X, Fei D, Kang K, Wang Q, Zhao M. Lycorine attenuates lipopolysaccharide-induced acute lung injury through the HMGB1/TLRs/NF-κB pathway. Biotech 2020;10(8):1-10.
33. Meng L, Li L, Lu S, Li K, Su Z, Wang Y, et al. The protective effect of dexmedetomidine on LPS-induced acute lung injury through the HMGB1-mediated TLR4/NF-κB and PI3K/Akt/mTOR pathways. Molecular Immunology 2018;94:7-17.
34. Ding J, Cui X, Liu Q. Emerging role of HMGB1 in lung diseases: friend or foe. Journal of Cellular and Molecular Medicine. 2017;21(6):1046-57.
35. Li L, Zhang H, Jin S, Liu C. Effects of crocin on inflammatory activities in human fibroblast-like synoviocytes and collagen-induced arthritis in mice. Immunologic Research 2018;66(3):406-13.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 279-286
https://doi.org/10.30621/jbachs.1237830
RESEARCH ARTICLE

RELIABILITY AND VALIDITY OF THE TURKISH VERSION OF THE COMPREHENSIVE LOWER LIMB AMPUTEE SOCKET SURVEY

Senem Demirdel [1], Ertuğrul Demirdel [2], Osman Söyler [3]

[1] University of Health Sciences, Gulhane Faculty of Physiotherapy and Rehabilitation, Ankara, Turkey
[2] Ankara Yıldırım Beyazıt University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey
[3] Lokman Hekim University, Health Sciences Institute, Ankara, Turkey

ORCID: S.D. 0000-0001-7395-8859; E.D. 0000-0002-7139-0523, O.S. 0000-0002-2798-0649

Corresponding author: Senem Demirdel, **E-mail:** senem.demirdel@sbu.edu.tr
Received: 17.01.2023; **Accepted:** 12.02.2024; **Available Online Date:** 31.05.2024

Cite this article as: Demirdel S, Demirdel E, Söyler O. Reliability and Validity of the Turkish Version of the Comprehensive Lower Limb Amputee Socket Survey. J Basic Clin Health Sci 2024; 8: 279-286.

ABSTRACT

Purpose: The aim of this study was to translate the Comprehensive Lower Limb Amputee Socket Survey (CLASS) into Turkish and examine its reliability and validity in lower limb amputees.
Materials and Methods: This cross-sectional study included 97 lower limb amputees. Cronbach's alpha coefficient was used to evaluate internal consistency, and intraclass correlation coefficient was used to evaluate test-retest reliability. The retest of the CLASS was applied one week later. The satisfaction with the prosthesis subscale of the Trinity Amputation and Prosthesis Experience Scale (TAPES) was used to assess convergent validity.
Results: The mean age of the participants was 46.78±15.04 years and 71.1 % were male. Internal consistency was found to be high for all domains of the Turkish CLASS (Cronbach's alpha ranged from 0.81 to 0.90). Test-retest reliability was found to be high (intraclass correlation coefficient ranged from 0.82-0.95). A significant relationship was found between all domains of the CLASS and TAPES prosthesis satisfaction subscale (r=0.553 for stability domain, r=0.509 for suspension domain, r=0.482 for comfort domain, r= 0.444 for appearance domain, p<0.001).
Conclusion: The results of this study showed that the Turkish version of the CLASS is a reliable and valid tool for assessing user's perception about socket fit in lower limb prosthesis users.

Keywords: Prostheses, surveys, socket fit, amputee, reliability, validity

INTRODUCTION

In individuals with lower extremity amputation, walking ability is affected due to the loss of part of the locomotor system. Prosthetic rehabilitation is required to restore mobility and functional restoration (1, 2). In the rehabilitation process, prosthesis satisfaction plays an important role in the functional use of the prosthesis. Socket features must be suitable for fit, which is one of the most important factors affecting prosthesis satisfaction (3). The socket is very important as it is the part of the prosthesis that comes into contact with the user. The socket is the part where the prosthesis comes into contact with the residual limb and body weight is transferred to the prosthesis through the socket (4). Transmission of movements in the residual limb to other prosthetic elements is also achieved through the socket (5). Socket fit is the most considerable factor affecting rehabilitation for both clinicians and amputees (6, 7). In individuals with lower extremity

amputation, a safe and comfortable socket provides stable transfer of the load from the residual limb to the prosthesis, increasing functionality in daily living activities (8). If the socket is not a good fit, ulcers may occur on the residual limb due to localized pressure and shear stresses. These conditions complicate the use of prosthesis, and have a negative effect on mobility and daily activities (9).

The design, manufacture, and implementation of the socket is a time-consuming process for both the user and the prosthetist, and may require multiple service visits for individuals with amputations (8, 10). Socket-related evaluations are of great importance to ensure socket fit in the shortest time and most effectively. An initially well fitting socket can become incompatible over time due to volume changes in the residual limb, which can lead to skin-related discomfort and gait disturbances (11). Therefore, socket-related evaluations should be carried out at regular intervals. There are many techniques that for the biomechanical evaluation of socket fit (10, 12, 13). However, it is also necessary to evaluate the feedback of the prosthesis user about the socket. Patient-reported outcome measures are of great importance in ensuring patient-centred clinical management, evaluating the effectiveness of clinical interventions from the patient's perspective, and improving health care quality (14).

Various socket designs and suspension systems are currently available for individuals with lower extremity amputation (5, 15-17). User experiences should be evaluated to make it easier for clinicians to make decisions about prosthetic parts (18). There are various scales evaluating prosthesis satisfaction in Turkey (19, 20). However, since the socket is in contact with the residual limb and is the most important part for the comfort of the prosthesis, it should be evaluated in detail. The pressure distribution between the residual limb and the socket may vary during stair climbing and walking activities (21). Therefore, querying the socket-related parameters during different activities provides more accurate results. The Comprehensive Lower Limb Amputee Socket Survey (CLASS) is an easy and quick patient reported outcome measurement for the evaluation of the stability, suspension, comfort and appearance of the prosthetic socket during different activities (22). The purpose of the current study was to examine the reliability and validity of the Turkish version of CLASS.

MATERIAL AND METHODS

Study Design and Ethical Approval

This prospective cross-sectional screening study was conducted in a Prosthesis-Orthosis Service in Ankara between June 2021 and December 2022. The study was approved by Ethics Committee of Ankara Yıldırım Beyazıt University, in accordance with the Declaration of Helsinki (Decision Date: 14.06.2021, No: 68).

Translation and cultural adaptation

Translation was carried out in accordance with the Patient Reported Outcomes Measures principles of translation and cultural adaptation (23). Translation permission was received from the CLASS developers by the project manager in December 2020. After obtaining translation permission, the necessary Ethics Committee permission was obtained to start the study. Two forward translations were made by two native Turkish speaker translators living in Turkey who are experienced in translation in the field of health. The translators were informed about lower extremity prostheses, sockets and the purpose of the study. The forward translations were checked for inconsistencies, and discrepancies were resolved by consensus. Reconciliation decisions were reviewed by the project manager. Two back translations were then made by two native English speaker translators who are experienced in translation in the field of health. The back translations were compared with the original version and reviewed for inconsistencies, and again discrepancies were resolved by consensus. All the translations were compared with each other and with the original version. Conceptual equivalence between source and target language was achieved. In the original version of the CLASS, statements about stability, suspension, comfort, and appearance are written once, and the activities of sit, stand, walk, ascending and descending stairs are listed at the bottom (My socket is comfortable when I "…"). In the Turkish version, it was decided that it could not be understood because "…" is at the beginning of the sentence, and it was decided to repeat the phrase for each activity. (My socket is comfortable when I sit, My socket is comfortable when I stand etc.) The obtained translation was applied to 12 lower extremity prosthesis users who were Turkish native speakers and its comprehensibility was evaluated. All the prosthesis users stated that the questionnaire items were comprehensible and clear. The project manager

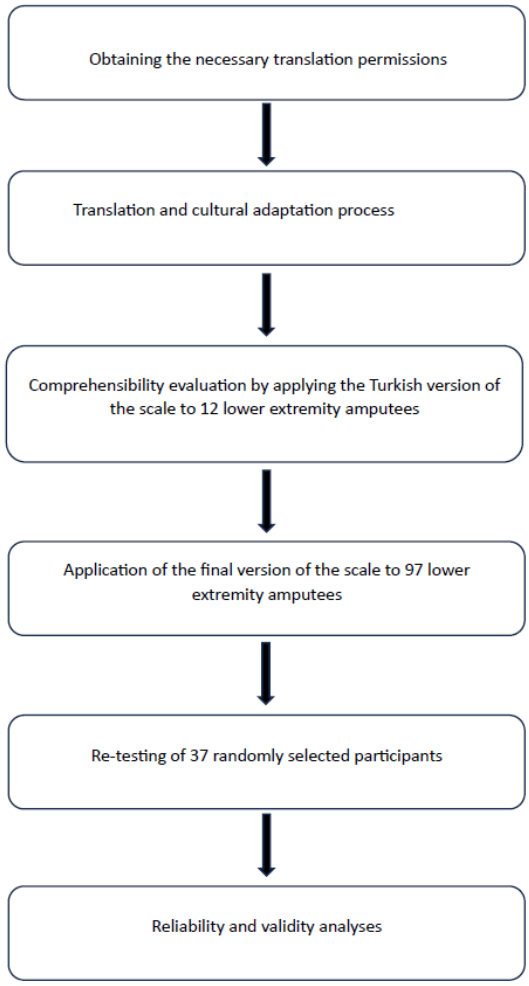


Figure 1. Flow Chart of the study

reviewed the results of the cognitive debriefing, and no changes were required at this stage. Proofreading was performed to correct minor errors before the translated questionnaire was used among the target population.

Participants

Criterion sampling method was used in the study. The study included individuals aged ≥18 years, who had unilateral lower extremity amputation, had been using their current prosthesis for at least 3 months, and were literate in Turkish. The informed consent was obtained from volunteers. After applying the Turkish version of CLASS, the retest was applied one week later to 37 randomly selected participants.

Outcome measures

The demographic and prosthesis-related information of the individuals was questioned and recorded. The CLASS and the satisfaction with the prosthesis subscale of the Trinity Amputation and Prosthetic Experience Scale (TAPES) were applied after questioning age, gender, level of amputation, reason for amputation, duration of prosthesis use, Medicare Functional Classification Level (24).

CLASS is an easy and quick self-report questionnaire that assesses the stability, suspension, comfort, and appearance of the prosthetic socket in lower extremity prosthesis users. It includes a total of 15 items; 12 items evaluating stability, suspension and comfort in sitting, standing, walking and stair climbing activities, and 3 items evaluating appearance during sitting, standing and wearing tight trousers. The questionnaire is scored using a 4-point Likert-type scale of 1= strongly disagree, 2= Disagree, 3= Agree, 4= Strongly agree. The percentage system equivalent of each subscale score and the total score were calculated. A high score indicates high socket satisfaction (22).

The TAPES satisfaction with the prosthesis subscale was used to assess criterion-based validity. This subscale includes 10 items scored with a 5-point Likert-type scale. A high score indicates high prosthesis satisfaction (20). The TAPES satisfaction with the prosthesis subscale was selected because prosthesis satisfaction is related to socket fit and this scale was previously used as a validation measure in the Persian version of CLASS (25).

Statistical Analysis

The obtained data were analyzed using IBM SPSS 25.0 for Windows software (SPSS Inc., Chicago, IL, USA). Internal consistency for homogeneity and test-retest reliability for reprodubility were analyzed. Internal consistency was assessed using the Cronbach's alpha coefficient, with values >0.80 considered as high internal consistency (26). The intraclass correlation coefficient (ICC) was used for test-retest reliability, with values >0.75 accepted as good reliability (27). Item-total correlation coefficient was used to evaluate the contribution of each item to the total subcale score (28). The item-total correlation coefficient is expected to be >0.25 (29). If more than 15% of the participants obtained the minimum score, the floor effect was considered to be present, and if more than 15% of the participants obtained the maximum score, the ceiling effect was considered to be present (30).

Convergent construct validity was evaluated by using the correlation between the TAPES satisfaction with the prosthesis subscale and the CLASS domains.

Table 1. Demographic and clinical features of the study population

		Mean	Standart deviation
Age (years)		46.78	15.04
Time since first prosthesis use (years)		17.25	15.06
Daily prosthesis use time (hours)		12.7	3.74
		n	**%**
Gender	Female	28	28.9
	Male	69	71.1
Cause of amputation	Trauma	63	64.9
	Vascular	14	14.4
	Congenital	6	6.2
	Other reasons	14	14.4
Amputation level	Transtibial	55	56.7
	Knee disarticulation	6	6.2
	Transfemoral	36	37.1
Activity level	K2	29	29.9
	K3	63	64.9
	K4	5	5.2

Spearman's correlation coefficient (r) was calculated to determine convergent construct validity. The correlation coefficients were considered as strong (r>0.76), good (0.51<r<0.75), moderate (0.26<r<0.50) and poor (r<0.25) correlation (31).

RESULTS

Evaluation was made of 97 lower extremity amputees. Of the individuals with transtibial amputation, 69.1% used the vacuum system, 7.3% the suction system, 16.4% the pin and lock system, and 7.3% other suspension systems. Of the individuals with knee disarticulation, 33.3% used the vacuum system, 33.3% the suction system, and 33.3% the soft insert mechanism. Of the individuals with transfemoral amputation, 19.4% used the vacuum system, 47.2% the suction system, and 33.3% the pin and lock system. The demographic characteristics of the participants and information about the amputations are presented in Table 1.

It was seen that the lowest score in the CLASS stability, suspension and comfort domains was obtained from the ascending or descending stairs item. In the Appearance domain, the lowest score was seen in the item related to wearing tight trousers. The item statistics are shown in Table 2.

The lowest score among the CLASS subscales was obtained from the appearance subscale. Cronbach's alpha was >0.80 in all the subscales, and the ICC was >0.80 in all the subscales. No floor effect was observed in any of the CLASS subscales, and the ceiling effect was observed only in the suspension subscale (Table 3).

The TAPES satisfaction with the prosthesis subscale was completed by 96.9% of the study participants. The total score of the TAPES satisfaction with the prosthesis subscale was mean 37.87±6.35 points (minimum:20, maximum:50). A statistically significant, positive correlation was found between the satisfaction with the prosthesis subscale and the CLASS stability subcale (r=0.553, p<0.001), suspension subscale (r=0.509, p<0.001), comfort subscale (r=0.482, p<0.001), and appearance subscale (r=0.444, p<0.001).

DISCUSSION

The aim of the current study was to translate the CLASS into Turkish, to adapt it cross-culturally, and to examine its psychometric properties for individuals with unilateral lower extremity amputation. The results of the current study demonstrated that the internal consistency and test-retest reliability Turkish

Table 2. Item statistics of domains of the CLASS

Items of the stability domain	Mean	Standart Deviation	Item-total correlation
Sit	3.11	0.71	0.656
Stand	3.11	0.69	0.794
Walk	3.03	0.68	0.782
Ascend or descent stairs	2.91	0.70	0.780
Items of the suspension domain			
Sit	3.20	0.67	0.661
Stand	3.18	0.66	0.800
Walk	3.07	0.73	0.859
Ascend or descent stairs	2.94	0.74	0.793
Items of the comfort domain			
Sit	3.03	0.74	0.575
Stand	3.14	0.59	0.764
Walk	3.06	0.65	0.779
Ascend or descent stairs	2.88	0.64	0.646
Items of the appearance domain			
Sit	2.75	0.82	0.731
Stand	2.98	0.74	0.709
Wear tight pants	2.45	0.90	0.578

version of CLASS was good. A moderate to good correlation was found between the Turkish CLASS domains and the TAPES satisfaction with the prosthesis subscale in the criterion-based validity analysis.

This study included unilateral lower extremity amputees with different demographic characteristics and clinical features. This increases the generalizability of the results of the study and shows that the psychometric properties of the Turkish CLASS are suitable for use in individuals with unilateral lower extremity amputations with different characteristics.

Various scales are used in Turkey to evaluate prosthesis satisfaction (19, 20). Although there are items related to socket fit in these scales, it is not possible to obtain a detailed assessment of the socket (3). Since the socket is the part where the prosthesis comes into contact with the user, it should be evaluated holistically during different activities. With the use of CLASS, the prosthesis users can better express their socket-related problems and it becomes easier for the prosthetist to resolve the problem. Since satisfaction with use is related to ambulation ability, and socket fit is an important factor affecting saticfaction with use, evaluation of socket fit is also important in terms of increasing functionality (3, 32).

It was determined that the lowest score in the comfort, suspension and stability subscales was obtained from the item related to stairs. The ascent and descent of stairs is an activity where intra-socket pressure is increased compared to walking on a flat surface (21). Therefore, low CLASS scores for ascending and descending stairs is an expected result. However, it has been shown that different interface systems have different effects on interface pressure when climbing and descending stairs (33). The evaluation of socket fit during different activities with CLASS can guide prosthesis prescribing. The score obtained from the Appearance subscale was found to be lower than the other subscale scores. In previous evaluations of prosthesis satisfaction in lower extremity amputees, the satisfaction scores regarding the appearance of the prosthesis have been reported to be low (3). The current study also showed that the satisfaction with socket appearance scores were the lowest of the socket-related parameters. This issue should be

Table 3. Reliability indicators of domains of the CLASS

Domains of the CLASS	Mean (SD)	Median	Range	Cronbach's Alpha	ICC (95% CI)	% with floor effect	% with ceiling effect
Stability	76.09 (15.09)	75	25-100	0.886	0.951 (0.907-0.974)	1	14.4
Suspension	77.57 (15.48)	75	25-100	0.900	0.871 (0.764-0.931)	1	18.6
Comfort	75.77 (13.68)	75	25-100	0.846	0.832 (0.700-0.910)	1	11.3
Appearance	68.29 (17.66)	66.66	25-100	0.815	0.825 (0.687-0.906)	4.1	8.2

SD: Standart Deviation, ICC: Intraclass Correlation Coefficient, CI: Confidence Interval

considered in new socket and prosthesis designs in order to increase user satisfaction.

The internal consistency of the CLASS subscales was found to be good. This result confirmed that the CLASS items were interrelated and consistent. The Cronbach's alpha coefficient ranged from 0.85 to 0.92 in the original version and 0.86-0.92 for the Persian version of the CLASS (22, 25). The value obtained in the current study is close to these values. The item-total score correlations show that the predictive utility of CLASS items is as strong as those of the original version (22). The test-retest reliability of the Turkish version of CLASS was found to be higher than the Persian version of CLASS for the stability and suspension subscales. For the comfort and appearance subscales, the ICC values were lower than those of the Persian version (25). The ICC value >0.80 obtained in all the subscales indicates high reproducibility.

No floor effect was found for any subscale in the Turkish version of CLASS, and the ceiling effect was seen only for the suspension subscale. Similarly in the Persian version of CLASS, there was no floor effect and the ceiling effect was found only in the suspension subscale (16.1%) (25). This could be attributed to the fact that the suspension systems used by the participants are up-to-date and advanced systems.

A moderate to good correlation was found between the TAPES satisfaction with the prosthesis subscale, which is also used in the Persian version for convergent validity, and the CLASS Turkish version. This result is similar to the results of Rouhani et al. The TAPES satisfaction with the prosthesis subscale is a general measure of prosthesis satisfaction (25). It contains items that may be related to the socket fit, such as the fit and comfort of the prosthesis, but since it does not provide a direct assessment of the socket, the moderate to good correlation is an expected result.

This study presents important results from examination of the reliability and validity of the Turkish CLASS. However, that the study was conducted in a single centre can be considered a limitation. The service where the study was conducted is located in the capital city of Turkey and is a preferred centre for prosthesis application by many individuals with lower extremity amputations residing in different cities. However, it is a private centre where high-tech prostheses are applied. It can be recommended that in future studies, the psychometric properties of the Turkish CLASS can be evaluated in amputees who apply to different centres. Additionally, it is a limitation that only certain psychometric properties were examined in the study. Further analyzes should be included in future studies.

Study Limitation

In this study, limitation that only certain psychometric properties were examined in the study. Further analyzes should be included in future studies..

CONCLUSION

The Turkish CLASS is a reliable and valid survey that can be used to evaluate socket fit in individuals using unilateral lower extremity prosthesis. The use of the Turkish version of CLASS may be useful for both evaluating the socket, which is the prosthesis component that lower extremity amputees have the most problems with, and for measuring the effectiveness of interventions.

Acknowledgement: None.

Author contribution: Study Design: SD, ED; Data Collection: SD, ED, OS; Statistical Analysis: SD; Manuscript Preparation: SD, ED, OS; Funds Collection: SD, ED, OS.

Conflict of interests: The authors hereby declare that there was no conflict of interest in conducting this research.

Ethical approval: The study was approved by the Ethics Committee of Ankara Yıldırım Beyazıt University, in accordance with the Declaration of Helsinki (Decision Date: 14.06.2021, No: 68).

Funding: The authors declare that the study received no funding.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Ülger Ö, Yıldırım Şahan T, Celik SE. A systematic literature review of physiotherapy and rehabilitation approaches to lower-limb amputation. Physiother Theory Pract 2018;34(11):821-34.
2. Van Velzen J, van Bennekom CA, Polomski W, Slootman J, van der Woude LH, Houdijk H. Physical capacity and walking ability after lower limb amputation: a systematic review. Clin Rehabil 2006;20(11):999-1016.
3. Baars EC, Schrier E, Dijkstra PU, Geertzen JH. Prosthesis satisfaction in lower limb amputees: A systematic review of associated factors and questionnaires. Medicine 2018;97(39).
4. Jia X, Zhang M, Lee WC. Load transfer mechanics between trans-tibial prosthetic socket and residual limb—dynamic effects. J Biomech 2004;37(9):1371-7.
5. Klotz R, Colobert B, Botino M, Permentiers I. Influence of different types of sockets on the range of motion of the hip joint by the transfemoral amputee. Ann Phys Rehabil Med 2011;54(7):399-410.
6. Turner S, McGregor AH. Perceived effect of socket fit on major lower limb prosthetic rehabilitation: A clinician and amputee perspective. Arch Rehabil Res Clin Transl 2020;2(3):100059.
7. Legro MW, Reiber G, del Aguila M, Ajax MJ, Boone DA, Larsen JA, et al. Issues of importance reported by persons with lower limb amputations and prostheses. J Rehabil Res Dev 1999;36(3):155-63.
8. Dickinson AS, Steer JW, Woods CJ, Worsley PR. Registering a methodology for imaging and analysis of residual-limb shape after transtibial amputation. J Rehabil Res Dev 2016;53(2):207-18.
9. Meulenbelt HE, Dijkstra PU, Jonkman MF, Geertzen JH. Skin problems in lower limb amputees: a systematic review. Disabil Rehabil 2006;28(10):603-8.
10. Papaioannou G, Mitrogiannis C, Nianios G, Fiedler G. Assessment of amputee socket–stump–residual bone kinematics during strenuous activities using Dynamic Roentgen Stereogrammetric Analysis. J Biomech 2010;43(5):871-8.
11. Sanders J, Zachariah S, Jacobsen A, Fergason J. Changes in interface pressures and shear stresses over time on trans-tibial amputee subjects ambulating with prosthetic limbs: comparison of diurnal and six-month differences. J Biomech 2005;38(8):1566-73.
12. Al-Fakih EA, Abu Osman NA, Mahmad Adikan FR. Techniques for interface stress measurements within prosthetic sockets of transtibial amputees: A review of the past 50 years of research. Sensors 2016;16(7):1119.
13. Binedell T, Ghazali MFB, Wong C, Subburaj K, Blessing L. Measuring discomfort—An objective method for quantifying peak pressure discomfort and improved fit in adults with transtibial amputation. PM&R 2022.
14. Kingsley C, Patel S. Patient-reported outcome measures and patient-reported experience measures. Bja Education 2017;17(4):137-44.
15. Gholizadeh H, Osman NA, Eshraghi A, Ali S, Razak N. Transtibial prosthesis suspension systems: systematic review of literature. Clin Biomech 2014;29(1):87-97.
16. Nia A, Toetschinger G, Kubinec T, Domayer S. Evaluation of the new, patient-adjustable socket system Varos in the early phase of prosthetic rehabilitation: a pilot study. Eur J Phys Rehabil Med 2022;58(3):462-469.
17. Kahle J, Miro RM, Ho LT, Porter M, Lura DJ, Carey SL, et al. The effect of the transfemoral prosthetic socket interface designs on skeletal motion and socket comfort: A randomized clinical trial. Prosthet Orthot Int 2020;44(3):145-54.
18. Richardson A, Dillon MP. User experience of transtibial prosthetic liners: a systematic review. Prosthet Orthot Int 2017;41(1):6-18.
19. Demirdel S, Ulaş K, Erol Çelik S, Karahan S, Topuz S. Reliability and validity of the Turkish version of the satisfaction module of the Orthotics and Prosthetics Users' Survey. Prosthet Orthot Int 2022;46(2):170-4.
20. Topuz S, Ülger Ö, Yakut Y, Gül Şener F. Reliability and construct validity of the Turkish version of the Trinity Amputation and Prosthetic Experience Scales (TAPES) in lower limb amputees. Prosthet Orthot Int 2011;35(2):201-6.
21. Dou P, Jia X, Suo S, Wang R, Zhang M. Pressure distribution at the stump/socket interface in transtibial amputees during walking

on stairs, slope and non-flat road. Clin Biomech 2006;21(10):1067-73.
22. Gailey R, Kristal A, Lucarevic J, Harris S, Applegate B, Gaunaurd I. The development and internal consistency of the comprehensive lower limb amputee socket survey in active lower limb amputees. Prosthet Orthot Int 2019;43(1):80-7.
23. Wild D, Grove A, Martin M, Eremenco S, McElroy S, Verjee-Lorenz A, et al. Principles of good practice for the translation and cultural adaptation process for patient-reported outcomes (PRO) measures: report of the ISPOR task force for translation and cultural adaptation. Value Health 2005;8(2):94-104.
24. Hafner BJ, Smith DG. Differences in function and safety between Medicare Functional Classification Level-2 and-3 transfemoral amputees and influence of prosthetic knee joint control. J Rehabil Res Dev 2009;46(3):417-33.
25. Rouhani N, Esfandiari E, Babaee T, Khosravi M, Moradi V, Balouchkayvan B, et al. The comprehensive lower limb amputee socket survey: reliability and validity of the persian version. Prosthet Orthot Int 2021;45(2):131-137.
26. Alpar R. Applied Statistics and Validity and Reliability with Examples from Sports, Health and Educational Sciences. Detay Publishing, Ankara; 2016.
27. Portney LG, Watkins MP. Foundations of clinical research: applications to practice: Pearson/Prentice Hall Upper Saddle River, NJ; 2009.
28. Ebel RL. Estimation of the reliability of ratings. Psychometrika. 1951;16(4):407-24.
29. Alpar R. Applied statistics in sports sciences: Nobel Publishing, Ankara; 2006.
30. Terwee CB, Mokkink LB, Knol DL, Ostelo RW, Bouter LM, de Vet HC. Rating the methodological quality in systematic reviews of studies on measurement properties: a scoring system for the COSMIN checklist. Qual Life Res 2012;21(4):651-7.
31. Nunnally JC. Psychometric theory 3E: Tata McGraw-hill education; 1994.
32. Harness N, Pinzur MS. Health related quality of life in patients with dysvascular transtibial amputation. Clin Orthop Relat Res 2001;383:204-7.
33. Ali S, Osman NAA, Eshraghi A, Gholizadeh H, Abas WABBW. Interface pressure in transtibial socket during ascent and descent on stairs and its effect on patient satisfaction. Clin Biomech 2013;28(9-10):994-9.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 287-295
https://doi.org/10.30621/jbachs.1240204
RESEARCH ARTICLE

A NEW FIELD TEST WITH DIFFERENT FLOORS TO MEASURE DYNAMIC BALANCE AMONG PRESCHOOL CHILDREN

Zehra Güçhan Topcu[1], Hatice Hacıküçük[1], Erdoğan Çetintaş[1], Hayriye Tomaç[1], Tuğba Obuz[1], Nazan Şeker[1], Levent Eker[1]

[1] Eastern Mediterranean University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Famagusta, Cyprus

ORCID: Z.G.T. 0000-0001-8587 -7407; H.H. 0000-0002-9212-8049, E.Ç. 0000-0002-3228-1455, H.T. 0000-0002-8245-9995, T.O. 0000-0001-9371-7964, N.Ş. 0000-0002-7320-8991, L.E. 0000-0001-7301-4073

Corresponding author: Zehra Güçhan Topcu, **E-mail:** zehraguchan@hotmail.com / zehra.guchan@emu.edu.tr
Received: 24.01.2023; **Accepted:** 02.02.2024; **Available Online Date:** 31.05.2024

Cite this article as: Güçhan-Topcu Z, Hacıküçük H, Çetintaş E, Tomaç H, Obuz T, Şeker N, Eker L. A New Field Test With Different Floors To Measure Dynamic Balance Among Preschool Children. J Basic Clin Health Sci 2024; 8: 287-295.

ABSTRACT

Purpose: This study aimed to assess the test-retest reliability and inter-rater reliability of a newly designed balance test named the Paediatric Tandem Balance (PTB) test.
Material and Methods: 108 children (girls: 54, boys: 54) with a mean age of 4.08±0.78 were included in the study. Two raters measured the same children for inter-rater reliability, and the first rater retested the same children after two days for test-retest reliability. Time and sway numbers were recorded as the variables of the PTB test.
Results: The inter-rater reliability was good in both parameters of PTB which were duration (r=0.836) and number of sways (r=0.840). The test-retest reliability was good in both duration (r=0.727) and number of sways (r=0.705). The PTB test is a reliable test to measure dynamic balance in 3-5 years old children.
Conclusion: This test will bring a new point of view for tests of dynamic balance.

Keywords: balance, balance test, dynamic balance, postural control

INTRODUCTION

Balance supports the development of the motor systems of children as it is a prerequisite to learn and control fundamental motor skills in daily life (1,2). Static balance is defined as the ability to provide body balance in a specific location or position, whereas dynamic balance exists during the movement or execution of the movement (3). Both sensory and motor regions of the brain should give correct information to muscles which are the main active elements of body. When muscles obtain correct information from brain, they should arrange amount of their contractions in an adequate time interval (1,2). Postural control which needs visual, vestibular and somatosensory (e.g., plantar cutaneous, proprioception) input plays a fundamental role in the maintenance of balance (3,4). Cognition has an important role to perceive and integrate these sensory inputs in order to maintain balance so cognition is like a bridge from sensory to motor behaviour (5).

Both balance and some cognitive functions like attention are controlled by the same central region, the cerebellum (6). Thus, it may be stated that there is a relationship between balance and cognitive tasks and that many daily activities require a good balance

control with cognitive skills (7). In addition, an increase in balance may contribute to some cognitive skills such as memory and spatial cognition (8). Lima et al. (9) also stated that there is a positive association between the dynamic balance and academic performance of children. Shortly, balance skills may affect attention, memory, spatial performance, and learning skills for academic performance.

Gallahue (1) states that babies detect their body parts and their movements with reflexes and rudimentary movements like crawling and walking during the first two years of life. The first form of rudimentary movements are immature, but babies get more experience with practices and start to develop postural reactions to keep in balance in these movements. Thus, until 2 years old, babies should gain balance in rudimentary movements. From 2 to 7 years old, children start to develop fundamental motor skills which are important movements for sport activities like running, jumping and hopping (1). The practices and experiences of these movements develop better balance in these movements until 7 years old. The late development of balance among children leads to the late and inadequate learning of complicated motor skills like running, jumping and climbing. This negatively affects the participation of children in athletics activities and causes more injuries (2). As a result, monitoring balance development and determining potential factors which may prevent this development is important in childhood (10).

Dynamic balance develops in a complicated way as it needs the integration of sensory systems and experience in motor learning (3,11). There are many tests used in clinical practice to measure dynamic balance (10,12-15). For example, in two systematic reviews of dynamic balance tests in children, fourteen tests were investigated, and among them, three tests, the Timed-Up and Go (TUG) test, Pediatric Balance Reach test and Pediatric Balance Scale, showed good reliability in children (10,15). In both reviews by Verbecque et al. (10,15), it was stated that standardisation is needed in the criteria of balance tests for children as children need motivation to follow directions and speed. Although balance is affected by many environmental factors, and the floor where a test is conducted is one of the most important factors among these, none of the existing tests has focused on this parameter (16). Particularly, the effects of the floor should be measured in children as their balance develops during growth, and it is a prerequisite for many motor skills as mentioned before; so, when this factor is added to measurements, it will increase the strength of analyses carried out on balance in

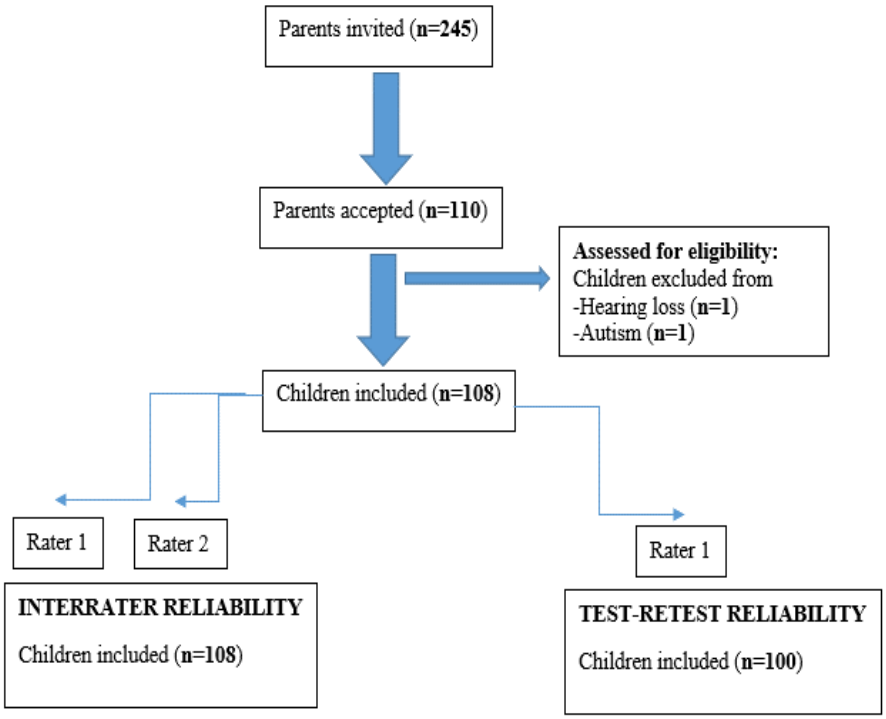


Figure 1. Flowchart of the reliability study

children (1,2,11). Moreover, in daily life, people need to improve balance reactions and protect their balance on many types of surfaces (such as snowy, wet, stony, hard, foam ground) (16).

As the first five years of life plays a critical role in the development of motor skills, the use of accurate tests which reflect performance as much as possible is required to see the actual level and progression that are aimed to be measured (17). Compared to laboratory tests, field tests present better options for the examiner as they are cost-effective, easy to administer and usually portable with minimal equipment. Although dynamic balance is important to adapt the body on different floors in mobile conditions, there is no field test to measure this balance involving variations of floor materials. The Paediatric Tandem Balance (PTB) test was designed with this aim, and it was hypothesised that this test would demonstrate reliability to measure dynamic balance in children.

MATERIAL AND METHODS

Study Design and Participants

Children living in Famagusta were included in this study. They were children registered to kindergartens of the city of Famagusta. According to the inclusion criteria, children who were 3-5 years old were included. H1 hypothesis = 0, H1 hypothesis = 0.3 and $\alpha = 0.05$, $\beta = 0.20$ were calculated for the sample size, and 84 people were obtained. The initial value was increased by 20% for the second assessment, resulting in 100 healthy children aged 3-5.

Children who had sensory loss which would prevent them from taking the test or understanding the explanations, had communication problems in understanding the test, orthopaedic, neurological, or mental problems were excluded from the study (Figure 1).

Age, sex, height and weight were firstly recorded. Then, the PTB test was applied to the children. Two raters used a stopwatch (Catiga CG-503) to record time. The test was firstly explained with short sentences that were the same for all children and then the raters showed the test practically. The tests were conducted in barefoot condition. The PTB test is explained below in details.

PTB Test

This test was designed by considering the need of testing dynamic balance on different surfaces. The standardization of this field test was challenging.

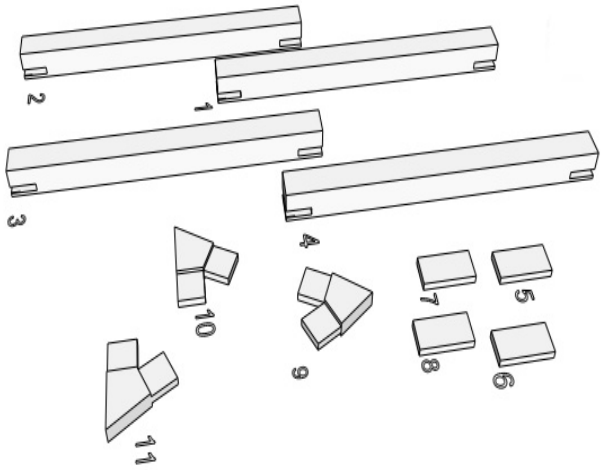


Figure 2. The pieces of the Paediatric Tandem Balance test platform. Numbers 1-4: Long pieces, Numbers 5-8: Straight connectors, Numbers 9-11: 60-degree angle connectors.

Tandem walking was chosen to standardize steps on the platform and the dimensions were arranged according to single foot. Then, the floors were chosen and connections were considered. In the end, 4 different floors with 4 different hardness grades (wood, hard sponge, soft sponge, and fibre) were created using four 100-cm-long, 8-cm-high and 8-cm-wide blocks (Figure 2, shapes 1-4). One piece was completely produced from wood material with 8 cm. Other three pieces have 4 cm wood bases and 4 cm different materials (as mentioned above sponge and fibre) on the wood base. All four long pieces of the PTB test platform were covered with same leather in the same color.

The platform could be brought to different shapes as a line or a square (Attachment 1). There were seven connector parts. Four straight connecters (Figure 2, shapes 5-8) were used to make various shapes like a square or a line. The other three connectors (Figure 2, shapes 9-11), which had a 60-degree angle, were used to make W and triangle shapes (Figure 2). Since we tried different shapes in the tests of some children before deciding the shape for testing and saw that the W shape had a clear start and end point, we decided to use the W shape (Figure 3). Moreover, this shape gave the message to the child that they were going to a new floor, so that planning about the floor could be done more easily, and the risk of falling was reduced in comparison to the use of other shapes. The ability to walk on this test platform was measured by time completion and sway numbers from platform. The W platform was assembled from the difficulty level easy

Table 1. Descriptive characteristics recorded in the PTB test

Variables	N	Range	Minimum	Maximum	Mean	Std. Deviation
RATER 1 - TIME (PTB) (sec.)	108	81.77	17.32	99.09	38.22	15.17
RATER 1 - SWAY NUMBER (PTB)	108	18	0	18	5.17	3.64
RATER 2 - TIME (PTB) (sec.)	108	94.18	11.08	95.26	35.18	13.06
RATER 2 - SWAY NUMBER (PTB)	108	18	0	18	5.08	3.49
RATER 1 SECOND ASSESSMENT - TIME (PTB) (sec.)	100	73.15	14.16	87.31	37.56	14.25
RATER 1 SECOND ASSESSMENT - SWAY NUMBER (PTB)	100	17.00	0	17.00	5.29	3.35

Figure 3. The Paediatric Tandem Balance Test and a child in the test.

to the level of hard. Hence, the child was asked to make a tandem walk in the following order: on wood, hard sponge (density=28 DNS), soft sponge (density=22 DNS), and fibre. The raters used the same commands and similar instructions to children since these would affect results. At first, the raters explained to the children how they would be assessed on the platform. The children were permitted to do any kind of tandem walk (full tandem, semi-tandem) and walk on only long pieces without touching the connectors of the peak points of the W-shape. Standing with any region of the heel of one foot touching the big toe of the other foot in front is defined as semi-tandem position, while standing with the heel of one foot in front of the fingers of other foot is full tandem (18).

For the starting position, the children were ready on the ground without any contact with the platform. Following the “START” command was given, they were asked to step onto the platform with their preferred leg and complete test platform carefully without swaying out of the platform. If they could not prevent to sway out, they would continue from the same point with stepping onto the platform back. The platform did not allow running as its base of support was narrow for running. When they complete the W shape, they were asked to change direction by going down from the platform to the ground and walk again to the starting location from the most difficult floor to the easiest. Words for motivation were not permitted before, during or after test.

First of all, the first walk was carried out as a practice for the children to learn the platform and understand

what to do. In this first experience, the rater walked next to them to guide them and reassure them without any touching or holding (Figure 3). After this experience, the children were asked whether they understand the test and have any question about the test. Additionally, some children were curious about the platform, and the raters did not prevent them from touching the platform if they wanted to do so. Then, the next attempt was recorded for the test result. As soon as the children stepped onto the platform, timing was started, and when they returned to the point where they were standing before stepping on the platform, it was stopped. The duration was recorded in seconds. The numbers of sways of the children to the ground with any foot or both feet were counted without stopping the time recorded on the track. The durations and numbers of sways were recorded as the outcomes. After every child, the platform was cleaned as the covering material allowed easy hygiene. For the reliability of the PTB test, every included child was assessed three times. For inter-rater reliability, two raters (the second and third authors) assessed the children two times with at one-hour intervals on the same day. The order of the raters was randomly decided by tossing a coin and the raters were blind to each other's results.

The first rater (the second author) also assessed the same children after two days to measure test-retest reliability. The measurement results of the test were recorded as the first rater, the second rater and the second assessment of the first rater.

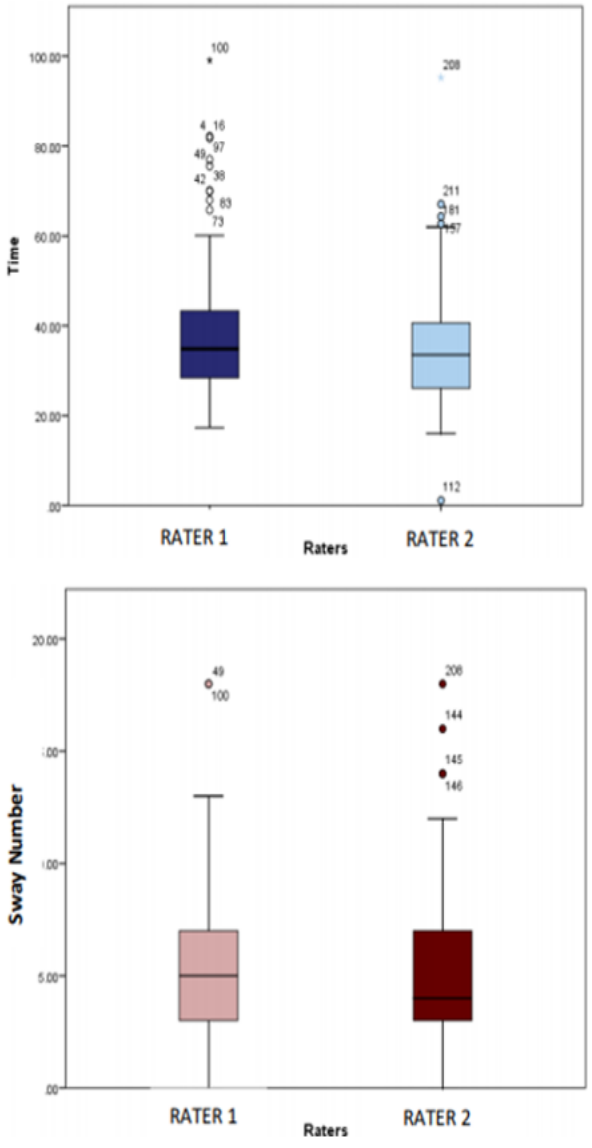


Figure 4. Distribution of the data for both raters with boxplot which indicates some points in terms of normality (Boxplot for inter-rater reliability)

Statistical Analysis

The data were analysed using the IBM Statistical Package for the Social Sciences (SPSS) 22.0. The categorical data are presented as percentages (%). The continuous data are presented as means and standard deviations. Since all variables were normally distributed, Pearson's correlation analysis was used (Table 1). The intraclass correlation coefficient (ICC) with two-way random effects was used to analyse test-retest and inter-rater reliability. Paired-samples t-test and Pearson's test were used to support the evidence about test-retest reliability. Bland-Altman plot analysis was used to evaluate the agreement between the values of the test and retest measurements.

Ethical Consideration

The study was approved by the Research and Publication Ethics Committee of Eastern Mediterranean University, in accordance with the Declaration of Helsinki (Decision Date: 24.05.2018, No: 2018/59-19). Informed consent, approved by the university's ethics committee, was taken from the parents of all children after explaining the aim and procedures of the study in detail. This study was also registered on ClinicalTrials.gov (NCT03777995).

RESULTS

Participation flow of the children

The parents of 245 children were invited to the study. The parents (n=110) who agreed for their children to participate in the study and their children (n=110),

including 55 girls and 55 boys, were assessed. One child (girl) had hearing loss, and one child (boy) had autism, so they were excluded. A total of 108 children were tested on the first assessment day. Twenty-eight (25.9%) children were three years old, 43 (39.8%) were 4 years old, and 37 (34.3%) were 5 years old. Eight of the children did not attend the second assessment. So, the data of 100 children were used for the test-retest reliability analysis (Figure 1).

Demographic characteristics of the sample

The mean age of the children who were included in this study was 4.08±0.78 years. The mean height of the children was measured as 104.28±7.81 cm, and their mean weight was 18.35±3.44 kg. Their body mass index values were 16.77±1.75 kg/m2.

Descriptive findings obtained by the raters

Table 1 shows the descriptive statistics for the variables. A wide dispersion of the measurements was seen, which led to quite high standard deviation values especially for Rater 1-Time, Rater 2-Time, and rater 1 second assessment-Time as 15.17, 13.06, and 14.25, respectively. In relation to how the data for both raters were distributed, it was considered that boxplots can clearly explore such distributions and describe normality. Both measurements from both raters were quite similar, and the plot definitely not showing concrete evidence to be perfectly normal (Figure 4). We also plotted the first rater's score with the second assessment with respect to time and number of sways. This method was used to analyse test-retest reliability as well. The two assessments looked very much like each other as seen in Figure 5.

Test-retest reliability of the PTB test

An ICC model was established to analyse the intraclass correlation coefficient (ICC) calculations. Table 2 shows that there was a quite strong consistency level between the first and second assessments for the time measurements with a coefficient of 0.842 in a 95% CI (0.765 – 0.894). Additionally, there was high consistency between the first and second assessments of the sway numbers by the first rater with an ICC value of 0.826 in a 95% CI (0.742 – 0.883). The differences between repetitions and the relationship between differences and correlation values are shown in Table 3.

Another useful test involves drawing Bland-Altman plots. If the points on the Bland–Altman plot are all

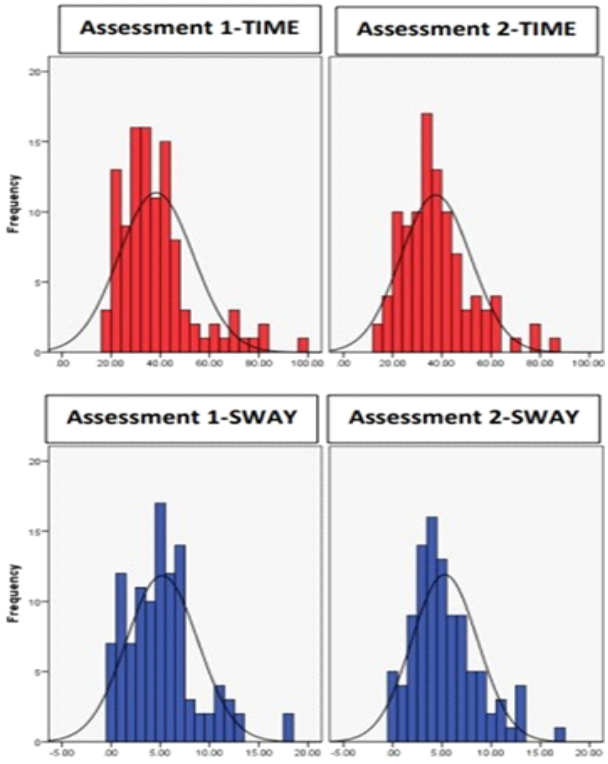


Figure 5. Plotting the first rater's first and second assessments to see the distribution in terms of time and sway numbers (plotting for test-retest reliability)

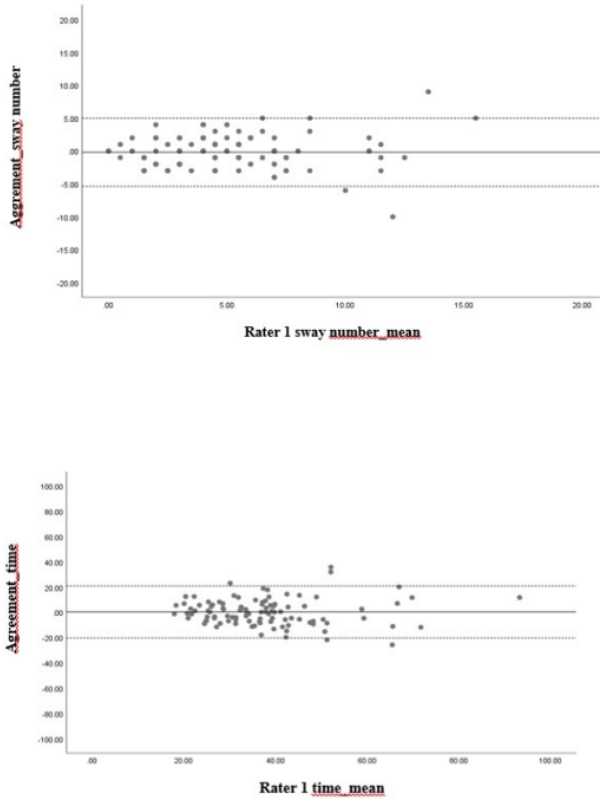


Figure 6. Bland-Altman plot analysis to see the level of agreement for the first and second day assessments

over the place, above and below zero, it means that there is no consistent bias in favour of one strategy over the other. It can be seen on the plot that there was consistency between the rater's first and second assessment measurements (Figure 6).

Inter-rater reliability of the PTB test

Inter-rater reliability of the measurements of both time and sway numbers was also analysed by determining the interclass correlation coefficient (ICC). The value of ICC in a 95% CI was 0.836 (0.760-0.888) for time, which indicated a strong agreement between the two raters. For the sway numbers, the ICC value in a 95% CI was recorded to be 0.840 (0.766 – 0.891). Accordingly, the method was determined to be reliable, and it could be used for overall assessments (Table 4).

DISCUSSION

tandem, full tandem) for balance. Thus, the PTB test included different somatosensory systems by reducing the base of support and visual input. As mentioned in the methods, all four pieces of the PTB test platform were covered with the same material and the same colour, so that the pieces would appear in the same from the outside, and the children needed more somatosensory feedback from the plantar region. The test limits the measurement in a variety of components of balance so it can be stated that this probably causes high reliability of the PTB test.

Visual feedback is reduced in many balance tests to investigate whether other sensory systems (e.g., proprioceptive, vestibular) can be used and integrated for postural control and balance (19). Existing tests usually use "closed eyes" while reducing the degree of this feedback. Thus, this new platform brings a new testing model for dynamic balance in terms of lowering visual input and varying the floor material. Visual input is completely non-existent when one's eyes are closed, whereas it is diminished in the PTB test because children experience the platform before the test and learn that its pieces have different hardness levels. Nevertheless, it does not provide the same amount of visual input as walking on floors with different appearances, for example, pink wood and blue sponge.

As the prevalence of measurement procedures of balance in children at the ages of 3-5 is low, the TUG test has been recommended more for this age group,

Table 2. Test-retest reliability testing using ICC

	Intraclass Correlation Coefficient			
	Intraclass Correlation	95% Confidence Interval		
		Lower Bound	Upper Bound	
First & Second Assessments (Time)	0.842	0.765	0.894	0.000
First & Second Assessments (Sway number)	0.826	0.742	0.883	0.000

Table 3. Differences between repetitions and the relationship between differences and correlation values

	Mean ± SD	Correlation with first assessment	Sig	Correlation with second assessment	Sig
Difference between first and second assessments (time)	3.44±16.41	0.430	0.000	0.375	0.000
Difference between first and second assessments (sway number)	0.27±3.28	0.489	0.000	0.330	0.001

Table 4. Inter-rater reliability testing for both time and sway numbers by the first and second raters

	Intraclass Correlation Coefficient						
	Intraclass Correlation	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Time by first and second raters	0.836	0.760	0.888	6.108	107	107	0.000
Sway number by first and second raters	0.840	0.766	0.891	6.244	107	107	0.000

but there may be some variations in the turning points of the TUG test, where some children made wider turns around the chair, and others made narrower turns (20). The raters stated regarding the PTB test that it was easy to control the children's route as it had a platform. Moreover, since the platform looked the same even though it was made of different materials, this mysterious structure caused motivation in the children according to the statements of the raters. Similarly, a recent paper proposed the use of a red Duplo brick for motivation in the TUG test (21). In general, according to our raters, the PTB test was easy to be understood by children.

The children were asked to walk with one trial test and one real test. In many balance tests (10), three repetitions are allowed for children, and the best result is recorded. On the other hand, the learning effect, which is prominent at younger ages, was avoided in this study with fewer repetitions as this test had sensorial feedback, and it could have been very easy to learn in further repetitions.

The main strength of this paper was the presentation of the psychometric analysis results of a newly designed dynamic balance test, the PTB test, with high test-retest and inter-rater reliability. These findings are likely to encourage the use of this field test to see the balance of pre-schoolers in the conditions of different somatosensory inputs to their feet.

The PTB test offers a simple use with various advantages. First of all, this is the first dynamic balance test which includes different floor materials and creates an advantage to show progression this way. Many professions like physiotherapists, physical educators and occupational therapists can use a progressive procedure for the development of balance by changing the floor material. Thus, this test provides this opportunity. Secondly, since this is low-tech field test, it is a much more inexpensive test than high-tech balance test devices, whereas it is also easy to use this test and make comments on results for users. Thirdly, in this study, there was no risk/injury about the test reported by the raters. Lastly, although the "test" shape was determined as W, the platform can be brought to different shapes like a triangle, a square and a straight line for working on balance (Attachment 1).

Limitations

A limitation of this paper was the need for a gold standard test for balance in preschool children as high-tech/digital devices are required to get more objective results to investigate the validity of the PTB test. Researchers who have training and adequate opportunities in terms of high-tech devices could conduct further studies to investigate the validity of the PTB test for more accurate results (22,23)..

CONCLUSION

In conclusion, the PTB test may be used as a reliable test in clinical practice for pre-school children. Although it is easy to manufacture this test platform, the practitioners who wonder to use this test are suggested to contact the authors to learn more details. Lastly, the psychometrics and clinical utility of the test may also be investigated in older children, or children with developmental delays and special needs in further papers.

Acknowledgement: We would like to thank the administrators of the kindergartens "Gelişim Eğitim Merkezi", "Kids Dream Education", "Lucky Duck", "Petit Baby Montessori School" and "Uçan Balon Kreş ve Anaokulu". We also would like to thank Prof. İlker Etikan for the statistical analyses.

Author contribution: ZGT: Planning, design of platform, interpretation of the results, writing, publication procedures. HH: Design of platform and data collection (rater 2). EÇ: Design of platform and data collection (rater 1). HT: Support to the management of study and writing. TO: Ethical approval and support in data collection. NŞ: Ethical approval and writing. LE: Power Analysis for sample size and support for ethical approval.

Conflict of interests: The authors declare that there was no conflict of interest.

Ethical approval: The study was approved by the Research and Publication Ethics Committee of Eastern Mediterranean University, in accordance with the Declaration of Helsinki (Decision Date: 24.05.2018, No: 2018/59-19).

Funding: None.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Gallahue D, Ozmun J, Goodway J. Understanding motor development: Infants, children, adolescents, adults. Boston, MA: Mcgraw-hill, New York, 2006.
2. Jiang GP, Jiao XB, Wu SK, et al. Balance, proprioception, and gross motor development of chinese children aged 3 to 6 years. J Motor Behav 2018;50(3),343-352.
3. Bozkurt S, Erkut O, Akkoç O. Relationships between Static and Dynamic Balance and Anticipation Time, Reaction Time in School Children at the Age of 10-12 Years. Univers J Educ Res 2017;5(6),927-931.
4. Sharma K, Samuel AJ, Midha D, Aranha VP, Narkeesh K, Arumugam N. Multi-directional

reach test in South Asian children: Normative reference scores from 5 year to 12 years old. Homo 2018;69(1-2),62-69.
5. Martínez K, Martínez-García M, Marcos-Vidal L, Janssen J, Castellanos FX, Pretus C, Villarroya Ó, Pina-Camacho L, Díaz-Caneja CM, Parellada M, Arango C. Sensory-to-cognitive systems integration is associated with clinical severity in autism spectrum disorder. JAACAP 2020;59(3):422-33.
6. Goetz M, Schwabova JP, Hlavka Z, Ptacek R, Surman CB. Dynamic balance in children with attention-deficit hyperactivity disorder and its relationship with cognitive functions and cerebellum. Neuropsychiatr Dis Treat 2017;13:873.
7. Niederer D, Plaumann U, Seitz T, et al. How does a 4-week motor–cognitive training affect choice reaction, dynamic balance and cognitive performance ability? A randomized controlled trial in well-trained, young, healthy participants. SAGE Open Med 2019;7:2050312119870020.
8. Rogge AK, Röder B, Zech A, Nagel V, Hollander K, Braumann KM, Hötting K. Balance training improves memory and spatial cognition in healthy adults. Scientific reports. 2017;18:7(1):5661.
9. Lima RA, Stodden DF, Pfeiffer KA, et al. Dynamic Balance, but Not Precision Throw, Is Positively Associated with Academic Performance in Children. Int J Env Res Pub He 2020;17:2790.
10. Verbecque E, Schepens K, Theré J, Schepens B, Klingels K, Hallemans A. The Timed Up and Go test in children: does protocol choice matter? A systematic review. Pediatr Phys Ther 2019;31:22-31.
11. Roberts D, Veneri D, Decker R, Gannotti M. Weight status and gross motor skill in kindergarten children. Pediatr Phys Ther 2012;24:353-360.
12. Brandsma R, Van Egmond ME, Tijssen MA, et al. Diagnostic approach to paediatric movement disorders. Dev Med Child Neurol 2021;63(3):252-258.
13. Dehnavi M, Sadeghi H, Taghva M. Reliability of Functional Balance Tests and Their Correlation With Selected Anthropometric Parameters in Children Aged 7-10 Years. J Sport Biomech 2020;5:216-227.
14. Tyson SF, Connell LA. How to measure balance in clinical practice. A systematic review of the psychometrics and clinical utility of measures of balance activity for neurological conditions. Clin Rehabil 2009;23:824-840.
15. Verbecque E, Lobo Da Costa PH, Vereeck L, Hallemans A. Psychometric properties of functional balance tests in children: a literature review. Developmental Medicine & Child Neurology, 2015;57:521-529.
16. Maïano C, Hue O, Lepage G, Morin AJ, Tracey D, Moullec G. Do exercise interventions improve balance for children and adolescents with Down syndrome? A systematic review. Phys Ther 2019;99:507-518.
17. Wood AP, Imai S, Mcmillan AG, Swift D, Dubose KD. (2020). Physical activity types and motor skills in 3-5-year old children: National Youth Fitness Survey. J Sci Med Sport 2020;23:390-5.
18. Warmerdam E, Schumacher M, Beyer T, Nerdal PT, Schebesta L, Stürner KH, Zeuner KE, Hansen C, Maetzler W. Postural sway in Parkinson's disease and multiple sclerosis patients during tasks with different complexity. Front Neurol 2022;13:857406.
19. Emery CA, Cassidy JD, Klassen TP, Rosychuk RJ, Rowe BH. Development of a clinical static and dynamic standing balance measurement tool appropriate for use in adolescents. Phys Ther 2005;85:502-514.
20. Lei Y, Lam CKY, Lams MHS, et al. Validity and Reliability of Timed Up and Go Test on Dynamic Balance in 3-5 Years Old Preschool Children. J Yoga Phys Ther 2017;7:1-5.
21. Hallemans A, Klingels K, Van Criekinge T, Vereeck L, Verbecque E. Reliability and concurrent validity of a modified timed up and go test for healthy preschoolers. EJPEDT 2020;179:1579-86.
22. Hu SY, Hınojosa J, Chiang PY, Leu CS. Validity of the Sensory Balance Test to Screen Children for Sensory Processing Impairments. J Occup Ther Sch Early Interv 2010;3:139-153.
23. Dewar RM, Tucker K, Claus AP, Van Den Hoorn W, Ware RS, Johnston LM. Evaluating validity of the Kids-Balance Evaluation Systems Test (Kids-BESTest) Clinical Test of Sensory Integration of Balance (CTSIB) criteria to categorise stance postural control of ambulant children with CP. Disabil and Rehabil 2021;1-8.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 296-307
https://doi.org/10.30621/jbachs.1256495
RESEARCH ARTICLE

SERUM CHEMERIN, VASPIN, OXIDATIVE STRESS AND INFLAMMATION MARKERS IN SUBCLINICAL HYPOTHYROIDISM/ HYPERTHYROIDISM

Sümeyye Tamer[1], Taylan Turan[1], Tuba Taşkan[1], Mehmet Ayhan Karakoç[2], Emre Arslan[2], Aymelek Gönenç[1*]

[1] Gazi University, Faculty of Pharmacy, Department of Biochemistry, Ankara, Turkey
[2] Gazi University, Faculty of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey

ORCID: S.T. 0000-0003-4956-2015; T.T. 0000-0001-7335-1213; T.T. 0000-0003-1677-5356; M.A.K. 0000-0002-0601-6893; E.A. 0000-0003-4460-8598; A.G. 0000-0001-9661-8291

Corresponding author: Aymelek Gönenç, **E-mail:** aymelek@gazi.edu.tr
Received: 27.02.2023; **Accepted:** 30.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Tamer S, Turan T, Taşkan T, Karakoç M A, Arslan E, Gönenç A. Serum Chemerin, Vaspin, Oxidative Stress and Inflammation Markers in Subclinical Hypothyroidism/Hyperthyroidism. J Basic Clin Health Sci 2024; 8: 296-307.

ABSTRACT

Purpose: Subclinical thyroid diseases constitute the first stage of clinical thyroid, so it is important to investigate underlying mechanisms. Clinical studies have revealed changes in some adipokines concerning thyroid disorders. Relationship chemerin and vaspin adipokines with thyroid hormones needs to crarify. So, it was aimed to evaluate chemerin, vaspin, oxidative stress, and inflammation markers in subclinical hypothyroidism/hyperthyroidism.
Material and Methods: The study included 38 subclinical hyperthyroidism, 31 subclinical hypothyroidism, and 44 healthy controls. Serum chemerin, vaspin, interleukin-10, C-reactive protein, and Oxidized LDL were measured with ELISA method, while total antioxidant status, and total oxidant status were spectrophotometric methods.
Results: Serum chemerin levels were higher in the subclinical hypothyroidism group, whereas lower in the subclinical hyperthyroidism compared to the controls. Vaspin levels of subclinical thyroid patients were lower than the controls. Interleukin-10 levels of subclinical hyperthyroidism were lower, conversely C-reactive protein levels were higher in both patient groups than the control group. Total antioxidant status were higher in the subclinical hypothyroidism group; total oxidant status and oxidative stress index were lower in subclinical hyperthyroidism patients.
Conclusion: Increased total antioxidant and C-reactive protein levels in the subclinical hypothyroidism group and decreased total oxidants, interleukin-10, and oxidative stress index in the subclinical hyperthyroidism group indicated that oxidant-antioxidant balance is impaired, suggesting that subclinical thyroid diseases may cause changes in inflammation and defense mechanism. The decreases in chemerin levels in the subclinical hyperthyroidism patients and vaspin levels in the both patient groups show that chemerin and vaspin may be candidates as biomarkers in subclinical thyroid diseases.

Keywords: Chemerin, vaspin, oxidative stress markers, inflammation markers, subclinical hypothyroidism/hyperthyroidism

INTRODUCTION

Thyroid hormones have functions on metabolic rate, heat production, cell differentiation and development, response to other hormones, carbohydrate, protein, and lipid metabolism (1). Thyroid-stimulating hormone (TSH) directly provides the synthesis and secretion of adipokines. The positive relationship between TSH level and adiposity is biologically important. Clinical studies reveal changes in some adipokine levels accompanying thyroid diseases (2,3). The most recently discovered chemerin, vaspin are members of adipokines this group. Chemerin is

encoded by the G protein-coupled receptor 1 (GPR1) gene and, acts as an endogenous ligand for GPR and is known to have pro-inflammatory and insulin resistance inducing properties. It was found that physiological amounts of chemerin are secreted from adipose tissues in early adipocyte differentiation, and the level of secreted chemerin increases with the maturation of cells. Another adipokine synthesized in adipose tissue, vaspin is known for its insülin-sensitizing effects and modulator role on glucose tolerance. There are limited studies in the literature investigating the role of serum levels of chemerin and vaspin in thyroid diseases. Serum chemerin levels were suggested to be significantly higher in patients with hyperthyroidism compared to controls (4). Vaspin mRNA levels were shown as significantly lower in rats with hyperthyroidism while higher in rats with hypothyroidism compared to rats with euthyroidism (5).

Cytokines are pro-inflammatory mediators which play a central role in inflammatory and immune processes. Interleukin-10 (IL-10) is recognized as one of the most important anti-inflammatory immunomodulatory cytokines. It has been reported that IL-10 mRNA expression has an important role in thyroid autoimmune diseases (6). C-reactive protein (CRP) is involved in inflammatory processes in some thyroid disorders. Serum CRP values were shown as high in patients with subclinical hypothyroidism (SubHypo) compared to controls (7). Oxidized LDL (Ox-LDL) has vasoconstrictor, mitogenic, and proinflammatory properties. It has been reported that dysfunction of thyroid hormones may cause an increase in Ox-LDL levels (8). Therefore, it is essential to specify the possible risk factors for increased Ox-LDL. Recent studies have suggested that Ox-LDL may trigger endoplasmic reticulum stress in endothelial cells and macrophages (9), and this may have an effect on the secretion of some adipokines (10). Measurement of the Ankle Brachial Index (ABI) is the most used method in diagnosing peripheral artery disease (PAD). There are few studies in the literature to explain the relationship between thyroid dysfunction and PAD determined by ABI measurement (11).

Metabolic changes accompanying thyroid dysfunction may cause changes in the antioxidant defense of the organism. Cebeci et al. found reduced antioxidant defense in SubHypo patients (12). Supportively, a decrease in serum antioxidant activity was observed due to the decrease in body antioxidant defense system capacity in patients with hyperthyroidism by Marcocci et al. (13). Total antioxidant status (TAS), total oxidant status (TOS) and Oxidative Stress Index (OSI) are among the critical parameters that can be used to assess the redox status. OSI is an indicator of the degree of oxidative damage. Several studies have indicated that OSI is responsible for the formation of endothelial dysfunction (14,15).

In the light of these informations, it is crucial to investigate the roles of some new adipokines, proinflammatory, and oxidant/antioxidant indicators in the progression of subclinical thyroid to clinical thyroid diseases. So, it was aimed to measure chemerin, vaspin, IL-10, CRP, Ox-LDL, ABI, TAS, TOS, and OSI in subclinical hyperthyroidism (SubHyper) and SubHypo.

MATERIAL AND METHODS

Characteristics of Study Participants

The study group consisted of 38 SubHyper, 31 SubHypo patients, and 44 healthy individuals. The patient group consisted of applied to the Thyroid Clinic of Gazi University Medical Faculty Hospital, were over the age of 18, were newly diagnosed, and did not receive treatment. Patients were excluded from the study if they had a history of diabetes, chronic hyperlipidemia, Chronic Artery Disease (CAD), or PAD. The control group composed of healthy volunteers had never transmitted a systemic and/or thyroid disease.

Ethical Consideration

The study was approved by the Ethics Committee of Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital with decision number 2017-03/06, and all participants or their relatives gave their informed consent before participating in the study.

Anthropometric Measurements

Body weight was measured with a TANITA weighing device while hungry in the morning and after defecation with less clothed, dry, and bare feet. The height of individuals was measured with a TANITA brand portable wall stadiometer with feet side by side and head on the Frankfort plane, with eye triangle and top of the auricle aligned. Body Mass Index (BMI) was calculated as weight (kg) divided by the square of height (m2). Waist circumference (WC) of individuals; with arms on both sides and feet together, the middle point of the area between the lowest rib and navel

Table 1. Characteristic features and biochemical measurements of the study group

Parameter	SubHyper (N=38)	SubHypo (N=31)	Control (N=44)
Age (X±SD)	46.37±2.28	44.39±2.55	45.41±1.95
Gender (F/M)	31/7	25/6	12/32
BMI (kg/m^2)	26.52±0.78	27.77±0.68	26.14±0.78
WC (cm)	79.94±1.98	92.16±2.49§	86.11±1.93
WC/HC (X±SD)	0.82±0.01	0.88±0.27	0.84±0.02
SBP (mmHg)	112.68±0.56	116.03±4.67*,§	113.77±0.59
DBP (mmHg)	77.24±0.80*	68.55±0.44*,§	72.95±0.89
FBG (mg/dL)	99.78±2.62*	93.47±1.80	91.95±1.98
TC (mg/dL)	146.07±7.29	168.71±7.29	162.77±6.16
HDL-C (mg/dL)	45.62±1.02	47.11±1.64	44.93±1.15
LDL-C (mg/dL)	110.24±4.53	111.73±6.01	104.40±4.64
TG (mg/dL)	148.91±10.04	127.73±8.99	140.12±11.73
fT_3 (pg/mL)	3.46±0.07**	3.26±0.05**	2.87±0.06
fT_4 (ng/dL)	0.93±0.02**	0.84±0.28**	1.18±0.04
TSH (mIU/mL)	0.20±0.02**	7.68±0.64**,§§	1.93±0.13

*Significant difference from control, p<0.05, **significant difference from control, p<0.01, §Significant difference from SubHyper, p<0.05, §§significant difference from SubHyper, p<0.01. SubHyper (Subclinical Hyperthyroidism), SubHypo (Subclinical Hypothyroidism), BMI (Body Mass Index), WC (Waist circumference), HC (Hip circumference), SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), FBG (Fasting Blood Glucose), TC (Total Cholesterol), HDL-C (HDL cholesterol), LDL-C (LDL cholesterol), TG (Triglycerides), fT_3 (Free Triiodothyronine), fT_4 (Free Thyroxine) TSH (Thyroid-stimulating hormone)

was determined and measured on a flat surface. Hip circumference (HC) was measured with the arms of the individuals on their sides, their feet side by side and standing upright, individual's gaze was directed towards the front and parallel to the ground by a non-stretch tape from the highest point. Blood pressure was measured two times intermittently with an Omron brand blood pressure device after all individuals had been in rest for at least 20 minutes in a sitting position and, the average of the two measurements was taken to determine the result. Limit values were determined according to NCEP ATP III diagnostic criteria.

Biochemical Measurements

5 ml of peripheral venous blood was taken from patient groups and the healthy controls into red-capped flat serum tubes with the help of professional health personnel. The blood samples were immediately transported to the Gazi University Faculty of Pharmacy Biochemistry Department Laboratory under appropriate storage conditions and centrifuged at +4ºC, 3000 rpm, for 15 minutes.

Serums were kept in deep freeze at -80ºC until to be analyzed. The biochemical parameters of fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), LDL cholesterol (LDL-C), and HDL cholesterol (HDL-C) were analyzed in Gazi Hospital Biochemistry Laboratory from the residue part of blood samples. FBG was measured with the hexokinase method and BeckmanCoulter kit, AU5800 analyzer (Beckman Coulter, CA, USA). TG, TC, LDL-C, and HDL-C analyses were performed by using the spectrophotometric method with the same device. TSH, free triiodothyronine (fT3), and free thyroxine (fT4) were measured by using a Beckman Coulter kit with the CLIA method (Abbott Architecht I200 autoanalyzer, USA).

Serum Chemerin/Vaspin/IL-10/CRP/Ox-LDL Concentrations

Human serum chemerin levels were measured spectrophotometrically using a commercial ELISA kit (Elabscience Biotechnology Co. Ltd, USA, E-EL-H0698) according to the manufacturer's instructions. The sensitivity of the chemerin ELISA assay is 0.10 ng/mL, and the detection range is 0.16-10 ng/mL. The intra-assay CV is <4.8%, and inter-assay precision is <5.3%.

Using a sandwich-ELISA (Elabscience Biotechnology Co. Ltd, USA, E-EL-H1762), vaspin levels in serum were measured. The detection range is 62.50-4000 pg/mL, and the sensitivity of the vaspin sandwich-ELISA assay is 37.50 pg/mL. The intra-assay CV is <5.3%, and inter-assay precision is <4.7%.

Detection of human IL-10 levels in serum was performed with an ELISA kit (Elabscience Biotechnology Co. Ltd, USA, E-EL-H0103). Kit sensitivity for IL-10 is 4.69 pg/mL, and the detection range is between 7.81 and 500 pg/mL. Intra-assay CV is <5.4%, and inter-assay precision is <4.7%.

Serum CRP concentrations were determined with a commercially available ELISA (Elabscience Biotechnology Co. Ltd, USA, E-EL-H0043) according to the manufacturer's instructions. Human CRP ELISA kit has 0.23 ng/mL sensitivity with a detection range of 0.39-25 ng/mL. Intra-assay CV is <3.9%, and inter-assay precision is <6.1%.

Commercial ELISA kits (Elabscience Biotechnology Co. Ltd, USA, E-EL-H0124) were used for the quantification of serum levels of Ox-LDL. All the tests were performed according to the manufacturer's instructions. Intra-assay CV is <5.3%, and inter-assay precision is <5.0%.

Measurements of ABI Value

The ABI value of participants was inflated to 220 mmHg by tying cuff to the left upper arm or 20-30 mmHg above expected Systolic Blood Pressure (SBP). Air of cuff was decreased 10 mmHg in 5 seconds by placing a Doppler device on the brachial artery, and SBP was recorded. Later, it was inflated to 220 mmHg by tying cuff under the left knee cap or 20-30 mmHg above the expected SBP. Doppler device was placed on the dorsalis pedis, and air of cuff was evacuated in 5 seconds with a decrease of 10 mmHg. Pulsed SBP was noted when a pulse was taken on a Doppler device. Two SBPs are divided with pressure in the arm at the top. The figure obtained has been noted as ABI (11). ABI Value=Ankle Systolic $Pressure_{(max)}$/Brachial Systolic $Pressure_{(max)}$.

Serum TAS/TOS/OSI Concentrations

TAS measurement in serum was performed according to the decolorization method of 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) cation radical modified by Re et al. (16). In the total antioxidant measurement method, suppression of the generated radical by antioxidants in serum was determined using a spectrophotometer. Absorbance measurements were done at 734 nm in 6th minute. The phosphate buffer solution was used in measurements as a blank solution.

10 µL of serum was added to 1 ml of ABTS radical solution whose absorbance was adjusted to be 0.70(±0.02), and absorbance was read at 6th minute. Based on the results, %Inhibition was calculated by the formula: %Inhibition=100–[(Abs_{sample}/Abs_{ABTS})x100]

TOS measurement in serum was made according to the fully automatic colorimetric method developed by Erel et al. (17). Oxidants present in the sample oxidize ferrous ion-o-dianisidine complex to ferric ion. Glycerol in the environment accelerates this reaction approximately three times. Ferric ions form a colorful complex with xylenol orange in an acidic environment. The intensity of the color associated with the amount of oxidants in the sample is measured spectrophotometrically. By calibrating the measurement with hydrogen peroxide, results are expressed in micromolar hydrogen peroxide equivalent per liter (µmol H2O2 Equivalent/L) (17). OSI value was calculated as the ratio of TOS to TAS level. Specifically, OSI (arbitrary unit)=TOS (µmol H2O2 Eq/L)/TAS (µmol Trolox Eq/L).

Statistical Analysis

Statistical analysis of data was performed using the SPSS statistical package program (version 22 software, SPSS Inc. Chicago, Illinois, USA). The normality of the data was tested by Kolmogorov-Smirnov. Differences among the three groups were evaluated using one-way analysis of variance ANOVA followed by Post Hoc and Tukey test for multiple comparisons between groups. To evaluate the correlation between parametric and nonparametric variables, Pearson and Spearman correlation tests were used, respectively. Results were considered statistically significant at $p<0.05$ at 95% confidence interval.

RESULTS

The clinical characteristics and some biochemical parameters of the study group were given in Table. Statistical differences were found between SubHyper and control groups in Diastolic Blood Pressure (DBP), FBG, fT3, fT4, and TSH levels. DBP, FBG, and fT3 levels were significantly higher ($p<0.05$, $p<0.05$, $p<0.01$, respectively), while fT4, and TSH were lower in SubHyper when compared to control ($p<0.01$, $p<0.01$, respectively). Similarly, significant differences were found between SubHypo and control groups in SBP, DBP, fT3, fT4 and TSH levels. SBP, fT3, and TSH levels were higher ($p<0.05$, $p<0.01$, $p<0.01$, respectively), while DBP and fT4 were lower in SubHypo than control ($p<0.05$, $p<0.01$). SBP, WC,

and TSH levels were higher (p<0.05, p<0.05, p<0.01, respectively), whereas DBP was lower in SubHypo compared to SubHyper (p<0.05). No significant differences were found between groups in age, BMI, WC/HC, TC, HDL-C, LDL-C, and TG levels (p>0.05). Serum chemerin levels of SubHyper, SubHypo, and control groups are given in Figure 1. In the study, serum chemerin levels were found 2.58±0.14 ng/mL in SubHypo, 1.42±0.19 ng/mL in SubHyper, and 2.22±0.16 ng/mL in the control group. Serum chemerin levels were significantly lower in the SubHyper group compared to the control group (p<0.01). Chemerin levels in patients with SubHypo were found to be higher than patients with SubHyper (p<0.01). No significant difference was found between SubHypo, and the healthy control group in terms of serum chemerin levels (p>0.05). Figure 2

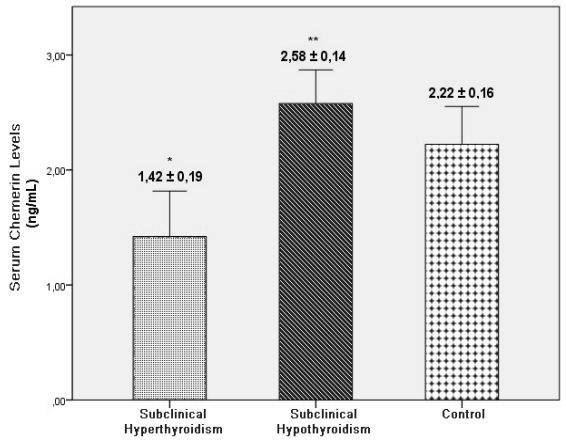


Figure 1. Comparison of serum chemerin levels in study groups. Boxes represent the means of the serum Chemerin levels and error bars indicate±standart deviation. Significant difference from control group and from SubHyper group were shown with an asterisk and double asterisks, respectively. The value of p<0.05 was considered as statistically significant, in all statistical analyses. *Significant difference from control group, p<0.01. **Significant difference from SubHyper, p<0.01.

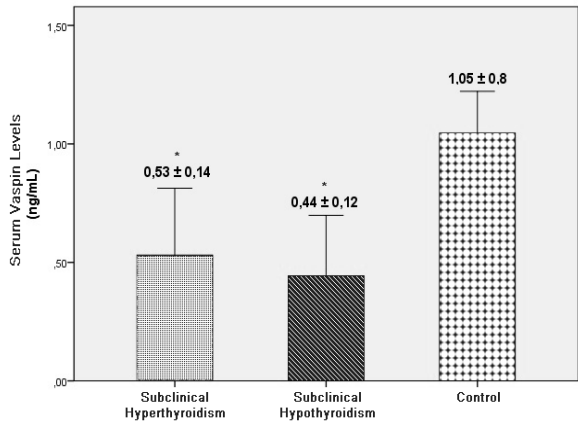


Figure 2. Comparison of serum vaspin levels in study groups. Boxes represent the means of the serum vaspin levels and error bars indicate±standart deviation. Significant difference from control group was shown with an asterisk. The value of p<0.05 was considered as statistically significant, in all statistical analyses. *Significant difference from control group, p<0.01.

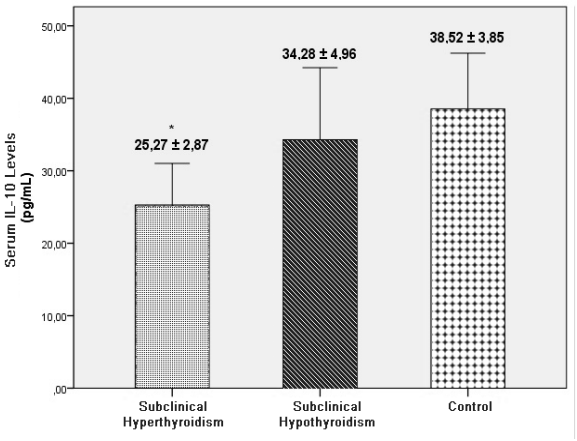


Figure 3. Comparison of serum IL-10 levels in study groups. Boxes represent the means of the serum IL-10 levels and error bars indicate±standart deviation. Significant difference from control group was shown with an asterisk. The value of p<0.05 was considered as statistically significant, in all statistical analyses. *Significant difference from control group, p<0.01, IL-10 (Interleukin-10).

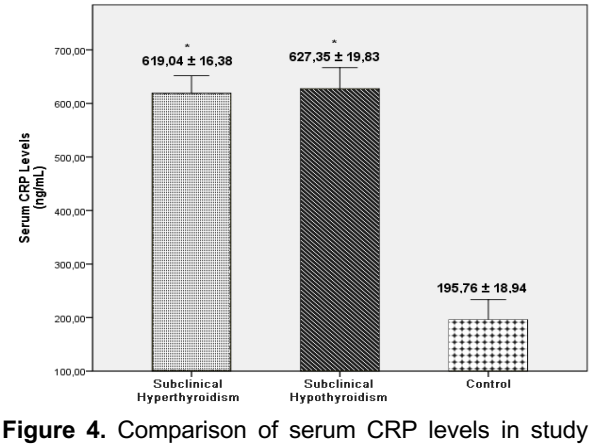


Figure 4. Comparison of serum CRP levels in study groups. Boxes represent the means of the serum CRP levels and error bars indicate±standart deviation. Significant difference from control group was shown with an asterisk. The value of p<0.05 was considered as statistically significant, in all statistical analyses. *Significant difference from control group, p<0.01, CRP (C-reactive protein).

shows serum vaspin levels in SubHyper, SubHypo and healthy control groups. Serum vaspin levels were found as 0.44±0.12 ng/mL in patients with SubHypo, 0.53±0.14 ng/mL in patients with SubHyper and, 1.05±0.8 ng/mL in the control group. Serum vaspin levels were found to be statistically lower in both patients with SubHypo and SubHyper as compared to control ($p<0.01$). There was no significant difference in serum vaspin levels between SubHyper and SubHypo ($p>0.05$).

In Figure 3, serum IL-10 levels of SubHyper, SubHypo, and control groups are given. Serum IL-10 levels were found to be 34.28±4.96 pg/mL in SubHypo patients, 25.27±2.87 pg/mL in SubHyper patients, and 38.52±3.85 pg/mL in controls, respectively. Serum IL-10 levels were found lower in SubHyper patients compared to the control group. There was no significant difference in serum IL-10 levels between SubHypo and healthy control ($p>0.05$), SubHyper and SubHypo ($p>0.05$). Serum CRP levels in SubHyper, SubHypo, and control groups are given in Figure 4. In our study, serum CRP levels were found as 627.35±19.83 ng/mL in SubHypo, 619.04±16.38 ng/mL in SubHyper, and 195.76±18.94 ng/mL in the control group. Serum CRP levels were found to be importantly higher in patients with SubHypo and SubHyper compared to controls ($p<0.01$).

In Figure 5, serum Ox-LDL levels are given in study groups. Serum Ox-LDL levels were found to be 8.33±0.11 ng/mL in patients with SubHypo, 8.27±0.66 ng/mL in patients with SubHyper, and 8.34±0.13 ng/mL in the control group, respectively. There was no difference between all groups in serum Ox-LDL levels ($p>0.05$).

Figure 6 shows the ABI values in SubHyper, SubHypo, and healthy control groups. ABI values were found 1.055±0.02 in SubHypo, 1.020±0.02 in SubHyper, and 1.040±0.02 in the control group, in our study. No statistically significant difference was observed between the groups in terms of ABI values ($p>0.05$).

Figure 7 demonstrates serum TAS levels in study groups. Serum TAS levels were 2.27±0.26 mmol/L in SubHypo, 2.20±0.58 mmol/L in SubHyper, and 2.07±0.57 mmol/L in the control group, respectively. Serum TAS levels were significantly higher in patients with SubHypo compared to control ($p<0.01$). Although TAS levels of patients with SubHyper were higher than the control group, were not significant ($p>0.05$). The comparison of TOS levels in SubHyper, SubHypo, and healthy controls were given in Figure 8. TOS levels were found 10.43±0.63 µmol/L in patients with SubHypo, 4.44±0.31 µmol/L in patients with SubHyper, and 9.90±0.52 µmol/L in the control group, respectively. Serum TOS levels were found to be significantly lower in patients with SubHyper compared to the control group ($p<0.01$). There was no statistically significant difference between SubHypo and healthy control groups in terms of serum TOS levels ($p>0.05$). Figure 9 shows the serum OSI values in SubHyper, SubHypo, and healthy control groups. Serum OSI values were calculated as 4.58±0.26 in patients with SubHypo, 2.00±0.15 in patients with SubHyper, and 5.06±0.36 in the control group, respectively. Serum OSI values were significantly lower in patients with SubHyper compared to controls ($p<0.01$). No statistically significant difference was obtained between SubHypo and healthy control groups in terms of serum OSI values ($p>0.05$).

Using bivariate correlation analysis among measured parameters in patients with SubHyper, a positive correlation was found between TOS and OSI ($r=0.887$, $p<0.01$), and a negative correlation was found between IL-10 and TOS ($r=-0.318$, $p<0.05$). Positive correlation was found between TOS and OSI ($r=0.978$, $p<0.01$), and negative correlations were found between IL-10 and Ox-LDL ($r=-0.470$, $p<0.01$) in patients with SubHypo. In healthy controls, positive correlations were found between vaspin and TOS ($r=0.303$, $p<0.05$), Ox-LDL and TOS ($r=0.344$, $p<0.05$), TOS and OSI ($r=0.479$, $p<0.01$), and negative correlations were found between IL-10 and Ox-LDL ($r=-0.439$, $p<0.01$), IL-10 and TOS ($r=-0.395$, $p<0.01$), TAS and OSI ($r=-0.685$, $p<0.01$).

DISCUSSION

There is a tight interaction between thyroid hormones and adipokines (3). Clinical studies have revealed changes in apelin, adiponectin, and leptin adipokines accompanying thyroid disorders (2,3,18). The pathophysiological role of thyroid hormones regulating chemerin and vaspin in subclinical thyroid diseases has not been clarified yet. Thus, we mainly aimed to demonstrate the clinical significance of chemerin and vaspin adipokines in SubHyper and SubHypo. Additionally, serum levels of IL-10, CRP, Ox-LDL, TAS, and TOS were measured to show the changes in inflammation and oxidative stress in subclinic thyroid disorders.

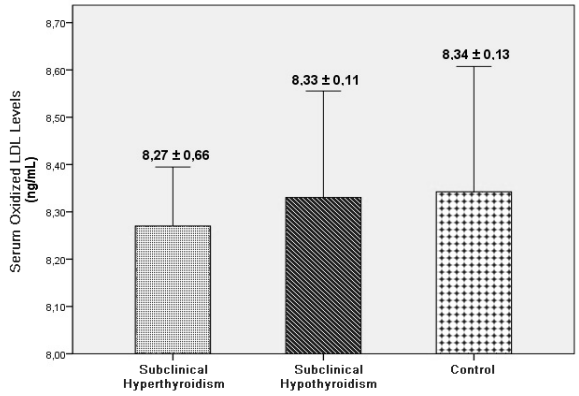


Figure 5. Comparison of serum Ox-LDL levels in study groups, Ox-LDL (Oxidized LDL). Boxes represent the means of the serum Ox-LDL levels and error bars indicate±standart deviation. The value of p<0.05 was considered as statistically significant, in all statistical analyses.

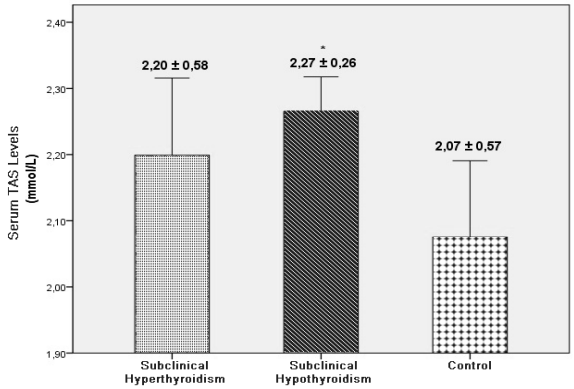


Figure 7. Comparison of serum TAS levels in study groups. Boxes represent the means of the serum TAS levels and error bars indicate±standart deviation. Significant difference from control group was shown with an asterisk. The value of p<0.05 was considered as statistically significant, in all statistical analyses. *Significant difference from control group, p<0.01, TAS (Total Antioxidant Status)

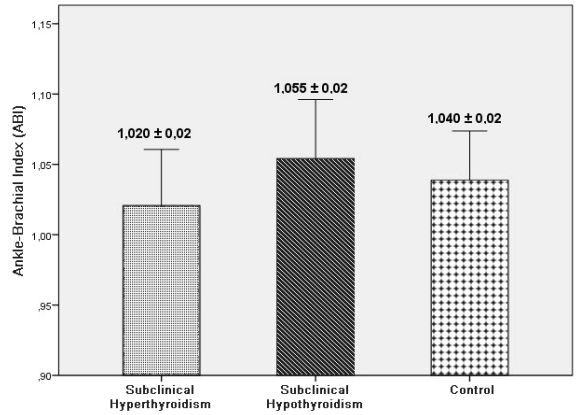


Figure 6. Comparison of serum ABI levels in study groups, ABI (Ankle Brachial Index). Boxes represent the means of the serum ABI levels and error bars indicate±standart deviation. The value of p<0.05 was considered as statistically significant, in all statistical analyses.

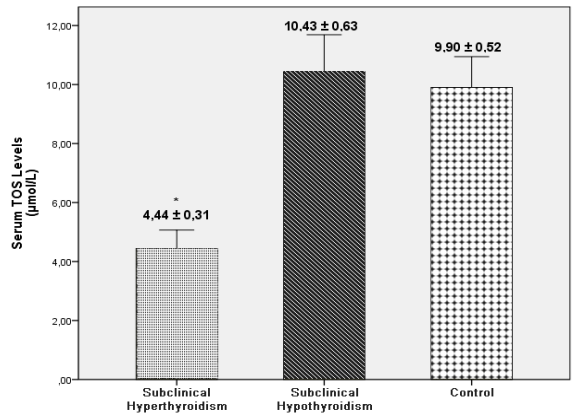


Figure 8. Comparison of serum TOS levels in study groups. Boxes represent the means of the serum TOS levels and error bars indicate±standart deviation. Significant difference from control group was shown with an asterisk. The value of p<0.05 was considered as statistically significant, in all statistical analyses. *Significant difference from control group, p<0.01, TOS (Total Oxidant Status).

Many inflammatory molecules circulating in the blood are might be a potential markers. In many studies conducted in recent years, it has been shown that human plasma chemerin levels have a significant relationship with BMI, inflammation, and metabolic syndrome (19,20). Nevertheless, there are limited studies in the literature investigating the role of serum levels of chemerin and vaspin in thyroid diseases. Berta et al. evaluated serum chemerin levels in patients with Hashimoto's Thyroiditis (HT) and found no differences between patients and controls. It was also reported by the authors that no correlation was observed between chemerin and TSH, fT_3, and fT_4 levels (21). On the other hand, Alshaikh et al. stated that serum chemerin levels were higher in patients with hyperthyroidism compared to controls. Moreover, serum chemerin concentrations were positively correlated with total triiodothyronine (TT_3), total thyroxine (TT_4), and fT_3 and negatively correlated with TSH and fT_4 (4). In a study conducted on rats with experimentally induced thyroid dysfunction, a significant increase in chemerin was

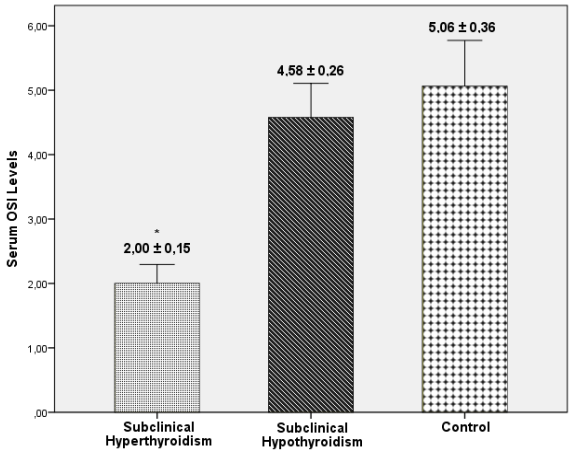


Figure 9. Comparison of serum OSI values in study groups. Boxes represent the means of the serum OSI levels and error bars indicate±standart deviation. Significant difference from control group was shown with an asterisk. The value of $p<0.05$ was considered as statistically significant, in all statistical analyses. *****Significant difference from control group, $p<0.01$, OSI (Oxidative Stress Index).

observed in clinical hypothyroidism, while a decrease in hyperthyroidism. Additionally, a positive correlation was found between chemerin and TSH in hyperthyroidism, hypothyroidism, and healthy control groups. They indicated that chemerin may be a marker in thyroid hormone disorders since experimentally induced thyroid dysfunction affects chemerin (22). Similarly, higher serum chemerin levels were found in three groups of SubHypo rats administered increasing doses of methimazole compared to euthyroid rats. Additionally, it has been reported that there is a positive relationship between chemerin levels and TSH in study groups (23). In another study with different doses of methimazole, gene expression of chemerin and serum levels were measured. Compatible results with the previous studies in terms of serum chemerin levels and expressions were obtained (24). Considering the literature, there are very few clinical studies examining the relationship between chemerin and thyroid diseases. Our study was the first to investigate chemerin levels in SubHyper and SubHypo cases. In the study, serum chemerin levels were significantly higher in patients with SubHypo compared to patients with SubHyper. Serum chemerin was significantly lower in patients with SubHyper compared to healthy controls. Although there were higher chemerin levels in SubHypo patients compared to healthy controls, no significant difference was found.

Higher/lower serum vaspin levels were obtained in hypothyroidism/hyperthyroidism compared to the control group in the study of Jowari et al.. They thought that these changes in vaspin levels may be due to the effect of thyroid hormone disorder (25). Çınar et al. analyzed serum vaspin in clinical hypothyroidism, SubHypo patients, and euthyroid healthy controls. They found higher serum vaspin levels in SubHypo and clinical hypothyroidism compared to controls, but there were no significant differences between groups. Also, there was no correlation between vaspin levels and TSH (26). Salam et al. examined the effects of experimentally induced hyperthyroidism and hypothyroidism on vaspin, adiponectin, and visfatin levels in rats. They reported increased/decreased vaspin levels in hypothyroidism/hyperthyroidism compared to controls. In addition, serum vaspin levels were found negatively correlated with T_3 and T_4 levels and positively correlated with TSH levels in all study groups. They concluded that the decrease in vaspin production in hyperthyroid rats might be due to the dominant effect of T_3 on adipocytes (27). Likewise, Gonzalez et al. stated that vaspin mRNA levels were significantly decreased in rats with hyperthyroidism compared to rats with euthyroidism and increased significantly in rats with hypothyroidism although there was no change in glucose and insulin levels, and this was explained as thyroid dysfunction may affect vaspin expression (5). In our study, serum vaspin levels were found to be significantly lower in patients with SubHypo and SubHyper compared to the control group. While the data obtained from our study are consistent with the results obtained by Salam et al., Jowari et al., and Gonzalez et al. in terms of decreasing vaspin levels in the hyperthyroid model, decreasing serum vaspin levels in patients with SubHypo were first shown.

IL-10 is a mediator that regulates the systemic inflammatory response. It has an important role in autoimmune thyroid diseases and regulates the growth and development of both normal and neoplastic thyroid cells (28). CRP, which is a nonspecific marker of inflammation, is synthesized by the liver. The changes in serum CRP levels have not been routinely used to monitor thyroid disease, whereas inflammation occurs in many thyroid diseases. In a study conducted by Marchiori et al., serum CRP and IL-10 levels were measured at the end of 6 and 12 months to examine the changes in some inflammatory markers in hypothyroid patients

receiving levothyroxine treatment. Researchers found an increase in serum IL-10 levels in measurements after 6 and 12 months of levothyroxine treatment, but no significant difference was observed in CRP over time. They postulated that the changes in cytokine levels may be due to thyroid hormones (29). The serum concentration of IL-10 levels was measured in patients with extreme obesity in a study performed by Gómez-Zamudio et al. (30). For analyzing the effect of the presence of hypothyroidism on IL-10, patients with hyperthyroidism were excluded from the study, and euthyroid and hypothyroidism patients were compared. They reported that serum IL-10 levels did not differ in patients with hypothyroidism compared to euthyroid individuals (30). Tuzcu et al. aimed to determine CRP concentrations in SubHypo. It was shown that serum CRP values were higher in patients with SubHypo compared to the control group (7). According to the study of Kvetny et al. SubHypo was associated with higher concentrations of CRP (31). In our study, significantly decreased serum IL-10 levels were obtained in patients with SubHyper compared to the control group. This decline in IL-10 levels may be related to the increased antioxidant defense mechanism in patients with SubHypo. Serum CRP levels were found as statistically high in patients with both SubHypo and SubHyper compared to controls. Serum CRP results observed in SubHypo from our study are consistent with studies of Tuzcu et al. and Kvetny et al. We think that the increased serum CRP levels in the study are due to the increased inflammation in both subclinical groups.

Many studies to date have demonstrated that high oxidative stress supports oxidative modification of LDL levels. There are studies showing that excessive secretion of thyroid hormones may cause an increase in Ox-LDL levels (8,32). Itterman et al. measured the Ox-LDL levels of participants to determine the relationship between serum TSH and Ox-LDL levels and noted a positive relationship between them. They also suggested that Ox-LDL levels elevated with the increase in serum TSH levels, especially in the range of subclinical thyroid disease (33). Uçan et al. measured serum Ox-LDL before and after thyroid hormone therapy in HT patients and controls. They found no difference in serum Ox-LDL levels between patient and control groups (34). In another study, plasma Ox-LDL levels were evaluated in SubHypo, clinical hypothyroidism, and healthy individuals. It was reported that plasma Ox-LDL levels were significantly higher in clinical hypothyroid patients compared to the control group. They also found that plasma Ox-LDL was higher in SubHypo patients compared to controls but not significant. It was suggested that thyroid hormone deficiency affects Ox-LDL levels (35). In our study, there was no significant difference in serum Ox-LDL levels among individuals with SubHyper, SubHypo, and control. Our results are consistent with data obtained from the study of Uçan et al. and Duntas et al.

There are few studies in the literature investigating the relationship among thyroid dysfunction, ABI measurement, and PAD. In a study by Ittermannet al., ABI values were measured, and no significant relationship was found between TSH concentrations and ABI values (11). Compatible with this study, no significant difference was found between the groups in terms of ABI values in our study.

In thyroid diseases, TAS plays an essential role in protecting the organism from damage caused by oxidative stress and is an important parameter that can be used to assess redox status with TOS and OSI. In a study involving SubHypo and healthy individuals, TAS, TOS, and OSI were determined. TAS and OSI were found higher in SubHypo patients compared to controls. They reported that OSI showed a strong positive correlation with TSH levels in both groups (12). In another study, Cheserek et al. examined oxidative stress status in SubHypo and euthyroid individuals. Although studies detected higher serum levels of TAS in SubHypo patients compared to the control group, they did not find a significant difference between the groups (36). Ateş et al. studied the association between HT and oxidative stress parameters in euthyroid, subclinical, and overt hypothyroid stages. It was noted that TOS and OSI levels were higher, while TAS levels were lower in the overt hypothyroid group, whereas it was similar in control, euthyroid, and SubHypo groups. Also, it was shown that TOS and OSI were higher in SubHypo compared to controls, while TAS levels were similar in these groups (37). Aslan et al. evaluated the oxidative status of patients with hyperthyroidism and healthy controls. Serum TAS levels were found significantly lower in the hyperthyroidism group than controls, while serum TOS and OSI levels were significantly higher (38). In our study, serum TAS levels were found significantly higher in the SubHypo group compared to controls. While our results are compatible with the results of Cebeci et al. (12), there is a study with opposing-view

by reporting that there is no significant difference between groups (36). Changes in serum TAS levels in SubHypo may have occurred due to increased oxidative stress in SubHypo. We found that TOS and OSI were found to be significantly lower in SubHyper patients as compared to healthy controls. These controversial results in the study obtained by Aslan et al. may be due to increased oxidative stress.

Limitations

There is no doubt that the limitations of the original research were insufficient sample size, so these findings should be confirmed with further studies, especially with a larger population.

CONCLUSION

In conclusion, our study is the first in the literature to investigate the levels of serum chemerin and vaspin adipokines in subclinical thyroid diseases in humans. Although the conditions that affect the parameters evaluated in the study were excluded in the selection of the patient group, decreases were observed in Subhyper in serum chemerin levels and in both Subhyper and Subhypo in vaspin levels. CRP levels increased in both groups in subclinical thyroid patients as expected due to inflammation, while IL-10 levels decreased only in the Subhyper group. High TAS levels in the subhypo group and low TOS and OSI levels in the subhyper group indicate that the oxidative balance is impaired in subclinical thyroid diseases.

It is thought that new studies to be conducted with more patients in which serum chemerin and vaspin levels are investigated will contribute to evaluating the diagnosis and prognosis of thyroid diseases in which many factors participate in the etiology.

Acknowledgement: None.

Author contribution: Author Aymelek Gönenç and Mehmet Ayhan Karakoç were responsible for study conception and design; authors Sümeyye Tamer, Taylan Turan, Tuba Taşkan and Emre Arslan were responsible for acquisition of data; authors Sümeyye Tamer, Taylan Turan, Tuba Taşkan and Aymelek Gönenç were responsible for data analysis and drafting and revision of the manuscript.

Conflict of interests: The authors have no conflicts of interest to declare that are relevant to the content of this article.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Clinical Research Ethics Committee of the Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital (Decision Date: 24.03.2017, No. 2017-03/06).

Funding: This work was supported by GAZI University Projects of Scientific Investigation (GÜBAP) (Project No: 02/2017-24)
Peer-review: Externally peer-reviewed.

REFERENCES

1. Obregon MJ. Adipose tissues and thyroid hormones. Frontiers in Physiology 2014;5:1–12.
2. Chen Y, Wu X, Wu R, et al. Changes in profile of lipids and adipokines in patients with newly diagnosed hypothyroidism and hyperthyroidism. Scientific Reports 2016;19(6):1–7.
3. Edrees HM, Fahmy EK, Esmaeel SE. A Study on Serum Level of Chemerin in Experimentaly-Induced Thyroid Dysfunctions. Basic Sciences of Medicine 2018;7(2):21–6.
4. Alshaikh EM, Omar UM, Alsufiani HM, et al. The potential influence of hyperthyroidism on circulating adipokines chemerin, visfatin, and omentin. International journal of health sciences 2019;13(2):44–7.
5. González CR, Caminos JE, Vázquez MJ, et al. Regulation of visceral adipose tissue-derived serine protease inhibitor by nutritional status, metformin, gender and pituitary factors in rat white adipose tissue. Journal of Physiology 2009;587(14):3741–50.
6. De la Vega JR, Vilaplana JC, Biro A, Hammond L, Bottazzo GF, Mirakian R. IL-10 expression in thyroid glands: protective or harmful role against thyroid autoimmunity? Clin Exp Immunol. 1998;113(1):126–35.
7. Tuzcu A, Bahceci M, Gokalp D, Tuzun Y, Gunes K. Subclinical hypothyroidism may be associated with elevated high-sensitive C-reactive protein (low grade inflammation) and fasting hyperinsulinemia. Endocrine Journal 2005;52(1):89–94.
8. Barış N, Demir M, Ataytay A, Çuhadar S, Köseoğlu M. Hipotiroidizm ve hipertiroidizmde kardiyovasküler risk faktörleri. Yeni Tıp Dergisi 2011;28:30–3.
9. Ghiselli A, Serafini M, Natella F, Scaccini C. Total antioxidant capacity as a tool to assess redox status: Critical view and experimental data. Free Radical Biology and Medicine 2000;29(11):1106–14.
10. Patra RC, Swarup D, Dwivedi SK. Antioxidant effects of α tocopherol, ascorbic acid and L-methionine on lead induced oxidative stress to the liver, kidney and brain in rats. Toxicology 200
11. Ittermann T, Lorbeer R, Tiller D, et al. Serum Thyrotropin Concentrations Are Not Associated

with the Ankle-Brachial Index: Results from Three Population-Based Studies. European Thyroid Journal 2015;4(1):101–7.
12. Cebeci E, Alibaz-Oner F, Usta M, Yurdakul S, Erguney M. Evaluation of Oxidative Stress, the Activities of Paraoxonase and Arylesterase in Patients With Subclinical Hypothyroidism. J Investig Med 2012;60(1):23–8.
13. Marcocci C, Leo M, Altea MA. Oxidative Stress in Graves' Disease. European Thyroid Journal 2012;1(2):80–7.
14. Vassalle C, Bianchi S, Bianchi F, Landi P, Battaglia D, Carpeggiani C. Oxidative stress as a predictor of cardiovascular events in coronary artery disease patients. Clinical Chemistry and Laboratory Medicine 2012;50(8):1463–8.
15. Rani AJ Mythili SV. Study on total antioxidant status in relation to oxidative stress in type 2 diabetes mellitus. Journal of Clinical and Diagnostic Research 2014;8(3):108–10.
16. Re R, Pellegrini N, Proteggente A, Pannala A, Yang M, Rice-Evans C. Antioxidant Activity Applying an Improved ABTS Radical Cation Decolorization Assay. Free Radical Biology & Medicin. 1999;26:1231–7.
17. Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin Biochem. 2004;37(4):277–85.
18. Gürel A, Doğantekin A, Özkan Y, Aydın S. Serum apelin levels in patients with thyroid dysfunction. International Journal of Clinical and Experimental Medicine 2015;8(9):16394–8.
19. Sanson M, Augé N, Vindis C, et al. Oxidized low-density lipoproteins trigger endoplasmic reticulum stress in vascular cells: Prevention by oxygen-regulated protein 150 expression. Circulation Research 2009;104(3):328–36.
20. Chen Y, Chen M, Wu Z, Zhao S. Ox-LDL induces ER stress and promotes the adipokines secretion in 3T3-L1 adipocytes. PLoS ONE 2013;8(10):1–8.
21. Berta E, Harangi M, Varga VE, et al. Evaluation of serum chemerin level in patients with hashimoto's thyroiditis. Atherosclerosis 2016;252(2016):e168.
22. Lehrke M, Becker A, Greif M, et al. Chemerin is associated with markers of inflammation and components of the metabolic syndrome but does not predict coronary atherosclerosis. European Journal of Endocrinology 2009;161(2):339–44.
23. Chen X, Gao C, Gong N, Wang Y, Tian L. The change of left ventricular function in rats with subclinical hypothyroid and the effects of thyroxine replacement. International Journal of Endocrinology 2018;2018:1–10.
24. Gong N, Gao C, Chen X, Wang Y, Tian L. Adipokine expression and endothelial function in subclinical hypothyroidism rats. Endocrine Connections 2018;7(2):295–304.
25. Al-Jowari SA. Determination of the level of some adipokines in hypo-and hyperthyroids patients in Baghdad city. Baghdad Science Journal 2017;14(4):713–6.
26. Çinar N, Gülçelik NE, Aydín K, Akín Ş, Usman A, Gürlek A. Serum vaspin levels in hypothyroid patients. European Journal of Endocrinology 2011;165(4):563–9.
27. Salam MHA, Edrees HM. Effect of Different Conditions of Thyroid Function on Serum Adiponectin, Visfatin and Vaspin Levels in Rats. Basic Sciences of Medicine 2015;4(1):12–9.
28. Lumachi F, Basso SMM, Orlando R. Cytokines, thyroid diseases and thyroid cancer. Cytokine 2010;50(3):229–33.
29. Marchiori RC, Pereira LAF, Naujorks AA, et al. Improvement of blood inflammatory marker levels in patients with hypothyroidism under levothyroxine treatment. BMC Endocrine Disorders 2015;15(1):1–9.
30. Gómez-Zamudio JH, Mendoza-Zubieta V, Ferreira-Hermosillo A, et al. High Thyroid-stimulating Hormone Levels Increase Proinflammatory and Cardiovascular Markers in Patients with Extreme Obesity. Archives of Medical Research 2016;47(6):476–82.
31. Kvetny J, Heldgaard PE, Bladbjerg EM, Gram J. Subclinical hypothyroidism is associated with a low-grade inflammation, increased triglyceride levels and predicts cardiovascular disease in males below 50 years. Clinical Endocrinology 2004;61(2):232–8.
32. Şahin DA, Başpınar O. Thyroid Diseases. Turkiye Klinikleri Pediatric Sciences 2015;11(2):23–8.
33. Ittermann T, Baumeister SE, Völzke H, et al. Are serum TSH levels associated with oxidized low-density lipoprotein? Results from the study of health in Pomerania. Clinical Endocrinology 2012;76(4):526–32.
34. Ucan B, Kebapci MN, Uslu S, Kara M, Akcar Degirmenci N, Oner S. Hipotiroid hastalarda plazma visfatin konsantrasyonlarının tiroid

otoimmünitesi ve ateroskleroz ile ilişkisi. Ortadoğu Tıp Dergisi 2018;10(4):498–505.
35. 35. Duntas LH, Mantzou E, Koutras DA. Circulating Levels of Oxidized Low-Density Lipoprotein in Overt and Mild Hypothyroidism. Thyroid 2002;12(11):1003–7.
36. 36. Cheserek MJ, Wu GR, Ntazinda A, Shi YH, Shen LY, Le GW. Association between Thyroid Hormones, Lipids and Oxidative Stress Markers in Subclinical Hypothyroidism. Journal of Medical Biochemistry 2015;34(3):323–31.
37. Ates I, Yilmaz FM, Altay M, Yilmaz N, Berker D, Güler S. The relationship between oxidative stress and autoimmunity in Hashimoto's thyroiditis. European Journal of Endocrinology 2015;173(6):791–9.
38. Aslan M, Cosar N, Celik H, et al. Evaluation of oxidative status in patients with hyperthyroidism. Endocrine 2011;40(2):285–9.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 308-318
https://doi.org/10.30621/jbachs.1257886
RESEARCH ARTICLE

EVALUATION OF THE EFFECTIVENESS OF HOSPITAL RECYCLING PROGRAM FOR IMPROVING NURSES' RECYCLING BEHAVIOURS

Hatice Gürgen Şimşek[1], Süheyla Altuğ Özsoy[2]

[1] Manisa Celal Bayar University, Faculty of Health Sciences, Department of Midwifery, Manisa, Turkey
[2] Ege University, Faculty of Health Sciences, Department of Public Health Nursing, Izmir, Turkey

ORCID: H.G.S. 0000-0002-2084-4097; S.A.O. 0000-0001-5615-1893

Corresponding author: Hatice Gürgen Şimşek, **E-mail:** hatice.simsek@cbu.edu.tr
Received: 28.02.2023; **Accepted:** 27.02.2024; **Available Online Date:** 31.05.2024

Cite this article as: Gurgen-Simsek H, Ozsoy SA. Evaluation of the Effectiveness of Hospital Recycling Program for Improving Nurses' Recycling Behaviours. J Basic Clin Health Sci 2024; 8: 308-318.

ABSTRACT

Purpose: To evaluate the effect of the Hospital Recycling Program conducted for the wastes generated during the practice of nurses on the recycling behavior and waste amounts of the nurses.
Material and Methods: A quasi-experimental study with a pre-test and post-test control group was conducted with 64 nurses. Data were collected by the Nurse Descriptive Characteristics Form, Recycling Scale for Sustainable Hospital, and Unit Waste Registration Form. The Hospital Recycling Program based on the Theory of Planned Behaviour was applied to the intervention group.
Results: The Hospital Recycling Program had a positive effect on attitudes/behavior intention, and recycling behavior scores of nurses in the intervention group; the amount of recyclable waste was significantly increased compared to the control group ($p<0.05$). It was found that perceived behavioral controls of all nurses affected the intention to recycle and the Hospital Recycling Program had a significant effect on the attitudes of the nurses in the intervention group ($p<0.05$).
Conclusion: The Hospital Recycling Program based on the Theory of Planned Behaviour has a positive effect on the recycling behaviors of the nurses and the amount of recyclable waste.

Keywords: attitude, hospitals, intention, nurse, recycling.

INTRODUCTION

Today, one of the most important causes of environmental pollution is the increase in the amount of waste. Hospitals are open 365 days, 7 days a week, twenty-four hours a day, because they offer hotel services, restaurants, and office services as well as clinical services and there are too many employees, they are also among the places where intensive waste production as well as energy and water consumption (1, 2). Sterile procedures, surgeries, patient hygiene, and numerous other services require a wide range of materials that are contaminated or disposable, even if they are opened and not used (3). Particularly among the nursing care activities, many wastes that can be recycled and non-recyclable are produced during drug treatment/drug procedures (4). Given that nurses often represent the majority of employees in a hospital and participate directly in patient care, the fact that they are an important source of consumer and waste producer is emerging (5-7).

Nurses have professional responsibilities for waste management (2). Studies show that nurses have low levels of knowledge/practice on environmental protection, rational use of resources and waste management practices (8, 9). In particular, there is

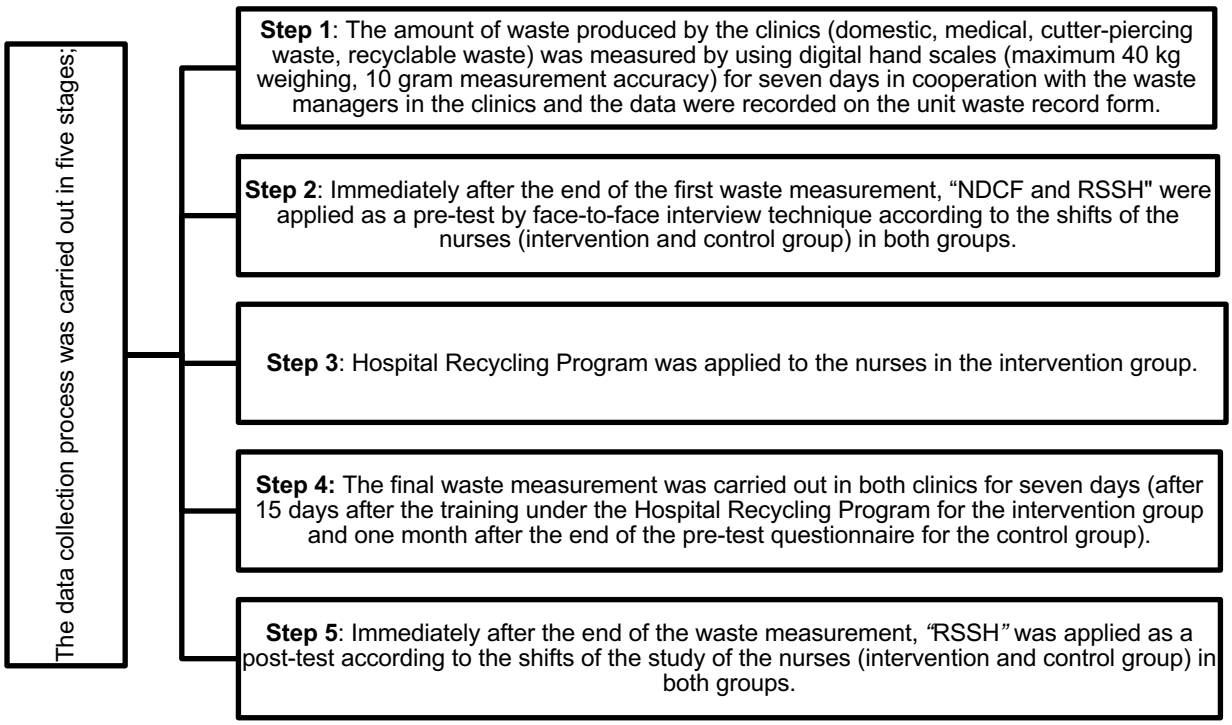


Figure 1. Data Collection Stages

evidence that there are problems with effective recycling practices and the separation of waste at the source (7,10). To reduce the risk of disease transmission, nurses dispose of some of the waste in domestic waste and recycling and unnecessarily waste them into medical waste bags. The inclusion of recyclable wastes in domestic waste and medical wastes brings economic and environmental burdens, so the separation of wastes at the source is important (9-11). However, it is stated that nurses are generally unaware of waste and energy costs (12). However, nurses need to be an active part of cost-effective efforts (13).

Nurses should be involved in waste management practices to improve environmental sustainability in health care (5, 6). Since environmental problems cannot be solved only by technology and laws, individual behavior changes are required. There should also be a change in knowledge and attitude for behavior change. Developing a positive attitude towards the environment is possible with environmental education (14). Environmental education aims to increase the awareness of the individual about environmental problems (15). Theory-based studies need to be conducted and tested to understand the mechanism responsible for recycling behavior. In this context, in many studies, the Theory of Planned Behavior (TPB) has been successfully applied to understand the behavior of recycling (16-18). In our country, it is determined that studies on recycling behavior are concentrated in educational sciences and there is no study on nursing (19-21). For a sustainable future, it is important to explain the recycling behavior of nurses based on the model (16). Supporting nurses with a professional and motivating approach is thought to positively affect their recycling behavior. It is thought that nurses who are role models in hospitals will improve their recycling behaviors and contribute to gaining these behaviors in student nurses. This study aimed to evaluate the effect of the Hospital Recycling Program prepared by the researcher on the recycling behavior of the nurses and their waste amounts.

MATERIAL AND METHODS

Design

The study was conducted as a quasi-experimental study with a pre-test, and post-test control group.The research hypotheses were:

-H_1: The Hospital Recycling Program affects the recycling behaviors of nurses.

-H_1: The Hospital Recycling Program affects the amount of recyclable waste in the clinic.

Table 1. Distribution of Nurses in the Intervention and Control Group by Descriptive Characteristics

Characteristics		**Intervention (n = 32)**	**Control (n = 32)**	**Total (n = 64)**	***Test value p***
Age (year)	***Min-Max (Median)***	23-49 (33.5)	23-58 (35)	23-58 (34)	*t=-0.473*
	x̄±SD	33.97±6.74	34.88±8.48	34.42±7.62	[a]*p =0.638*
Gender	**Female**	31	31	62	χ^2*=0.001*
	Male	1	1	2	[b]*p =1.000*
Marital status	**Married**	14	20	34	χ^2*=2.259*
	Single	18	12	30	[c]*p= 0.133*
Education	**University**	25	30	55	χ^2*=3.232*
	Graduate	7	2	9	[b]*p =0.148*
Professional working time (year)	***Min-Max (Median)***	1-30 (10)	1-36 (12)	1-36 (10)	*t=-0.624*
	x̄±SD	11.17±7.49	12.44±8.70	11.80±8.08	[a]*p =0.535*
Department	**Clinic**	13	12	25	χ^2*=2.127*
	Intensive care	9	14	23	[c]*p =0.345*
	Operating room	10	6	16	
Professional position	**Clinic nurse**	18	21	39	χ^2*=1.363*
	Supervisor nurse	1	2	3	[a]*p =0.562*
	Other	13	9	22	
Membership in the environmental group	**Yes**	1	2	3	χ^2*=0.350*
	No	31	30	61	[b]*p =1.000*
Thinking that nurses should take an active role in protecting environmental health	**Yes**	27	28	55	χ^2*=0.129*
	No	5	4	9	[b]*p =1.000*
Evaluation of hospital recycling activities	***Min-Max (Median)***	*1-7 (3)*	*1-7 (4)*	*1-7(4)*	*Z=-2.158*
	x̄±SD	*3.09±1.61*	*4.03±1.71*	*3.56±1.72*	[e]*p =**0.031****

[a]Student t Test. [b]Fisher's Exact Test. [c]Pearson Chi-Square Test. [d]Fisher Freeman Halton Test. [e]Mann Whitney U Test
**p<0.05*

Place and Time of Study

The study was conducted between June 2017 and February 2018 at a University Medical Faculty Hospital General Surgery and Cardiovascular Surgery Clinics (service, intensive care, and operating room).

Sample

The sample of the intervention group consisted of nurses at the Cardiovascular Surgery Clinic and the control group at the General Surgery Clinic. Because of the high number of recyclable medical products in these clinics, nurses working in these units were sampled and randomly determined. The most intensive clinics of the hospital in terms of patient circulation and working nurse were selected. The nurses here were chosen because they would support the researcher in data collection.The study sample was composed of 64 nurses based on a confidence interval of 95%, moderate effect size (d=0.50), and a statistical power of 80%. The study was started with 72 nurses and was completed with 64 nurses (intervention = 32, control = 32) due to health problems and unit change. Power analysis (G*Power v3.1.7) made at the end of the study showed a statistical power of 81% based on a confidence interval of 95%.

Inclusion criteria. Voluntary nurses working in cardiovascular and general surgery clinics who accepted to participate in the study were included in the study.

Exclusion criteria. Nurses who were leaving work, on sick leave, on annual/unpaid leave were excluded from the study.

Table 2. Evaluation of Recycling Scale for Sustainable Hospital Sub-Dimension and Scale Scores By Groups

Sub-dimensions		Intervention (n = 32)	Control (n = 32)	Test value p
		Median/ x̄±SD	*Median/x̄±SD*	
1. Attitude	Pretest	6.1	6.4	
	Posttest	6.7	6.6	*Z=-3.213* [e]*p =**0.001***
	Point difference	0.73±0.63	0.25±0.57	
2. Behavior results	Pretest	7	7	
	Posttest	7	7	*Z=-0.195* [e]*p=0.846*
	Point difference	0.20±0.50	0.17±0.45	
3. The importance of the results of behavior	Pretest	7	7	
	Posttest	7	7	*Z=-0.904* [e]*p=0.366*
	Point difference	0.18±0.46	0.07±0.31	
4. Subjective norm	Pretest	5.5	6.5	
	Posttest	6	7	*Z=-1.296* [e]*p=0.195*
	Point difference	0.73±1.45	0.41±0.93	
5. Perceived expectations	Pretest	5.4	5.6	
	Posttest	6.2	6.1	*Z=-0.949* [e]*p=0.343*
	Point difference	0.63±1.34	0.29±0.95	
6. The importance of expectations	Pretest	6.1	6	
	Posttest	6.7	6.8	*Z=-0.189* [e]*p=0.850*
	Point difference	0.62±1.57	0.46±1.30	
7. Perceived behavior control	Pretest	4.88±1.02	5.19±1.19	
	Posttest	5.70±1.10	5.24±1.11	*t=2.479* [a]*p=**0.016****
	Point difference	0.81±1.26	0.05±1.18	
8. Perceived conditions/situations	Pretest	4.55±1.02	5.16±0.89	
	Posttest	5.59±0.52	5.21±0.91	*t=4.101* [a]*p=**0.001***
	Point difference	1.04±1.01	0.05±0.91	
9. Facilitating conditions/ situations	Pretest	6.3	6.3	
	Posttest	6.3	6.3	*Z=-1.926* [e]*p=0.054*
	Point difference	0.28±0.66	-0.01±0.42	
10. Behavior intention	Pretest	6	6	
	Posttest	7	7	*Z=-2.053* [e]*p=**0.040****
	Point difference	0.96±1.15	0.40±0.88	
11. Recycling behavior	Pretest	5	5.8	
	Posttest	6.2	6	*Z=-2.184* [e]*p=**0.029****
	Point difference	1.25±1.72	0.29±1.11	
Scale Total	Pretest	5.64±0.50	5.93±0.49	
	Posttest	6.32±0.27	6.15±0.44	*t=3.947* [a]*p=**0.001***
	Point difference	0.68±0.52	0.22±0.39	

[a]*Student t Test* [e]*Mann Whitney U Test. *p<0.05. **p<0.01*

Data Collection Tools

Nurse Descriptive Characteristics Form (NDCF): The form consisted of 10 questions that were developed in light of the relevant literature (20, 22).

Recycling Scale for Sustainable Hospital (RSSH): Tekkaya et al. (2011), the 7-point Likert-type scale, created according to TPB, is intended to determine the recycling behavior of university students on campus and consists of 11 sub-dimensions and 90 questions (20). The average score for the scale sub-dimensions was obtained by summing all the items in the sub-dimension and dividing by the total number of items. The mean score for the whole scale was obtained by summing all items in the scale and dividing it by the total number of items. Negative expressions (4 items) were reverse coded. Some expressions in the Perceived Expectations and Importance of Expectations sub-dimensions were changed with the permission of the scale owner as the study was conducted in the hospital environment: university management=hospital management, faculty members=nursing, services directorate, responsible nurses, campus=hospital. The Recycle Behavior sub-dimension included a blue wrap, glass vial, IV bag, medical packaging, and oxygen mask (Cronbach's Alpha coefficient = 0.83). Cronbach's Alpha coefficient values of each sub-dimension were calculated in the original scale, and no calculation was made for the scale total. In this study, Cronbach's Alpha coefficient of the scale was calculated as 0.92 in the pre-test.Cronbach's Alpha coefficient values are as follows: the attitude (original:0.87, this study: 0.89), behavior results (original:0.93, this study: 0.94), the importance of the results of the behavior (original:0.95, this study: 0.96), subjective norm (original: 0.67, this study: 0.75), perceived expectations (original:0.89, this study: 0.86), the importance of expectations (original:0.92, this study:0.96), perceived behavior control (original:0.72, this study: 0.77), perceived conditions/conditions (original: 0.76, this study: 0.75), facilitating conditions/situations (original: 0.92, this study: 0.83), behavior intention (original: 0.93, this study: 0.94),recycling behavior (original:0.90, this study: 0.80) (20).

Unit Waste Registration Form: The form was developed considering the relevant literature (23). It is a form in which seven-day measurements of the unit name, collector and waste types (domestic, medical, sharp-drilling, recyclable) are written.

Data Collection

Figure 1 presents data collection stages.

Implementation of Hospital Recycling Program

The content of the program consists of seven interference packages;

1. Recycling Training for Nurses: The training (individual or group) was conducted with 8 different groups interactively with 45 minutes PowerPoint presentation, video demonstration and 15 minutes discussion on the subject (a total of one hour, one time). Nurses were allowed to express their concerns and ask questions. In the presentation of 51 slides prepared by scanning the literature; waste management, legal responsibilities in waste management, the definition of recycling, benefits of recycling, recyclable medical materials, examples of recycling practices in hospitals around the world, nurses' responsibilities in recycling practices are included (7, 9, 10-12, 23-25).

2. 'Support recycling you too' Video: It was taken by the researcher with the technical support of a University Information and Communication Technologies Application and Research Center to emphasize the professional responsibilities of nurses and to realize the institutional impact on subjective norms. In this video, a member of the Department of Cardiovascular Surgery, head nurse and nurse responsible for intensive care unit, an environmental engineer working in the hospital environmental management unit, director of Environmental Problems Application and Research Center of our university, dean of nursing faculty, thesis supervisor and thesis student were included and the messages which were determined in line with the literature and thought to increase the sensitivity to recycling in hospitals were included. The video duration was 4.36 seconds. Watching the video during the training nurses were encouraged to recycle.

3. Recycling Board, Posters, and Brochures: The board was formed from recyclable medical materials (blue wrap, oxygen mask, intravenous bag, medical packaging material, glass vial) for use in training. It was aimed that the nurses could identify the recyclable materials and examine the recycling codes. Nurses were given a plastic code list with recycling numbers (23). Posters obtained from environmental non-governmental organizations were hung in the treatment and restrooms of the nurses for reminding and warning.

Table 3. Model Fit Indexes and Interpretation

Compliance index	Evaluation criteria	Values of the model in this study	Conformity in this study
χ2 p value	0≤χ2 ≤2df 0.05≤p≤1.00	8.78 0.19 (p >0.05)	Good
χ2 /df	0≤χ2 /df≤2	8.78/6 (1.46)	Good
RMSEA	0.05≤RMSEA≤0.10 (Acceptable)	0.086	Acceptable
CFI	0.95≤CFI≤0.97 (Acceptable)	0.93	-
GFI	0.95≤GFI≤1.00 (Good)	0.96	Good

RMSEA: Root Mean Square Error of Approximation, CFI: Comparative Fit Index, GFI: Goodness of Fit Index

4. The slogan of the Hospital Recycling Program: Inspired by literature, the following slogan created by the researcher was used in the video and on cloth bags (26). The slogan was "Economically sustainability, Ecologically sensitive, Socially sensitive for Nursing Applications Support Recycling You Too".

5. Recycling Reminder Badge: It was prepared by the investigator collecting the vial caps from the cardiovascular surgery clinic.

6. Supply and Increasing the Number of Recycle Bins: As it was found out that there were no recycle bins in the operating room, 7 recycle bins were placed in the operating room and an additional one was placed in the service and intensive care units. Also, waste battery boxes obtained from an environmental non-governmental organization were placed in the common room used by the operating room and intensive care nurses.

7. Encouragement of behavior: A stimulating environment was created for the nurses by using educational materials (posters, brochures, recyclable medical equipment board, plastic recycling code list) that contain information parallel to the content of the program. At the end of the training, nurses, brochures obtained from environmental non-governmental organizations, pencils (larch seed, obtained from recycling), a notepad, a reminder name badge, a cloth bag with the slogan of the program, booklet created in 2015 by a University Environmental Problems Application and Research Center distributed for motivation purposes.

While the program was applied to the intervention group, no intervention was applied to the control group. Routine hospital operation continued.

Statistical analysis

SPSS 20.0 software, LISREL 8.8 software for path analysis, and G-Power software for power analysis were used for data analysis. Numbers, percentages, mean, median, minimum, maximum, and standard deviation values were used to evaluate descriptive characteristics. The suitability of the data for normal distribution was determined by Shapiro-Wilk's test. Data were evaluated by Student t-Test, Mann Whitney U test, Wilcoxon Signed Ranks, Pearson Chi-Square test, Fisher-Freeman-Halton (post hoc Bonferroni method) test, and Fisher's Exact test. Confirmatory factor analysis was performed to assess the compatibility of the model, $p<0.05$ was considered significant.

Ethical considerations

Ethical approval was obtained from the Clinical Research Ethical Committee of a University Medical School Research and Training Hospital (Dated 30.05.2017 and No:17-5.2/20). Written permission was obtained for conducting the study in the same hospital (dated 29.06.2017 and No:69631334-302.99) and from the researchers who developed the scale used in the study. Verbal and written informed consent were obtained from nurses included in the study. The research conforms to the provisions of the Declaration of Helsinki (as revised in Brazil 2013).

RESULTS

Activities for the Environment and Personal Information of Intervention and Control Group Nurses

It was found that nurses in the intervention and control groups were similar in terms of personal information and environmental activity characteristics ($p>0.05$). It was found that nurses in the intervention group found the recycling activities in the hospital less adequate ($p<0.05$) (Table 1).

Recycling Behavior of Nurses in the Intervention and Control Group

Table 4. Distribution of Waste Amount of the Intervention and Control Group (kg)

Waste Types		Intervention Group (n=32)	Control Group (n=32)	*Between Groups Test value*
		x̄±SD	*x̄±SD*	
Domestic waste	Pretest Posttest	23.49±16.56	33.23±27.89	*Z=-0.616. [e]p = 0.538*
	In-group	22.80±17.12	31.24±26.80	*Z =-0.968 [e]p = 0.333*
	First-Last waste difference	*[g]p = 0.543*	*[g]p = 0.476*	
		-0.69±8.47	-1.99±8.23	*Z =-0.013 [e]p =0.990*
Medical waste	Pretest Posttest	115.09±74.03	112.27±41.74	*Z=-0.541 [e]p =0.589*
	In-group	57.33±27.37	100.85±23.07	*Z=-4.138 [e]p =**0.001****
	First-Last waste difference	*[g]p = **0.001****	*[g]p* = 0.244	
		-57.76±53.07	-11.42±35.31	*Z=-2.956 [e]p =**0.003****
Sharp waste	Pretest Posttest	9.83±7.64	8.62±5.08	*Z=-0.050 [e]p =0.960*
	In-group	12.12±3.87	12.81±7.25	Z=-0.176 *[e]p* = 0.860
	First-Last waste difference	*[g]p =0.224*	*[g]p = **0.012****	
		2.29±7.19	4.19±7.01	*Z=-0.138 [e]p = 0.890*
Recyclable waste	Pretest Posttest	2.14±1.77	2.26±0.65	*Z=-1.287 [e]p =0.198*
	In-group	6.45±3.97	2.30±0.79	*Z= -3.400 [e]p =**0.001****
	First-Last waste difference	*[g]p =**0.002****	*[g]p =0.730*	
		4.30±3.73	0.04±0.92	*Z=-3.446 [e]p = **0.001****

*[e]Mann Whitney U Test. [g]Wilcoxon Signed Ranks. *p<0.05. **p<0.01*

As seen in Table 2, the attitude, perceived behavior control, perceived conditions/conditions, behavior intention, recycling behavior dimensions and total scale scores of the intervention group were significantly higher than the control group after the Hospital Recycling Program (p<0.05). Behavior results, the importance of the results of the behavior, subjective norm, perceived expectations, the importance of expectations, and facilitating conditions/situations subscale scores were not significantly different in the intervention and control groups (p>0.05).

Comparison of Recycling Behavior of Nurses in Intervention and Control Groups with Path Analysis

In order to evaluate the effectiveness of the TPB-based Hospital Recycling Program, a model was established by Path Analysis by taking the RSSH post-test scores of all nurses in the intervention and control groups and the model was found to be in good agreement (Table 3).

In Model 1, the direct impact of the Hospital Recycling Program on attitude, subjective norm, perceived behavioral control, intention, and behavior; the direct effect of attitude, subjective norm, perceived behavioral control on intention; the direct effect of perceived behavioral control on behavior and the direct effect of intention on behavior were evaluated together. It was found that Hospital Recycling Program (β=2.14, S.E= 5.57) had a significant effect on attitude (p<0.05), but it did not directly affect subjective norm (β=-1.71, S.E.=5.57), perceived behavioral control (β=1.64, S.E.=5.57), intention (β =0.96, S.E.=7.87) and behavior (β=0.75, S.E.=5.57) (p>0.05). It was determined that perceived behavioral control (β=0.94, S.E.=5.57) and intention (β=1.92, S.E.=5.57) did not affect behavior (p>0.05). Subjective norms (β=-0.08, S.E.= 7.87) and attitudes (β=1.10, S.E.=7.87) did not have a direct effect on intention (p>0.05), and perceived behavioral control (β=2.57, S.E.=7.87) had a significant effect on intention (p<0.05). 16% of the total change in the intent variable is explained by perceived behavioral control (INTENTION=0.31* PERCEIVED

BEHAVIORAL CONTROL -0.0095* SUBJECTIVE NORM +0.14*ATTITUDE+0.12*GROUP, Errorvar.=0.87, R^2=0.16). 7% of the total change in attitude variable is explained by the Hospital Recycling Program (ATTITUDE=0.25*GROUP, Errorvar.=0.87, R^2=0.069) (Model 1).

Intervention and Control Group Average of the amount of waste belonging to the units where nurses work

The distribution of domestic, medical, sharp, and recyclable waste amounts (kg) belonging to the intervention and control groups was shown in Table 4. It was observed that the amount of waste in the pretest was similar. In line with these results, there was no statistically significant difference between the intervention and control groups in terms of domestic and sharp waste amounts after the Hospital Recycling Program ($p>0.05$), and there was a statistically significant difference between the intervention and control groups in terms of the amount of recyclable and medical waste ($p<0.05$).

DISCUSSION

Recycling Behavior of Nurses

It was stated in the literature that nurses had very important roles in waste management in hospitals and that the positive attitude of nurses increases the success of separation practices at the source (27). Nevertheless, some studies show that nurses have negative attitudes towards waste management (28, 29). At this point, the importance of education is emphasized for proper separation of wastes in hospitals. In a study of 255 health workers in Pakistan with a pre-test-post-test-control group design conducted for 3 months; the intervention group received training on medical waste management. At the end of the training, there was a significant difference in the attitudes of the intervention group (30). Six months after the training on hazardous waste to 69 healthcare workers in Egypt, positive attitudes of participants were found to increase (31). In this study, it was determined that the Hospital Recycling Program applied to the intervention group had a positive effect on the attitudes of nurses, in accordance with the literature.

Knowing how wastes should be separated and which wastes are recyclable, the presence of recycling bins in the immediate environment contributes to the individual's perception of recycling behavior as easy (28, 32, 33). When the resources and opportunities of the individual increase or the barriers decrease, the perception of control over the behavior increases (34). In a study conducted with anesthesiologists working in private and public hospitals in Australia, New Zealand, and the UK, the greatest obstacle to recycling waste was the inadequacy of recycling bins (28). The reason for the high amount of waste in a medical center in Nigeria has been attributed to waste bins in unsuitable places and a lack of information on medical waste (33). In a study conducted with 164 healthcare workers in America, the rate of discard of glass vials in recycling bins increased from 33% to 58% after the training initiative (32). In this study, in the scope of Hospital Recycling Program, supplying and increasing the number of recycling bins, showing which medical equipment is recyclable by plastic recycling code list, and explaining the hospital samples from the world, it was ensured that nurses in the intervention group scored high on perceived behavior control and perceived conditions/situations.

Investigation of Nurse's Recycling Behavior by Path Analysis

One of the most common models used to predict and explain recycling behavior is TPB (20). In a study conducted with 163 health personnel working in a hospital in Uganda, perceived behavioral control was found to affect intent (16). In this study, in accordance with the literature, it was found that perceived behavioral control affected intent (17, 18). However, although this study did not show the effect of attitude on intention, the fact that the study was conducted experimentally shows that the effect of the initiative on attitude was achieved through the "Hospital Recycling Program". It is thought that this positive attitude will turn into behavior in the long run.

Waste Amount of Units

Considering the high amount of waste produced daily by the surgical units in hospitals, it is stated that the initiatives to be carried out regarding waste management will have a positive impact on the environment as well as reduce the waste disposal costs and contribute to the saving of hospitals (32). The studies propose the use of initiatives to reduce the amount of waste in hospitals (training, number/availability of waste bins, availability of hospital procedures, institutional support) (25). Through these initiatives, it was observed that the attitudes and behaviors of the personnel were changed the amount of medical waste was reduced,

and recycling was increased (32, 35, 36). It has been shown that the systematic separation of wastes identified as having a recycling sign in a hospital operating room in Korea can lead to a reduction in medical waste production and an increase in recyclable waste rates (36). Waste measurement was carried out for two weeks following the training initiative with the Recycling in the Operating Room Project carried out in 16 operating theaters of Harborview Medical Center in the USA. As a result, medical waste decreased by 59%, and recyclable waste increased by 19% (32). After a one-month online waste management training program conducted by the Association of Perioperative Registered Nurses with 66 perioperative employees (nurses, anesthesiologists, technicians), there was a 40.68% reduction in the amount of medical waste measured on any day (35). In this study, nurses' awareness of recycling was increased, recycling behaviors were improved and the amount of recyclable waste was increased by conducting research-specific initiatives (such as reminder badges, video) in addition to similar initiatives in the literature. Following the Hospital Recycling Program, the amount of recyclable waste increased, and the amount of medical waste decreased. It was concluded that the Hospital Recycling Program was effective in creating behavior change in nurses.

Limitations

Only the recycling step in the waste management hierarchy and the fact that it only includes nurses among health professionals constituted the limitation of the research.

CONCLUSION

The Hospital Recycling Program developed according to the Theory of Planned Behavior, has affected the attitudes of nurses, has significantly improved recycling behavior, increased the amount of recyclable waste, and reduced the amount of medical waste. However, it was a good example of how nurses could lead in project development aiming at reducing waste in the hospital. In this respect, hospitals may prefer to use this program in waste management practices. It has also enabled raising awareness about the appropriate waste segregation that provides environmental and economic benefits.

This study not only emphasizes the importance and feasibility of the implementation of an appropriate waste separation program in the surgical units in the hospital, but it is also important in terms of minimizing the cost of institutional disposal and showing what should be done to reduce the carbon footprint created by the health sector. For future research, it may be suggested to conduct research (qualitative and quantitative) to identify conditions that prevent nurses from recycling behavior, to investigate the amount of waste in internal clinics as well as surgical units, and to investigate the determinants of recycling behaviors of all healthcare workers in larger sample groups.

Acknowledgement: This study was funded by Ege University Faculty Member Training Program and presented as a Doctoral dissertation at Ege University Health Sciences Institute. We would like to thank the nurses who participated in the study, the waste personnel performing waste measurements, and the environmentalist non-governmental organizations (ÇEVKO, ELDAY, TUKÇEV) that provided posters, brochures, notebooks, pens, and recycling bins support. We would also like to acknowledge Assoc. Prof. Dr. Timur Köse, Assoc. Prof. Dr. Hakan BAYDUR, Assoc. Prof. Dr. Aynur Çetinkaya, Assoc. Research Assistant Semiha Özgül for their valuable contribution to the statistical analysis of the data. This study presented as an oral presentation and full text statement at 6th International 17th National Nursing Congress, 19-21 December 2019 Ankara in Turkey

Author contribution: Conceptualization HGS, SAÖ; Formal analysis HGS; Methodology HGS, SAÖ; Resources HGS; Writing - original draft HGS; Writing - review & editing HGS, SAÖ.

Conflict of interests: None.

Ethical approval: This research was approved by the Clinical Research Ethical Committee of Ege University Medical School Research and Training Hospital (Dated 30.05.2017 and No:17-5.2/20).

Funding: This study was funded by Ege University Faculty Member Training Program and presented as a Doctoral dissertation at Ege University Health Sciences Institute. Also the environmentalist non-governmental organizations (ÇEVKO, ELDAY, TUKÇEV) provided posters, brochures, notebooks, pens, and recycling bins support.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Johnson SW. Summarizing green practices in US hospitals. Hospital Topics 2010;88(3):75-81.
2. Shaner-McRae H, McRae G, Jas V. Environmentally safe health care agencies: Nursing's responsibility, Nightingale's legacy. Online Journal of Issues in Nursing 2007;12(2).
3. Bentley T, Effros R, Palar K, Keeler E. Waste in the US health care system: A conceptual framework. The Millbank Quarterly 2008; 86(4):629-659.
4. Kwakye G, Brat GA, Makary MA. Green surgical practices for health care. The Archives of Surgery 2011; 146(2):131-6.

5. Anaker A, Elf M. Sustainability in nursing: a concept analysis. Scandinavian Journal of Caring Sciences 2014;28(2):381-9.
6. Kangasniemi M, Kallio M, Pietila AM. Towards environmentally responsible nursing: a critical interpretive synthesis. Journal of Advanced Nursing 2014;70(7):1465-78.
7. Kubicki MA, McGain F, O'Shea CJ, Bates S. Auditing an intensive care unit recycling program. Critical Care and Resuscitation 2015;17(2):135-40.
8. Maroufi M, Javadi M, Yaghoubi M, Karimi S. Function of nurses and other staff to minimize hospital waste in selected hospitals in Isfahan. Iranian Journal of Nursing and Midwifery Research 2012;17(6):445-50.
9. Vogt J, Nunes KRA. Recycling behaviour in healthcare: Waste handling at work. Ergonomics 2014; 57(4): 525-35.
10. Albert MG, Rothkopf DM. Operating room waste reduction in plastic and hand surgery. Plastic Surgery 2015;23(4):235-8.
11. McDermott-Levy R. The nurse's role on green teams: An environmental health opportunity. Pennsylvania Nurse 2011;66(1):17-21.
12. Huffling K, Schenk E. Environmental sustainability in the intensive care unit: Challenges and solutions. Critical Care Nursing Quarterly 2014;37(3):235–250.
13. Brady DJ, Cornett E, DeLetter M. Cost reduction: What a staff nurse can do. Nursing Economics 1998; 16(5):273.
14. Erten S. Research on about energy saving of intention toward the behaviour at homes for male and female students by the application of the theory of planned behaviour. Hacettepe University Journal of Education 2002;22:67-73.
15. Byerne S, Regan B. Attitudes and actions towards recycling behaviours in the Limerick, Ireland region. Resources, Conservation and Recycling 2014; 87:84-96.
16. Akulume M, Kiwanuka SN. Health care waste segregation behavior among health workers in Uganda: An application of the Theory of Planned Behavior. Journal of Environmental and Public Health 2016; 1-8.
17. Arı E, Yılmaz V. A proposed structural model for housewives' recycling behavior: A case study from Turkey. Ecological Economics 2016;129:132-42.
18. Mahmud SD, Osman K. The determinants of recycling intention behavior among the Malaysian school students: an application of theory of planned behaviour. Procedia-Social and Behavioral Sciences 2010; 9:119-124.
19. Öztürk DK. A study on preservice preschool teachers' recycling intentions in relation to parents' educational level and recycling opportunities. International Journal of Environmental and Science Education 2016;11(5):949-956.
20. Tekkaya C, Kılıç DS, Şahin E. Explanation of recycling behavior with Planned Behavior Theory: Recycling survey for a sustainable campus. Proceedings of the 2nd International Conference on New Trends in Education and Their Implications; 2011 April 27-19; Antalya, Turkey.
21. Yılmaz V, Doğan M. Investigation of recycling behavior using Theory of Planned Behavior with a Proposed Structural Equation Model. Anadolu University Journal of Social Sciences 2016;191-205.
22. Uzun N, Sağlam N. Development and validation of an environmental attitudes scale for high school students. Hacettepe University Journal of Education 2006;30:240-250.
23. Chartier Y, Emmanuel J, Pieper U, et al. Safe management of wastes from health-care activities. 2nd edition.Geneva:World Health Organization;2014.14-69. https://www.who.int/publications/i/item/9789241548564
24. International Council of Nurses. [Internet]. Health care waste: role of nurses and nursing. [Accessed date: 15 November 2016]. Available from: http://www.icn.ch/images/stories/documents/publications/position_statements/E07_Medical_Waste.pdf.
25. McGain F, Story D, Hendel S. An audit of intensive care unit recyclable waste. Anaesthesia 2009;64(12): 1299-1302.
26. Furukawa PD, Cunha IC, Pedreira MD, Marck PB. Environmental sustainability in medication processes performed in hospital nursing care. Acta Paulista de Enfermagem 2016;29(3):316-24.
27. Shivalli S, Sanklapur V. Healthcare waste management: Qualitative and quantitative

appraisal of nurses in a tertiary care hospital of India. The Scientific World Journal 2014; 1-6.
28. McGain F, White S, Mossenson S, Kayak E, Story DA. Survey of anesthesiologists' views of operating room recycling. Anesthesia & Analgesia 2012;114(5):1049-1054.
29. Wyssusek KH, Foong WM, Steel C, Gillespie BM. The gold in garbage: Implementing a waste segregation and recycling initiative. AORN Journal 2016;103(3):316.
30. Kumar R, Somrongthong R, Shaikh BT. Effectiveness of intensive healthcare waste management training model among health professionals at teaching hospitals of Pakistan: a quasi-experimental study. BMC Health Services Research 2015;15(1):81.
31. Tabash MI, Hussein RA, Mahmoud AH, El-Borgy MD, Abu-Hamad BA. Impact of an educational program on knowledge and practice of health care staff toward pharmaceutical waste management in Gaza, Palestine. Journal of the Air & Waste Management Association 2016;66(4):429-438.
32. Martin DM, Yanez CND, Treggiari MM. An initiative to optimize waste streams in the operating room: Recycling in the operating room (RECOR) project. American Association of Nurse Anesthetists Journal 2017;85(2):108-112.
33. Oraegbune OM, Waziri AI. Alternative disposal system of hospital medical solid waste–A case study of Federal Medical Center, Gombe, Gombe State, Nigeria. International Journal of Health, Safety and Environments 2017;3(4);57-69.
34. Ajzen I. Theory of planned behavior. Organizational Behavior and Human Decision Processes 1991;50:179-211.
35. Perrego K. Improving staff knowledge of perioperative regulated-waste management. AORN Journal 2017;105(1):85-91.
36. Shinn HK, Hwang Y, Kim BG., et al. Segregation for reduction of regulated medical waste in the operating room: A case report. Korean Journal of Anesthesiology 2017;70(1):100-104.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 319-326
https://doi.org/10.30621/jbachs.1264683
RESEARCH ARTICLE

WHICH POLYMORPHISM IS THE DISTINGUISHING FACTOR FOR FITNESS ATHLETES: THE ACE INDEL OR ACTN3 RS1815739?

Onur Eroğlu[1,2], Raif Zileli[2,3], M. Ali Nalbant[1], Tolga Polat [4], Özlem Özge Yılmaz[4], Beste Tacal Aslan[5], Korkut Ulucan [4,5]

[1] Bilecik Seyh Edebali University, Faculty of Science and Letters, Department of Molecular Biology and Genetics, Bilecik, Turkey
[2] Bilecik Seyh Edebali University, Biotechnology Application and Research Center, Bilecik, Turkey
[3] Bilecik Seyh Edebali University, Faculty of Health Science, Bilecik, Turkey.
[4] Marmara University, Health Sciences Institute, Department of Basic Medical Sciences, Istanbul, Turkey
[5] Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Istanbul, Turkey

ORCID: O.E. 0000-0002-3451-8540; R.Z. 0000-0003-4178-5468; M.A.N. 0000-0002-4713-1492; T.P. 0000-0002-1257-5384; O.O.Y. 0000-0002-4085-6159; B.T.A. 0000-0001-5271-7917; K.U. 0000-0002-1304-9386

Corresponding author: Korkut Ulucan, **E-mail:** korkutulucan@hotmail.com
Received: 13.03.2023; **Accepted:** 21.02.2024; **Available Online Date:** 31.05.2024

Cite this article as: Eroğlu O, Zileli R, Nalbant MA, Polat T, Yılmaz ÖÖ, Aslan BT, Ulucan K. Which Polymorphism is The Distinguishing Factor For Fitness Athletes: The ACE Indel or ACTN3 rs1815739? J Basic Clin Health Sci 2024; 8: 319-326.

ABSTRACT

Purpose: The purpose of this research was to investigate the occurrence of ACE InDel and ACTN3 rs1815739 in sub-elite fitness athletes and to determine which gene is distinctive by comparing genotype and allele frequencies with sedentary individuals.

Material and Methods: Forty-one sub-elite fitness athletes and the same number of the sedentary volunteers participated in the study. Genetic analyzes of the athletes were determined using molecular-based methods such as DNA isolation from peripheral blood samples by using a commercial kit and genotyping with real-time polymerase chain reaction (Real-Time PCR), and conventional polymerase chain reaction (PCR). The Chi-Square test was used to compare the genotype distribution and I, D, C, and T allele frequencies of ACE InDel and ACTN3 rs1815739 polymorphisms for statistical significance.

Results: No statistical difference was found for ACE I/D polymorphism in terms of both genotype distribution (p=0.4438). A comparison of sub-elite fitness athletes and control groups showed that the ACTN3 rs1815739 polymorphism had a statistically significant difference in terms of genotype distribution (p=0.0313).

Conclusion: In conclusion, we suggest that the ACTN3 rs1815739 polymorphism is more effective than the ACE InDel polymorphism in fitness athletes.

Keywords: ACE, ACTN3, fitness, gene, polymorphism, power

INTRODUCTION

Since the completion of the Human Genome Project, there has been research examining the relationship between athletic performance and genetics; and those led sports scientists to consider many factors that affect athletic performance, including physiological and environmental factors (1). In addition, the effects of genetic factors that determine

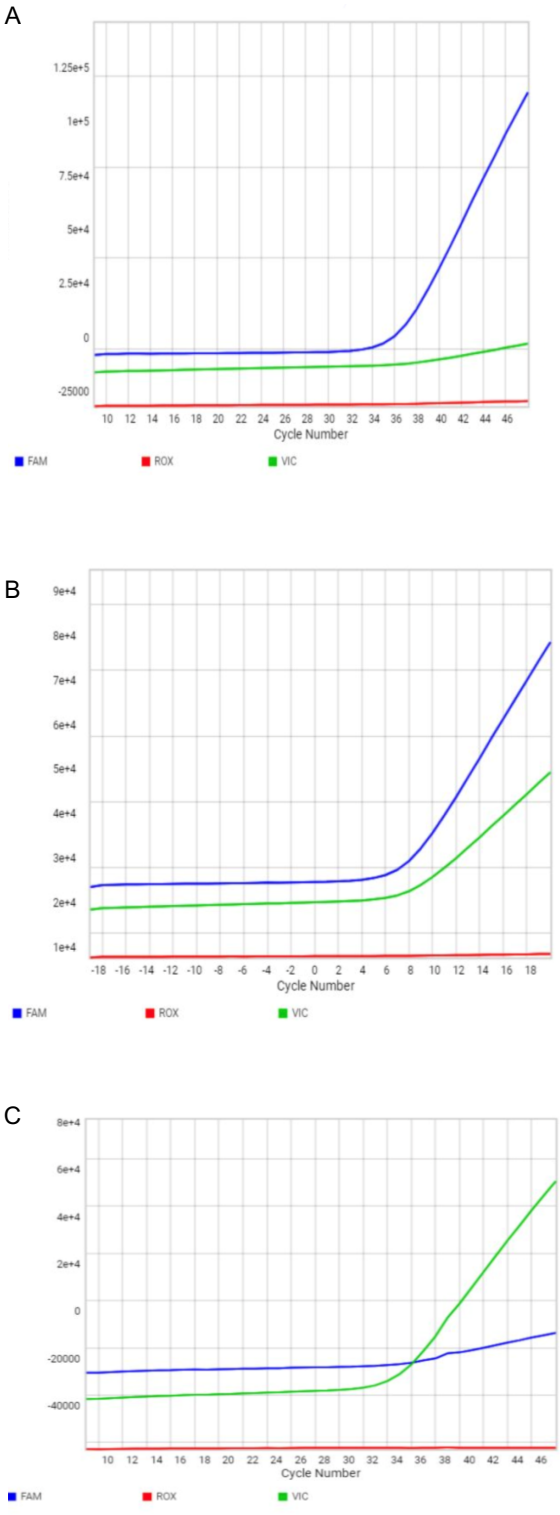


Figure 1. Quantitative PCR amplification of the ACTN3 rs1815739 polymorphism. FAM indicates the C allele (blue curve), whereas VIC (green curve) indicates the T allele). (A) The single blue curve indicates the homozygous genotype of RR (CC), whereas (B) the blue and green curves indicate the heterozygous genotype of RX (CT); (C) the green curve for homozygous genotype of TT (XX).

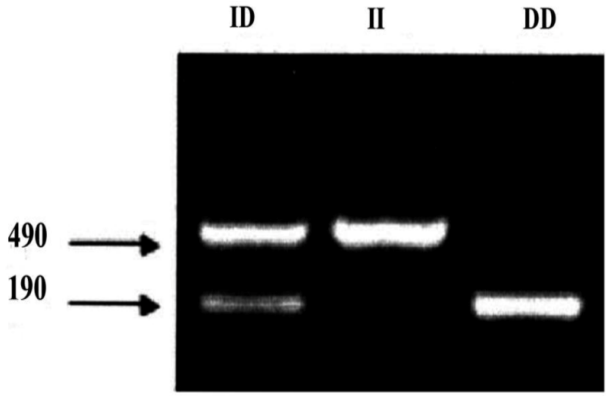


Figure 2. Representative image amplification products of the ACE InDel polymorphisms on agarose gel. The band 490 bp in length is the I allele, with a 287 bp insert. The 190 bp band is the D allele.

oxygen consumption, glucose/lipid metabolism, and fast and slow twitch fibers on athletic performance have been reported in studies. These studies formed the basis of sports genetics. The aim of sports genetics studies is the determination of the candidate genes affecting athletic performance, comparing the determined gene regions in successful athletes and sedentary individuals to assess the genetic effects. To have those, it is usually aimed to develop athletes or sedentary individuals in their optimal form by establishing an association between athletic performance and genetic endowments (2, 3).

Environmental and genetic factors influence muscle function and reveal large differences in physical performance phenotypes between individuals. It is known that only a small part of the effect of genetic variants (polymorphism) affecting athletic performance on phenotype can be explained. Various methodological techniques were used to identify correlations between genetic variations and the performance of athletes. Case-control association studies are based on the assumption that candidate gene alleles are more or less common in a group of elite athletes (cases) than in the general population (controls). Cross-sectional association studies examine whether athletes with specific genotypes/alleles exhibit different levels of phenotypic traits compared to other athletes (4, 5).

Along with genetic and environmental factors involved in muscle function and performance metabolism, phenotypic differences arise between individuals. These phenotypic differences reveal the predisposition of individuals regarding athletic performance. To better explain these predispositions,

Table 1. Genotype distribution and allele frequency of ACE InDel polymorphism in sub-elite fitness athletes.

	Genotype			*p* Value	Allelic Frequency		*p* Value
	II	ID	DD		I	D	
Athletes (n=41)	11	16	14	0,4438	38	44	0,1596
Percentage	26,8%	39,0%	34,2%		46,3%	53,7%	
Control Group (n=41)	16	15	10		47	35	
Percentage	39,0%	36,6%	24,4%		57,3%	42,7%	

* The results were considered statistically significant if the $p<0.05$. The $\chi 2$ test was utilized to compare the results with the control group.

case-control studies were conducted between candidate genes and athletic performance. These studies are based on the assumption that the distribution of the candidate gene's allele in the athlete group and control group is correlated and statistically significant (6).

Angiotensin-converting enzyme gene insertion/deletion (ACE InDel) and alpha-actinin-3 (ACTN3) rs1815739 polymorphisms are two of the most widely analyzed genes to explain the relationship between superior athletic performance and the genetics of strength training (7, 8, 9, 10, 11). Therefore, we focused on the two most studied genes, ACE and ACTN3, to explain the relationship between sportive performance and genes in athletes. The ACE gene is situated on chromosome 17q23 and its encoded protein forms a major part of the renin-angiotensin system (RAS) (11). The RAS is responsible for controlling physiological blood pressure. Renin, an enzyme, is released into the bloodstream by particular cells which line the arterioles at the glomerulus, the filtering unit in the kidney. It facilitates the transformation of angiotensinogen, a plasma protein, into angiotensin I, a decapeptide. Following the action of the angiotensin-converting enzyme (ACE) in the blood, angiotensin Ⅰ is converted to an octapeptide, leading to the formation of angiotensin II (9). The hormone Angiotensin II interacts with receptors in the adrenal gland to cause the release of aldosterone, which prompts the kidneys to take up salt and water, narrows the arterioles, and raises blood pressure (13). Effects of ACE InDel polymorphisms are reported in various studies and populations (11, 14, 15). The ACE I allele leads to low ACE enzyme levels and is thought to be linked to better endurance performance. Research has demonstrated that people with the ACE D allele tend to exhibit greater amounts of strength and muscle mass, as well as a higher proportion of fast-twitch fibers. The ACE D allele has also been linked to athletes who are elite-strength (14).

The ACTN3 gene is located at 11q13.1 and is responsible for producing the α-actinin-3 protein. This protein, which is expressed in fast-twitch and type II fibers, is a sarcomere protein and is essential for producing forceful and intense muscle contractions. ACTN3 rs1815739 polymorphism is the result of cytosine-to-thymine exchange in exon 16 of the gene. A stop (X) codon is created in place of the arginine (R) codon, which was previously encoding amino acid 577 of the protein (16). This polymorphism causes ACTN3 deficiency in an individual. ACTN3 rs1815739 polymorphism is a strong candidate for impacting the performance of elite athletes performance (11, 17). The severity of α-actinin-3 deficiency (TT genotype) decreases muscle mass and diameter of fast-twitch fibers and increases the proportion of slow-twitch fibers (15).

In literature, there are some information about the effect of the given polymorphisms on different sports types; most of which have controversial results (19). In addition, the genomic profiles of the fitness athletes are restricted in this term. This report will be the first to have an association with the given polymorphisms and Turkish-based fitness athletes. We hypothesized the link between the given polymorphisms and the power/strength ability of the fitness athletes. Therefore the current study aimed to identify the distribution of ACE InDel and ACTN3 rs1815739 polymorphisms among sub-elite fitness athletes' and compare the results with sedentary people's genetic polymorphisms.

MATERIAL AND METHODS

Study Group and Ethical Consideration

Forty-one sub-elite male fitness athletes and the same number of sedentary males (as controls) were included in the study. The main inclusion criteria were the average training sessions of 4-5 days/week and

Table 2. Genotype distribution and allele frequency of ACTN3 rs1815739 polymorphism in sub-elite fitness athletes

	Genotype			*p* Value	Allelic Frequency		*p* Value
	CC	**CT**	**TT**		**C**	**T**	
Athletes (n=41)	14	24	3	**0,0313**	52	30	**0,0187**
Percentage	34,2%	58,5%	7,3%		63,4%	36,6%	
Control Group (n=41)	7	23	11		37	45	
Percentage	17,1%	56,1%	26,8%		45,1%	54,9%	

* The results were considered statistically significant if the p<0.05. The χ2 test was utilized to compare the results with the control group.

the ones who regularly train within the past 2 years. Eskişehir Osmangazi University, Clinical Research Ethics Committee approved the study protocol (Decision Date: 08.02.2016, No: 01) and the research was performed in line with the Declaration of Helsinki II. All participants signed a written consent form detailing the objectives and procedures of the study. This work was supported by the Scientific Research Organization of Bilecik Şeyh Edebali University (2015-02.BSEÜ.13-01).

Genotyping

DNA samples were isolated from peripheral blood samples using a commercial DNA isolation kit (Invitrogen, Van Allen Way, Carlsbad, CA, USA). Conventional A260/A280 ratio spectrophotometer values were used to determine the purity of the isolated DNAs. All the isolates had the results between 1.6- 2.0 and all were accepted to have the required purity for the genotyping process. DNA samples have been saved at −20 °C till used for genotyping. The ACTN3 rs1815739 polymorphism was determined using a Real-time PCR (Applied Biosystems StepOne™ Real-Time PCR, Foster City, CA, USA) method using isolated DNA material and the Taqman genotyping assays genotyping kit (Thermo Fisher Scientific Inc., Waltham, Massachusetts, USA). The commercially available primers for the amplification were as previously described (8). Genotyping was performed using 5 µL master mix, 3.50 µL H2O, 0.50 µL assay, and 1 µL (10 ng) DNA for a total of 10. The T (X) allele was determined with FAM primers and the C (R) allele was determined with VIC primers (Figure 1).

The polymerase chain reaction (PCR) was used to genotype the ACE InDel polymorphism from the isolated DNA sample. Briefly, the genotyping reaction was performed in a total volume of 50µL using dNTP concentration 0.5 mM, primer concentration 10 pmol, total DNA amount 100ng, 2U Taq DNA polymerase (Fermentas, Vilnius, Lithuania). The PCR process requires a preliminary denaturation at 95°C for 3 minutes, followed by 35 cycles that consist of 30 seconds at 95°C, 45 seconds at 53°, 1 minute at 72°C, and 10 minutes at 72°C after the last cycle applied as final elongation. The primers for the amplification were as previously described (20). Amplicons were examined using agarose gel electrophoresis with ethidium bromide (0.2g/mL) staining and then visualized under Ultraviolet (UV) light. A genotyping procedure was carried out involving a 490-bp band (representing the II genotype), a 190-bp band (indicative of the DD genotype), or a combination of both bands (indicative of the I/D genotype) (Figure 2).

Statistical Analysis

The SPSS software package 22 (SPSS Inc., Chicago, IL, USA) was used in the data analysis. The statistical significance of ACE and ACTN3 genes genotype distribution and I, D, C, and T allele frequencies were compared with the Chi-Square test, and the significance was tested at the p<0.05 level at 95% confidence interval.

RESULTS

In sub-elite fitness athletes (n=41), the numbers and percentages of ACE Indel polymorphism II, ID, and DD genotypes were 11 (26.8%), 16 (39.0%,) and 14 (34.2%), respectively. The D allele (53.7%) was counted with a higher percentage than the I allele (46.3%). The number and percentages of II, ID, and DD genotypes for the control group (n=41) were 16 (39.0%), 15 (36.6%,) and 10 (24.4%), respectively. In the control group, the I allele (57.3%) was counted with a higher percentage than the D allele (42.7%). In the statistical analysis between sub-elite fitness athletes and control groups, no statistical difference was found for ACE I/D polymorphism in terms of both genotype distribution (p=0.4438) and allelic

Table 3. Combined distribution of ACE InDel and ACTN3 rs1815739 polymorphisms in sub-elite fitness athletes.

***ACE* I/D**	***ACTN3* rs1815739**		
Polymorphisms, n (%)	**CC**	**CT**	**TT**
DD	6 (14,63%)	8 (19,51%)	-
ID	5 (12,20%)	9 (21,95%)	2 (4,88%)
II	3 (7,32%)	7 (17,07%)	1 (2,44%)

frequency (p=0.1596). ACE InDel polymorphism results are listed in Table 1.

In sub-elite fitness athletes (n=41), the numbers and percentages of ACTN3 rs1815739 polymorphism CC, CT, and TT genotypes were 14 (34.2%), 24 (58.5%), and 3 (7.3%), respectively. The C allele (63.4%) was counted with a higher percentage than the T allele (36.6%). The number and percentages of CC, CT, and TT genotypes for the control group (n=41) were 7 (17.1%), 23 (56.1%), and 11 (26.8%), respectively. In the control group, the T allele (54.9%) was counted with a higher percentage than the C allele (45.1%). A comparison of sub-elite fitness athletes and control groups showed that the ACTN3 rs1815739 polymorphism had a statistically significant difference in terms of genotype distribution (p=0.0313) and allelic frequency (p=0.0187). The outcomes of the ACTN3 rs1815739 variation are shown in Table 2.

DISCUSSION

Human strength and power are multifactorial concepts that are influenced by both multiple genes and environmental factors (9, 10). Resistance exercise is an effective way to build up skeletal muscle mass because it stimulates muscle protein synthesis (21). The link between individual genome on athletic ability is currently a subject of worldwide investigation. The amount of research on how the ACE and ACTN3 genes associate with the success of power athletes is still limited (4). The current research is a genetic case-control study conducted on Turkish fitness athletes. The novelty of the present study was the evaluation of the ACE InDel and ACTN3 rs1815739 polymorphisms on sub-elite fitness athletes.

ACE InDel polymorphism ID genotype and the ACTN3 rs1815739 CT genotypes are probably the preferred genotypes for Turkish fitness athletes (39.0%; 58.6%, respectively). To date, ACE and ACTN3 polymorphisms had been associated with power, strength, and endurance in determining athletic performance. Those findings suggest that the ACE I allele was linked to endurance, while the D allele was associated with sprinting and power/strength performance. Additionally, ACTN3 CC and CT genotypes were found to be connected to elite power/strength athletes (22, 23). In the present study, we detected no statistically significant difference in the ACE InDel polymorphism (Table 1) between sub-elite fitness athletes and sedentary people (p=0.4438). However, we detected a statistically significant difference in the ACTN3 rs1815739 polymorphism (p=0.0313). Therefore, our results do not support the hypothesis that the ACE InDel polymorphism is related to power/strength ability. However, when the literature is examined, it was that the relationship between ACE and ACTN3 genes and sportive performance is not clear and more studies are needed.

Polat et al. (24) analyzed the same polymorphisms in 11 Turkish bodybuilders. They reported that CT (54%) genotype was higher than the CC (45%) genotype in ACTN3 polymorphism, and the TT genotype was not detected in their cohort. For the ACE I/D polymorphism, 73% of bodybuilders had ID, 18% had II, and 9% had DD genotypes. They highlighted the significance of ACE and ACTN3 polymorphisms associated with stamina in bodybuilders. These findings were in agreement with our findings in the terms of genotype percentage, suggesting the importance of ethnicity in selected polymorphisms.

Muhan et al. (25) investigated the determination of ACTN3 rs1815739 polymorphism in football players and the relationship between the genotypes of football players and their positions. The TT genotype (55.0%) and T allele (72.5%) were found to be higher in football players, while the CT genotype (53.9%) and T allele (53.3%) was higher in the control group. It was determined that midfielders who require endurance are mostly in the TT genotype, while the sprinter strikers are in the CC genotype. Due to the

same ethnicity, nonsimilar results of ACE InDel polymorphism with the current findings may indicate the advantageous the genetic variations in different sports.

Kim et al. (26), reported that they found more DD genotype and D allele in ACE I/D polymorphism in elite strength athletes compared to the control group. Papadimitriou et al., (27), 200 and 400 m. in their study with elite male sprinters compared the sprint times of the athletes with their genotypes. It was revealed that athletes who had the ACE DD genotype in 200 m events had shorter individual running times than those who had the ACE II genotype. Unlike our results, which showed the superiority of the ID genotype, the results of the study supported most of the previous findings.

In another cohort, Scott et al. (11) found that the ACE I/D polymorphism does not have a significant effect on the performance of 114 Jamaican and 113 American sprinter athletes in their study. In a study of 32 female non-elite Turkish athletes, Çam et al. (28) examined the relationship between athletes sprinting and middle-distance running and ACE I/D polymorphism. They found that there were no major variations between genotypes of the ACE I/D polymorphisms in connection to either sprint or middle-distance performance. Similar findings Shahmoradi et al. (29) and Wang et al., (30) both reported that short-distance swimmers have a greater abundance of ACE I alleles compared to the control group.

Studies have revealed the relationship between athletic performance and factors such as ability selection and training response between the ACTN3 gene (31, 32). Some research has indicated that strength athletes have a higher prevalence of the ACTN3 gene CC genotype and a lower prevalence of the ACTN3 TT genotype than the control group (17, 22, 23). Elite wrestlers and competitive bodybuilders had more CC genotypes compared to the control group (33). Yang et al. (23) reported that sprinters had more CC (50%, 30%) and less CT (45%, 52%) and TT (6%, 18%) genotypes than controls. Elite athletes who focused on power-based sports had a higher frequency of the C allele than the control group (34). Some studies did not support the relationship between ACTN3 rs1815739 polymorphism TT genotype and endurance performance in elite strength athletes (29, 30). On the other hand, there are also studies reporting a relationship between ACTN3 rs1815739 polymorphism and power performance in athletes (31,32). Our findings showed the high frequency of CT genotype in fitness athletes, which does not support the previous studies.

There are some previous studies that suggest the unsufficient role of ACTN3 rs1815739 polymorphism on exercise performance. Norman and colleagues (2009) reported that there was no relationship between the ACTN3 gene and power output, fatigue, or power features. They contended that alpha actors have little to no influence on deciding muscle fiber type (31). Contrary to studies reporting that ACTN3 is the "speed gene" in the literature, Lucia et al. (39), discovered that a Spanish long jumper who had participated in the Olympics twice had the TT genotype for the ACTN3 rs1815739 polymorphism. In a similar finding, Druzhevskaya and his friends reported that the world-recorded Russian hammer shooter had TT genotype in ACTN3 rs1815739 polymorphism in a study in 2008.

Strengths and Limitations

The previous studies were mostly conducted on athletes like sprinters- marathons, and football players; there is not enough information about fitness athletes in terms of genetic research. In the present study, ACE ID and ACTN3 CT genotypes were associated with an advantage for fitness. But our cohort did not reveal any explanation in terms of alleles. The low athletes' number and the lack of biochemical or physical parameters are the main limitations of the present study.

CONCLUSION

In conclusion, to have a more predictable evaluation of the effect of the given polymorphisms and athletic performance, more studies are needed. In addition, we believe that this first report will help to further investigate the relationship between ACE and ACTN3 genes and physical fitness in athletes.

Acknowledgement: None.

Author contribution: All authors contributed equally to the process.

Conflict of interests: No conflict of interest was declared by the authors.

Ethical approval: Eskişehir Osmangazi University, Clinical Research Ethics Committee approved the study protocol (Decision Date: 08.02.2016, No: 01)

Funding: This work was supported by the Scientific Research Organization of Bilecik Şeyh Edebali University (2015-02.BSEÜ.13-01).

Peer-review: Externally peer-reviewed.

REFERENCES

1. Corak A, Kapıcı S, Sercan C, Akkoç O, Ulucan K.. A pilot study for determination of anxiety related SLC6A4 promoter "S" and "L" alleles in healthy Turkish athletes. Cellular and Molecular Biology 2017; 63(5): 29-31.
2. Melián Ortiz A, Laguarta-Val S, Varillas-Delgado D. Muscle work and its relationship with ACE and ACTN3 polymorphisms are associated with the improvement of explosive strength. Genes 2021;12(8): 1177.
3. Ulucan K, Topal ES, Aksulu BK, Yaman B, Çiftci İC, Bıyıklı T. Atletic Performance, Genetics and Gene Doping. IKSST J 2015;7(2):58-62.
4. Gineviciene V, Jakaitiene A, Aksenov MO, Aksenova AV, Druzhevskaya AM, Astratenkova IV, Utkus A. Association analysis of ACE, ACTN3 and PPARGC1A gene polymorphisms in two cohorts of European strength and power athletes. Biology of Sport 2016;33(3):199-206.
5. Bulgay C, Kasakolu A, Kazan HH, Mijaica R, Zorba E, Akman O, Bayraktar I, Ekmekci R, Koncagul S, Ulucan K, et al. Exome-Wide Association Study of Competitive Performance in Elite Athletes. Genes 2023; 14(3):660.
6. 6.Semenova EA, Hall ECR, Ahmetov II. Genes and Athletic Performance: The 2023 Update. Genes 2023;14(6):1235.
7. Dogan M, Aslan BT, Ulucan K. Comparison of potential biomarker, ACTN3 rs1815739 polymorphism, for athletic performance of Turkish athletes. Cellular and Molecular Biology 2022;68(5):54-59.
8. Eroğlu O, Zileli R, Ali Nalbant M, Ulucan K. Prevalence of alpha actinin-3 gene (ACTN3) R577X and angiotensin converting enzyme (ACE) insertion/deletion gene polymorphisms in national and amateur Turkish athletes. Cellular and Molecular Biology 2018;64(5):24-28.Ahmetov II, Fedotovskaya ON. Current progress in sports genomics. Advances in Clinical Chemistry 2015;70:247-314.
9. Hughes DC, Day SH, Ahmetov II, Williams AG. Genetics of muscle strength and power: polygenic profile similarity limits skeletal muscle performance. Journal of Sports Sciences 2011;29(13):1425-1434.
10. Scott RA, Irving R, Irwin L, Morrison E, Charlton V, Austin K, Pitsiladis YP. ACTN3 and ACE genotypes in elite Jamaican and US sprinters. Medicine & Science in Sports & Exercise 2011;42(1):107-112.
11. Woods DR, Humphries SE, Montgomery HE. The ACE I/D polymorphism and human physical performance. Trends in Endocrinology & Metabolism 2000;11(10):416-420.
12. Goessler KF, Cornelissen VA, de Oliveira EM, de F Mota G, Polito MD. ACE polymorphisms and the acute response of blood pressure to a walk in medicated hypertensive patients. Journal of the Renin-Angiotensin-Aldosterone System 2015;16(4):720-729.
13. Pescatello LS, Kostek MA, Gordish-Dressman H, Thompson PD, Seip RL, Price TB, Hoffman EP. ACE ID genotype and the muscle strength and size response to unilateral resistance training. Medicine & Science in Sports & Exercise 2006;38(6):1074-1081.
14. Drozdovska SB, Dosenko VE, Ahmetov II, Ilyin VN. The association of gene polymorphisms with athlete status in Ukrainians. Biology of Sport 2013;30(3):163-167.
15. Ulucan K, Bayyurt GM, Konuk M, Güney AI. Effect of alpha-actinin-3 gene on trained and untrained Turkish middle-school children's sprinting performance: a pilot study. Biological Rhythm Research 2014;45(4):509-514.
16. Eynon N, Ruiz JR, Femia P, Pushkarev VP, Cieszczyk P, Maciejewska-Karlowska A, Lucia A. The ACTN3 R577X polymorphism across three groups of elite male European athletes. PLoS ONE 2012;7(8):e43132.
17. Vincent B, De Bock K, Ramaekers M, Van den Eede E, Van Leemputte M, Hespel P, Thomis MA. ACTN3 (R577X) genotype is associated with fiber type distribution. Physiological Genomics 2007;32(1):58-63.
18. Ulucan K. Literature review of Turkish sportsmen in terms of ACTN3 R577X polymorphism. Clinical and Experimental Health Sciences 2016; 6(1), 144-147.
19. Guney AI, Ergec D, Kirac D, Ozturhan H, Caner M, Koc G, Kaspar K, Ulucan K, Agirbasli M. Effects of ACE polymorphisms and other risk factors on the severity of coronary artery disease. Genet Mol Res 2013;12:6895–6906.
20. Damas F, Phillips S, Vechin FC, Ugrinowitsch C. A review of resistance training-induced changes in skeletal muscle protein synthesis and their contribution to hypertrophy. Sports Medicine 2015;45:801-807.

21. Cieszczyk P, Sawczuk M, Maciejewska-Karlowska A, Ficek K. ACTN3 R577X polymorphism in top-level Polish rowers. Journal of Exercise Science & Fitness 2012;10(1):12-15.
22. Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Easteal S, North K. ACTN3 genotype is associated with human elite athletic performance. The American Journal of Human Genetics 2003;73(3): 627-631.
23. Polat T, Dogan CS, Dogan M, Akcay T, Ulucan K. Distribution of α-actinin-3 rs1815739 and angiotensin-1 converting enzyme InDel polymorphisms in Turkish bodybuilders. Biomedical Reports 2020;13(6):1-1.
24. Muhan A, Polat T, Yılmaz ÖÖ, Tacal Aslan B, Ulucan K. Investigation of ACTN3 rs1815739 polymorphism, physical characteristics, and position—relation in football players: A team sample. Research in Sport Education and Sciences. 2023;25(1):14-18.
25. Kim CH, Cho JY, Jeon JY, Koh YG, Kim YM, Kim HJ, Kim C. ACE DD genotype is unfavorable to Korean short-term muscle power athletes. International Journal of Sports Medicine 2010;31(01):65-71.
26. Papadimitriou ID, Lucia A, Pitsiladis YP, Pushkarev VP, Dyatlov DA, Orekhov EF, Eynon N. ACTN3 R577X and ACE I/D gene variants influence performance in elite sprinters: a multi-cohort study. BMC Genomics 2016;17(1):1-8.
27. Cam S, Colakoğlu M, Colakoğlu S, Berdeli A. The ACE I/D gene polymorphism and physical performance in a non-elite female cohort. Turkish Journal of Sports Medicine 2005;40(1):1-8.
28. Shahmoradi S, Ahmadalipour A, Salehi M. Evaluation of ACE gene I/D polymorphism in Iranian elite athletes. Advanced Biomedical Research 2014;3:207.
29. Wang G, Mikami E, Chiu LL, De Perini A, Deason M, Fuku N, Galloway SD. Association analysis of ACE and ACTN3 in elite Caucasian and East Asian swimmers. Medicine and Science in Sports and Exercise 2013;45(5):892-900.
30. Norman B, Esbjornsson M, Rundqvist H, Osterlund T, Von Walden F, Tesch P. A. Strength, power, fiber types, and mRNA expression in trained men and women with different ACTN3 R577X genotypes. Journal of Applied Physiology 2009;106(3):959-965.
31. Gómez-Gallego F, Santiago C, González-Freire M, Muniesa CA, Del Valle MF, Perez M, Lucia A. Endurance performance: genes or gene combinations?. International Journal of Sports Medicine 2009;30(01):66-72.
32. Djarova T, Watson G, Basson A, Grace J, Cloete J, Ramakoaba A. ACTN3 and TNF gene polymorphism association with C-reactive protein, uric acid, lactate and physical characteristics in young African cricket players. Afr J Biochem Res 2011;5(1):22-27.
33. Papadimitriou ID, Papadopoulos C, Kouvatsi A, Triantaphyllidis C. The ACTN3 gene in elite Greek track and field athletes. International Journal of Sports Medicine 2008;29(04):352-355.
34. Yang N, Macarthur D, Wolde B, Onywera VO, Boit MK, Wilson RH, North K. ACTN3 genotype ıs not associated with elite endurance athlete status in Ethiopians and Kenyans. Medicine & Science in Sports & Exercise. 2005;37(5):472.
35. Schneider AJ, Rupert JL. Constructing winners: The science and ethics of genetically manipulating athletes. Journal of the Philosophy of Sport 2009;36(2):182-206.
36. Druzhevskaya AM, Ahmetov II, Astratenkova IV, Rogozkin VA. Association of the ACTN3 R577X polymorphism with power athlete status in Russians. European Journal of Applied Physiology 2008;103(6):631-634.
37. Fiuza-Luces C, Ruiz JR, Rodríguez-Romo G, Santiago C, Gómez-Gallego F, Yvert T, Lucia A. Are 'endurance'alleles 'survival'alleles? Insights from the ACTN3 R577X polymorphism. PloS One 2011;6(3):e17558.
38. Lucia A, Oliván J, Gómez-Gallego F, Santiago C, Montil M, Foster C. Citius and longius (faster and longer) with no α-actinin-3 in skeletal muscles?. British Journal of Sports Medicine 2007;41(9):616-617.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 327-335
https://doi.org/10.30621/jbachs.1283363
RESEARCH ARTICLE

EFFECT OF INSTRUMENT ASSISTED SOFT TISSUE MOBILIZATION IN PATIENTS WITH CERVICAL DISC HERNIATION: A RANDOMIZED CONTROLLED TRIAL

Yasin Algantekin[1], Mehmet Ozkeskin[2], Adem Akturk[3,4], Emre Şenocak[5]

[1] Special Ilgi Hospital, Department of Physical Therapy and Rehabilitation, Istanbul, Turkey
[2] Ege University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Izmir, Turkey
[3] Istanbul Gelisim University, Vocational School of Health Services, Department of Podology, Istanbul, Turkey
[4] Medilife Beylikdüzü Hospital, Department of Physical Therapy and Rehabilitation, Istanbul, Turkey
[5] Karadeniz Technical University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Trabzon, Turkey

ORCID: Y.A. 0000-0003-3951-2313; M.O. 0000-0002-6892-0108; A.A. 0000-0002-2487-5720; E.S. 0000-0003-3677-9813

Corresponding author: Mehmet Ozkeskin, **E-mail:** mehmet.ozkeskin76@gmail.com
Received: 14.04.2023; **Accepted:** 26.02.2024; **Available Online Date:** 31.05.2024

Cite this article as: Algantekin Y, Ozkeskin M, Akturk A, Senocak E. Effect of Instrument Assisted Soft Tissue Mobilization in Patients with Cervical Disc Herniation: A Randomized Controlled Trial. J Basic Clin Health Sci 2024; 8: 327-335.

ABSTRACT

Purpose: The effects of Instrument Assisted Soft Tissue Mobilization (IASTM) on cervical disc herniation (CDH) have not been extensively studied. The study aimed to investigate the effect of the IASTM technique on pain, functionality and psychology in CDH.
Methods: A two-armed randomized controlled trial was carried out with 24 patients with CDH. Participants were randomized into two groups: conventional physiotherapy (n=12) and IASTM plus conventional physiotherapy (n=12). A conventional rehabilitation consists of a hot pack, electrotherapy, and exercises five days a week for four weeks. IASTM technique has been used for two sessions per week for four weeks. Patients were assessed with Visual Analogue Scale (VAS), Neck Disability Index (NDI), Copenhagen Neck Functional Disability Scale (CNFDS), Hospital Anxiety and Depression Scale (HADS).
Results: Both groups had improvements in VAS scores ($p<0.05$). IASTM group yielded more reduction in resting and activity pains ($p_{resting}=0.001$, $p_{activity}=0.001$). Disability scores of both groups improved ($p<0.05$). However, no difference was encountered between the groups regarding function and disability ($p>0.05$). Both the intervention and control groups showed a decrease in anxiety and depression symptoms ($p<0.05$). The anxiety and depression score of the intervention group yielded better results than the control group ($p<0.05$).
Conclusion: IASTM improved patients' rest and activity pain, anxiety and depression symptoms. On the other hand, IASTM provided advancement on function and disability scores simply as effective as conventional physiotherapy.

Keywords: Anxiety, cervical pain, disability, instrument-assisted soft tissue mobilization

INTRODUCTION

Neck pain is a significant public health problem (1). Approximately 48.5% of people experience neck pain at some point in lifespan (2). Cervical disc pathologies are the most common factor triggering neck pain (3). Therefore, patients with neck pain should be handled

in terms of biomechanical features of the anatomical region (4). The cervical region has less stability and greater mobility than other spinal cord segments. This specific condition causes an increase in both compression and rotational forces on the intervertebral discs. Increased compression and rotational forces protrude the nucleus pulposus to the contralateral side, promoting degeneration (5, 6). In addition, external mechanical factors such as overuse of spinal cord segments, posture disorders, and repetitive traumas directly affect disc mechanics and cause disc degeneration (7). Cadaver studies determined the existence of free nerve endings in the annular part of degenerated discs. This anatomical finding helps to further understand the mechanism of pain formation due to cervical disc degeneration (8).

There is a direct relationship between chronic pain and the functional status of individuals with cervical disc herniation (9). Long-term neck pain causes inhibition in deep flexor and extensor muscle groups, resulting in decreased functional capacity (10). Depending on the decreased function, basic and instrumental activities of daily living of individuals might be affected (11). Correspondingly, possible secondary psychosocial disorders, including anxiety and depression, could entail more ominous actual clinical results (12).

Various treatment modalities, including medication, invasive techniques, and conventional physiotherapy, are commonly applied to heal these frequent symptoms in patients with cervical disc herniation (13, 14). In recent years, "Instrument-Assisted Soft Tissue Mobilization (IASTM)" has become a trending technique with a positive effect on soft tissue pathologies (15). Recent studies have been demonstrated the effect of IASTM on cervical symptoms, including cervicogenic pain, pain threshold, disability muscle tone (16-18). IASTM is a highly applicable and cost-effective technique in low back and neck pain (15, 19). However, studies on the effect of the IASTM in neck pathologies are limited. The physical and psychosocial effects of IASTM on cervical disc herniation have not been extensively studied. A holistic consideration of the psychological state with the basic physical clinical parameters (e.g., pain, function) would provide essential clinical practical output. The aim of the study was to investigate the effectiveness of the IASTM technique on pain, functionality and psychosocial status in patients with cervical disc herniation.

METHODS

Study Design

A randomized controlled trial was conducted in *"blinded for peer review"*. The study was reported regarding the "Consolidated Standards of Reporting Trials (CONSORT) stages and SPIRIT (Statement of Recommendations for Interventional Trials)" guidelines (20). The study protocol was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Decision Date: 03.05.2019, No: 09.2019.491). The study was carried out in accordance with the ethical principles and the Helsinki Declaration. This research was also registered to the "clinicaltrials.gov" (Registration No: NCT04803669)

Participants

Twenty-eight patients who applied to the physical therapy outpatient clinic with cervical disc herniation diagnosis were enrolled in the study. Inclusion criteria of the study were; (1) a radiological diagnosis of bulging or protrusion, (2) pain score >2 regarding the visual analog scale, and (3) neck pain >3 months. The exclusion criteria of the study were; (1) a history of neck-shoulder surgery/injury, (2) cortisone usage, (3) extrude/sequestered disc, (4) a history of fibromyalgia. After the eligibility procedure, 24 patients were randomized into two groups: conventional physiotherapy (n=12) and conventional physiotherapy plus IASTM group (n=12). All included patients completed the follow-up process and enrolled in the statistical analysis stage. The CONSORT flow chart of the study is given in Figure 1.

Recruitment process

The steps of the recruitment procedure are as follows: All individuals are informed about the objectives of the program (e.g., intervention, duration, assessments, potential risks). Documented, and a verbal statement was given. After the consent was obtained from the individuals, the voluntary consent form was signed. The study started after diagnosing individuals with cervical disc herniation via radiological evaluations by a specialist physician. The patients were directed to a physiotherapist from the physical therapy outpatient clinic.

Randomization and blinding

A simple randomization method was used in this trial.

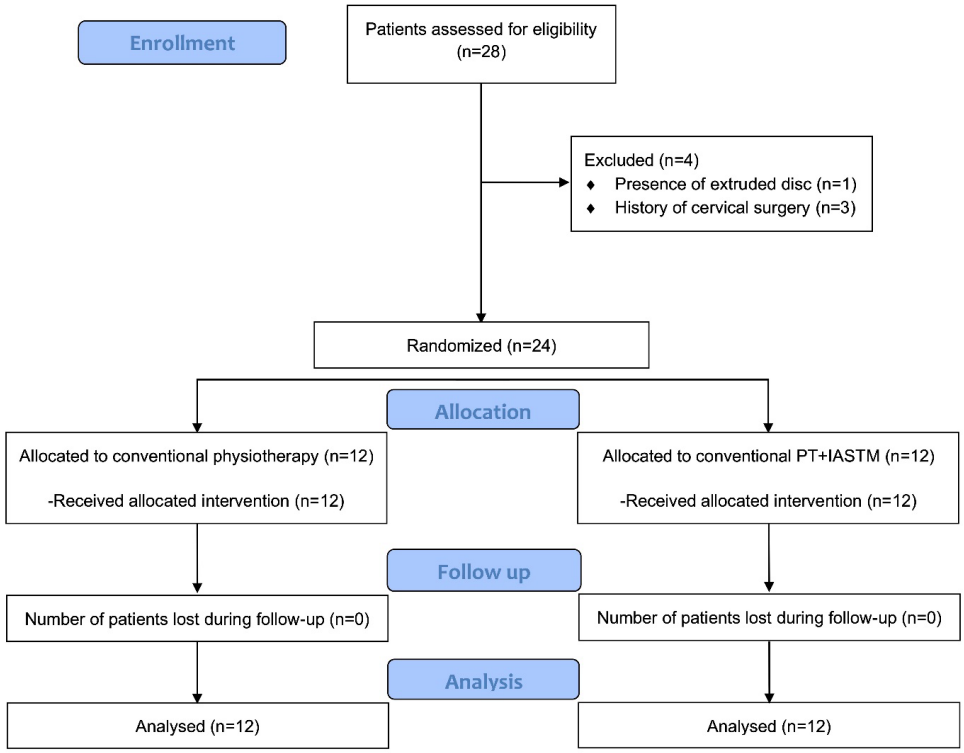


Figure 1. CONSORT FLOW CHART OF THE TRIAL

Participants were randomized using the sealed envelope method and divided into two groups. The blinding of the therapist was not possible due to the essence of the study. On the other hand, evaluator blinding was not possible due to the existing facilities of the setting.

Sample size

G-Power 3 was used to calculate the required minimum sample size of the study (21). Regarding the visual analog scale based difference values of the mean and standard deviation score of the referenced similar study (17), the effect size was determined as 1.09. Consequently, a total of 24 patients (minimum 12 individuals in each group) were calculated with a power of 0.80 and a confidence interval of 0.05.

Interventions

Conventional physiotherapy group (control group):

"The conventional treatment program consisted of a hot pack, electrotherapy agents, and an exercise program (22). The heat application was applied to the neck and upper back area by wrapping hot water bags and a towel for 25 minutes. The electrotherapy program consisted of transcutaneous electrical stimulation (TENS) and ultrasound (US). Conventional TENS (Acu Tens, 100 Hz, 200 ms, 1-100 mA) was applied for 25 minutes with two channels and four electrodes on the neck and upper trapezius muscle. The current intensity was adjusted not to cause disturbance in the patient. The US technique was applied (1-2.5 W/cm2, 1 MHz) for 5 minutes. The exercise program was applied after every electrotherapy session for 25 minutes under the supervision of a physiotherapist. This exercise program consisted of deep flexor and extensor strengthening, posture, stretching, and mobilization exercises with iso-flex bands."

Conventional physiotherapy plus IASTM group (intervention group):

"The identical conventional physiotherapy protocol was applied to the intervention group. IASTM was performed with a stainless-steel instrument (PTR medical, Turkey) using the brushing technique (short brushing made at an angle of 30°) to the superficial and deep fascia and muscle fibers between the C1-T1 neck-shoulder segments (23). A water-based gel was used to prevent the adverse effects that may occur due to friction in the tissue. This technique was applied in two weekly sessions and 5 minutes each for four weeks, totaling eight sessions (16)."

Figure 2. IASTM intervention illustration: the application material and technique

Assessments

"All patients were evaluated at baseline and four weeks after the intervention. Sociodemographic data form was used to record the patient's gender, age, body mass index, onset of pain, and herniation types.

Visual Analog Scale (VAS): VAS is a practical and reliable assessment used to determine patients' pain severity. Scoring is accomplished between 0-10 points. "0" represents the absence of pain, and "10" represents the maximum pain. The time of neck pain onset, resting, and activity pain was questioned using the VAS (24).

Neck Disability Index (NDI): NDI has been prepared in 10 main sections as pain intensity, self-care, lifting, reading, headache, attention, working, driving, sleeping and recreation. The patients included in the study are asked to give a score between 0 (no disability) and 5 (disability) for each item. The total score varies between 0 (no disability) and 50 (disability). Telci-Aslan et al. Turkish validity and reliability was performed by (25).

Copenhagen Neck Functional Disability Scale (CNFDS): CNFDS evaluates the disability of patients due to neck pain (26). The scale consists of 15 items. Items are answered as "Yes, No, Sometimes" and scored between 0 to 2 points. Those who answer "Yes" to the first five questions of the scale receive "0", those who answer "sometimes" get "1 point," and those who answer "no" get "2 points". For the other ten questions, scoring is done in reverse. The total score is between 0 and 30 points. If the total score is "0", it means "no neck pain and disability," and "30" means "maximum neck pain and disability" (27).

Hospital Anxiety and Depression Scale (HADS): HADS includes anxiety and depression subscales. The scale consists of 14 items in total. Even-numbered items assess depression, and odd-numbered items assess anxiety. The answers are in a four-point Likert format and are scored between 0 to 3. The cut-off point for the anxiety subscale of the scale is 10, and 7 points for the depression subscale (28)."

Statistical Analysis

In classifying the data obtained in the study, qualitative and quantitative statistical methods were evaluated with the "Statistical Package for the Social Sciences (SPSS) 11.0 statistical program", and significance was assessed at $p<0.05$ level. The normality distributions of the data were analyzed with the "Kolmogorov-Smirnov test". "The Mann-Whitney U" test was used because the data between groups did not show normal distribution. The "Wilcoxon Signed Rank Test" was used for in-group comparison. "Fisher's exact chi-square test" was used to analyses non-quantitative data.

Whether the results were clinically significant or not was determined according to Cohen's effect size calculation. The effect size for each variable was calculated based on the average changes in the results obtained before and after treatment. This calculation suggests the effect size as small 0.2, medium 0.5, and large 0.8.

RESULTS

The median age of the individuals in the control and intervention groups were 34.50 and 40 years, respectively. Body Mass Index (BMI), gender, pain

Table 1. Baseline characteristics of the patients

	Control	Intervention	p
Age	34.50	40.00	0.285
BMI	25.34	28.51	0.028
Pain Onset	5.50	18.00	0.087
Gender (n,			
Female	5 (41.70)	6 (50.00)	0.500
Male	7 (58.30)	6 (50.00)	
Herniation			
Bulging	2 (16.66)	1 (8.33)	0.381
Protrusion	10 (83.33)	11 (91.66)	

n: number of individuals, BMI: body mass index

onset and clinical features of herniation are presented in Table 1. There was no difference between groups regarding baseline characteristics ($p>0.05$), except BMI ($p=0.028$).

Resting and activity pain decreased in both groups at the end of the intervention ($p<0.05$). Also, the pain score of the intervention group improved better than the control group ($p_{rest}=0.001$, $p_{activity}=0.001$). The change occurring during both rest pain and activity pain was clinically in favor of the IASTM group (Cohen's $d_{resting}$: 2.12; Cohen's $d_{activity}$: 1.86). Disability scores of both groups improved ($p<0.05$). However, no difference was encountered between the groups regarding function and disability ($p>0.05$). Both the intervention and control groups showed a decrease in anxiety and depression symptoms ($p<0.05$). The anxiety and depression score of the intervention group yielded better results than the control group ($p=0.015$) and effect sizes were shown at Table 2.

DISCUSSION

The present study examined the effects of IASTM in patients with cervical disc herniation on pain, disability, anxiety, and depression. The literature suggests that IASTM improves pain severity and disability levels in patients with musculoskeletal disorders (29,31). The physical effect of IASTM has been widely demonstrated (15, 29-31). However, its effect on cervical disc herniation-related pain and function is not well-studied. In addition, our study is unique in terms of evaluating the psychosocial effect of IASTM on cervical disc herniation. According to the present study results, IASTM thoroughly improved patients' rest and activity pain, depression and anxiety symptoms. On the other hand, IASTM provide advancement on function and disability scores simply as effective as conventional physiotherapy.

First, the improvement in resting and activity pain in the 4-week follow-up brought along the expectation of also on the functional status. However, the additional pain-related gains of IASTM did not improve functional status and disability. This outcome might be due to our trial's short to medium-term evaluation period. Longer-term monitoring and intervention may be required to observe the intervention's effect on daily living activities. On the other hand, the additional advantage of IASTM was observed in terms of depression and anxiety score. However, more comprehensive psychological screening tests and more detailed analyzes for the evaluation of psychological state can provide precise clinical outcomes (32).

IASTM applications are widely used as an alternative method in musculoskeletal disorders (15-17, 29-31, 33). Lauche et al. and Abdelhamid et al. emphasized the effect of IASTM therapy on pain in individuals with chronic neck pain (29, 34). On the other hand, Mylonas et al. reported the significant positive effect of IASTM on posture and function in patients with neck pain (31). These results provide the further benefits of IASTM on pain, posture and function. However, our study only proved the clinical effectiveness of IASTM in terms of pain and depression. The disability and postural status of Mylonas and colleagues may also have resulted in greater clinical output by performing combined IASTM and neuromuscular exercises. Examining the psychological state in our study provides a unique advantage. In particular, the decrease in pain intensity may have led to improvements in depression and anxiety (35).

Crothers et al. and El-Hafez et al. emphasized no additional advantage of IASTM on pain and disability in individuals with thoracic spinal pain and myofascial pain syndrome, respectively (15, 16). Emshi et al. focused on the positive effect of IASTM on clinical symptoms such as pain severity, range of motion and disability (36). On the other hand, Erden et al. also applied IASTM to the trapezius muscle of patients with myofascial pain syndrome and noted a decrease in trigger point pain (37). This inflammatory process causes the blood supply of the zone and increases fibroblastic activity. Thus, collagen synthesis and maturation in the soft tissue are facilitated, and the

Table 2. Comparison of the results between the groups (median values)

		Control (n=12)	IASTM (n=12)	p[a]	d
VAS-at rest	Baseline	6.50	8.00	0.746	
	6. week	6.00	3.00	0.001	2.12
	p[b]	0.003	0.002	-	
VAS-at activity	Baseline	7.50	7.50	0.500	
	6. week	6.00	3.50	0.001	1.86
	p[b]	0.002	0.003	-	
CNFDS	Baseline	14.00	18.50	0.046	
	6. week	8.00	6.00	0.384	-
	p[b]	0.002	0.002	-	
NDI	Baseline	17.50	21.00	0.418	
	6. week	10.50	7.00	0.258	-
	p[b]	0.002	0.002	-	
HADS-Anxiety	Baseline	10.00	11.00	0.601	
	6. week	7.00	7.00	0.044	0.44
	p[b]	0.003	0.002	-	
HADS-Depression	Baseline	10.50	9.00	0.595	
	6. week	8.00	4.50	0.015	0.30
	p[b]	0.003	0.002	-	

[a]: Wilcoxon Signed-Rank Test, [b]: Mann-Whitney U Test, d: Cohen's effect size, IASTM: Instrument-assisted soft tissue mobilization, CNFDS: Copenhagen Neck Functional Disability Scale, NDI: Neck Disability Index, HADS: Hospital Anxiety and Depression Scale, VAS: Visual Analog Scale.

healing process is supported (38-40). This physiological effect may have resulted in positive gains. The application method of the IASTM technique, in which different results were observed in studies on the neck and its circumference, is another issue that should be addressed in clinical effectiveness. The positive effect of the brushing technique we used in our study, especially on pain, should also be considered.

Studies have reported a strong correlation between neck pain and disability (41). Pain intensity is a dimension of disability (42). This technique reduces pain and disability by acting on the active myofascial trigger points of the upper trapezius muscle (36). As a result of our study, it was observed that the disability levels of the patients decreased. The decrease in pain after treatment may have affected disability levels.

IASTM was reported to effectively reduce pain, especially in patients with nonspecific low back pain (43). Zlatkov et al. also emphasized the effectiveness of IASTM on pain and disability in low back pain patients (33). It is noticed that similar results with the neck region are also observed in low back pain. However, there is a lack of results related to evaluating psychological status in chronic low back pain. In this respect, our study is essential in terms of revealing the effect of IASTM on psychosocial status, including diverse spinal conditions.

Chronic pain negatively affects the workforce, social isolation, quality of life, and psychological health (44). Different physiotherapy modalities used in pain treatment aim to improve quality of life, regulate pain, and reduce anxiety and depression complaints (45). In our study, conventional methods and the IASTM protocol, in addition to these methods, caused a decrease in anxiety and depression scores. However, it is proposed that it would be more appropriate to evaluate anxiety and depression with more comprehensive assessment methods in individuals with chronic neck pain in future studies.

Limitations

The limitations of the study should be handled. In this study, the evaluation of the joint range of motion of the cervical region might be appropriate to support

the changes in pain and disability parameters. Also, the HADS scale we used for anxiety and depression included questions about the patient's psychological complaints, preventing the evaluation of physical factors' effects on anxiety and depression. Another limitation concerns the long-term effects of the study. The long-term effects of the IASTM technique on parameters such as pain intensity and disability are unknown. In our study, we evaluated the short-term effectiveness of the technique. Evaluation of the technique's long-term effect will help reveal the actual effect. Long-term follow-up studies can also be a reference for cost-effectiveness analysis studies of treatment. On the other hand, some methodological limitations should be acknowledged. The lack of blinding in the study may suggest measurement-based bias problems. On the other hand, in terms of baseline characteristics, there is a possibility that a significant difference between the groups in BMIs may disrupt the homogeneity. However, we can express that our results provide critical clinical outcomes since BMI does not primarily affect clinical status in cervical disc herniation.

CONCLUSION

According to the results of our study, the IASTM protocol was found to be effective on pain severity and depression in patients with cervical disc hernia. However, the same positive effects were not observed on function and anxiety. It would be beneficial for physiotherapists to add the method to conventional physiotherapy programs as an alternative method since it is low cost, accessible, practical, easily tolerated by the patient, and has high clinical benefits.

Acknowledgements: None.
Author Contributions: Concept development: YA, MÖ; Literature search: YA, MÖ; Design: YA, MÖ; Recruitment: YA, AA; Interventions and participant management: YA, AA; Data collection: YA, AA; Data analysis: YA, MÖ; Manuscript preparation: YA, MÖ, AA, EŞ; Commented/edited final manuscript: YA, MÖ, AA, EŞ.
Conflict of Interest: The authors report no conflicts of interest and certify that no funding has been received for this study and/or preparation of this manuscript.
Ethical Approval: The study protocol was approved by the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Decision Date: 03.05.2019, No: 09.2019.491). The study was carried out in accordance with the ethical principles and the Helsinki Declaration. Informed consents of the patients were obtained. This research was also registered to the "clinicaltrials.gov" (Registration No: NCT04803669)
Funding: None.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Vassilaki M, Hurwitz EL. Insights in public health: perspectives on pain in the low back and neck: global burden, epidemiology, and management. Hawai'i Journal of Medicine & Public Health. 2014;73(4):122.
2. Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: a systematic critical review of the literature. European spine journal. 2006;15(6):834-48.
3. Peng B, DePalma MJ. Cervical disc degeneration and neck pain. Journal of pain research. 2018;11:2853.
4. Whiting WC, Zernicke RF. Biomechanics of musculoskeletal injury: Human Kinetics; 2008.
5. Papadakis M, Sapkas G, Papadopoulos EC, Katonis P. Pathophysiology and biomechanics of the aging spine. The open orthopaedics journal. 2011;5:335.
6. Frost BA, Camarero-Espinosa S, Foster EJ. Materials for the spine: anatomy, problems, and solutions. Materials. 2019;12(2):253.
7. Choi W-H. The Effects of the Cervical Deep Muscle Flexion Exercises on Pain and Cervical Function in Patients with Chronic Cervical Pain. Journal of Korean Society for Neurotherapy. 2019;23(1):55-9.
8. Yang L, Yang C, Pang X, Li D, Yang H, Zhang X, et al. Mechanoreceptors in diseased cervical intervertebral disc and vertigo. Spine. 2017;42(8):540-6.
9. Pampati K, is an Interventional IDM, Manchikanti L. A randomized, double-blind, active control trial of fluoroscopic cervical interlaminar epidural injections in chronic pain of cervical disc herniation: results of a 2-year follow-up. Pain Physician. 2013;16:465-78.
10. Amiri-Arimi S, Bandpei MAM, Rezasoltani A, Javanshir K, Biglarian A. Asymmetry of cervical multifidus and longus colli muscles size in participants with and without cervical radicular pain. Journal of Manipulative and Physiological Therapeutics. 2020;43(3):206-11.
11. Bible JE, Biswas D, Miller CP, Whang PG, Grauer JN. Normal functional range of motion of the cervical spine during 15 activities of daily living. Clinical Spine Surgery. 2010;23(1):15-21.
12. Liu F, Fang T, Zhou F, Zhao M, Chen M, You J, et al. Association of depression/anxiety symptoms with neck pain: a systematic review

and meta-analysis of literature in China. Pain Research and Management. 2018;2018.
13. Cohen SP, editor Epidemiology, diagnosis, and treatment of neck pain. Mayo Clinic Proceedings; 2015: Elsevier.
14. Gebremariam L, Koes BW, Peul WC, Huisstede BM. Evaluation of treatment effectiveness for the herniated cervical disc: a systematic review. Spine. 2012;37(2):E109-E18.
15. El-Hafez HM, Hamdy HA, Takla MK, Ahmed SEB, Genedy AF, Al Shaymaa S. Instrument-assisted soft tissue mobilisation versus stripping massage for upper trapezius myofascial trigger points. Journal of Taibah University Medical Sciences. 2020;15(2):87-93.
16. Crothers AL, French SD, Hebert JJ, Walker BF. Spinal manipulative therapy, Graston technique® and placebo for non-specific thoracic spine pain: a randomised controlled trial. Chiropractic & manual therapies. 2016;24(1):1-9.
17. Abdel-Aal NM, Elsayyad MM, Megahed AA. Short-term effect of adding Graston technique to exercise program in treatment of patients with cervicogenic headache: a single-blinded, randomized controlled trial. European Journal of Physical and Rehabilitation Medicine. 2021;57(5):758-66.
18. Kim D-H, Lee B-H. The effects of mechanical stimulation using graston on changing trigger point pressure pain threshold and muscle tone of the same spinal segment in neck disk patient. The Journal of the Korea Contents Association. 2019;19(10):198-205.
19. Davies CC, Brockopp DY. Use of ASTYM® treatment on scar tissue following surgical treatment for breast cancer: a pilot study. Rehabilitation Oncology. 2010;28(3):3.
20. Liu X, Faes L, Calvert MJ, Denniston AK. Extension of the CONSORT and SPIRIT statements. The Lancet. 2019;394(10205):1225.
21. Faul F, Erdfelder E, Lang A-G, Buchner A. G* Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behavior research methods. 2007;39(2):175-91.
22. Noori SA, Rasheed A, Aiyer R, Jung B, Bansal N, Chang K-V, et al. Therapeutic ultrasound for pain management in chronic low back pain and chronic neck pain: a systematic review. Pain Medicine. 2020;21(7):1482-93.
23. Nitsure P, Welling A. Effect of gross myofascial release of upper limb and neck on pain and function in subjects with mechanical neck pain with upper limb radiculopathy: A clinical trial. Int J Dental Med Res. 2014;1(3):8-16.
24. Kane RL, Bershadsky B, Rockwood T, Saleh K, Islam NC. Visual Analog Scale pain reporting was standardized. Journal of clinical epidemiology. 2005;58(6):618-23.
25. Aslan E, Karaduman A, Yakut Y, Aras B, Simsek IE, Yaglý N. The cultural adaptation, reliability and validity of neck disability index in patients with neck pain: a Turkish version study. Spine. 2008;33(11):E362-E5.
26. Yapali G, Günel MK, Karahan S. The cross-cultural adaptation, reliability, and validity of the Copenhagen Neck Functional Disability Scale in patients with chronic neck pain: Turkish version study. Spine. 2012;37(11):E678-E82.
27. Misterska E, Jankowski R, Glowacki M. Cross-cultural adaptation of the Neck Disability Index and Copenhagen Neck Functional Disability Scale for patients with neck pain due to degenerative and discopathic disorders. Psychometric properties of the Polish versions. BMC musculoskeletal disorders. 2011;12(1):1-8.
28. Aydemir Ö, Güvenir T, Küey L, Kultur S. Hospital Anxiety and Depression Scale Turkish form: validation and reliability study. Türk Psikiyatri Der. 1997;8(4):280e7.
29. Youssef EF MN, Mohamed MM, Ahmad HA. Trigger Point Release versus Instrument Assisted Soft Tissue Mobilization on Upper Trapezius Trigger Points in Mechanical Neck Pain: A Randomized Clinical Trial. The Medical Journal of Cairo University. 2020;88(December):2073-9.
30. Ramadan SM, El Gharieb HA, Labib AM, Embaby EA. Short-term effects of instrument-assisted soft tissue mobilization compared to algometry pressure release in tension-type headache: a randomized placebo-controlled trial. Journal of Manual & Manipulative Therapy. 2022:1-10.
31. Mylonas K, Angelopoulos P, Billis E, Tsepis E, Fousekis K. Combining targeted instrument-assisted soft tissue mobilization applications and neuromuscular exercises can correct forward head posture and improve the functionality of patients with mechanical neck pain: a randomized control study. BMC musculoskeletal disorders. 2021;22(1):1-9.

32. Smith SR, Little JA, Nowinski LA, Walker SJ. The comprehensive psychological assessment. Handbook of clinical rating scales and assessment in psychiatry and mental health: Springer; 2009. p. 287-301.
33. Zlatkov Y, Zlatkova K. Monitoring the effect of the ERGON IASTM technique in patients with lumbar disc herniation. Journal of Physical Education and Sport. 2021;21(5):2706-11.
34. Lauche R, Wübbeling K, Lüdtke R, Cramer H, Choi K-E, Rampp T, et al. Randomized controlled pilot study: pain intensity and pressure pain thresholds in patients with neck and low back pain before and after traditional East Asian" gua sha" therapy. The American Journal of Chinese Medicine. 2012;40(05):905-17.
35. Crombez G, Eccleston C, Van Damme S, Vlaeyen JW, Karoly P. Fear-avoidance model of chronic pain: the next generation. The Clinical journal of pain. 2012;28(6):475-83.
36. Emshi ZA, Okhovatian F, Kojidi MM, Baghban AA, Azimi H. Comparison of the effects of instrument assisted soft tissue mobilization and dry needling on active myofascial trigger points of upper trapezius muscle. Medical Journal of the Islamic Republic of Iran. 2021;35:59.
37. Erden A, Şenocak E, Kalaycıoğlu A, Aktürk A. Effectiveness of instrument assisted soft tissue mobilization in myofascial pain syndrome: preliminary results of a randomized controlled trial. Sports Medicine Journal/Medicina Sportivâ. 2020;16(1).
38. Melham TJ, Sevier TL, Malnofski MJ, Wilson JK, Helfst Jr RH. Chronic ankle pain and fibrosis successfully treated with a new noninvasive augmented soft tissue mobilization technique (ASTM): a case report. Medicine and science in sports and exercise. 1998;30(6):801-4.
39. Gross MT. Chronic tendinitis: pathomechanics of injury, factors affecting the healing response, and treatment. Journal of Orthopaedic & Sports Physical Therapy. 1992;16(6):248-61.
40. Hammer WI. The effect of mechanical load on degenerated soft tissue. Journal of Bodywork and Movement Therapies. 2008;12(3):246-56.
41. Yip CHT, Chiu TTW, Poon ATK. The relationship between head posture and severity and disability of patients with neck pain. Manual therapy. 2008;13(2):148-54.
42. Hermann KM, Reese CS. Relationships among selected measures of impairment, functional limitation, and disability in patients with cervical spine disorders. Physical therapy. 2001;81(3):903-12.
43. Moon JH, Jung J-H, Won YS, Cho H-Y. Immediate effects of Graston Technique on hamstring muscle extensibility and pain intensity in patients with nonspecific low back pain. Journal of physical therapy science. 2017;29(2):224-7.
44. Dunn AL, Trivedi MH, O'Neal HA. Physical activity dose-response effects on outcomes of depression and anxiety. Database of Abstracts of Reviews of Effects (DARE): Quality-assessed Reviews [Internet]. 2001.
45. Chiu TT, Hui-Chan CW, Cheing G. A randomized clinical trial of TENS and exercise for patients with chronic neck pain. Clinical rehabilitation. 2005;19(8):850-60.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 336-348
https://doi.org/10.30621/jbachs.1284274
RESEARCH ARTICLE

DECISION TREE-BASED CLASSIFICATION APPROACH TO DISCOVER FACTORS AFFECTING VITAMIN D LEVEL WITH MACHINE LEARNING

Ceyda Unal[1], Cihan Cilgin[2], Suleyman Albas[3], Esra Meltem Koc[4]

[1] Dokuz Eylul University Faculty of Economics and Administrative Sciences, Department of Management Information Systems, Izmir, Türkiye

[2] Bolu Abant Izzet Baysal University, Faculty of Applied Sciences, Department of Management Information Systems, Bolu, Türkiye

[3] Family Health Center, Karabaglar No 17, Izmir, Türkiye

[4] Izmir Katip Celebi University, Faculty of Medicine, Department of Family Medicine, Izmir, Türkiye

ORCID: C.U. 0000-0002-5503-8124; C.C. 0000-0002-8983-118X; S.A. 0000-0002-6779-5309; E.M.K. 0000-0003-3620-1261

Corresponding author: Ceyda Unal, **E-mail:** ceyda.unal@deu.edu.tr
Received: 16.04.2023; **Accepted:** 25.04.2024; **Available Online Date:** 31.05.2024

Cite this article as: Unal C, Cilgin C, Albas S, Koc EM. Decision Tree-Based Classification Approach to Discover Factors Affecting Vitamin D Level with Machine Learning. J Basic Clin Health Sci 2024; 8: 336-348.

ABSTRACT

Purpose: Vitamin D level is emphasized as an important biomarker in determining risk factors for different diseases. Vitamin D is an important vitamin for human health and its deficiency is associated with serious health problems. Therefore, it is of great importance to detect vitamin D deficiency, which can be easily prevented and treated. The possible relationship between vitamin D deficiency and musculoskeletal pain, osteoporosis, diabetes mellitus, hypertension is frequently discussed in researches. Enhanced availability of health data and decreased data processing expenses facilitate the extraction of valuable patterns related to vitamin D from extensive datasets. To illustrate, decision trees are commonly used for explainability and explainable AI (XAI) purposes. In this research, it is aimed to analyze the factors in determining the vitamin D level and the decision rules related to it.

Materials and Methods: A descriptive framework based on one of the machine learning techniques, that is decision tree is followed. The data used to create the decision rules were obtained from volunteers between the ages of 18-85 who applied to Izmir Katip Çelebi University Atatürk Training and Research Hospital Infectious Diseases and Family Medicine Polyclinics and agreed to participate in the study between 01.03.2017 and 01.09.2017. The sample size was calculated as 172 with 80% power, 5% error margin using NCSS and PASS software. The following parameters were examined: AST, ALT, ALP, BUN, creatine, total protein, albumin 25 (OH) D, PTH, TSH, Ca, Mg, phosphate, uric acid and VDR gene polymorphism. An investigator-designed socio-demographic data questionnaire was administered in-person interviews with 172 participants as a consequence of the research conducted with that total number of individuals.The validity of the models were assessed according to “accuracy scores” for each model.

Results: It was observed that age, gender and laboratory test values are strong predictors for vitamin D level. As a result of two CART (Classification and Regression Trees) models, %90.47 and %95 predictive accuracy were observed respectively. In the first model, uric acid, age and creatine; in the second model TSH, ALP and smoking(yes) were the most important three biomarkers affecting vitamin D level.

Conclusion: The collected features give a comprehensive list of variables that influence vitamin D in the dataset under consideration. Important findings of the study include not only the identification of these variables, but also the effective categorization determination procedures. Final decision tree models were constructed using two distinct feature sets. The initial model was created with 12 features (Age, ALP, TSH, URICACID, PHOSPHATE, AST, Cigarette Consumption, CA, CREATIN, TOTALPROTEIN, MG, BUN) that had over 4% importance, resulting in a classification accuracy rate of 92.7%. The second model was built using all features in the dataset and achieved a classification accuracy rate of 88.37%. In contrast to previous research, the Age variable is the most influential factor within the scope of this dataset, which includes demographic information on patients and their existing disorders.

Keywords: Machine learning, decision trees, decision rules, vitamin D.

INTRODUCTION

Big data in healthcare is crucial for processing and analyzing vast volumes of data. Artificial intelligence advancements contribute to clinical decision support systems, revealing valuable patterns from health data. Electronic health records and clinical analytics enable the analysis of large-quantitative data for new insights. As a result of this, reducing cost in healthcare domain has been inevitable in United States and other countries (1). Machine learning methods are transforming healthcare by identifying biomarkers in laboratory tests, with Vitamin D being a crucial biomarker for various healthcare situations.

Vitamin D deficiency is currently on increasing incidence globally, with a systematic review finding a prevalence of serum 25(OH)D < 30 nmol/L at 15.7% from 2000 to 2022. Vitamin D insufficiency is prevalent in Turkey as a consequence of restricted sunshine exposure and dietary effects. In Turkey, Vitamin D deficiency are quite common due to limited sunlight exposure and dietary factors (2). The primary factor contributing to the widespread occurrence of vitamin D deficiency is the failure to recognize that sun exposure has been and remains the primary source of vitamin D for the majority of adults and children [33–35]. Very few substances contain vitamin D naturally. These consist of cod liver oil, mushrooms that have been sun-dried or subjected to sunlight, and oily fish such as herring, mackerel, and salmon [1, 25, 34]. Meat, such as beef and pork, may contain an amount of vitamin D in the form of 25(OH)D, which can be significant at times [36, 37]. An increasing quantity of muscle 25(OH)D3 is being produced by numerous poultry, pigs, and cows as a result of the incorporation of 25(OH)D3 into diverse animal feeds. In addition to consuming polar bear liver and oily salmon, civilizations residing in the far Northern and Southern latitudes also obtain vitamin D from seal and whale blubber and polar bear liver.(3) The possible relationship between vitamin D deficiency and musculoskeletal pain, osteoporosis, diabetes mellitus, hypertension, cardiovascular diseases, autoimmune diseases, sleep disorders, cancer and increased mortality is frequently discussed in researches. However, there are limited number of researches about the factors related to Vitamin D level from the machine learning perspective.

In the literature various studies focused on identifying risk factors and associations related to vitamin D deficiency in different populations. Several studies found that factors like black race, female gender, winter season, and hypoalbuminemia were strong predictors of vitamin D deficiency in dialysis patients using decision tree-based algorithms (4-5-6-7-8-9). It was also indicated that vitamin D deficiency in the cities of Mashhad and Sabzevar in the northeast of Iran using the decision tree method based on 14 characteristics. 70% of the participants that is 618 cases were used as a random training dataset to form the decision tree, while the remaining 30% that is 285 cases were used as a test dataset to evaluate the performance of decision making. Using the test dataset, sensitivity, specificity, accuracy and AUC values were obtained as 79.3%, 64%, 77.8% and 72%, respectively. A study consisting of 31540 data presented a framework based on rules in the Apriori algorithm. A total of 22 association rules were generated with an 80% confidence level using WEKA software. The rule with the highest confidence level (98%) highlighted that among 1199 female patients aged 18 to 35 with vitamin D deficiency. (4-5-6). In addition, logistic regression and the XGBoost algorithm also used for detecting factors related to vitamin D level. The XGBoost algorithm identified stroke severity, age, and 25-hydroxyvitamin D level as important predictors (ROC/AUC of 0.805 versus 0.746). (7). A study conducted in Birjand, Iran, analyzing a healthy population to identify risk factors for vitamin D3 deficiency among chronic hepatitis B (CHB) patients. The study included 292 CHB patients and 330 vaccinated individuals, with serum biochemical characteristics measured. Data mining techniques were used, with 60% of the data used for training using the decision tree method. The model's performance was evaluated using the Receiver Operating Characteristics (ROC) curve, which yielded a 78% accuracy rate. The prevalence of vitamin D3 deficiency was found to be 63% among CHB patients and 32.9% among healthy individuals. The study concluded that serum zinc levels are predictive variables for vitamin D3 deficiency and emphasized the high accuracy in predicting the risk of vitamin D3 deficiency (8). It was also stated that Vitamin D was highlighted as a factor that reduces the risk of COVID-19. Countries were categorized into low or high COVID-19 cases, deaths, or case fatality rates based on the 40th and 60th percentiles (9).

The framework presented is identical as mentioned in previous studies but more focused on rule-based approach. In this context, a descriptive study is conducted. One of the purposes of the research is

analyzing the factors in determining the vitamin D level and decision rules behind them. The second is benefiting from the advantage of decision trees in terms of explainability and explainable AI (XAI). In order to do this, the remaining of article will emphasize the materials and methods in detail and discuss the results. Suggestions for further studies at the end of the research, could shed light on various researches.

MATERIALS AND METHODS

Dataset

The data used within the scope of the research were composed of volunteers between the ages of 18-85 who applied to the Infectious Diseases and Family Medicine Outpatient Clinics of İzmir Katip Çelebi University Atatürk Training and Research Hospital between 01.03.2017 and 01.09.2017 and agreed to participate in the research. Ethical approval obtained by İzmir Kâtip Çelebi University, Non-interventional Clinical Research Ethics Committee (Decision Date: 18.11.2021, Number: 0470). As a result of the research conducted with 172 people in total, a socio-demographic data questionnaire prepared by the researchers using the face-to-face interview technique was carried out. Exclusion criteria for study included: autoimmune disease, metabolic bone disease, chronic kidney disease, chronic liver disease, thyroid-- parathyroid disease, diabetes mellitus, malignancy, alcoholism, immunosuppression, liver transplantation, pregnancy or breastfeeding, psychiatric disease that disrupts the ability to answer questions, using medication that vitamin D, calcium, hormone therapy, glucocorticosteroid, antituberculosis, antiepileptic the last six months. In addition, as seen in detail in Table 1, it has been obtained from various biochemical data. The sample size used in this study was determined based on model tests performed as each new observation was added. Data collection was discontinued after a certain model performance was partially (approximately 90%) achieved.

Important factor considered within the scope of the purpose of the research is to discover the factors that affect the vitamin D level, so the dataset used in the research has a wide variable set consisting of 46 independent and 1 dependent variable. During the data preparation process, 25 (OH) D continuous variable was determined as one class and those with lower than 10 ng / ml as determining the vitamin D level, which is primarily used as an independent variable, while those higher than this threshold value were determined as another class. According to Turkey Endocrinology and Metabolism Association (TEMD) Osteoporosis and Metabolic Bone Diseases Working Group, a 25(OH)D level of at least 20 ng/ml (50 nmol/L) is accepted as sufficient for maintaining bone health. For non-bone effects, a level ranging from 30 to 50 ng/ml (75 to 125 nmol/L) is called adequate. A level between 10 and 20 ng/ml (25 to 50 nmol/L) indicates vitamin D insufficiency, while a value below 10 ng/ml (25 nmol/L) indicates vitamin D deficiency (10) Thus, the value “10 ng/ml” was chosen as threshold. The dependent variable, which is a continuous variable, has been transformed into a binary variable for the purpose of the research. In addition, variables in categorical form are organized as binary variables.

As stated in Table 1, the ages of the participants vary between 19-85 with an average age of 41.5 ± 13.6 years, consisting of 80 men and 92 women. In line with the information obtained from the participants, while 0 was determined for those who do not smoke, the number of daily use of cigarettes was used for smokers. Individuals were assigned with alcohol use habits, while 0 was assigned for individuals who did not consume alcohol.

In addition, all variables used in the dataset for the participants' existing diseases were determined as binary variables and a value of 1 was assigned in the presence of disease, while the opposite was indicated as 0. According to the test results obtained in the biochemical data, it was included in the dataset as a continuous variable in the relevant variable range as shown in Table 1. In addition, the DVit variable, which is used as the target variable within the scope of this research, is a binary variable and 84 of the participants are below the specified threshold value and represented by 0 value, while 88 of them are above the threshold value and represented with a value of 1.

Feature Selection

In machine learning problems, the representation of data often uses many features and only a few of them represent the target variable (11). Feature selection reflects the process of discovering a subset of related features or attributes as dependent variables in a predictive model, thereby helping to reduce the overfitting of the model and increase the prediction accuracy (12). Especially, as it is within the scope of

Table 1. Information about the Features used in the scope of the Dataset

Feature	Type	Range
Age	Continuous	19-81
Gender	Binary	0,1
Cigarette Consumption	Continuous	0-40
Alcohol	Binary	0,1
HBV (Hepatitis B virus)	Binary	0,1
CAH (Congenital Adrenal Hyperplasia)	Binary	0,1
HT (Hypertension)	Binary	0,1
ASTHMA	Binary	0,1
GOR	Binary	0,1
GASTRITIS	Binary	0,1
PANICDIS	Binary	0,1
ANEMIA	Binary	0,1
MIGRAINE	Binary	0,1
HL (Hodgkin Lenfoma)	Binary	0,1
LDH (Lactate Dehydrogenase)	Binary	0,1
DEPRESSION	Binary	0,1
PPI (Proton Pump Inhibitor)	Binary	0,1
ANTIHT	Binary	0,1
INHALER	Binary	0,1
ANTIAGREAGAN	Binary	0,1
SSRI (Selective Serotonin Reuptake Inhibitor)	Binary	0,1
FE	Binary	0,1
NSAII	Binary	0,1
STATIN	Binary	0,1
TOTALPROTEIN	Continuous	6.3 – 8.7
ALBUMIN	Continuous	3.2 – 4.8
CREATINE	Continuous	0.5 -1.2
AST (Aspartat Aminotransferaz)	Continuous	10 – 60
BUN (Blood Urea Nitrogen)	Continuous	1 – 30
CA (Calcium)	Continuous	5.9 – 10.5
PHOSPHATE	Continuous	1.9 – 5.1
MG (Magnesium)	Continuous	1.6 – 3.7
TSH (Thyroid Stimulating Hormone)	Continuous	0.24 – 5.85
PTH (Parathormon)	Continuous	0.1 – 99
ALP (Alkalen Fosfataz)	Continuous	9.1 – 179
URICACID	Continuous	1 – 8.94
ALT (Alanine Aminotransferase)	Continuous	3 - 82
AA	Binary	0,1
Aa	Binary	0,1
Aa	Binary	0,1
TT	Binary	0,1
Tt	Binary	0,1
Tt	Binary	0,1
FF	Binary	0,1
Ff	Binary	0,1
Ff	Binary	0,1
BB	Binary	0,1
Bb	Binary	0,1
Bb	Binary	0,1
Dvit	Binary	0,1

this study, feature selection phase is critical both in increasing the classification performance in datasets with huge variable sets and in the discovery process of important variables in the existing dataset.

Although there are substantial amount of feature selection methods in the literature, these methods can differ according to the types of variables in the dataset, the target variable and the machine learning approach to be applied to the dataset. In this context, Classification and Regression Trees (CART) -- a type of decision tree -- was used in both the classification task of the dataset and the feature extraction. As pointed out in the literature (13,14), the use of decision trees in feature selection is common and positively affects the performance in classification or regression tasks. In line with the discovery of the important variables that affect the target variable, which is one of the main objectives of the research, the feature selection process followed a unique framework different from the decision tree approaches in the literature. Especially ignoring the time complexity, the focus has been on determining the variable dataset that affects the prediction performance. Particularly, in the decision tree and feature selection approaches in the literature, the feature set is considered as a whole and the decision tree is evaluated on the tree structure formed with the variables in this whole set of variables, while the effect of different variable set combinations on the prediction performance and therefore on the feature selection is ignored. As a result of this, evaluation was made with all possible combinations of variable sets determined with the approach used in the research. It would be more informative to list the approach used in feature selection in the following steps:

Primarily, variables are divided into specified clusters according to determined similarities. (For example, variables belonging to diseases in the dataset can be considered as a single set.)

With all possible combinations of these cluster variable groups, decision trees were created with k-fold cross validation with the CART method. (the k value was determined as 20)

The decision trees created were evaluated according to the accuracy metric and the results that provided a certain accuracy rate (87% specified) were selected, and the percentage of variables that were effective in the decision rules used in the formation of these trees were determined.

Finally, the final variable significance were calculated by taking the mean values of variable significance obtained from decision trees created as a result of each different variable set combination.

Thus, a variable selection decision was not made over a single set of variables, and the attitudes of variables that occur in all possible sets of variables were examined through a comprehensive examination. At this point, it should be emphasized again that this process takes a lot of time (about one month in our research) but offers a robust approach in terms of reliability. Consequently, the feature selection methodology suggested would also be a contribution to the literature, especially in the process of determining independent variables effective on the target variable rather than time complexity.

Considering the trees created as a result of k-fold cross validation in the specified feature selection process, approximately 72.577.600 trees were evaluated and feature importance given in Table 2 were obtained. As can be seen in Table 2, Age, ALP, TSH and Uric Acid values are more than 7% importance in determining the target variable (Vitamin D), respectively. All variables (features) not included in the table were not reported to the research framework, as their importance were lower than 1%.

Table 2. The Order of Feature Importance Used in the Context of Dataset

Feature	Importance
Age	0,07954
ALP	0,07923
TSH	0,07267
URICACID	0,07015
PHOSPHATE	0,06826
AST	0,06157
Cigarette Consumption	0,05716
CA	0,05538
CREATINE	0,05224
TOTALPROTEIN	0,04402
MG	0,04386
BUN	0,04285
ALBUMIN	0,03892
PTH	0,03756
Aa	0,03163
ALT	0,02777
Gender	0,02736
HBV	0,02217
Tt	0,02011

Decision Trees- CART (Classification and Regression Trees)

Decision trees are one of the frequently used methods in data mining and machine learning. Finance (15,16), education (17,18), real estate (19,20), energy (21,22) and many similar areas, as well as in healthcare (23–26) preferred as a data mining technique. Decision Trees represents a tree-nodes corresponding to the order of decision rules in the simplest terms (27).

Today, decision trees are popularly preferred by researchers in the field of data mining because it has the advantage of ease of interpretation and visualization (28), does not require a preliminary process with its non-parametric modeling structure (29), requires very little data preparation, can process both numerical and categorical data and perform very well with a large dataset in a short time (15). One of the advantages of decision tree analysis is that the relationship between the binary dependent variable and the related independent variables is clearly demonstrated using a tree structure (29). In other words, it can be considered as a white box structure. In particular, unlike Black Box-type algorithms such as neural networks; decision trees are a white-box type machine learning algorithm, which is highly beneficial in evaluating the results and discovering the occurrence patterns (decision-making logic) of the results (30). In this way, a complex decision-making process can be divided into a collection of simpler decisions and decision rules, that are generally simpler to interpret (31) and understandable can be created. Decision trees can basically be designed for two task processes: classification tree analysis and regression tree analysis (15,20,24). Decision trees developed with the recursive partioning process provide a high-power tool for the definition, classification, regression and prediction of data (19). Decision trees generate the classification or regression process by using a set of hierarchical rules on variables, organized in tree structure (32).

Decision tree is one of the various approaches that can be used to develop a classification model for multi-stage decision making (31). It creates a tree-like structure model using inductive reasoning, focusing on existing data records (24). For this purpose, the decision tree starts with a root node where users can act, and from this node, users divide each node recursively according to the decision tree learning algorithm (33). The attribute/variable/feature is first classified (branched) in terms of groups and then the next important one is reconsidered and classified under information gain (17). In decision tree algorithms, the dataset is divided into two or more subgroups that are mutually exclusive at each split. The goal is to produce subsets of data that are as homogeneous as possible with respect to the target (dependent) variable (29). While performing this division function, it is necessary to determine how to divide trees that separates the decision tree algorithms from each other. Today many different various splitting criteria such as Entropy, Twoing, Gini; Gini Index, which is a binary splitting criterion, is more frequently preferred in datasets with continuous variables and is also used in this research.

For use in classification and regression tasks, decision tree theory is well suited for making medical predictions and data analysis statements in the field. Although there are many decision tree algorithms such as, ID3, C4.5, C5, CART, Random Forest and CHAID (Chi-square Automatic Interaction Detection) in literature, each of these algorithms can be applied to different datasets for different purposes. In this paper, CART (34) method, which can work easily with continuous variables and can also be used in regression problems, was preferred. The structure of the CART algorithm takes the independent variables into account in terms of predictive power; therefore it serves as a powerful discovery tool to understand the basic structure of the data. This algorithm is basically a series of carefully prepared questions about the features of the data, and after an answer has been generated for a question, a subsequent question is asked until the class is determined on the observation. These questions can be framed in the form of a hierarchical structure of nodes and directed edges (35). The CART procedure performs "binary recursive partitioning". The term "binary partitioning" means that the master node is continuously divided into two child nodes, and the term "recursive" means that the process is repeated, treating each child node as a parent node in the next step. This process is repeated until further partitioning is impossible, that is, until leaf nodes are formed or limited by some criteria determined by the user (36).

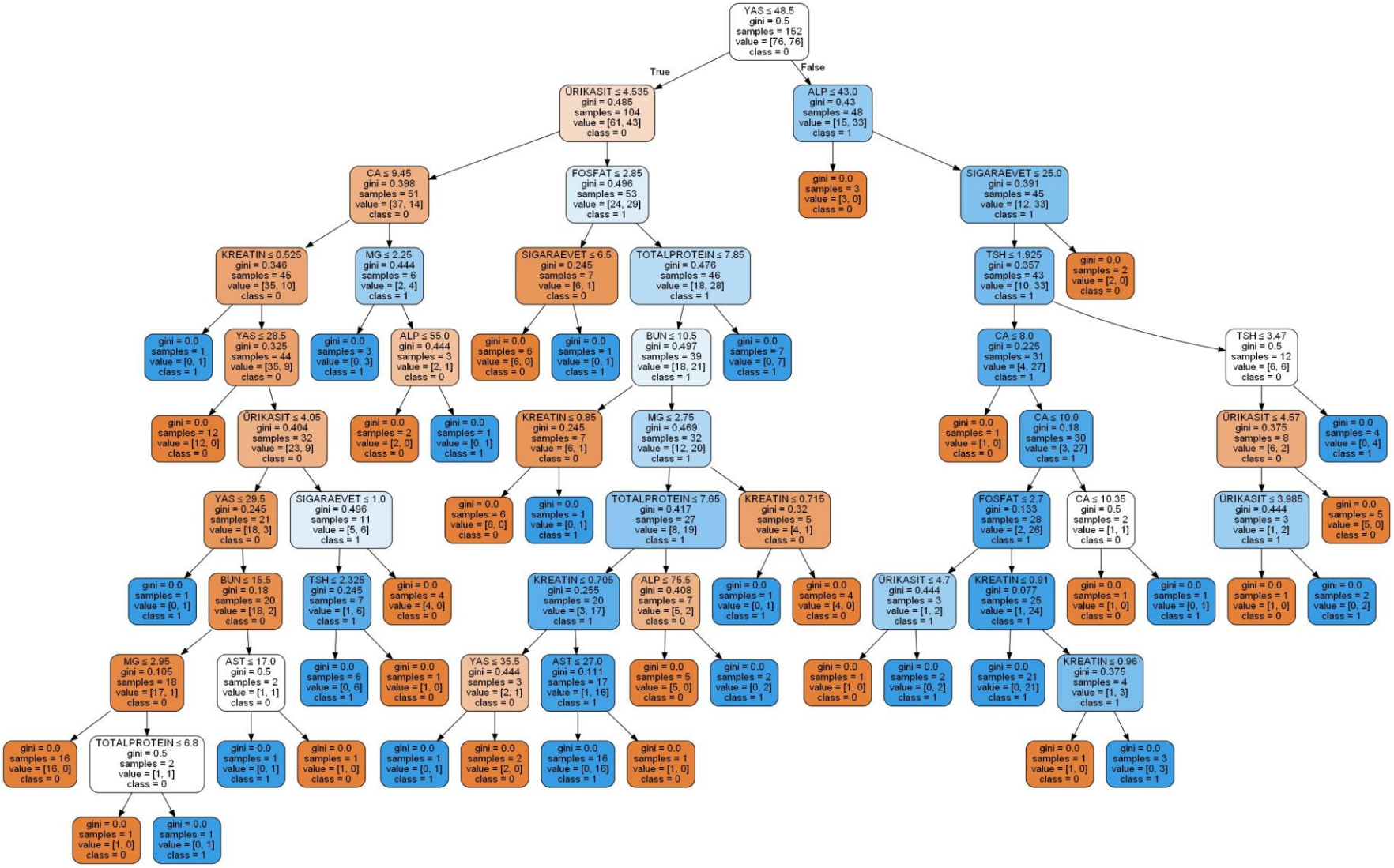


Figure 1. Initial CART Model (12 Features)

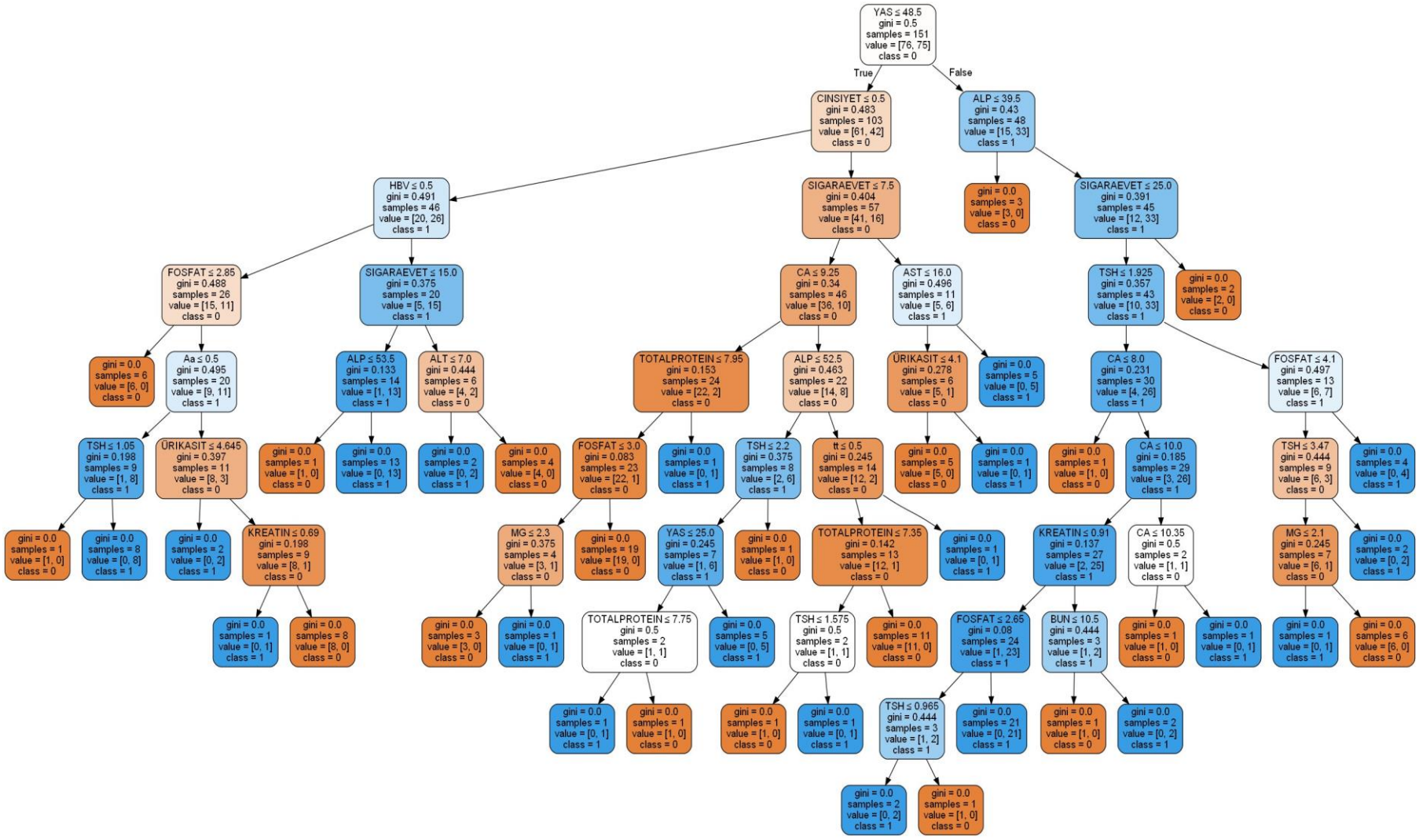


Figure 2. CART Model (All Features)

various splitting criteria such as Entropy, Twoing, Gini; Gini Index, which is a binary splitting criterion, is more frequently preferred in datasets with continuous variables and is also used in this research.

For use in classification and regression tasks, decision tree theory is well suited for making medical predictions and data analysis statements in the field. Although there are many decision tree algorithms such as, ID3, C4.5, C5, CART, Random Forest and CHAID (Chi-square Automatic Interaction Detection) in literature, each of these algorithms can be applied to different datasets for different purposes. In this paper, CART (34) method, which can work easily with continuous variables and can also be used in regression problems, was preferred. The structure of the CART algorithm takes the independent variables into account in terms of predictive power; therefore it serves as a powerful discovery tool to understand the basic structure of the data. This algorithm is basically a series of carefully prepared questions about the features of the data, and after an answer has been generated for a question, a subsequent question is asked until the class is determined on the observation. These questions can be framed in the form of a hierarchical structure of nodes and directed edges (35). The CART procedure performs "binary recursive partitioning". The term "binary partitioning" means that the master node is continuously divided into two child nodes, and the term "recursive" means that the process is repeated, treating each child node as a parent node in the next step. This process is repeated until further partitioning is impossible, that is, until leaf nodes are formed or limited by some criteria determined by the user (36).

RESULTS

Within the scope of the research, final decision tree models were carried out on two different feature set. Primarily, the first model was developed with 12 variables (Age, ALP, TSH, URICACID, PHOSPHATE, AST, Cigarette Consumption, CA, CREATIN, TOTALPROTEIN, MG, BUN) above 4% importance from the set of variables shown in Table 2. The second model was created with a total of 19 feature sets in the table. Within the framework of both models, 80% of the entire dataset was used as the training dataset, while 20% was used as the test dataset. Additionally, a 5-fold cross validation approach was adopted in the study to evaluate the model training results. In addition, the maximum depth of the decision tree is limited to 10 to prevent the complexity of the rules created by decision trees. Thus, the tree was completed after 10 branches. The tree was splitted according to Gini index as previously stated. In consequence of model implemented with the feature set within the first model, a high classification accuracy rate of 92,7% was achieved. The decision tree structure obtained as a result of this model is shown in Figure 1. As shown in Table 2, the “Age” feature has been assigned as the root node within the scope of the model.

Within the second model, a relatively high classification accuracy rate of 88.37% was achieved as a result of the model performed with the set of features included in the model. Although this accuracy rate is lower compared to the first model, it proves that the increase in the number of feature sets affects the model prediction performance as mentioned in the feature selection process. The decision tree structure obtained as a result of this model is shown in Figure 2. As in the first model, the “Age” feature, which is determined as the most important feature, was formed as the root node.

Alternative machine learning approaches were also applied within the scope of this study. In this way, it is possible to compare the results obtained with alternative methods, and the robustness of the results obtained can also be tested. For this purpose, analyzes were carried out with XGBooost, Random Forest (RF) and Support Support Vector Machine (SVM) models. The accuracy scores obtained as a result of these models are presented in Table 3.

For each model presented in Table 3, hyper parameter optimization was performed separately for two different feature sets with Grid-Search approach. As a result of this process, hyper-parameter values that provide the best model performance were selected. As seen in Table 3, SVM was the model with the lowest prediction performance. The main reason for this situation is the use of a tree-based approach in feature selection. Although RF and XGBoost showed relatively similar results, both models outperformed CART at a lower rate.

Although the results obtained within the scope of RF and XGBoost presented relatively better performance values, they did not provide a exceptionally increase in accuracy. Therefore, compared to CART, they require a large number of hyperparameter settings and therefore higher processing power and time. However, as another aim of this study, CART offers easy and fast use for many stakeholders. However, it should not be forgotten that the feature selection

Table 3. Accuracy scores obtained from alternative models

Models	Selected Hyper-Parameters	Accuracy Rate
SVM (1. Feature Set)	Kernel: Linear C: 1000 Gamma: 0.001	0,829
SVM (2. Feature Set)	Kernel: Linear C: 100 Gamma: 1	0,882
RF (1. Feature Set)	n_estimators: 50 Max_features: Sqrt Min_samples_leaf: 1 Max_depth: 2	0,931
RF (2. Feature Set)	n_estimators: 100 Max_features: Sqrt Min_samples_leaf: 2 Max_depth: 3	0,914
XGBoost (1. Feature Set)	Eta:0.01 Max_depth: 4 Subsample: 0,7	0,933
XGBoost (2. Feature Set)	Eta:0.01 Max_depth: 5 Subsample: 0,8	0,908

process within the scope of this study was carried out solely on the basis of the CART model. For this reason, it is expected that the accuracy rate provided by CART is high. Repeating similar feature selection processes for other tree-based approaches will further increase the accuracy rates of these models. In addition, modeling results performed with RF and XGBoost without any feature selection are much higher than both CART and SVM accuracy rates. This result is also an indicator of how effective the feature selection approach adopted in this study is, especially in improving the performance of CART.

DISCUSSION

This research aims to evaluate the factors influencing vitamin D levels and the corresponding the criteria for decision- Two separate feature sets were used to build the final decision tree models. The first model consisted of 12 features (Age, ALP, TSH, URICACID, PHOSPHATE, AST, Cigarette Consumption, CA, CREATIN, TOTALPROTEIN, MG, BUN) with overall importance above 4%, leading to a classification accuracy of 92.7%. The second model, utilizing all features in the dataset, had a classification accuracy rate of 88.37%. In the study, a significant relationship between high age, presence of chronic disease, being at university or higher education level, and high ALP and vitamin D levels was found. It is thought that this relationship may be due to the awareness of the retired and unemployed elderly population living in the province of Izmir, where the sociocultural level is high, about nutrition and benefiting from sunlight adequately. It is an expected situation that the average of vitamin D is determined to be higher in individuals with university and higher education level. Since the blood of the participants was collected within 2 months (March-April 2017), the seasonal variation was minimized. It was thought that vitamin D deficiency may have been detected more frequently, because the blood samples of the participants were taken after the winter season.

Moreover, unlike other studies in the literature, this study applies a high-precision feature selection process using decision trees. However, as presented in Table 2, the features obtained provide a complete list of variables that have an impact on vitamin D in the analyzed dataset. In addition to the identification of these variables, the decision rules that are effective in classification are also important findings of the study. Unlike the existing studies, the Age variable is the most important determinant within the scope of this dataset, which considers the demographic data of the patients as well as their existing diseases. Although Age has been used by many studies to determine vitamin D levels, it has not been identified as a factor, except for a few studies (8). Similar to other studies (9), Uric Acid (URICACID) and Calcium (CA) levels are other variables that affect the classification outcome. According to the empirical findings of the study conducted by (37) in which no

other variables were used except for various measurement values, ALBUMIN and ALT variables were the most influential variables on vitamin D levels, while these two variables were found to be relatively less influential variables in our study. In particular, this supports the conclusion that some demographic characteristics of the patients may be more effective as determinants of vitamin D levels. In addition to the highly interpretable findings of this study, the empirical results demonstrate classification performance with a high accuracy rate (95% accuracy).

The number of observations and variables used in this study constitute the main limitations. The data used in the study were conducted in a hospital environment, especially on people who performed certain laboratory tests. Therefore, the number of data is limited due to the data collected only from volunteers among those who performed these laboratory tests. Another limitation of this study is that different laboratory test results cannot be added as variables.

Studies on vitamin D prevalence and vitamin D cut-off value should be done in Turkey. In addition, this study needs to be repeated with new studies that measure vitamin D levels with a different method.

CONCLUSION

At the present time where data is highly apparent, healthcare services are also going through a big data revolution. Patients are also among the most critical elements of this ecosystem. Patients are constantly generating data and transferring their data to different applications. With regard to healthcare, it takes important steps towards personalized care, which is guided by an evidence-based approach to decision-making.

Artificial intelligence applications in healthcare bring about an important discussion. How these technologies can be included in the clinical workflow has become a critical issue studied by different researchers. As a result of this; two ways of positioning artificial intelligence in medicine / health are emerging: first, artificial intelligence is positioned as an aid for physicians and patients, second, and more radical, it replaces doctors as soon as it is sufficiently developed. The first is that artificial intelligence; as an irreplaceable component primarily in medicine, it assumes that human beings follow the principle of physicians, because it is above all a technology created by humans and humans are too complex structures to be analyzed from all aspects required by any artificial system. In this research, a framework supporting the first opinion for the purpose of determining Vitamin D level were proposed.

The research developed two decision tree models using two different feature sets. The first model had 12 variables with a 4% importance, while the second had 19 variables. 80% of the dataset was used as the training dataset, and 20% as the test dataset. A 5-fold cross validation approach was used to evaluate the model training results. The decision tree was split according to Gini index. The first model achieved a high classification accuracy rate of 92.7%, with the "Age" feature as the root node. The second model achieved a higher accuracy rate of 88.37%, indicating that increasing the number of feature sets affects model classification performance.

Based on these results, the decision tree method can serve as important and useful references in diagnosis for physicians to avoid the use of unnecessary medical supplies and improve healthcare quality. The empirical findings of this paper try to provide a reference index system for physicians in clinical diagnosis by using the decision tree, which is a machine learning approach. For example, it is possible that the factor rules generated from the decision tree model can be used in the judgment process to reduce human errors and avoid medical waste. In addition to the comprehensive examinations performed by specialist physicians, it is possible to provide a decision support to make the final diagnosis with higher accuracy with the information provided by this research, and this information can also be used to formalize and optimize the healthcare process.

Acknowledgements: The article was presented as an abstract at II. International Artificial Intelligence in Health Congress (2021).
Author Contributions: Concept- CC, CU; Design- CC; Supervision– EMK; Resource– EMK, SA; Materials– EMK, SA; Data Collection and/ or Processing- SA; Analysis and/or Interpretation- CC, CU; Literature Search- CC,CU EB; Writing– CC, CU, EMK; Critical Reviews- EMK.
Conflict of interest: None.
Ethical approval: Ethical approval obtained by Izmir Katip Celebi University, Non-interventional Clinical Research Ethics Committee (Decision Date: 18.11.2021, Number: 0470)
Funding: No financial funding.
Peer-Review: Externally peer-reviewed.

REFERENCES

1. Bates DW, Saria S, Ohno-Machado L, Shah A, Escobar G. Big data in health care: using analytics to identify and manage high-risk and high-cost patients. Health Aff (Millwood) 2014;33(7):1123–1131.
2. Cui A, Zhang T, Xiao P, Fan Z, Wang H, Zhuang Y. Global and regional prevalence of vitamin D deficiency in population-based studies from 2000 to 2022: A pooled analysis of 7.9 million participants. Front Nutr 2023;10:1070808.
3. Holick MF. The vitamin D deficiency pandemic: Approaches for diagnosis, treatment and prevention. Rev Endocr Metab Disord 2017;18(2):153-165.
4. Bhan I, Burnett-Bowie Sam, Ye J, Tonelli M, Thadhani R. Clinical measures identify vitamin D deficiency in dialysis. Clin J Am Soc Nephrol CJASN 2010;5(3):460–467.
5. Gonoodi K, Tayefi M, Saberi-Karimian M, et al. An assessment of the risk factors for vitamin D deficiency using a decision tree model. Diabetes Metab Syndr Clin Res Rev 2019;13(3):1773–1777.
6. Kaya B, Günay A, Ozudogru, O. Analysis of the association between vitamin D deficiency and other diagnoses of patients by data mining techniques. Sakarya University Journal of Computer and Information Sciences 2020;3(1):51-59.
7. Kim C, Lee SH, Lim JS, et al. Impact of 25-hydroxyvitamin D on the prognosis of acute ischemic stroke: machine learning approach. Front Neurol 2020;11:37.
8. Osmani F, Ziaee M. Assessment of the risk factors for vitamin D3 deficiency in chronic hepatitis B patient using the decision tree learning algorithm in Birjand. Inform Med Unlocked 2021;23:100519.
9. Rahimi Z, Abdolvand N, Sepehri MM, Khavanin Zadeh M. The association of vitamin-D level with catheter-related-thrombosis in hemodialysis patients: A data mining model. J Vasc Access 2023;24(4):606-613
10. Turkish Journal of Endocrinology and Metabolism [Internet]. Osteoporosis and Metabolic Bone Diseases Diagnosis and Treatment Guide. [Accessed Date: 25 February 2024]. Available from www.temd.org.tr/files/OSTEOPOROZ_web.pdf.
11. Kira K, Rendell LA. A practical approach to feature selection. In: Sleeman D, Edwards P, editors. Machine Learning Proceedings. San Francisco (CA): Morgan Kaufmann; 1992. p. 249–256.
12. Guyon I, Elisseeff A. An introduction to variable and feature selection. J Mach Learn Res 2003; 3: 1157-1182
13. Ratanamahatana C “ann”, Gunopulos D. Feature selection for the naive bayesian classifier using decision trees. Appl Artif Intell 2003;17(5–6):475–487.
14. Sugumaran V, Muralidharan V, Ramachandran KI. Feature selection using decision tree and classification through proximal support vector machine for fault diagnostics of roller bearing. Mech Syst Signal Process. 2007;21(2):930– 942.
15. Delen D, Kuzey C, Uyar A. Measuring firm performance using financial ratios: A decision tree approach. Expert Syst Appl. 2013;40(10):3970–3983.
16. Liu C, Hu Z, Li Y, Liu S. Forecasting copper prices by decision tree learning. Resour Policy. 2017 ;52:427–434.
17. Agarwal S, Pandey GN, Tiwari M. Data mining in education: data classification and decision tree approach. Int. J. e-Educ. e-Bus. e-Manag. e-Learn 2012; 2(2): 140.
18. Kolo KD, Adepoju SA, Alhassan J. A Decision Tree Approach for Predicting Students Academic Performance. Int. J. Edu. Mng Eng. 2015;5: 12-17.
19. Fan GZ, Ong SE, Koh HC. Determinants of house price: a decision tree approach. Urban Stud. 2006;43(12):2301–2315.
20. Shinde N, Gawande K. Survey on predicting property price. In: 2018 International Conference on Automation and Computational Engineering (ICACE). 2018 Oct 3-4. India p. 1–7.
21. Li X, Chan CW, Nguyen HH. Application of the neural decision tree approach for prediction of petroleum production. J Pet Sci Eng. 2013; 104:11–16.
22. Mikučionienė R, Martinaitis V, Keras E. Evaluation of energy efficiency measures sustainability by decision tree method. Energy Build. 2014;76:64–71.
23. Razavi AR, Gill H, Ahlfeldt H, Shahsavar N. Predicting metastasis in breast cancer: comparing a decision tree with domain experts. J Med Syst. 2007; 31(4):263–273.

24. Chang CL, Chen CH. Applying decision tree and neural network to increase quality of dermatologic diagnosis. Expert Syst Appl. 2009; 36(2):4035–4041.
25. Bayat S, Cuggia M, Rossille D, Kessler M, Frimat L. Comparison of bayesian network and decision tree methods for predicting access to the renal transplant waiting list. Stud Health Technol Inform. 2009;150:600–604.
26. Chaurasia V, Pal S, Tiwari BB. Chronic kidney disease: a predictive model using decision tree. Int. J. Res. Eng. Technol. 2019; 11(11): 1781-1794.
27. Singh D, Choudhary N, Samota J. Analysis of data mining classification with decision tree technique. Glob J. Comp Sci 2013; 13(13): 7-14.
28. Koh HC, Tan G. Data mining applications in healthcare. J Healthc Inf Manag JHIM. 2005;19(2):64–72.
29. Gandomi AH, Fridline MM, Roke DA. Decision tree approach for soil liquefaction assessment. Sci World J. 2013; 1-9.
30. Kurt AS, Cilgin C. Dış Ticaret Verileri İçin Kümeleme Analizi: Türkiye, Azerbaycan ve Kazakistan Örneği. Sosyoekonomi. 2021; 29(48): 511-540.
31. Safavian SR, Landgrebe D. A survey of decision tree classifier methodology. IEEE Trans Syst Man Cybern. 1991;21(3):660–674.
32. Aggarwal CC. Data mining: The textbook Springer International Publishing; 2015.
33. Singh S, Gupta P. Comparative study ID3, CART and C4.5 decision tree algorithm: A survey. Int. J. Adv. Sci; 27(27): 97-103.
34. Breiman L, Friedman J, Stone CJ, Olshen RA. Classification and regression trees. Taylor & Francis; 1984. Chapman and Hall/CRC.
35. Sarkar S, Patel A, Madaan S, Maiti J. Prediction of occupational accidents using decision tree approach. In: 2016 IEEE Annual India Conference (INDICON). 2016 Dec 16-18. Bangalore, India.p. 1–6.
36. Waheed T, Bonnell RB, Prasher SO, Paulet E. Measuring performance in precision agriculture: CART—A decision tree approach. Agric Water Manag. 2006; 16;84(1):173–85.
37. Hoffmann G, Bietenbeck A, Lichtinghagen R, Klawonn F. Using machine learning techniques to generate laboratory diagnostic pathways—a case study. J Lab Precis Med. 2018; 3(6). 58.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 349-357
https://doi.org/10.30621/jbachs.1298818
RESEARCH ARTICLE

THE CONCURRENT VALIDITY AND RELIABILITY OF THE SMARTPHONE MEASUREMENT APPLICATION TO EVALUATE ILIOTIBIAL BAND TIGHTNESS: A CROSS-SECTIONAL STUDY

Bayram Sonmez Unuvar[1], Hasan Gercek[2], Ertugrul Demirdel[3]

[1] KTO Karatay University, Faculty of Health Sciences, Department of Audiology, Konya, Turkiye
[2] KTO Karatay University, Vocational School of Health Services, Department of Therapy and Rehabilitation, Konya, Turkiye
[3] Ankara Yıldırım Beyazıt University, Faculty of Health Sciences, Physiotherapy and Rehabilitation Department, Ankara, Turkiye

ORCID: B.S.U. 0000-0003-2095-3645; H.G. 0000-0001-7459-4452; E.D. 0000-0002-7139-0523

Corresponding author: Bayram Sonmez Unuvar, **E-mail:** sonmezunuvar@gmail.com
Received: 18.05.2023; **Accepted:** 09.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Unuvar BS, Gercek H, Demirdel E. The Concurrent Validity and Reliability of the Smartphone Measurement Application to Evaluate Iliotibial Band Tightness: A Cross-Sectional Study. J Basic Clin Health Sci 2024; 8: 349-357.

ABSTRACT

Purpose: In recent years, the medical use of smartphones has increased with the development of hardware. The study aims to evaluate the reliability and concurrent validity of iPhone® measurement application to measure iliotibial band tightness.
Materials and Methods: This was a cross-sectional study. Thirty athletes with iliotibial band tightness (17 males, 13 females) between 20 and 45 years old were included and assessed in this study. The iliotibial band tightness was measured with Ober test using a bubble inclinometer and iPhone® measurement application and evaluated by two experienced physiotherapists. Three measurements were taken for both extremities using both the bubble inclinometer and the iPhone® measurement application by the researchers. The intraclass correlation coefficient (ICC) was used to evaluate the reliability of each smartphone measurement, and Bland–Altman analysis was used to examine measurement errors.
Results: The iPhone® measurement application has strong inter-rater (ICC=0.941) and intra-rater (ICC=0.986) reliability and concurrent validity (r=0.945) in measuring iliotibial band tightness.
Conclusion: From the cross-sectional study's results, it can be concluded that the iPhone® measurement application possesses strong intra-rater and inter-rater reliability and concurrent validity and can be used for measuring iliotibial band tightness.

Keywords: Assessment, iliotibial band tightness, musculoskeletal abnormalities, smartphone

INTRODUCTION

A longitudinal fibrous sheath running along the lateral thigh is the iliotibial band (ITB) tract, an essential structure involved in the lower limb motion. The ITB derives fascial inputs from the deep thigh fascia, gluteus maximus, and tensor fascia lata proximally in the thigh and implants them distally around the leg, including on the proximal tibia (1,2). Therefore, limitations in sports activities occur due to ITB tightness, which increases the incidence of overuse knee injuries in different sports branches (3,4).

The direct association between ITB tightness and limitations in sports activities supports the preference for using the Ober or modified Ober tests in measuring ITB tightness (5). The initial Ober test was identified to investigate the relationship between

tightness in the ITB and sciatica and low back pain (6). Today, this measure is not only used to measure ITB flexibility for those with low back pain but also to examine ITB flexibility in all people (5). Due to the increase in ITB tightness, the movement of the extremity measured with the Ober test in the horizontal plane is limited and the adduction movement of the hip joint decreases (7).

The ITB tightness measure may be conducted through visual inspection or by using a variety of measuring methods, including observation, goniometer, tape measurement, and inclinometer (5,8). Bubble inclinometers are compact, lightweight, and affordable. The inclinometer drawbacks include usability, as many clinics do not have them, and the clinicians' experience with the unique measuring techniques for these methods (9). A body of evidence reported good reliability of a gravity-based bubble inclinometer for calculating ITB tightness in symptomatic and asymptomatic individuals (10). A study by Samo et al. (11) found that the investigator and/or technological errors could be responsible for causing great measurement uncertainties. Procedural and technological errors result in inaccurate measurements. So, smartphones can be a realistic solution to inclinometer from an accessibility viewpoint.

Using sensors embedded in standard smartphones, this technology has the potential to provide clinicians and sports professionals with easy access to more accurate and precise measurements. Its development has not been studied as a clinical instrument for measuring ITB tightness, despite smartphones' increasing popularity in recent years. To the authors' knowledge, there is no study in the literature investigating the Concurrent Validity and Reliability of a Smartphone Measurement Application to Evaluate Iliotibial Band Tightness. To use smartphone applications such as bubble inclinometers in a clinical setting, its effectiveness must be evaluated. Therefore, the aim of this cross-sectional observational study was to determine the inter-observer and intra-observer reliability of a smartphone application iPhone® Measurement Application and determine the correlation between iPhone® Measurement Application and bubble inclinometer regarding active ITB tightness in athletes. In addition, for the two measuring instruments, we tried to analyze the concurrent validity and 95% consensus rate. We hypothesizes that the iPhone® measurement application will exhibit strong concurrent validity and reliability when assessing iliotibial band (ITB) tightness, demonstrating a robust correlation with the bubble inclinometer measurements in athletes.

MATERIALS AND METHODS

Study design and participants

This cross-sectional study was conducted across two sessions at KTO Karatay University Physical Therapy Laboratory between March 2021 and April 2021. This study was approved by KTO Karatay University Faculty of Medicine Drug and Non-Medical Device Research Ethics Committee (Decision Date: 27.12.2019, Number 2019/012) and prospectively registered at www.clinicaltrials.gov (NCT04787900).

A priori power analysis suggests a minimum enrollment of 16 or more athletes for a correlation of 0.7, an α level of 0.05, and a power of 95% (12). Inclusion criteria for this study were being between the ages of 20 and 45, having an ITB inclination angle below 24.59 degrees (10) and consenting to participate. Exclusion criteria included a history of hip or knee surgery and a history of lower extremity trauma within the last three months. Thirty athletes with ITB tightness between 20 and 45 years old were included in this study. The study protocol complied with the Declaration of Helsinki for human experimentation. All athletes provided written informed consent.

Procedure

This study employed a concurrent validity and reliability design to assess the iPhone® measurement app's reliability and accuracy in evaluating ITB tightness. The bubble inclinometer, recognized for its validity and reliability in OBER test assessments, was chosen for comparison. Athletes underwent a standardized 2-minutes warm-up with a cycle ergometer before the measurements (13). Additionally, prior to data collection, all athletes were introduced to the testing procedures and equipment. This familiarization process aimed to ensure athletes' comfort and understanding of the tests and devices, potentially enhancing the reliability of the collected data. The ITB flexibilities of both the dominant and nondominant limbs were evaluated by two independent blinded researchers, each in a separate room. One researcher used the iPhone® measurement application, while the other utilized a bubble inclinometer for measurements. The assessments were conducted sequentially by the first

Figure 1. A) Measurement procedure for the Ober test with a bubble inclinometer. B) Measurement procedure for the Ober test with iPhone® measurement application

investigator followed by the second investigator, ensuring consistency and comparability in the evaluation process. All measurement values were recorded by a third investigator to maintain impartiality and accuracy in data collection. For each extremity of the athletes, three measurements were taken, with a 5-minutes passive rest period provided between each measurement. This practice aimed to minimize any potential fatigue effects and ensure reliable and consistent assessments. Following data collection, a rigorous comparative analysis was performed utilizing statistical methods established in prior studies (14,15). This analysis involved a comprehensive examination of the data obtained from both devices to determine their validity and reliability in assessing ITB tightness.

Before the initial measurement, the athlete warmed up for 2 minutes. After warming up, the athlete lay on his side and flexed his knee to 90°. The researcher stabilized the patient from the pelvis with one hand and, with the other hand, brought the athlete's flexed leg to adduct and extend. The non-measured extremity was stabilized with the aid of a belt. Bubble inclinometer was first used for measurement. Researcher 3 recorded the result by placing the device to be measured on the lateral projection of the midpoint of the femur with a 90-degree angle (Figure 1a).

After the first bubble inclinometer measurement, the second and third measurements were taken with 5-minutes passive intervals.

Following the completion of the first researcher's evaluation, the athletes moved to the second researcher's room. The protocol applied for the bubble inclinometer was used for the measurements of the athletes (Figure 1b). The primary outcome of this study was concurrent validity, and the secondary outcome was reliability.

Instruments

We used two devices to measure ITB tightness, namely, bubble inclinometer (Baseline, Fabrication Enterprises Inc., New York) and iPhone® measurement applications (Apple Inc., California). The iPhone® measurement application measurements were made with the iPhone 6s plus running in IOS 13.3.1 (Apple Inc., California).

Statistical analysis

The SPSS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, version 25.0. Armonk, NY: IBM Corp.) software was used to evaluate the data and the Shapiro-Wilk test to examine the conformity

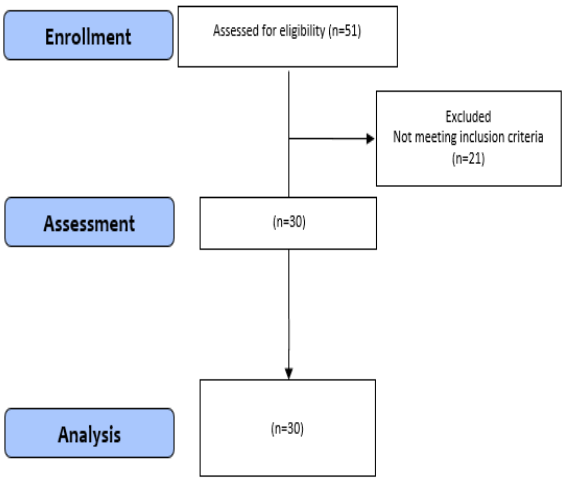


Figure 2. Flow diagram

of variables to normal distribution. All data were normally distributed. We analyzed using the mean ± standard deviation for the demographic data of the athletes. Descriptive data (mean ± standard deviation) were determined for the measuring angles of both devices.

The criterion and concurrent validity of the bubble inclinometer and iPhone® measurement applications were compared with the reference standard and were calculated using the Pearson product-moment correlation coefficient (r, two-tailed). The correlations were interpreted as weak (0.1–0.39), moderate (0.4–0.69), or strong (0.7– 0.99) (16).

The reliability of all measurements was tested using the ICC models (3, k and 2, k, respectively) for the intra-rater and inter-rater analyses. Using the SPSS software, the ICC model (2, k) was computed by selecting the options two-way random, average measure, and absolute agreement and the ICC model (3, k) the options two-way mixed and average measure (17).

The Bland-Altman plots were used to visually assess the mean differences and 95% limits of agreement between the bubble inclinometer and iPhone® measurement applications (18). A standard measurement error (SEM) calculated in the SD X √(1-ICC) form was used to examine the instruments' precision (19). The minimum detectable change (MDC95) representing the magnitude of the change required to provide confidence that a change is not caused by a random variation or measurement error was calculated with the formula form √2 X 1.96 X SEM at 95% confidence level. The level of significance was set at 0.05 (20).

RESULTS

The demographic information of 30 athletes with ITB tightness between the ages of 20 and 45 in this study was given in Table 1. (N = 30; 17 males, 13 females; age = 26.3 ± 4.6 years; body mass index = 23.5 ± 1.6 kg/m2). The flow diagram is shown in Figure 2. The measuring angles for each device by two researchers are given in Table 2.

Concurrent validity

One of the outcomes of this study is concurrent validity. The analysis of the whole dataset showed a strong correlation between the bubble inclinometer and iPhone® measurement application for ITB tightness measurement (r = 0.945, 95% CI = 0.058–0.575).

The Bland-Altman plot illustrated the agreement between the iPhone® measurement application and bubble inclinometer, with most values falling within the 95% limits of agreement (Figure 3). The mean difference between the iPhone® measurement application and bubble inclinometer measurement angle were −0.310.

Reliability

Another of the outcomes of this study was reliability, which was analyzed both inter-rater and intra-rater.

Intra-rater reliability

A strong intra-rater reliability was found with both the bubble inclinometer (ICC:0.983, %95CI:0.960–0.992) and iPhone® measurement application (ICC: 0.986, %95CI: 0.971–0.993) (Table 3).

Inter-rater reliability

A strong inter-rater reliability was found with both the bubble inclinometer (ICC:0.992, %95CI:0.987–0.995) and iPhone® measurement application (ICC: 0.941, %95CI: 0.902–0.965). (Table 4).

DISCUSSION

This is the first study that investigated the intra-rater and inter-rater reliability and concurrent validity of iPhone® measurement applications in measuring ITB tightness in individuals without ITB-related pathology The iPhone® measurement application was found to be highly valid, reliable, and accurate in measuring ITB tightness compared to a bubble inclinometer. The concurrent validity for ITB tightness between the bubble inclinometer and iPhone® measurement application was strong. These results are consistent

Table 1. Demographic characteristics of the participants

	Mean	SD
Age (year)	26.36	4.62
Height (m)	1.77	.05
Weight (kg)	71.30	7.38
BMI (kg/m^2)	23.52	1.68
Gender	n	%
Male	17	56.67
Female	13	43.33

n, number of participants; SD, standard deviation; BMI, body mass index; kg, kilogram, m:meter %, percentage

Table 2. Measurements of iliotibial band tightness for each device

	Right		Left	
	Mean	SD	Mean	SD
Bubble inclinometer (degree) Researcher 1	18.96	3.14	18.93	3.03
Bubble inclinometer (degree) Researcher 2	18.93	3.21	19.1	3.17
iPhone® measurement applications (degree) Researcher 1	19.23	2.93	19.36	2.67
iPhone® measurement applications (degree) Researcher 2	19.26	2.91	19.6	3.99

SD, Standard deviation

Table 3. Intra-rater reliability

Intra-rater	Bubble inclinometer	iPhone® measurement application
ICC (95% CI)	0.983 (0.96–0.992)	0.986 (0.971–0.993)
SEM	0.797	0.680
MDC_{95}	2.098	1.884

ICC, intraclass correlation coefficient; CI, confidence interval; SEM, standard error of measurement; MDC95, minimum detectable change

Table 4. Inter-rater reliability

Inter-rater	Bubble inclinometer	iPhone® measurement application
ICC (95% CI)	0.992 (0.987–0.995)	0.941 (0.902–0.965)
SEM	0.555	1.445
MDC_{95}	1.538	4.005

ICC, intraclass correlation coefficient; CI, confidence interval; SEM, standard error of measurement; MDC95, minimum detectable change

with various studies showing similar levels of correlation between smartphone applications and inclinometers and goniometers for measuring different ranges of motion (21,22).

Stresses from the daily living activities and sports, traumas, and pathologies can affect ITB mechanics and function. ITB tightness causes sports injuries, especially in the knee and hip joints. Measuring ITB tightness using valid and reliable tools can help clinicians and physiotherapists to provide an accurate clinical evaluation of athletes with knee and hip injuries occurring during competition or training (23,24). In the literature, the intra-rater and inter-rater reliability values of the bubble inclinometer used to measure ITB tightness have been reported to be strong (5,8). In this study, the ICC values for intra-rater and inter-rater reliability of measuring ITB tightness using the bubble inclinometer were 0.983 and 0.992, respectively. The reliability of the bubble inclinometer in this study aligns with prior research, showing consistently strong ICC values.

Several studies have evaluated the reliability and validity of smartphone ROM applications (25–27). Charlton et al. (28) evaluated the reliability and validity of a Smartphone for the assessment of hip ROM and found that intra-rater reliability ranged from 0.63 to 0.94. When compared to bubble inclinometer and motion analysis system, concurrent validity was 0.71 to 0.98. In another study of smartphone validity and reliability for the assessment of hip ROM, concurrent validity was excellent (r = 0.91-0.93). In addition, it showed excellent intra-rater and inter-rater reliability (ICC > 0.90) for all hip movements (29). The validity and reliability of the smartphone for the assessment of hip ROM were generally found to be valid and reliable in studies. We think that smartphones can be used in the evaluation of ROM of the hip joint due to the low compensation in the movements of the hip joint during measurement.

According to the results of the Ober test conducted by Reese and Bandy (5) the ITB tightness measured with the bubble inclinometer was 18.9°. In this study, the bubble inclinometer angle varied between 18.93° and 18.96°, and the tilt angle measured with iPhone® measurement applications was between 19.23° and 19.26°. The angular values obtained from this study are similar to the literature. The mean measurement values obtained from both devices used in this study were comparable. The results also revealed that both raters had a strong intra-rater reliability. In this study, the bubble inclinometer mean values were slightly

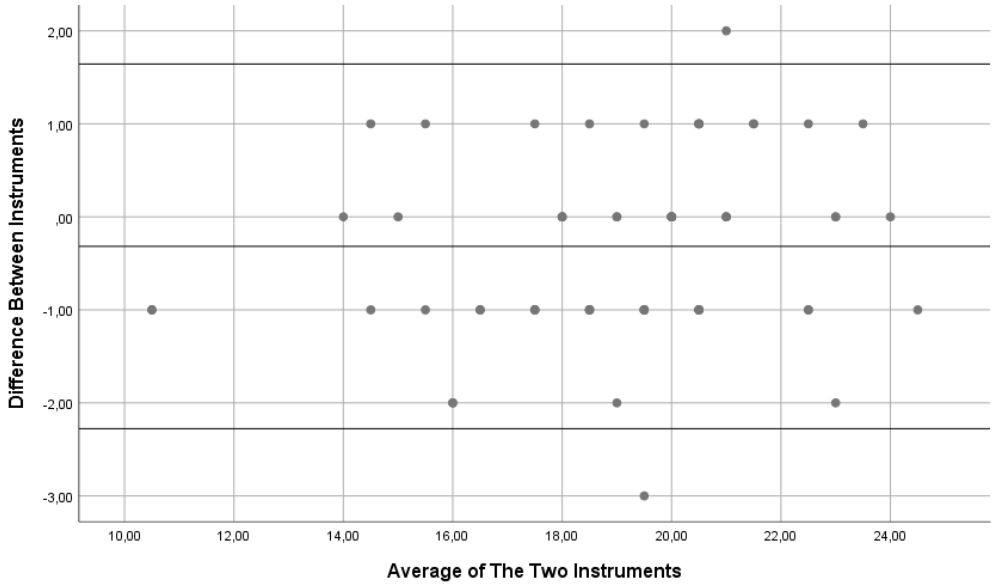


Figure 3. Bland-Altman plot for the iPhone® measurement application and bubble inclinometer

lower than that with the iPhone® measurement application. The distinct device structures and potential challenges in maintaining constant skin contact with the smartphone during measurement might explain the variance in average values obtained. We think that the high surface area of the smartphone and full contact make measurement easier. These results could have potential practical applications for physicians and physiotherapists wanting to simply monitor their patients' ITB tightness using their smartphones. Another reason for the high reliability may be due to more than 10 years of clinical experience of the investigators making the assessments. However, more research is needed in investigating the reliability of the existing iPhone® measurement applications for inexperienced examiner where reliability values cannot be predicted. Before the evaluations, the athletes were shown how to perform the application. To get more reliable results, we performed all measurements for three times. The averages of these measurements were analyzed. There are validity and reliability studies on the use of the iPhone® measurement application for range of motion evaluation, but there are no studies on the use of the application in ITB tightness (9,14,21,30,31). The findings of this study align with existing literature (9,17). The ICC values for the intra-rater and inter-rater reliability of measuring ITB tightness using the iPhone® were 0.986 and 0.941, respectively.

The intra-rater (0.971-0.993) and inter-rater (0.902-0.965) reliability of the iPhone® measurement applications were strong. The reliability achieved with the iPhone® measurement applications was comparable to that of the gravity-based inclinometer, partly owing to the absence of a smartphone case, a snug fit, and familiarity. The advantages of using the iPhone® measurement applications over the bubble inclinometer are being not limited in time and space and being a standard and free application of an iPhone®. It should be noted that millions of people can easily access the iPhone® measurement application from Apple's AppStore. Conversely, the limitations of using smartphones should be considered. Examiners may not want to use their smartphone for evaluation, as there will be direct contact between the smartphone and the individual's skin (9). Additionally, software and hardware problems may be encountered in smartphones regardless of the examiner. Depending on the increase in smartphone usage, the use of a valid and reliable application other than the medical devices used for clinical ROM measurement may make the evaluation easier and cheaper. Thus, based on this information, the iPhone® measurement application can be used validly and reliably for ITB tightness measurement without the need for additional medical equipment.

The strength of this study is that it reached a sufficient sample size, and it was a double-blind study. Despite its strengths, this study encountered several

limitations. Firstly, the iPhone Measurement application used for assessment was limited to the iOS operating system, restricting its application on other platforms like Android or HarmonyOS. Additionally, the expertise level of the examiners could potentially impact the study outcomes, raising uncertainties about whether less experienced raters would produce similar results. Furthermore, the study faced an imbalance in gender representation, with a larger number of male athletes compared to females. This disparity might have influenced the generalizability of the findings, considering potential anatomical and biomechanical variations between genders. While the study aimed to focus on ITB tightness regardless of gender-specific variations, future research should consider a more balanced gender representation for a comprehensive understanding of potential impacts on measurement outcomes.

Evaluation is important in the field of physiotherapy and sports. Before and after a problem occurs, the problem source is understood with a good evaluation, wherein many devices can be used (e.g., goniometers, inclinometers, measuring tapes, etc.) (10,22). Recently, the use of smartphone technology has become widespread due to its practicality and the large number of people using it. Thus, measurements can be made easily without the need for medical equipment. This study demonstrated that the iPhone® measurement applications in a ready-to-use smartphone are valid and reliable for measuring ITB tightness.

CONCLUSION

The study's hypothesis positing the strong concurrent validity and reliability of the iPhone® measurement application in evaluating ITB tightness has been confirmed. Our findings demonstrate a robust correlation between measurements obtained via the iPhone® application and the bubble inclinometer, supporting its effectiveness as a valid and reliable tool for assessing ITB tightness among athletes with ITB-tightness pathology. Therefore, the study's objectives have been met, affirming the utility of the iPhone® measurement application as a feasible alternative to traditional medical devices, offering clinicians and physiotherapists a convenient and reliable means of evaluating ITB tightness.

We recommend the incorporation of the iPhone® measurement application as a complementary assessment tool in clinical settings. Its accessibility, accuracy, and reliability make it a valuable addition to the array of traditional measurement devices. However, practitioners should consider the need for standardization in its usage and ensure familiarity with the application's methodology to optimize results. Additionally, future research should explore its efficacy in diverse populations and validate its use by practitioners with varying levels of experience.

Acknowledgements: Thanks to all participants.
Author contributions:
Conflict of interest: The authors have no conflict of interest to declare related to the present manuscript.
Ethical approval: This study was approved by KTO Karatay University Faculty of Medicine Drug and Non-Medical Device Research Ethics Committee (Decision Date: 27.12.2019, Number 2019/012) and prospectively registered at www.clinicaltrials.gov (NCT04787900). Informed consent was obtained from all patients for being included in the study.
Funding: None
Peer- review: Externally peer-reviewed.

REFERENCES

1. Flato R, Passanante GJ, Skalski MR, Patel DB, White EA, Matcuk GR. The iliotibial tract: imaging, anatomy, injuries, and other pathology. Skeletal Radiology 2017;46(5):605–22.
2. Hyland S, Varacallo M. Anatomy, Bony Pelvis and Lower Limb, Iliotibial Band (Tract). StatPearls. 2019.
3. Baker RL, Fredericson M. Iliotibial Band Syndrome in Runners. Physical Medicine and Rehabilitation Clinics of North America 2016;27(1):53–77.
4. Devan MR, Pescatello LS, Faghri P, Anderson J. A Prospective Study of Overuse Knee Injuries Among Female Athletes With Muscle Imbalances and Structural Abnormalities. Journal of Athletic Training 2004;39(3):263–7.
5. Reese NB, Bandy WD. Use of an Inclinometer to Measure Flexibility of the Iliotibial Band Using the Ober Test and the Modified Ober Test: Differences in Magnitude and Reliability of Measurements. Journal of Orthopaedic & Sports Physical Therapy 2003;33(6):326–30.
6. Ober FR. Back Strain and Sciatica. JAMA: The Journal of the American Medical Association. 1935;104(18):1580.
7. Willett GM, Keim SA, Shostrom VK, Lomneth CS. An Anatomic Investigation of the Ober Test. The American Journal of Sports Medicine 2016;44(3):696–701.
8. Melchione WE, Sullivan MS. Reliability of measurements obtained by use of an instrument

designed to indirectly measure iliotibial band length. Journal of Orthopaedic and Sports Physical Therapy 1993;18(3):511–5.
9. Salamh PA, Kolber M. The reliability, minimal detectable change and concurrent validity of a gravity-based bubble inclinometer and iphone application for measuring standing lumbar lordosis. Physiotherapy Theory and Practice 2014;30(1):62–7.
10. Ferber R, Kendall KD, McElroy L. Normative and Critical Criteria for Iliotibial Band and Iliopsoas Muscle Flexibility. Journal of Athletic Training 2010;45(4):344–8.
11. Samo DG, Chen SPC, Crampton AR, Chen EH, Conrad KM, Egan L, et al. Validity of Three Lumbar Sagittal Motion Measurement Methods. Journal of Occupational & Environmental Medicine 199739(3):209–16.
12. Erdfelder E, FAul F, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. Behavior Research Methods 2009;41(4):1149–60.
13. Kelly SB, Alvar BA, Black LE, Dodd DJ, Carothers KF, Brown LE. The Effect of Warm-Up With Whole-Body Vibration vs. Cycle Ergometry on Isokinetic Dynamometry. Journal of Strength and Conditioning Research 2010;24(11):3140–3.
14. Balsalobre-Fernández C, Romero-Franco N, Jiménez-Reyes P. Concurrent validity and reliability of an iPhone app for the measurement of ankle dorsiflexion and inter-limb asymmetries. Journal of Sports Sciences 2019;37(3):249–53.
15. Bland JM, Altman DG. Measuring agreement in method comparison studies. Statistical Methods in Medical Research 1999;8(2):135–60.
16. Pots P, Winter G. [Morphological investigation endometrial changes due to drugs]. Zeitschrift fur Geburtshilfe und Gynakologie 1956;147(1):44–51.
17. Kolber MJ, Pizzini M, Robinson A, Yanez D, Hanney WJ. The reliability and concurrent validity of measurements used to quantify lumbar spine mobility: an analysis of an iphone® application and gravity based inclinometry. International Journal of Sports Physical Therapy 2013;8(2):129–37.
18. Martin Bland J, Altman DouglasG. Statistical methods for assessing agreement between two methods of clinical measurement. The Lancet 1986;327(8476):307–10.
19. Pourahmadi MR, Taghipour M, Jannati E, Mohseni-Bandpei MA, Ebrahimi Takamjani I, Rajabzadeh F. Reliability and validity of an iPhone ® application for the measurement of lumbar spine flexion and extension range of motion. Peer J 2016;4:e2355.
20. Haley SM, Fragala-Pinkham MA. Interpreting Change Scores of Tests and Measures Used in Physical Therapy. Physical Therapy 2006;86(5):735–43.
21. Bucke J, Spencer S, Fawcett L, Sonvico L, Rushton A, Heneghan NR. Validity of the Digital Inclinometer and iPhone When Measuring Thoracic Spine Rotation. Journal of Athletic Training 2017;52(9):820–5.
22. Stanek JM, Parish J, Rainville R, Williams JG. Test-Retest and Intrarater Reliability of Assessing Tibial Rotation Range of Motion by Two Devices. International Journal of Athletic Therapy and Training 2020;25(5):263–9.
23. Beals C, Flanigan D. A Review of Treatments for Iliotibial Band Syndrome in the Athletic Population. Journal of Sports Medicine 2013;2013:1–6.
24. Strauss EJ, Kim S, Calcei JG, Park D. Iliotibial Band Syndrome: Evaluation and Management. American Academy of Orthopaedic Surgeon 2011;19(12):728–36.
25. Bruyneel AV. Smartphone applications for range of motion measurement in clinical practice: A literature review of inclinometer and goniometric tools. Annals of Physical and Rehabilitation Medicine 2018;61:e454.
26. Hahn S, Kröger I, Willwacher S, Augat P. Reliability and validity varies among smartphone apps for range of motion measurements of the lower extremity: a systematic review. Biomedical Engineering/Biomedizinische. Technik 2021;66(6):537–55.
27. Keogh JWL, Cox A, Anderson S, Liew B, Olsen A, Schram B, et al. Reliability and validity of clinically accessible smartphone applications to measure joint range of motion: A systematic review. Müller J, editor. PLOS ONE 2019;14(5):e0215806.
28. Charlton PC, Mentiplay BF, Pua YH, Clark RA. Reliability and concurrent validity of a Smartphone, bubble inclinometer and motion analysis system for measurement of hip joint range of motion. Journal of Science and Medicine in Sport 2015;18(3):262–7.
29. Sarac DC, Yalcinkaya G, Unver B. Validity and reliability of a smartphone goniometer application

for measuring hip range of motions. Work 2022;71(1):275–80.
30. Balsalobre-Fernández C, Marchante D, Muñoz-López M, Jiménez SL. Validity and reliability of a novel iPhone app for the measurement of barbell velocity and 1RM on the bench-press exercise. Journal of Sports Sciences 2018;36(1):64–70.
31. Pourahmadi M, Momeni E, Mohseni N, Hesarikia H, Ghanjal A, Shamsoddini A. The reliability and concurrent validity of a new iPhone® application for measuring active lumbar spine flexion and extension range of motion in patients with low back pain. Physiotherapy Theory and Practice 2021;37(1):204–17.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 358-366
https://doi.org/10.30621/jbachs.1303019
RESEARCH ARTICLE

EXAMINING PATIENTS' USE OF GRADUATED COMPRESSION STOCKINGS IN POSTOPERATIVE PERIOD

Filiz Salman Saraç[1], Altun Baksi[1], Faruk Durna[2], Nida Nur Yurt[2]

[1] Suleyman Demirel University, Faculty of Health Sciences, Department of Surgical Nursing, Isparta, Turkey.
[2] Suleyman Demirel University, Faculty of Health Sciences, Department of Nursing, Isparta, Turkey.

ORCID: F.S. 0000-0003-2107-0545; A.B. 0000-0001-8267-2254; F.D. 0000-0002-9470-7386; N.N.Y. 0000-0002-2795-0810

Corresponding author: Filiz Salman Saraç, **E-mail:** filizslmn@gmail.com
Received: 26.05.2023; **Accepted:** 27.02.2024; **Available Online Date:** 31.05.2024

Cite this article as: Salman F, Baksi A, Durna F, Yurt NN. Examining Patients' Use of Graduated Compression Stockings in Postoperative Period. J Basic Clin Health Sci 2024; 8: 358-366.

ABSTRACT

Purpose: This study aimed to examine the use of graduated compression stockings in patients after surgery.
Methods: Employing a descriptive research design, the study was conducted on a sample of 173 postoperative patients using compression stockings in the surgical departments of a university hospital. The data, obtained through the sociodemographic and clinical characteristics form, and the evaluation form assessing the use and knowledge level of graduated compression stockings, were collected via face-to-face interviews and observation.
Results: The mean age of the patients in the study sample was 58.84±13.67 years, and the number of days after wearing graduated compression stockings was 2.97±2.14. Among all the patients, 80.9% did not elevate their feet while in bed before putting on stockings, and 72.3% did not wear stockings before getting out of bed. The researchers observed that 50.9% of the patients correctly positioned the stockings on the heel, while 79.2% had folds in the stockings they wore. Additionally, during the removal of stockings for observations, 59.5% of the patients exhibited redness in the corresponding area. The patients who received information from healthcare providers had used the stocking accurately, and there was less tissue damage ($p<0.05$).
Conclusion: Patients experience some problems during the use of stockings, such as incorrect usage and tissue damage; however, these problems are less observed in educated patients. Consequently, it is advisable to implement comprehensive and effective patient education programs on compression stocking usage to address these issues and improve patient outcomes.

Keywords: Graduated compression stockings, Nursing, Postoperative, Venous thromboembolism

INTRODUCTION

Venous Thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism, is a preventable and significant health issue, often occurring in the lower extremity venous vessels (1). Three basic mechanisms which facilitate the development of VTE and which are defined as the Virchow triad are slowing of blood flow, endothelial damage and hypercoagulation (2, 3). When the clot formed as a result of this mechanism moves to other parts of the body, potentially fatal consequences occur (1). It is stated that 1-2/1000 cases of VTE are seen in the world every year (1, 4). In Turkey, the prevalence of VTE in postoperative patients varies between 0.56 and 1 per 1000 (5, 6). However, approximately 600 thousand cases of VTE are seen

in the United States every year, causing 7-10 billion dollars of expenditure in the area of health (1, 4). VTE leads to prolonged hospitalization, an increase in treatment costs, complications and an increase in mortality (1). Therefore, interventions to prevent VTE are important in the care and treatment of patients.

National and international health organizations periodically publish and update clinical guidelines for the prevention and management of VTE (2, 4, 7, 8). Primarily pharmacological treatment methods are recommended for the prevention of VTE (1, 2). The use of mechanical protective measures is recommended besides the use of pharmacological treatment or in patients who cannot use pharmacological treatment (2, 7). Graduated compression stockings (GCS), one of the mechanical protective measures, are easy-to-access and cost-effective medical products when compared to other mechanical protective measures such as the intermittent pneumatic compression. The use of GCS in patients at low risk for the development of VTE is controversial (9). In a large-scale study conducted with patients at moderate and high risk for DVT, it was stated that pharmacological treatment alone may be sufficient to prevent DVT and that the use of GCS may be unnecessary in many patients (10). However, GCS is now widely used in patients with moderate and high risk (8, 11).

When GCSs are used effectively and properly in patients in the postoperative period, they decrease the incidence of DVT by reducing not only the general cross-sectional area of the leg but also venous distension, by enhancing the venous return and by improving the venous valve function (12, 13). In order for GCSs to be effective, they must be in appropriate sizes for the patients' body and provide the appropriate compression (13, 14). In addition, for the effective use of stockings, patients should know the points to be considered regarding the use of GCS (11). Skin problems such as insufficient compression and support, ring-shaped compression marks, tourniquet effect, dryness of the skin, itching and compression ulcers are frequently encountered as a result of improper use of GCS (13, 15, 16). Injuries due to the use of GCS are among important injuries related to mechanical devices (17). Especially the problems experienced by patients with leg edema are more common (11).

Although the use of GCS is an effective method in the prevention of DVT, patients' insufficient knowledge about the use of stockings may cause undesirable harmful effects. Healthcare professionals have an important role in enabling patients to access adequate and appropriate information. Nurses have an important role in the care, education and follow-up of patients at risk for DVT, yet there are still deficiencies in the interventions made in relation to this subject (18). Compliance with a standard protocol during the use of stockings for the prevention of embolism may help reduce the skin problems seen in patients (19). It was observed during the use of GCS in the clinic that misapplications were made; those patients had insufficient knowledge about this subject; and that skin problems related to the use of stockings were experienced. In this respect, the purpose of this study was to examine the patients' use of GCS in the postoperative period.

MATERIALS AND METHOD

Research Design

The study was carried out using the descriptive research design. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the clinical research ethics committee of Suleyman Demirel University (Decision Date: 24.05.2022 and number 11/150). In addition, the consents of the institution where the study was carried out were obtained. The study was conducted in the surgical department of a university hospital (General Surgery, Neurosurgery, Orthopedics, Thoracic Surgery and Cardiovascular Surgery) in western Turkey between September 2022 and January 2023.

Participants

The research sample consisted of 173 patients who were treated in the surgical clinics of a university hospital at the time the research data were collected and who met the sampling criteria. The criteria for inclusion in the research sample included being 18 years or older, agreeing to participate in the study voluntarily, being in the postoperative period, having undergone elective surgery, using GCS for the last 48 hours, being able to understand and speak Turkish, and having orientation for person, place and time. Among the criteria for being excluded from the research sample was the presence of a disease (such as dementia/Alzheimer's, schizophrenia, etc.) that may influence the capability of making decisions. The patients were asked for their consents with the help of Informed Consent Form, which included information about the purpose of the study, the

Table 1. Socio-demographic and clinical characteristics of the patients (n:173)

Variable	n	%
Gender		
Female	95	54.9
Male	78	45.1
Marital Status		
Single	26	15.0
Married	147	85.0
Educational Background		
Literature	54	31.2
Elementary School/Secondary School	55	31.8
High School	39	22.5
Bachelor degree or above	25	14.5
Financial Status Perception		
Income lower than expenditures	12	6.9
Income equal to expenditures	103	59.5
Income higher than expenditures	58	33.5
Employment		
Employed	66	38.2
Unemployed	107	61.8
Chronic Disease		
Yes	92	53.2
No	81	46.8
Body mass index		
Lower than 18.9 kg/m^2 (weak)	3	1.7
Between 19-24.9 kg/m^2 (normal)	66	38.2
Between 25-29.9 kg/m^2 (a little fat)	56	32.4
Between 30-34.9 kg/m^2 (obese)	26	15.0
Higher than 35 kg/m^2 (extremely obese)	22	12.7
The clinic of treatment received	34	19.7
General surgery	45	26.0
Orthopedics	38	22.0
Brain and neurosurgery	38	22.0
Thoracic surgery	18	10.4
Cardiovascular		
Prior surgical experience		
Yes	90	52.0
No	83	48.0
Post-operative standing up/mobilization	108	62.4
Yes	65	37.6
No		
	Mean ± Standard Deviation	
Age	58.84±13.67 (min-max=22-85)	
Postoperative mobilization time (Hour)	5.70±1.75 (min-max=1 -11)	
Satisfaction with the health service	7.23 ±1.00 (min-max=4-9)	

duration of the research process, the implementation process, data collection, voluntary participation in the study, leaving the study at any time, and keeping the participants' names confidential.

Data Collection Tools

The research data were collected using the Socio-Demographic and Clinical Characteristics Form and the Use and Knowledge Level of Graduated Compression Stockings Evaluation Form, from the patients who met the sampling criteria. While collecting the data, the face-to-face interview method was used when the patients' general condition was stable and appropriate. The stockings were put off to observe whether there was a problem related to the use of GCS in the patients, and they put on the stockings again after the observation. In order to ensure the reliability of the observational data, the data were collected together by two researchers. The data collection process lasted an average of 10-15 minutes. Moreover, some of the research data were obtained from the patients' medical records (type of anesthesia, and so on).

Socio-Demographic and Clinical Characteristics Form

This form was prepared by the researchers in line with the literature. The form was made up of a total of 18 questions regarding the socio-demographic and clinical characteristics of the patients, such as "age, gender, educational background, employment status, chronic disease, type of chronic disease, body mass index, the clinic where the treatment was received, the type of anesthesia used in the surgery, previous experience in surgical intervention, and so on" (11, 13, 16, 20).

The Use and Knowledge Level of Graduated Compression Stockings Evaluation Form

This form was prepared by the researchers in line with the guidelines and studies on the use of GCS (7, 10, 11, 13, 15, 16, 19, 21, 22). There were 33 questions in the form to evaluate the patients' use of GCS and their knowledge level.

Data Analysis

The research data were analyzed in 25 package programs of SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL). In accordance with the purpose of the study, descriptive statistics are shown as number (n) and percentage (%) values in categorical data and mean±standard deviation (Mean±SD) values in continuous data. Pearson Chi-square analysis was used to compare categorical variables between groups.

Table 2. Evaluating patients' use of graduated compression stockings and their knowledge levels (n:173)

Variables	n	%
Previous use of GCS*		
Yes	55	31.8
No	118	68.2
Time when GCS was used for the first time		
A few hours before surgery	1	0.6
In the operating room	9	5.2
In the clinic after the operation	163	94.2
Kind of GCS		
Knee-length	112	64.7
Thigh-length	61	35.3
Type of GCS		
With toes open	173	100.0
Measuring the leg before the use of GCS		
Yes	51	29.5
No	122	70.5
Compression level of the stockings used		
Not known	173	100.0
Need for assistance while putting on and off GCS		
Yes	88	50.9
No	85	49.1
Difficulties/problems experienced during the use of GCS according to the patient's report		
Itching	76	45.0
Feeling warm	74	43.8
Redness	66	39.1
Inability to put on/ off stockings without help	49	28.5
Causing pain	42	24.9
Sweating	24	14.2
Color change	23	13.6
Slipping of stockings	21	12.4
Difficulty in wearing	20	11.8
Sensibility	19	11.2
Other**	60	35.6
Fit of the GCS size		
Yes	110	63.6
No	63	36.4
If the GCS size is not suitable, how is it?		
Too tight	54	85.7
Too loose	9	14.3
Whether informed about GCS or not?		
Yes	96	55.5
No	77	44.5
Do you know why you use GCS?		
Yes	148	85.5
No	25	14.5
Why are you using GCS? (n=148)		
Prevention of clot formation	114	65.9
Prevention of swelling	10	5.8
Eliminating pain	24	13.9
Do you know how you should use GCS?		
Yes	140	80.9
No	33	19.1
Before I put on GCS, I lifted my feet up for a while (in bed).		
Yes	33	19.1
No	140	80.9
I put on GCS before getting out of bed.		
Yes	48	27.7
No	125	72.3
I wore it by placing the heel area of GCS properly.		
Yes	132	76.3
No	41	23.7
After the operation, I removed GCS for such reasons as examination, massage, and so on.		
Yes	118	68.2
No	55	31.8
I checked my skin by removing GCS during the day.		
Yes	98	56.6
No	75	43.4
I checked the toe opening and the upper part of the legs skin for redness, and so on.		
Yes	128	74.0
No	45	26.0
I paid attention to whether there were folds/wrinkles.		
Yes	109	63.0
No	64	37.0
I made sure that they ended 2.5-5 cm below the patella (if the stockings were knee-length).		
Yes	21	18.8
No	91	81.3
I made sure that they ended 2.5-7.5 cm below the gluteal fold (if the stockings were thigh-length).		
Yes	18	29.5
No	43	70.5
I washed GCS with warm water without rubbing it when they got dirty.		
Yes	55	31.8
No	118	68.2
I know how to remove GCS.		
Yes	118	68.2
No	55	31.8

*GCS: Graduated compression stockings, **Other: Includes tingling, unaesthetic appearance, restriction of movement, edema, numbness and dryness of the skin.

Table 3. Observations of the researchers regarding the use of graduated compression stockings worn by the patients (n:173)

Variable	n	%
Wearing GCS* with proper placement on the heel		
Yes	88	50.9
No	85	49.1
Wearing GCS without folds		
Yes	36	20.8
No	137	79.2
In the case of knee-length GCS, ending 2.5-5 cm below the patella (n=112)		
Yes	17	15.2
No	95	84.8
In the case of thigh-length GCS, ending 2.5-7.5 cm below the gluteal fold (n=61)		
Yes	12	19.7
No	49	80.3
The presence of problems observed in the tissue		
Yes	112	64.7
No	61	35.3
Problems observed in the tissue		
Redness	103	59.5
Squeezing	48	27.7
Edema	18	10.4
Other**	7	4

* GCS: Graduated compression stockings, Other** includes compression ulcer and tourniquet effect.

RESULTS

The mean age of the patients in the study sample was 58.84±13.67 years. Of the patients in the postoperative period, 54.9% were women; 31.8% were primary school/secondary school graduates; 61.8% of 59.5% were unemployed; 53.2% had a chronic disease; and 38.2% were of normal weight. Among all the patients, 26% of them were treated in the orthopedic clinic; 77.5% received general anesthesia; 52% had undergone previous surgery; and 62.4% were able to stand up after surgery (Table 1). The socio-demographic and clinical characteristics of the patients in the postoperative period are given in Table 1 below.

Of all the patients in the study sample, 68.2% of them had not used GCS before; 94.2% wore the stockings in the clinical setting after the surgery; 64.7% used knee-length stockings and 100% used open-toed stockings; the leg circumference and length of 70.5% were not measured before using GCS; 100% did not know the compression level of the stockings; 50.9% needed help while putting on and putting off GCS; 97.1% did not use an apparatus to put on the stockings; and 45% experienced itching during the use of stockings. Of all the patients in the postoperative period, 63.6% said the size of the GCS was appropriate; 85.7% said the stockings were too tight; 55.5% were informed about GCS; 85.5% knew why they used the stockings; 65.9% used them to prevent clot formation; and 80.9% said they knew how to use the stockings (Table 2).

In addition, 80.9% of the patients did not lift their feet while in bed for a while before putting on the GCS; 72.3% did not wear the stockings before getting out of bed; 76.3% of them placed the stockings on the heel properly; 68.2% of them put off GCS after the operation for such purposes as control, massage and so on; 56.6% checked their skin by removing them during the day; 74% of them checked their skin from their toe opening or from the upper part of their legs where the stockings ended; 63% of them checked the stockings not to have folds/wrinkles while using them; 81.3% of them did not pay attention to the fact that the knee-length stockings should end 2.5-5 cm below the patella; 70.5% did not pay attention to the fact that the thigh-length stockings should end 2.5-7.5 cm below the gluteal fold; 68.2% of them did not wash the stockings with warm water when they got dirty; and 68.2% knew how to put off the stockings (Table 2). Moreover, it was seen that the number of days after GCS was worn was 2.97±2.14 (min-max=2 -18); the number of GCS removals was 2.02±0.92 (min-max=1 -6); and satisfaction level with the training provided by healthcare professionals on the use of GCS was 5.97±1.58 (min-max=1-9).

In the postoperative period, 50.9% of the patients placed GCS properly on the heel; 79.2% did not wear it without any folds; 84.8% did not wear the knee-length compression stockings 2.5-5 cm below the patella; and 80.3% did not wear the thigh-length compression stockings below the gluteal fold. In addition, 59.5% of the patients were observed to have redness in the area when the GCS was removed (Table 3).

According to the researcher observations, a statistically significant difference was found between the patients' proper use of stockings who received information from healthcare providers about GCS and those who did not. It was revealed that the patients who received training had significantly better results in terms of placing the stockings properly on the heel, wearing them without any fold, and wearing them as appropriate to the knee-length or thigh-length ($p<0.05$). In addition, it was found that the problems observed in the tissue related to the use of GCS in the patients were fewer in number in the group that received information ($p<0.05$) (Table 4). There was

Table 4. Comparison of researcher observations and informing patients about GCS* (n=173)

Variables		Informing about GCS		Analysis**
		Yes n (%)	No n (%)	x^2/p
Wearing GCS with proper placement on the heel	Yes	56 (58.3)	32 (41.6)	**4.81/ 0.028**
	No	40 (41.7)	45 (58.4)	
Wearing GCS without folds	Yes	32(33.3)	4(5.2)	**20.53/ 0.001**
	No	64(66.7)	73(94.8)	
In the case of knee-length GCS, ending 2.5-5 cm below the patella (n=112)	Yes	15 (24.6)	2 (3.9)	**9.21/ 0.002**
	No	46 (75.4)	49 (96.1)	
In the case of thigh-length GCS, ending 2.5-7.5 cm below the gluteal fold (n=61)	Yes	11 (31.4)	1 (3.8)	**7.18/ 0.007**
	No	24 (68.6)	25 (96.2)	
Observed problems	Yes	50 (52.1)	62(80.5)	**15.13/ 0.001**
	No	46 (47.9)	15 (19.5)	

* GCS: Graduated compression stockings ** Pearson Chi-square test

no statistically significant difference between the type of GCS (knee-length and thigh-length) and proper placement of stockings, wearing without any folds or having problems based on the use of stockings ($p>0.05$).

DISCUSSION

According to the reports of the patients in this study, only one third of the body measurements were taken before using GCS. In the literature, it is pointed out that the body measurements of patients should be taken in the preoperative period and that suitable stockings should be according to these measurements (13, 19, 23). Studies demonstrated that patients use stockings in the wrong size and that there is no documentation for the size of stockings used by patients (13, 16). Winslow and Brosz (2008) found that the stockings used in 26% of the postoperative patients were not suitable for the patient's size, and Miller (2011) reported that 36% of the patients did not use stockings appropriate to their size in the postoperative period. Miller (2011) stated that the stockings with the wrong size were one-size or two-size larger than the body measurements of the patients and that these stockings did not allow an effective use in terms of preventing VTE. GCS must be able to provide effective compression in order to reduce the risk of VTE (14).

According to the reports of the patients in the study, about half of them could not get enough information about GCS. The patients generally stated that they knew what the stockings were used for (85.5%). However, when their answers to the question of "Why do you use them" were considered, it was seen that some of the patients (19.7%) did not have accurate knowledge about the purpose of using stockings. Moreover, the patients did not have knowledge about the compression levels of the stockings used. These findings suggest that the patients did not have sufficient knowledge about GCS. Furthermore, the answers given by the patients to the questions about their use of GCS showed that the majority of them did incorrect practices such as wearing stockings after getting out of bed; that about half of them did not put off the stockings at all; that about half of them did not check their skin; or that more than one-third of the patients did not pay attention to the formation of folds. In a study conducted by Winslow and Brosz (2008), it was found that 20% of surgical patients did not know the purpose of using stockings and that 29% of them used stockings improperly (13). On the other hand, Özkan et al. (2016) found that patients in the postoperative period did practices regarding the use of stockings and that their knowledge about this subject was insufficient (16). Improper practices during the use of GCS may cause the use of stockings to be ineffective, the patient's risk of DVT to continue, or problems to occur such as skin problems related to the use (11). Similar to the research findings in the literature, it was seen that the patients had insufficient knowledge about the use of stockings and wore them wrongly.

In this study, it was revealed that the patients had a moderate level of satisfaction with the information they received about the use of GCS (5.97±1.58). The researcher observations demonstrated that the patients who received information about GCS had better use of GCS than the patients who were not informed. It was also seen that these patients placed the stockings properly, paid attention to the absence of folds, and wore the stockings according to the thigh-length or patella-length. In addition, it was found

that the problems observed due to the use of GCS were fewer in these patients. Nurses have important responsibilities in informing and monitoring patients who will use GCS in clinics (11, 14). Nurses should check the patient's skin before wearing GCS and should contact the doctor when there is a situation that prevents them from wearing stockings. In order for the stockings to be used effectively by the patients, they should be provided with adequate education and information, and they should continue their education at intervals during patient follow-up (11, 13). In the regulation on the Amendment of the Nursing Regulation (Official Gazette, 19 April 2011, Number: 27910), nurses' attempts to prevent embolism are legally recorded (24). In the literature, it is reported that although nurses' attitudes towards the use of GCS are positive, there are deficiencies in their knowledge and behaviors regarding this subject (25, 26). Karadogan et al. (2020) found that nurses had insufficient knowledge about the risk factors for venous thromboembolism, about pharmacological and non-pharmacological interventions for the prevention of venous thromboembolism, and about patients' education (20). Inadequacies in both knowledge and behavior are important obstacles that cause patients not to use graduated stockings properly in clinics. It was found that with the clinical use of the anti-embolism stockings care protocol developed by Akyüz and Tunçbilek (2021), the knowledge and practical skills of nurses increased and that the problems encountered by patients related to the use of stockings decreased (19). The guideline published by the American Society of Operating Room Nurses for the prevention of DVT advises establishing and implementing an evidence-based protocol in line with the research results, evaluating the patient in the preoperative period, applying mechanical and pharmacological prophylaxis effectively, providing patients with education, and recording the interventions (23). Parallel to the literature, the findings obtained in the study showed that patients' education was necessary to increase the proper use of GCS and to reduce the problems experienced, similar to the literature.

In the study, the patients stated that they experienced problems such as itching (45.0%), feeling of warmth (43.8%), redness (39.1%), inability to put on and off stockings without help (28.5%) and pain (24.9%) due to the use of GCS. The researchers' observations of the patients revealed that redness (59.5%) and squeezing (27.7%) were encountered most frequently. Studies demonstrated that similar problems were experienced due to the use of stockings in the postoperative period (11, 13, 15, 16, 27). Ozkan et al. (2016) found that patients in the postoperative period mostly experienced problems such as inability to put on and off stockings without help and sweating due to the use of stockings. On the other hand, Winslow and Brosz (2008) reported that most of the surgical patients experienced discomfort due to the use of stockings and that 20% of the patients had redness. In a study examining patients who needed to use compression stockings for a long time, it was revealed that the patients had problems such as difficulty in putting on and off stockings, tightening, sweating and itching (27). These problems were frequently seen in the areas of stockings that were under high compression locally (28). It was reported that the problems experienced in patients in the postoperative period were fewer in patients who used low-compression stockings (21). Improper use of stockings can also cause problems to increase. In a study, it was found that improper use of stockings was more common in patients who were overweight and who used thigh-length stockings and that problems related to the use of stockings were more common (13). In the literature, it is pointed out that the skin should be clean and dry before stockings are used and that stockings should be removed and re-worn daily for skin control (11). The findings obtained in the present study are similar to those reported in the literature, and ineffective use of GCS can lead to serious problems.

In the study, it was seen that mostly knee-length stockings were used by the patients (64.7%). Interventions for the prevention of venous thromboembolism should also ensure the comfort of patients (29). Studies showed that it was easier for patients to adapt to knee-length stockings and that they preferred to use knee-length stockings (13, 30, 31). In addition, it was reported that improper use was more common in patients who used thigh-length stockings (13). In this study, it was seen that regardless of the type of stockings, the patients had similar problems in terms of placing the stockings properly, wearing them without folds, and the problems experienced.

This study has some limitations. The study was performed in a single center, which limits the generalizability of the results. In the section where the patients' use of GCS was observed by the researchers, the form was filled in with two

researchers' consensus as a result of their observations. The fact that the researchers made observations individually and that inter-observer agreement was not examined was considered to be another limitation of the study.

CONCLUSION

In the study, the patients did improper practices such as wearing stockings improperly, not paying attention to folds, and not using stockings with appropriate compression, and they therefore experienced problems such as redness, itching and pain while using the stockings. These problems were less common in patients who received sufficient information about the use of GCS. It is recommended that nurses working in surgical clinics, as care providers, adequately inform their patients about the use of GCS. In addition, patients' use of GCS should be monitored; problems that may occur through daily skin check should be detected early; and preventive measures should be taken. It is also recommended that a protocol be developed and that this protocol be implemented in clinics so that all healthcare professionals can act jointly towards the use of GCS.

What did the study add to the literature?

- It has been revealed that the problems experienced in relation to the graduated compression stockings, which are widely used, still continue.
- Patients are in need of being informed about the use of graduated compression stockings.
- It has been found that training on the use of compression stockings increases their proper use and reduces the observed complications.

Acknowledgements: This research was presented as an oral presentation at 6th International Health Science and Life Congress (IHSLC 2023), Burdur /Türkiye, 2-5 March 2023.

Author Contributions: Concept: FS, AB; Design: FS, AB; Consulting/Supervision: FS, AB; Data collection and/or processing: FD, NNY, FS, AB; Data analysis and/or interpretation: AB, FS; Literature search: FS, AB, FD, NNY; Article writing: FS, AB, FD, NNY; Critical review: AB, FS.

Conflict of Interest: The authors declare no conflict of interest.

Ethical Approval: The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the clinical research ethics committee of Suleyman Demirel University (Decision Date: 24.05.2022 and number 11/150).

Funding: The authors did not receive any financial support in conducting this study.

Peer-Review: Externally peer-reviewed.

REFERENCES

1. Khan F, Tritschler T, Kahn SR, Rodger MA. Venous thromboembolism. The Lancet 2021;398(10294):64-77.
2. Demir M, Erdemli B, Kurtoğlu M, Öngen G. Ulusal venöz tromboembolizm profilaksi ve tedavi kılavuzu. İstanbul: Gü-Ven Platformu; 2010.
3. Roberts SH, Lawrence SM. Venous Thromboembolism. Am J Nurs 2017;117(5):38-47.
4. Ortel TL, Neumann I, Ageno W, et al. American society of hematology 2020 guidelines for management of venous thromboembolism: treatment of deep vein thrombosis and pulmonary embolism. Blood Adv 2020;4(19):4693-738.
5. Atılgan K, Demirdaş E, Er CZ, Çiçekçioğlu F. Evaluation of deep vein thrombosis incidence with respect to age and gender in light of regional factors in central Anatolia: A population-based study. Journal of Surgery and Medicine 2020;4(1):62-65.
6. Edeer AD, Comez S, Damar HT, Savcı A. Prevalence and risk factors of venous thromboembolism in postoperative patients: A retrospective study. Pak J Med Sci 2018;34(6):1539.
7. Sachdeva A, Dalton M, Amaragiri SV, Lees T. Elastic compression stockings for prevention of deep vein thrombosis. Cochrane Database Syst Rev 2010(7).
8. Sachdeva A, Dalton M, Lees T. Graduated compression stockings for prevention of deep vein thrombosis. Cochrane Database Syst Rev 2018(11).
9. Machin M, Peerbux S, Whittley S, et al. Examining the benefit of graduated compression stockings in the prevention of hospital-associated venous thromboembolism in low-risk surgical patients: a multicentre cluster randomised controlled trial (PETS trial). BMJ Open 2023;13(1):e069802.
10. Shalhoub J, Lawton R, Hudson J, et al. Graduated compression stockings as adjuvant to pharmaco-thromboprophylaxis in elective surgical patients (GAPS study): randomised controlled trial. BMJ 2020;369.
11. Akyüz E, Tunçbilek Z. Antiembolik çorap yönetiminde hemşirelerin rol ve sorumlulukları:

antiembolik çorap bakım protokolü. Turk J Cardiovasc Nurs 2018;9(20):96-104.
12. Lim CS, Davies AH. Graduated compression stockings. CMAJ. 2014;186(10):E391-E8.
13. Winslow EH, Brosz DL. Graduated compression stockings in hospitalized postoperative patients: correctness of usage and size. Am J Nurs 2008;108(9):40-50.
14. Geçit S, van Giersbergen MY. Cerrahi hasta bakımında venöz tromboembolizmin önlenmesi kanıt temelli uygulama önerileri. E.Ü. Hemşirelik Fakültesi Dergisi 2021;37(2):179-187.
15. Miller JA. Use and wear of anti-embolism stockings: a clinical audit of surgical patients. Int Wound J 2011;8(1):74-83.
16. Özkan ZK, Fındık Ü, Ünver S. Hastaların ameliyat sonrası kompresyon çorabı kullanma durumlarının değerlendirilmesi. Florence Nightingale Hemşirelik Dergisi 2016;24(1):30-37.
17. Hobson DB, Chang TY, Aboagye JK, et al. Prevalence of graduated compression stocking–associated pressure injuries in surgical intensive care units. J Crit Care 2017;40:1-6.
18. Morrison R. Venous thromboembolism: scope of the problem and the nurse's role in risk assessment and prevention. J Vasc Nurs 2006;24(3):82-90.
19. Akyüz E, Tunçbilek Z. Anti-embolism stocking care protocol to prevent associated skin problems: A quasi-experimental study. J Tissue Viability 2021;30(1):89-94.
20. Karadoğan K, Durna Z, Akın S. Hemşirelerin venöz tromboemboli risk faktörleri ve koruyucu girişimlere yönelik bilgi düzeylerinin değerlendirilmesi. JAREN 2020;6(1):36-43.
21. Ayhan H, Iyigun E, Ince S, et al. A randomised clinical trial comparing the patient comfort and efficacy of three different graduated compression stockings in the prevention of postoperative deep vein thrombosis. J Clin Nurs 2015;24(15-16):2247-2257.
22. National Institute for Health and Care Excellence (NICE). Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. NICE guideline: 2019 Aug. London (UK).
23. Association of Perioperative Registered Nurses (AORN). Guideline Quick View: Venous Thromboembolism. AORN J 2018;107(2):281-5.
24. Çalişilan birim/servis/ünite/alanlara göre hemşirelerin görev, yetki ve sorumluluklari. Hemşirelik yönetmeliğinde değişiklik yapılmasına dair yönetmelik. Resmi Gazete (TC): 2011 Nisan. Rapor No:27910.
25. Varghese BA, Ezhilarasu P, Rajan A, Jesudason MR, Jeyaseelan V. Knowledge, attitude, and practice of nurses regarding use of Anti-embolism stockings. Indian Journal of Continuing Nursing Education 2016;17(2):31.
26. Xu Y, Wang W, Zhao J, Wang J, Zhao T. Knowledge, attitude, and practice of healthcare professionals toward clinically applying graduated compression stockings: results of a Chinese web-based survey. J Thromb Thrombolysis 2019;47:102-108.
27. Yılmaz S, Yaylaci S, Diken A, Yalcinkaya A, Aksoy E. Alt ekstremite venöz yetmezligi tedavisinde kompresyon çoraplari ve kullanımını etkileyen faktörler. Damar Cerrahi Dergisi 2015;24(1):47-53.
28. Williams A, Davies P, Sweetnam D, et al. Knee-length versus thigh-length graduated compression stockings in the prevention of deep vein thrombosis. Journal of British Surgery 1996;83(11):1553.
29. Brady D, Raingruber B, Peterson J, et al. The use of knee-length versus thigh-length compression stockings and sequential compression devices. Crit Care Nurs Q 2007;30(3):255-262.
30. Hilleren-Listerud AE. Graduated compression stocking and intermittent pneumatic compression device length selection. Clin Nurse Spec 2009;23(1):21-24.
31. Wade R, Paton F, Woolacott N. Systematic review of patient preference and adherence to the correct use of graduated compression stockings to prevent deep vein thrombosis in surgical patients. J Adv Nurs 2017;73(2):336-348.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 367-379
https://doi.org/10.30621/jbachs.1327637
RESEARCH ARTICLE

THE EFFECT OF PHYSICAL ACTIVITY AND NUTRITION AWARENESS EDUCATION ON THE LEVEL OF PHYSICAL FITNESS AND NUTRITION KNOWLEDGE IN WOMEN AGED 50-60

Nurettin Konar[1], Sare Bostanci[2], Gizem Baskaya[3], Cigdem Aykut[4]

[1] Bandirma Onyedi Eylul University, Faculty of Sports Sciences, Department of Physical Education and Sports Teaching, Bandirma, Balıkesir.
[2] Bandirma Onyedi Eylul University, Manyas Vocational School, Private Security and Protection Program, Manyas, Balıkesir.
[3] Bandirma Onyedi Eylul University, Faculty of Sports Sciences, Department of Coaching Education, Bandirma, Balıkesir.
[4] Bandirma Onyedi Eylul University, Institute of Health Sciences, Department of Physical Education and Sports , Bandirma, Balıkesir.

ORCID: N.K. 0000-0001-7926-6677; S.B. 0000-0003-1844-1966; G.B. 0000-0002-6001-1727; C.A. 0009-0007-5965-5799

Corresponding author: Nurettin Konar, **E-mail:** nkonar@bandirma.edu.tr
Received: 14.07.2023; **Accepted:** 19.09.2023; **Available Online Date:** 31.01.2024

Cite this article as: Konar N, Bostancı S, Baskaya G, Aykut C. The Effect of Physical Activity and Nutrition Awareness Education on the Level of Physical Fitness and Nutrition Knowledge in Women aged 50-60. J Basic Clin Health Sci 2024; 8: 367-379.

ABSTRACT

Purpose: The aim of this study was to examine the effect of physical activity and nutrition awareness training on the motor skills and nutrition awareness of individuals related to healthy living in sedentary women aged 50-60 years.

Material and Methods: The study included 15 healthy sedentary women on voluntary basis; participants were divided into 2 groups as experimental (n=8) and control (n=7) groups by random sampling method. Participants in the experimental group were given physical activity 2 days a week (60 min/day) for 6 weeks and nutrition education 1 day a week (30 min/day). In the training programs applied during the week, strength was applied on the first day and aerobic exercise was applied on the second day. Age-appropriate motor skill tests (arm curl test, back scratch test, two-minutes step, 8 food up and go test, chair stand test, sit and reach test) and the "Nutrition Knowledge Level Scale for Adults" questionnaire were applied as pre-test and post-test. Whether the data obtained at the end of the study were normally distributed was determined by Shapiro-Wilks test, Paired Samples T-Test was used for intra-group comparisons of physical fitness tests before and after exercise, and Independent Samples T-Test was used for inter-group comparisons. Wilcoxon Test was used in the pre-test and post-test intra-group comparisons and Man Whitney U Test was used in inter-group comparisons of the parameters related to nutritional knowledge levels.

Results: As a result of the analysis, statistically significant improvements were found in the performance parameters of the participants in the experimental group in arm curl, back scratch, 2-min step and 8 food up and go test ($p<0.05$). In addition, the participants in the experimental group statistically significantly improved their 2-min step, 8 food up and go, chair sit and reach, chair stand tests and basic nutrition knowledge level scores compared to the participants in the control group ($p<0.05$).

Conclusion: In conclusion, it was determined that regular physical activity programs and regular nutrition education improved the health-related motor skill parameters and nutrition knowledge levels of sedentary women.

Keywords: Exercise, Nutrition, Physical Activity, Women

INTRODUCTION

Sedentary lifestyle has a negative impact on parameters related to physical fitness as it negatively affects mental, physical, and social well-being (1). Sedentary life, which is seen as one of the leading causes of premature death and chronic diseases, is a phenomenon that affects large masses in terms of public health in individuals over middle age (2).

Nutrition and physical activity are seen as the main factors to maintain existing health, minimize health-related risk factors and age healthily (1,3 4,5). In this direction, the World Health Organization recommends that individuals should do physical activity at least 2 days a week regarding sedentary life (6). When the parameters of relations with health are evaluated, it can be stated that bad eating habits and chronic diseases are more common in individuals with sedentary behavior (7). Changes in lifestyle, which are a result of modern life, are associated with sedentary life. In addition to long working hours and lack of physical activity, dietary habits seem to be a determining factor of sedentary behavior (8). In this context, physical activity is of great importance in preventing a sedentary life largely due to malnutrition and inactivity (9).

In addition to sedentary lifestyle, malnutrition also lies at the basis of health-related chronic diseases. Today, the general idea about healthy living is that exercise should be supported by regular nutrition programs and these programs should be followed in a healthy way (10). However, the lack of nutrition education and nutritional awareness causes unbalanced and inadequate nutrition in individuals and the consequences become more apparent (11, 12). Nutritional awareness refers to people's food intake and consumption habits independent of their physical and mental states. In parallel with the increase in the level of awareness, healthy food consumption habits also increase (13).

Although sedentary life is more common in developing countries, it is known that more than half of the adults in the world population do not participate in regular physical activity (14). It is seen that the causes of death due to lack of physical activity increase depending on the years. According to the data of the World Health Organization, the increase in alternatives in urbanization and transportation, depending on the economic development, causes the increase of physically inactive individuals (15,16). When obesity, which is one of the most common chronic diseases related to physical activity and nutrition in Turkey, is examined according to the gender factor, it has been observed that women are diagnosed as obese two times more than men (17). In addition, regular participation in physical activity is more limited in women than in men (15). In addition to all these, given that it is essential that physical activity practices that improve general health status and protect against chronic diseases are sustainable and continuous for middle-aged individuals (6) and that sports scientists, conditioners and coaches are constantly looking for new training methods that will improve the health-related parameters of sedentary people as well as athlete performance, this type of research, especially on female sedentary people, is important.

As in the rest of the world, life expectancy in our country has increased in recent years. This situation causes a parallel increase in age-related chronic diseases. Nutritional habits and physical activity, which are also related to sedentary life, are the leading prevention methods used in preventable chronic diseases, especially obesity and diabetes (18).

On the other hand, although there has been an increase in the number of studies focusing on women's health and physical activity in the literature in recent years (19,20,21,22), along with exercise practices for a certain period of time. No study was found in which nutrition education was given and the results were discussed. The aim of our study, which focuses primarily on women's health of sedentary life, is to examine the effects of physical activity and nutrition awareness training in sedentary women aged 50-60 on healthy life-related fitness levels, motor skills, nutritional preferences and nutritional awareness of individuals. Nutrition awareness education and physical activity practices are thought to have positive effects on health-related physical fitness parameters and nutritional awareness of sedentary women.

MATERIALS AND METHODS

Research Model: In this study, experimental model was used in accordance with the objectives. In the study, 8 women sedentary were not excluded from the training program for any reason, and the planned exercise program was performed 2 days a week (60 min/day) and nutrition awareness training were performed 1 day a week (30 min/day) for 6 weeks.

Study Group: The study included 15 volunteer women between the ages of 50-60 years who had not practiced sports before. The participants were divided into two groups as experimental (n=8) and control group (n=7) by random sampling method (Table 1). Inclusion criteria of permanents; It was determined as being in the 50-60 age range, being sedentary, not having any obstacles in doing sports, and being a woman.

Table 1. Demographic Information of Participants

Demographic Information	Experimental Group Mean ± ss	Control Group Mean ± ss
Age (years)	52.75 ± 5.898	58.14 ± 7.448
Height (cm)	171.25 ± 6.819	163.00 ± 7.528
Body Weight (kg)	82.38 ± 13.169	68.0 ± 6.733

Table 2. Exercise and Nutrition Program

Weeks	Days	Education	Number of Sets and Repetition	Education Content
Week 1	Tuesday	Education Nutrient		Nutrient elements basic education
		Exercise Program	2 sets / 25 sec	10 min warm-up + Step aerobics + 5 min cool down
	Thursday	Exercise Program	2 sets / 20 sec – 8-10 repetitions	10 min warm-up + Resistance exercise + 5 min cool down
Week 2	Tuesday	Education Nutrient		Proteins, Fats
		Exercise Program	2 sets / 25 sec	10 min warm-up + Step aerobics + 5 min cool down
	Thursday	Exercise Program	2 sets / 20 sec – 8-10 repetitions	10 min Warm-up + Resistance exercise + 5 min Cool down
Week 3	Tuesday	Education Nutrient		Carbohydrates
		Exercise Program	2 sets / 30 sec	10 min warm-up + Step aerobics + 5 min cool down
	Thursday	Exercise Program	2 sets / 25 sec – 10-12 repetitions	10 min Warm-up + Resistance exercise + 5 min Cool down
Week 4	Tuesday	Education Nutrient		Vitamins and Minerals
		Exercise Program	2 sets / 25 sec	10 min warm-up + Step aerobics + 5 min cool down
	Thursday	Exercise Program	2 sets / 25 sec – 10-12 repetitions	10 min Warm-up + Resistance exercise + 5 min Cool down
Week 5	Tuesday	Education Nutrient		Food Groups
		Exercise Program	3 sets / 30 sec	10 min warm-up + Step aerobics + 5 min cool down
	Thursday	Exercise Program	3 sets / 25 sec – 10-12 repetitions	10 min Warm-up + Resistance exercise + 5 min Cool down
Week 6	Tuesday	Education Nutrient		Healthy snacking suggestions
		Exercise Program	3 sets / 35 sec	10 min warm-up + Step aerobics + 5 min cool down
	Thursday	Exercise Program	3 sets / 30 sec – 10-12 repetitions	10 min Warm-up + Resistance exercise + 5 min Cool down

Protocol: During the current study, the "Directive on Scientific Research and Publication Ethics of Higher Education Institutions" was followed. Before the study prepared in accordance with this proposal, all participants and the study team were informed about the research in detail and voluntary consent forms were signed by the participants. After obtaining the necessary permissions, the age, height, and body weight of the participants were determined before starting the exercise program. Then, performance tests of the participants were taken, and scales were applied. Anthropometric tests (height and body weight) and the scale (YETBID) were administered on day 1, while healthy living-related motor skills tests

(arm curl, back scratch, 2-min step, 8-food up and go, chair stand and chair sit and reach tests) were taken on day 2. Before the performance tests, a 15–20-minute warm-up protocol was applied to the participants. In order to eliminate the learning effect on the first day of the study, physical fitness tests were explained to the participants and they were asked to try them. After the pre-test measurements were taken, the exercise program was performed by experienced coaches in the gymnasium of the Faculty of Sports Sciences in accordance with health and safety rules. The exclusion criteria from the study were determined to be the presence of a chronic disease of the participants. Participants were free to leave the study voluntarily at any part of the study.

The collected data were not used in any way other than for scientific purposes and were prepared in a way that would not harm personal rights. After the 6-week training period, the same measurements were taken as a post-test in the same protocol. During the 6-week period, in addition to the exercise program, the participants were given training on nutritional awareness by a nutritionist 1 day a week (30 min/day). Participants in the control group were not subjected to any application and were asked not to perform physical activity during this period.

Exercise Program and Nutrition Education: Participants underwent an exercise program for 6 weeks, 2 days a week for 60 minutes each. An exercise program was planned as 10 minutes warm-up, 45 minutes exercise practice and 5 minutes cool down. Participants were subjected to the exercise program shown in Table 2 and received nutrition education. The intensity of aerobic exercises was determined according to the heart rate values obtained with the Karvonen formula (Target Heart Rate = [(max Heart Rate − resting Heart Rate) × %Intensity] + resting Heart Rate example). Aerobic exercises were performed at 60% of the heart rate of the individuals. Resistance exercises were performed with body weight and low weight dumbbells (2 kg, 3 kg) in accordance with the program designed. In the following periods of the program, the program process was continued by changing the duration, repetition, and number of sets in line with the development and the program was terminated after 6 weeks. Throughout the whole study, attention was paid to breathing and exhaling with the correct method, technique and breathing and exhaling at the correct point of the movement.

Warm-up Protocol Applied Before the Tests: Participants performed a 10-minute warm-up protocol

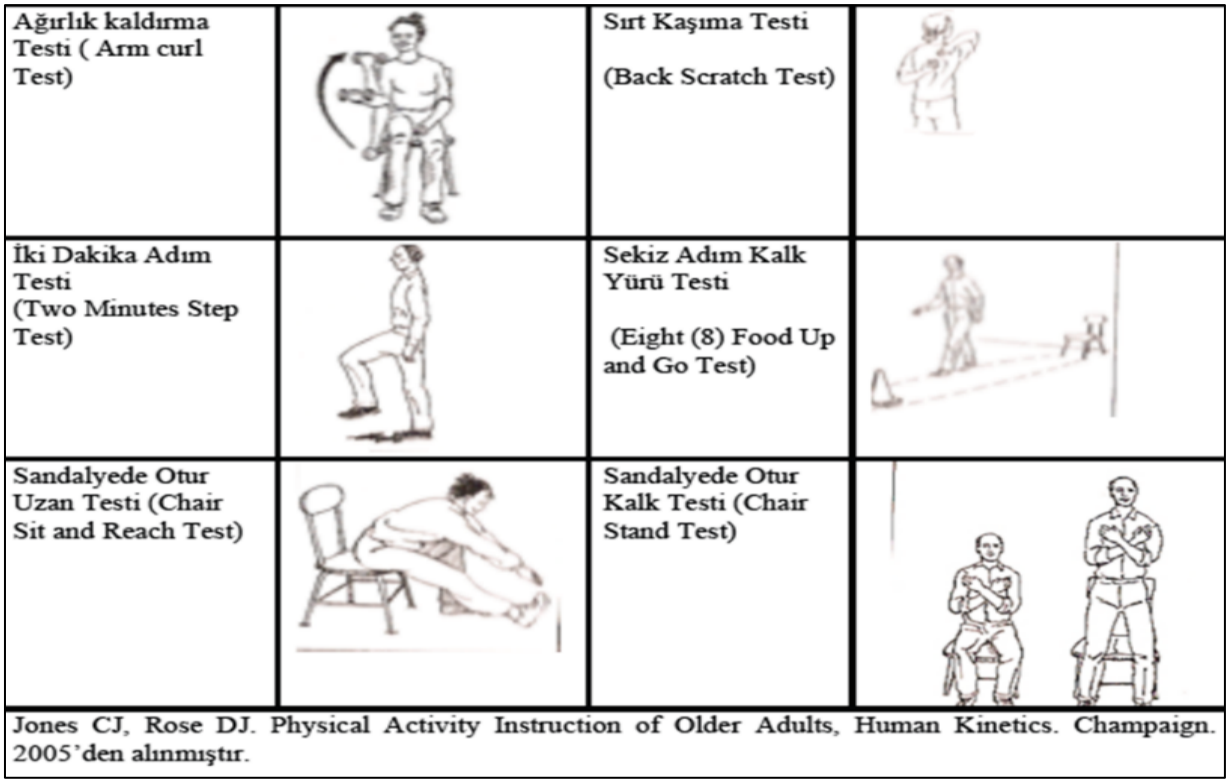


Figure 1. Health-Related Physical Fitness Tests (24).

Table 3. Pre-Test and Post-Test Results of Performance Parameters of the Control Group

Parameters	Pre-Test	Post-Test	t	p
	Mean ± ss	Mean ± ss		
Arm Curl Test (kg)	20.71 ± 4.348	21.00 ± 4.000	-.795	0.457
Back Scratch Test (cm)	-7.43 ± 12.095	-7.00 ± 12.396	-1.441	0.200
Two Minutes Step Test (count)	214.71± 33.270	223.71 ± 42.074	-.925	0.391
Eight Food Up and Go Test (sec)	6.45 ± .712	7.12 ± .808	-1.222	0.267
Chair Sit and Reach Test (sec)	9.43 ± 7.138	8.43 ± 4.237	.494	0.639
Chair Stand Test (count)	17.29 ± 2.138	14.00 ± 2.887	2.633	**0.039***

**Statistical significance value p<0.05*

Table 4. Pre-Test and Post-Test Results of Nutritional Parameters of the Control Group

Parameters	Pre-Test	Post-Test	Z	p
	Mean ± ss	Mean ± ss		
Basic Nutrition Knowledge (points)	49.86 ± 9.191	51.43 ± 8.753	-0.422	0.673
Nutrition and Health Relationship	8.14 ± .690	7.86 ± 1.345	-1.000	0.317

**Statistical significance value p<0.05*

Table 5. Pre-Test and Post-Test Results of Performance Parameters of the Experimental Group

Parameters	Pre-Test	Post-Test	t	p
	Mean ± ss	Mean ± ss		
Arm Curl Test (kg)	21.75 ± 8.172	25.75 ± 8.956	-2.733	**0.029***
Back Scratch Test (cm)	-1.88 ± 14.147	5.50 ± 10.650	-2.693	**0.031***
Two Minutes Step Test (count))	274.13 ± 74.455	316.63 ± 72.394	-2.471	**0.043***
Eight Food Up and Go Test (sec)	6.18 ± .780	4.47 ± .507	6.229	**0.000***
Chair Sit and Reach Test (sec)	16.13 ± 8.626	19.75 ± 7.906	-1.407	0.202
Chair Stand Test (count)	19.00 ± 3.024	21.25 ± 5.418	-1.741	0.125

**Statistical significance value p<0.05*

before all performance tests. Within the scope of the protocol, the participants ran for 5 minutes at 40-45% pace and performed dynamic warm-up movements for the upper and lower extremities. After the run, a 1-minute rest was given and dynamic warm-up movements for the lower extremities were performed first. After the warm-up, the participants were given a 2-minute rest period to make their final preparations before the test.

Data Collection Tools

***Height and Body Weight**:* Participants' height and body weight were measured using a Seca 769 electronic measuring device (Seca Anonim Company, Hamburg, Germany) with an accuracy of 0.1 cm for height and 0.1 kg for body weight. (23).

Arm Curl Test: The participant is seated on the edge of a chair slightly to the side of the dominant arm. The dumbbell weight was 2.27 kg for women and 3.63 kg for men. The participants were asked to complete the test by performing full lifts of the weight for 30 s using the dominant hand with the arm in full extension below and full flexion above (24). At the end of 30 s, the total number of lifts was noted (25).

Back Scratch Test: While the participant was in a standing position, one arm was made to rotate outward, over the shoulder, with the palm facing the back and the fingers in extension, the participant was asked to reach the lowest point on the back. The other arm was rotated internally, and the participant was asked to reach the highest point on his/her back with his/her fingers in extension and the palm facing forward. The participant tried to bring the fingertips as close together as possible and the distance between the middle fingers of both hands was measured. During the measurement, the participant was not helped to bring the fingertips closer together. If the middle fingers were not touching, the distance was recorded as (-) in cm; if the middle fingers were touching end to end, the value was zero (0); and if the middle finger crossed over the other, the value was recorded as (+) in cm for the distance the middle finger crossed (24).

***Two Minutes Step Test**:* In order to apply the test, while the participant was standing in an upright position, the distance from the front projection of the hip bone (iliac crest) to the midpoint of the kneecap (patella) was measured and the midpoint of the distance between these two bones was determined. The height of this point from the ground was measured and the step height of the subject was determined. In order to determine whether the step height reached the target height, a tape was drawn at the determined height, or the target height was marked on the wall, and it was checked whether the subject's step height (knee height) reached the target height. The participant was made to step in place for two minutes with both knees reaching the target height. The participant started the test with the right foot and was asked to lift both knees to the specified height. During the test, the participant was asked not to run but to perform the test as fast as he/she could, and at the end of two minutes, the total number of right steps performed correctly was recorded. If any of the participant's steps (right or left) failed to reach the desired height, these steps were considered invalid. The total number of right knees that reached the target height at the end of two minutes was recorded on the measurement sheet (24).

Eight Food Up and Go Test: The participant was seated in the center of the chair and his/her back was leaned back. The participant should have both hands on the knees and feet fully on the floor. In this position, with the start command, the participant was asked to turn around the funnel located 2.44 cm away and reach the chair again as soon as possible and sit down. The time started with the get up command was stopped when the participant sat on the chair again and the time was recorded in seconds (24).

Chair Sit and Reach Test: This test, which is a modified version of the sit-lie test, is used especially to determine the flexibility of the hamstring muscle group. The participant is seated on a chair with a height of 43.18 cm, which is placed against a wall or a solid floor, so that the junction of the thigh and hip bone is in front of the chair. At the participant's discretion (right left), one foot was extended forward in full extension with the heel of the foot on the floor and the ankle at approximately 90°. The other foot was placed towards the end of the chair with the knee flexed at approximately 90° and the sole of the foot on the floor. The participant's hands were placed on top of each other, and the middle fingers were aligned. The participant was instructed to reach towards the toe of the foot by extending the body forward with both hands without bending the knee, which was extended forward (extension), without

Table 6. Pre-Test and Post-Test Results of Nutrition Parameters of the Experimental Group

Parameters	Pre-Test	Post-Test	Z	p
	Mean ± ss	Mean ± ss		
Basic Nutrition Knowledge (points)	54.38 ± 6.479	57.88 ± 3.643	-1.524	0.128
Nutrition and Health Relationship	7.00 ± 3.024	8.38 ± 1.061	-1.604	0.109

**Statistical significance value p<0.05*

Table 7. Pre-test Comparison of Experimental and Control Group Performance Parameters

Parameters	Experimental Group	Control Group	t	p
	Mean ± ss	Mean ± ss		
Arm Curl Test (kg)	21.75 ± 8.172	20.71 ± 4.348	.299	0.769
Back Scratch Test (cm)	-1.88 ± 14.147	-7.43 ± 12.095	.811	0.432
Two Minutes Step Test (count)	274.13 ± 74.455	214.71± 33.270	1.941	0.074
Eight Food Up and Go Test (sec)	6.18 ± .780	6.45 ± .712	-.710	0.490
Chair Sit and Reach Test (sec)	16.13 ± 8.626	9.43 ± 7.138	1.623	0.129
Chair Stand Test (count)	19.00 ± 3.024	17.29 ± 2.138	1.249	0.234

**Statistical significance value p<0.05*

Table 8. Pre-test Comparison of Nutrition Parameters in Experimental and Control Groups

Parameters	Experimental Group	Control Group	Z	p
	Mean ± ss	Mean ± ss		
Basic Nutrition Knowledge (points)	54.38 ± 6.479	49.86 ± 9.191	-1.394	0.163
Nutrition and Health Relationship	7.00 ± 3.024	8.14 ± .690	-.909	0.364

**Statistical significance value p<0.05*

pushing the pain limit. If the fingertips of the participant's hand did not touch the toe, a value in centimeters (-) was taken as the distance between them; if the fingertips of the middle hand touched the toe, a value of zero (0) was taken; if the fingertip of the middle hand crossed the toe, a value in cm (+) was taken as the distance the middle fingertip crossed and recorded on the measurement sheet (24).

Chair Stand Test: The participant was made to sit in the center of a 43.18 cm highchair with his/her back straight, feet on the floor and arms crossed in front of the chest (right hand on the left shoulder, left hand on the right shoulder). In this position, the participant started the test with the start command and performed as many full take-offs as he/she could for 30 s. The number of full take-offs performed during 30 s was recorded as the participant's score (24)

Level of Nutrition Knowledge Scale for Adults - Basic Nutrition Section: It was developed by Batmaz (26) and a validity and reliability study were conducted. The scores obtained from the evaluation criteria of the nutrition knowledge level scale for adults are evaluated as poor, moderate, good, and very good. There are a total of 20 propositions in the "basic nutrition" section of the scale and the highest score that can be obtained from this section is 80. Those with a score less than 45 are considered to have poor knowledge, those with a score between 45 and 55 are considered to have fair knowledge, those with a score between 56 and 65 are considered to have good knowledge, and those with a score above 65 are considered to have very good knowledge. The reliability coefficient for the "Basic Nutrition" section of the YETBID was found to be 0.72**.**

Data Analysis: The data were analyzed in IBM SPSS 26.0 package program. After evaluating whether the obtained data showed normal distribution by looking at the kurtosis skewness values, Independent Samples T Test was applied at α=0.05 significance level to determine the difference between groups in performance tests, and Paired Samples T Test was applied in intra-group comparisons. In the parameters related to nutritional awareness, non-parametric tests were applied due to the small sample size; Man-Whitney U Test was used for inter-group comparisons and Wilcoxon Test was used for intragroup comparisons.

RESULTS

In Table 3, within-group analysis values of the performance parameters of the control group were compared. In the table, it was determined that there was a statistically significant difference between the participants' chair stand test (p=0.039) data due to pre-test measurements.

In Table 4, the intra-group analysis values of the nutritional parameters of the control group were compared. In the table, no statistical difference was found between the pre and post test values of the participants (p>0.05).

In Table 5, the intra-group analysis values of the performance parameters of the experimental group were compared. In the table, it was determined that there was a statistically significant difference between the participants' arm curl (p=0.029), back scratch (p=0.031), 2-minute step (p=0.043) and 8 food up and go test (p=0.0) data. Although there was no statistically significant difference between the chair sit and reach and chair stand test data, it was revealed that the post-test measurements were numerically higher (p>0.05).

In Table 6, the intra-group analysis values of the nutritional parameters of the experimental group were compared. Although no statistical difference was found between the pre and post test values of the participants (p>0.05), it was determined that there was a numerically improvement in the post test measurements.

Table 7 compared the pre-test performance parameters of the control and experimental groups. The table does not reveal any statistical difference between the pre-test values of the groups (p>0.05).

In Table 8, the pre-test nutritional parameters of the control and experimental groups were compared. The table does not reveal any statistical difference between the pre-test values of the groups (p>0.05).

In Table 9, the post-test values of the performance parameters of the control and experimental groups were compared. In the table, it was determined that there was a statistically significant difference in favor of the experimental group between the groups' 2-minute step (p=0.011), 8 food up and go (p=0.005), chair sit and reach (p=0.005) and chair stand tests (p=0.008). Although there was no statistically significant difference between the arm curl and back scratch test data, it was revealed that the numerically post-test measurements were higher in favor of the experimental group (p>0.05).

In Table 10, the post-test values of the nutritional parameters of the control and experimental groups were compared. In the table, it was determined that there was a statistically significant difference between the basic nutrition knowledge scores (p=0.036) of the groups in favor of the experimental group .

DISCUSSION

The aim of our study is to investigate the effects of physical activity and nutrition awareness training on health-related physical fitness parameters and nutrition awareness in female individuals aged 50-60 years. In our study, it was observed that 6-week physical activity practices created a significant difference in the performance values of arm curl, back scratching, 2-min step and 8 food up and go tests on sedentary women in health-related motor skills tests (p<0.05). It was revealed that sedentary women in the experimental group performed better in the 2-min step, 8 food up and go, chair stand and chair sit and

reach tests compared to the women in the control group and this difference between them was statistically significant ($p<0.05$). It was also found that nutrition awareness training caused significant improvements in the basic nutrition knowledge level scores of sedentary women ($p<0.05$).

Although this study analyzed the effect of physical activity and nutrition education intervention on physical fitness and nutrition awareness of sedentary women in relation to health and life, it has some limitations. Under normal conditions, the number of experimental groups receiving exercise and nutrition education under exercise increases every four months: Exercise group, nutrition education training group, participation in nutrition support training and exercise application group, and only exercise and nutrition support training group, which is expected to be a control group, and a nutrition awareness and exercise application group. There are two groups. The presence of 2 groups in the study is considered a limitation. The main reason for this limitation is that sufficient samples could not be reached in the specified age group. On the other hand, the necessity of practices encouraging participation is seen especially when the age group is taken into consideration. Based on this information, it can be suggested that researchers who want to study on this and similar subjects should study on the four different groups mentioned above in order to see the educational effects more healthy.

When the literature was examined, studies with similar results to the results of our study were found. In one study, a significant difference was found in the anthropometric measurements of menopausal women as their nutritional knowledge score and thus nutritional awareness increased. In other findings of the study, parameters such as lean body mass and body fat ratio of individuals who did and did not engage in physical activity were also evaluated and it was found that physical activity had a positive effect

Table 9. Post-test Comparison of Experimental and Control Group Performance Parameters

Parameters	Experimental Group	Control Group	t	p
	Mean ± ss	Mean ± ss		
Arm Curl Test (kg)	25.75 ± 8.956	21.00 ± 4.000	1.354	0.206
Back Scratch Test (cm)	5.50 ± 10.650	-7.00 ± 12.396	2.102	0.560
Two Minutes Step Test (count))	316.63 ± 72.394	223.71 ± 42.074	2.944	**0.011***
Eight Food Up and Go Test (sec)	4.47 ± .507	7.12 ± .808	-7.736	**0.000***
Chair Sit and Reach Test (sec)	19.75 ± 7.906	8.43 ± 4.237	3.378	**0.005***
Chair Stand Test (count)	21.25 ± 5.418	14.00 ± 2.887	3.160	**0.008***

**Statistical significance value p<0.05*

Table 10. Post-test Comparison of Nutrition Parameters in the Experimental and Control Groups

Parameters	Experimental Group	Control Group	Z	p
	Mean ± ss	Mean ± ss		
Basic Nutrition Knowledge (points)	57.88 ± 3.643	51.43 ± 8.753	-2.094	**0.036***
Nutrition and Health Relationship	8.38 ± 1.061	7.86 ± 1.345	-.610	0.542

**Statistical significance value p<0.05*

on the values (27). Kurt (28) applied step-aerobic exercise for eight weeks in their study on middle-aged sedentary women and examined the changes in physical fitness parameters of individuals. As a result of the study, a significant increase was observed in the strength, flexibility, endurance-related values of the individuals if continued regularly, while a decrease was observed in body fat percentages, resting and post-exercise pulse rates in relation to health. Vergili (29) examined the effects of Pilates and calisthenic exercise on the health-related quality of life of 153 women aged 25-55 years with sedentary behavior. The 15-D health-related quality of life questionnaire, whose sub-dimensions consisted of health-related parameters, was administered to the experimental group before and after the 12-week intervention. A significant increase in the health-related parameters of quality of life was found in the experimental group included in the exercise, while the values in the control group did not change.

In a study investigating the effects of aerobic exercise on body composition and blood values in young and middle-aged women, 30 minutes of running-walking exercise was practiced for 3 days for 12 weeks. Parameters related to physical fitness showed positive changes in both age groups. Especially in parallel with our study, an increase in HDL values and a parallel decrease in triglyceride values were observed in individuals evaluated in the middle age category, although not statistically significant (30). Akgül (31), it was seen that high-intensity interval training (HIIT) applied to sedentary women for 2 weeks, 3 days a week and 6 sessions in total, had a positive effect on the aerobic performance parameters of individuals.

It was observed that bosu exercises applied for 3 months in sedentary women had positive effects on the participants' hand grip strength, flexibility and circumference measurements (32).

A significant decrease in body mass index, body weight and fat mass amounts was observed in sedentary female individuals after exercise regularly applied for 3 days and 60 minutes for 12 weeks (33).

In a study investigating the effect of exercise applied 3 days a week for eight weeks on body composition in middle-aged sedentary women, significant changes were noted in the lean body weight and body mass index of individuals compared to pre-exercise (34).

In a study examining the relationship between the nutritional program determined in addition to 12-week resistance exercise and balance, three groups were formed as exercise and nutrition, nutrition and control, and a more significant improvement was observed in the balance parameter in the experimental group in which nutrition and exercise were combined than in the other groups (10). In the study findings, it was determined that the improvement in blood pressure and cardiovascular system in relation to health in individuals participating in resistance and aerobic exercise significantly changed in individuals diagnosed with hypertension (35).

Based on the increase in sedentary lifestyle with the pandemic, the effect of zumba exercise applied online for 8 weeks on total fat percentages, body image and eating attitudes of individuals was examined. The findings of the study showed a significant decrease in the waist-hip measurements, body mass index and body fat percentages of the individuals who participated in the exercise. Significant reductions were found not only in physical fitness and anthropometrics, but also in hunger sensitivity and emotional eating parameters of individuals in the experimental group (36). In another study on the dietary habits and physical activity levels of women in relation to the pandemic, it was observed that age had no effect on nutrition and physical activity levels. However, the variables of income, employment status and number of people in the household were found to be related to nutrition and participation in physical activity. In addition to the findings, it was observed that individuals consumed the food they enjoyed eating and had low physical activity levels during the pandemic period without calorie control (37).

In a study examining the nutritional knowledge and habits of obese women, low physical activity level was found to be among the factors in the formation of obesity together with factors such as dietary habits, meal frequency and number of births (38). In a study in which the effect of nutrition and physical activity level was investigated in a sample group over 65 years of age whose demographic structure was similar to our study, it was reported that the regular activity preference was generally walking and the increase in socio-economic level caused a decrease in the rate of physical activity (39). In a study conducted on women for 12 weeks, it was observed that the inclusion of physical activity in the diet program positively affected the weight loss and energy expenditure levels of individuals. In addition, in parallel with our study, a decrease in dietary habits, sugar and fat consumption and an increase in fruit,

milk and vegetable consumption occurred during the combination of nutrition and physical activity (40).
In the literature, it is seen that female individuals who participate in regular physical activity have higher scores than obese female individuals in nutrition awareness levels, cumulative physical activity scores, health responsibility, spiritual development, interpersonal communication and stress management, which are among the cognitive outcomes. This shows that healthy eating and participation in regular physical activity are associated with a healthy lifestyle in women (41,42).

CONCLUSION

In conclusion, physical activity and nutrition awareness training had a positive effect on nutrition awareness and motor skills related to physical fitness such as flexibility, endurance, and strength in sedentary female individuals aged 50 years and older. In the study, it was aimed to slow down the loss of flexibility and all motor skills in later ages. In addition to the findings, it is thought that the risk of falling, which is related to losses related to physical fitness, which is frequently seen in women aged 50 years and over, and which occurs with the decrease in bone density in the menopausal period, will also decrease. In addition to health-related physical fitness parameters, the positive effect of strength and endurance-based combination exercise models on bone and joint health should also be taken into consideration. In this context, considering both physiological, anatomical and motor outcomes, it is thought that the benefits of regular exercise will show its effect in many dimensions. It is thought that increasing the number of sample and control groups in future studies will positively affect the results of the study.

Acknowledgements: List all contributors who do not meet the criteria for authorship, such as technical assistants, writing assistants or head of department who provided only general support.

Author(s) contribution(s): NK: the conception and design of the study, revising it critically for important intellectual content, final approval of the version to be submitted. SB: the conception and design of the study, acquisition of data, drafting the article, revising it critically for important intellectual content, final approval of the version to be submitted. GB: the conception and design of the study, analysis and interpretation of data, revising the article critically for important intellectual content, final approval of the version to be submitted. ÇA: the conception and design of the study, final approval of the version to be submitted.

Conflict of interest: The authors declare that there is no conflict of interest

Ethical approval: Ethical approval was obtained from the İstanbul Esenyurt University, Non-Invasive Research Ethics Committee (Date: 12/09/2022, Decision no: 2022/08-6). The study was performed in accordance with the ethical standards as laid down in the 1965 Declaration of Helsinki and its later amendments. Informed consent was obtained from all individual participants included in the study.

Funding: The authors declare that there is no financial disclosure.

REFERENCES

1. Akyol A, Bilgiç P, Ersoy G. Fiziksel aktivite, beslenme ve sağlıklı yaşam. Klasmat Matbaacılık, Ankara.2008.
2. Lucas SR, Platts-Mills TA. Physical activity and exercise in asthma: Relevance to etiology and treatment. Journal of Allergy and Clinical Immunology 2005;115(5):928-9.
3. Çat G, Yıldırım İ. Ofis çalışanlarının yeme davranışları fiziksel aktivite düzeyleri ve yaşam kalitelerinin incelenmesi. Beden Eğitimi ve Spor Bilimleri Dergisi 2022;16(3):290-305.
4. Keogh JW, MacLeod RD. Body composition, physical fitness, functional performance, quality of life, and fatigue benefits of exercise for prostate cancer patients: A systematic review. Journal of Pain and Symptom Management 2012; 43(1):96-110.
5. Vural Ö, Eler S, Güzel AN. Masa başı çalışanlarda fiziksel aktivite düzeyi ve yaşam kalitesi ilişkisi. Spormetre Beden Eğitimi ve Spor Bilimleri Dergisi 2010;8(2):69-75.
6. Bull FC, Al-Ansari SS, Biddle S. et. al, J.F. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. British journal of sports medicine 2020;54(24):1451-1462.
7. Ünal B, Ergor G, Horasan G. D, Kalaca S, Sozmen K. Turkey incidence of chronic diseases and risk factors study. Ankara: Ministry of Health. 2013;84.
8. Ameer Arsalan Hadi P. Nutritional status and sedentary lifestyle of individuals a review. International Journal of Modern Agriculture. 2021;10(2).
9. Charansonney OL, Després JP. Disease prevention—should we target obesity or sedentary lifestyle?. Nature Reviews Cardiology 2010;7(8):468-472.
10. Dilican T. Egzersiz ve beslenmeye bağlı kilo kaybının sağlıklı sedanter kadınların denge performansına etkisi. Master's Thesis. Uludağ University. Bursa, Turkey 2023.

11. Baysal A. Beslenme. Hatiboğlu Yayınları, 14. Baskı, Ankara. 2012.
12. Beyhan, Y. İşçi sağlığı, iş güvenliği ve beslenme. Sağlık Bakanlığı Yayın, Ankara.2012.
13. Bor H, Saka M. Besin Okuryazarlığı, Yeme Farkındalığı ve Beslenme. Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi 2021;10(2): 307-313.
14. Lucas SR, Platts-Mills TA. Physical activity and exercise in asthma: Relevance to etiology and treatment. Journal of Allergy and Clinical Immunology 2005;115(5):928-9
15. World Health Organization. Global action plan on physical activity 2018-2030: more active people for a healthier world. World Health Organization, 2019.
16. Organisation for Economic Co-Operation and Development 2017, https://www.oecd.org/health/health-data.htm
17. Cengiz ŞŞ, Örcütaş H, Ulaş AG. Ateş B. Sedanter Bireylerin Yeme Bozukluğu, Beden Algısı ile Fiziksel Aktiviteye Karşı Tutum Ve Davranışlarının Belirlenmesi. Uluslararası Güncel Eğitim Araştırmaları Dergisi 2022;8(1), 198-214.
18. Durstine JL, Gordon B, Wang Z, Luo X. Chronic disease and the link to physical activity. Journal of sport and health science 2013;2(1), 3-11.
19. Grenier LN, Atkinson SA, Mottola et al. Be healthy in pregnancy: Exploring factors that impact pregnant women's nutrition and exercise behaviours. Maternal and Child Nutrition 2020; 17(1):e13068.
20. Kaya A, Aksu HS, Arslan F. Fiziksel aktivitelere düzenli ve düzensiz olarak katılım sağlayan kadınların fiziksel aktivite özdeğer algılarının incelenmesi. Sportive 2021;4(2):57-76.
21. Kong Z, Fan X, Sun S, Song L, Shi Q, Nie J. Comparison of high-intensity interval training and moderate-to-vigorous continuous training for cardiometabolic health and exercise enjoyment in obese young women: A randomized controlled trial. PLos One 2016;11(7):e0158589
22. McArthur D, Dumas A, Woodend, K., Beach, S., Stacey, D. Factors influencing adherence to regular exercise in middle-aged women: A qualitative study to inform clinical practice. BMC Women's Health 2014;14(1):1-8.
23. Bayrakdaroğlu S, Can İ, Albayrak AY, İmamoğlu R. Futbolcularda yo-yo aralıklı toparlanma testlerindeki (seviye 1-2) kalp atım hızı, laktat profili ve toparlanma sürelerinin incelenmesi. Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi 2021;10(3):550-559.
24. Rikli RE, Jones JC. Senior fitness test manual champaign, IL: Humann Kinetics.2001.
25. Sampaio A, Marques EA, Mota J, Carvalho J. Effects of a multicomponent exercise program in institutionalized elders with Alzheimer's disease. Dementia 2019;18(2):417-431.
26. Batmaz H. Yetişkinler için beslenme bilgi düzeyi ölçeği geliştirilmesi ve geçerlik-güvenirlik çalışması. Master Thesis. Marmara University. İstanbul, Turkey 2018.
27. Fakılı FE. Menepoza girmiş kadınların beslenme durumları ile fiziksel aktivite ve beslenme bilgi düzeylerinin belirlenmesi. Master's Thesis. Başkent University. Ankara, Turkey 2013.
28. Kurt S, Hazar S, İbiş S, Albay B, Kurt Y. Orta yaş sedanter kadınlarda sekiz haftalık step-aerobik egzersizinin bazı fiziksel uygunluk parametrelerine etkilerinin değerlendirilmesi. Uluslararası İnsan Bilimleri Dergisi 2010; 7(1):665-674.
29. Vergili Ö. Sağlıklı sedanter kadınlarda kalistenik ve pilates egzersizlerinin sağlıkla ilişkili yaşam kalitesi üzerindeki etkileri. Kırıkkale Üniversitesi Tıp Fakültesi Dergisi 2012;14(3):14-20.
30. Karacan S, Çolakoğlu FF. Sedanter orta yaş bayanlar ile genç bayanlarda aerobik egzersizin vücut kompozisyonu ve kan lipidlerine etkisi. Spormetre Beden Eğitimi ve Spor Bilimleri Dergisi 2003 1(2):83-88.
31. Akgül MŞ, Gürses, VV, Karabıyık H, Koz, M. İki haftalık yüksek şiddetli interval antrenmanın kadınların aerobik göstergeleri üzerine etkisi. International Journal of Sport Culture and Science 2016;4 (Special Issue 1):298-305.
32. Türk N. Sedanter bayanlarda bosu egzersizin fiziksel uygunluk ve psikososyal değişimlerine etkisi. Master Thesis. Hitit University. Çorum, Turkey 2016.
33. Aydemir İ, Dağ R. Düzenli pilates egzersizlerinin sedanter kadınlarda biyomotor ve fizyolojik parametreler üzerine etkisi. Spor Eğitim Dergisi. 2021;5(3):70-78.
34. Çolakoğlu F, Şenel Ö. Sekiz Haftalık Aerobik Egzersiz Programının Sedanter Orta Yaşlı Bayanların Vücut Kompozisyonu Ve Kan Lipidleri Üzerindeki Etkileri. Sportmetre Beden Eğitimi ve Spor Bilimleri Dergisi 2003;1(1):57-61.

35. Sharman JE, La Gerche A, Coombes JS. Exercise and cardiovascular risk in patients with hypertension. American Journal of Hypertension 2015;28(2):147-158.
36. Akyılmaz G. Kadınlarda online zumba egzersizlerinin vücut yağ oranları, yeme tutumları ve beden imajı üzerine etkisi. Master's Thesis. Hitit University. Çorum, Turkey 2021.
37. Tarhan M, Dursun Y. Covid-19 döneminde kadınların beslenme alışkanlıkları ve fiziksel aktiviteleri üzerindeki etkisi. Ankara Hacı Bayram Veli Üniversitesi İktisadi ve İdari Bilimler Fakültesi Dergisi 2022;24(1):428-459.
38. Pekcan G, Baltaoğlu S. Şişman kadınların beslenme bilgi düzeyi ve alışkanlıklarının saptanması. Beslenme ve Diyet Dergisi 1988;17(2):221-234.
39. Ersoy G, Akbulut GÇ. Farklı sosyo ekonomik düzeylerde yaşayan 65 yaş üstü bireylerin beslenme ve fiziksel aktivite durumlarının değerlendirilmesi. Beslenme ve Diyet Dergisi. 2006;34(1):41-51.
40. Akbulut G, Rakıcıoğlu N. On iki hafta süresince düşük kalorili diyet ve/veya fiziksel aktivite uygulayan hafif şişman/şişman kadınların besin ve besin ögesi tüketim durumlarının ve bazı antropometrik ölçümlerinin değerlendirilmesi. Türkiye Klinikleri 2011;23(1):29-39.
41. Akarsu G. Kadınlarda fiziksel aktivitenin beslenme alışkanlıkları ve obezite üzerine etkisi. Master's Thesis. Gazi University. Ankara, Turkey 2018.
42. Dubbert PM, Carithers T, Sumner AE, et al. Obesity, physical inactivity and risk for cardiovascular disease. American Journal of The Medical Sciences 2022;324(3):116-126.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 380-389
https://doi.org/10.30621/jbachs.1339191
RESEARCH ARTICLE

COMPARISON OF E-HEALTH LITERACY, DIGITAL HEALTH AND PHYSICAL ACTIVITY LEVELS OF UNIVERSITY STUDENTS IN DIFFERENT FIELDS

Ayse Kardelen Acar[1], Sema Savcı[2], Buse Ozcan Kahraman[3], Aylin Tanrıverdi[1]

[1] Dokuz Eylül University, Institute of Health Sciences, Izmir, Turkey
[2] Acibadem University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Istanbul, Turkey
[3] Dokuz Eylül University, Faculty of Physical Therapy and Rehabilitation, Izmir, Turkey

ORCID: A.K.A..0000-0002-7255-3590; S.S. 0000-0001-8675-1937; B.O.K. 0000-0002-0192-6740; A.T. 0000-0002-0220-0642

Corresponding author: Ayse Kardelen ACAR, **E-mail:** acar.kardelen@gmail.com
Received: 15.08.2023; **Accepted:** 20.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Acar AK. Savci S. Kahraman BO. Tanriverdi A. Comparison of E-Health Literacy, Digital Health and Physical Activity Levels of University Students in Different Fields. J Basic Clin Health Sci 2024; 8: 380-389.

ABSTRACT

Purpose: This study aimed to compare the health literacy, e-health literacy, digital health, and physical activity levels of undergraduate students in different departments.
Material and Methods: Undergraduate students 307 of whom were studying in the Physiotherapy department (PT), and 228 in the Faculty of Economics and Administrative Sciences (FEAS) participated in the study. Health literacy (HL) (European Health Literacy Scale), e-health literacy (E-Health Literacy Scale), digital literacy (Digital Literacy Scale), and physical activity level (International Physical Activity Questionnaire-Short Form (IPAQ-SF)) were assessed. Scales were applied to the participants electronically via Google Forms.
Results: There was no difference between the e-HL, digital, and HL levels of both department students($p>0.05$). 70.1% of all students did not have enough HL. PT department students' IPAQ-SF total score, severe physical activity, and walking activities were lower than FEAS students($p<0.05$). There was no difference between the moderate levels of physical activity and daily sitting times of the students of both departments($p>0.05$). 79.6% of all students did not have sufficient physical activity levels (PALs).
Conclusion: This study showed that HL and PALs were low in the majority of university students. HL education programs for university students before graduation and awareness studies to develop healthy behavior habits should be included in undergraduate education programs.

Keywords: Digital health, eHealth, health literacy, physical activity

INTRODUCTION

Health literacy (HL) is defined that individuals' sufficient motivation levels, social and cognitive skills to access, understand and use the information to improve and protect their health by the World Health Organization (WHO) (1). E-health literacy is "the capacity to access, understand, evaluate and implement information obtained from electronic sources to solve a health problem" and is evaluated under the scope of health literacy (2).

Thanks to the advancement of technology and its easy accessibility by all segments of society, the diversity of information sources is also increasing (3). There are many of uncontrollable data on the internet about health and considering the effect of the acquired data on human health, the importance of

digital literacy competence emerges (4). Within this framework of this competence, the individual is expected to have the skills to reach, produce and share accurate information by using technology appropriately (5).

Recently, digital health focuses on health literacy, lifestyle changes, preventive and individualized care approaches of many e-health applications (6). While digital health initiatives authorize individuals to monitor, manage and develop their quality of life and health, it is also considered that they will provide more individuality, higher efficiency, and usability in health service delivery at a lower cost (5), (6). Thus, it enables the active participation of the individual in terms of self-management in health (5).

With the widespread usage of the internet and technological improvements, it is thought that the continuation of some daily activities (use of virtual market, food orders, payments, social relations, etc.) in digital environments triggers an inactive attitude development (7).

Although physical inactivity is not contagious, it has been described as a pandemic because it affects the whole World. Among the causes of morbidity and mortality figures that the physical inactivity pandemic is one of the top important risk factors, and it also causes a great economic burden around the World (8).

It has been stated that if physical activity does orderly it can help to treat and prevent noncommunicable diseases. Besides, this is also an important step in preventive health services (9). WHO aims to decrease physical inactivity by 10% by 2025 and 15% by 2030 (8).

Health professionals' health literacy level is critical in effective communication with the patient and also contributes to the patient's health literacy (10). International studies indicated that there are major gaps in knowledge, awareness, and clinical identification among health professionals because of low health literacy levels (11).

In this context, there were limited studies on the health literacy of university students studying in different fields in our country (12), (13), and there is no research on university students who studied physiotherapy and social sciences evaluating the relationship between physical activity and health literacy in the electronic environment during the Covid-19 pandemic period. Therefore, the aim study was to compare university students studying in health and non-health departments of digital health, e-health literacy, and physical activity levels.

MATERIAL AND METHODS

Participants

The study's population consists of undergraduate students from two universities, the School of Physical Therapy and Rehabilitation at Dokuz Eylul University and the Department of Physiotherapy and the Faculty of Health Sciences and the Faculty of Economics and Administrative Sciences at Izmir Kâtip Celebi University.

Inclusion criteria were to be 18-25, volunteering to participate in research, and being literate in Turkish. Exclusion criteria were determined for individuals with the presence of vision-hearing problems and the presence of diagnosed chronic disease in the study.

According to a similar study comparing e-health literacy levels measured by the e-health literacy scale of university students with and without previous education in the field of health (14). the effect size was found as 0.58. The probability of type I error and the statistical power was deemed as 0.05 and 0.95, respectively. The minimum sample size of our study was estimated as at least 154 participants, 77 per group using G*Power Software (ver.3.1.9.2).

Design of the Study

The study was accepted by Dokuz Eylul University University Non-Interventional Clinical Research Ethics Committee (Decision Date: 05.10.2020, Number: 2020/24-17). The research is a cross-sectional study. The study collected descriptive data from students using a questionnaire based on relevant literature (15), (16). Participants were asked to provide their consent and complete validated scales to assess various parameters, all of which were administered electronically through Google Forms. The relevant links were shared with students through pre-existing WhatsApp groups for their respective classes.

Instruments

European Health Literacy Survey Questionnaire (HLS-EU-Q47), which has a Turkish version and whose validity-reliability study was performed by Abacıgil et al.(α: 0.95). It was prepared using a Likert scale and the scale includes a total of 47 items. The total score is in the range of 0-50 (16), (17).

E-Health Literacy Scale (eHEALS), involves 2 sections. A 5-point Likert-type rating was used.

Table 1. Descriptive characteristics of university students by department (n=535)

		PT (n=307)		FEAS (n=228)		Statistical Value	
Descriptive Characteristics		**n**	**%**	**n**	**%**	**χ2**	**p**
Gender	Female Male	259 48	84.4 15.6	142 86	62.3 37.7	33.989	0.01*
Age	Median(IQR): 20.00 (19.00-21.00) (min.=18;max=25)			Median(IQR): 20.00 (19.00-22.00) (min.=18;max=25)			0.010* z= -2.579
BMI (kg/m^2)	Median(IQR): 21.10 (19.28-23.45) (min.=10.13;max=44.28)			Median(IQR): 21.72 (19.48-24.60) (min.=16.13;max=44.58)			0.010* z= -1.601
Grade	1st Class 2nd Class 3rd grade 4th grade	109 71 61 66	35.523.1 19.9 21.5	93 57 37 41	40.8 25.0 16.2 18.0	2.915	0.40
Exercise Habit	Yes No	144 163	46.9 53.1	134 94	58.8 41.2	7.381	0.007*
Breakfast Habit	Yes No	272 35	88.6 11.4	190 38	83.3 16.7	3.079	0.079
Daily Sleep Time	Less than 6 Hours 7-8 Hours Over 9 Hours	25 258 24	8.1 84.0 7.8	29 170 29	12.7 74.6 12.7	7.356	0.025*
Cigarette	Yes No Give up	126 170 11	41.0 55.4 3.6	130 87 11	57.0 38.2 4.8	15.541	<0.001*
Alcohol	Yes No	131 171	42.7 57.3	124 104	54.4 45.6	7.198	0.007*
Access to Health Information Resource	Newspaper/ Magazine Radio/Television Book/ Brochure Health Worker (Doctor etc.) Social media Scientific Publication/ Article	1 7 11 34 76 178	3 2.3 3.6 11.1 24.8 58	0 10 1 42 23 152	0 4.4 4 18.4 10.1 66.7	30.118	0.01*
First Institution to Apply for a Health Problem	Community Health Center Public Hospital University Hospital Private Hospital Private Practice	113 152 21 18 3	36.8 49.5 6.8 5.9 1.0	64 125 12 26 1.0	28.1 54.8 5.3 11.4 4.0	9.651	0.04*

χ2: Chi-Square value. z: Mann-Whitney U test. p<0.05* PT: Department of Physiotherapy and Rehabilitation; FEAS: Faculty of Economics and Administrative Sciences. BMI: Body Mass Index

Between the 8 and 40 points are taken from the scale. A high score corresponds to a high level of health literacy (18). There is Turkish validity and reliability of this scale(α: 0.78) (19). Digital Literacy Scale (DLS), consists of four dimensions and 17 items, and seven sub-dimensions. It is a 5 points Likert-type rating type scale (20) Turkish validity and reliability study for this scale was carried out(α: 0.90) (21).

International Physical Activity Questionnaire Short Form (IPAQ-SF), consists of 4 separate parts and 7

questions developed for adults. The questions ask about the different activities done in the last week and the time spent in these activities. The time spent sitting daily is questioned in the last question (22). Turkish validity and reliability study was carried out by Saglam et al. (α: 0.69) (9).

Statistical analysis

Analyzes were made with the help of IBM SPSS 23.0. Kolmogorov Smirnov test and histograms were used to check the normality of distribution. As a result of the Kolmogorov-Smirnov test and histograms, it was determined that the data were not normally distributed ($p<0.05$). Categorical variables were expressed as numbers (n) and percentages (%) and were analyzed using the chi-squared test. Continuous variables were reported as median and interquartile range (IQR) because of their non-normal distributions. Differences between groups were specified by Mann–Whitney U test according to variable distributions. Spearman correlation analysis was used to evaluate the relationship between the scales. The effect size was calculated as follows: $z/\sqrt{N}$ (23). In all analyses, $p<0.05$ was considered statistically significant.

RESULTS

A total of 535 volunteers, including undergraduate students, studying at the School of Physical Therapy and Rehabilitation at Dokuz Eylul University and the Department of Physiotherapy and the Faculty of Health Sciences, and the Faculty of Economics and

Table 2. Comparison of internet-media time, e-Health, digital health and health literacy of students studying in different fields

	PT (n=307)			**FEAS (n=228)**			**Statistical Value**		
Findings	**Median(IQR)**	**Min**	**Max**	**Median(IQR)**	**Min**	**Max**	**z**	**p**	***effect size***
Internet Time (min.)	240.00 (180.00-360.00)	20	1200	200.00 (120.00-300.00)	0	1440	-3.862	0.000*	-0.170
Social Media Time (min.)	120.00 (60.00-180.00)	0	1440	120.00 (60.00-180.00)	0	780	-1.999	0.04*	-0.086
eHeals	29.00 (26.00-31.00)	8	40	29.00 (24.00-32.00)	8	40	-0.412	0.68	-0.018
DLS	63.00 (56.00-68.00)	17	85	64.00 (55.25-71.00)	17	85	-1.242	0.21	-0.054
HL	30.46 (24.79-34.05)	0	50	31.45 (25.49-35.41)	0	50	-1.054	0.29	-0.045

	PT (n=307)		**FEAS (n=228)**		**Statistical Value**	
HL Categorized Classification	**n**	**%**	**n**	**%**	**χ^2**	**p**
Inadequate HL (0-25)	85	27.7	57	25	1.682	0.64
Problematic HL (> 25-33)	133	43.3	100	43.9		
Sufficient HL (>33-42)	61	19.9	43	18.9		
Excellent HL (>42-50)	28	9.1	28	12.3		

Mann-Whitney U test.*$p<0.05$.
PT: Department of Physiotherapy and Rehabilitation; FEAS: Faculty of Economics and Administrative Sciences
Min.: Minute
eHeals: E-Health Literacy Scale; DLS: Digital Literacy Scale; HL:Health Literacy

Administrative Sciences at Izmir Kâtip Celebi University.

The descriptive characteristics of the students are given in Table 1. The median age of PT students was 20.00(19.00-21.00) years, and the median age of FEAS students was 20.00(19.00- 22.00) years. There was a significant difference in the mean age between the two groups ($p<0.05$, Table 1). A significant difference was found between the two groups in terms of gender, and BMI (kg/m2) ($p<0.05$, Table 1). When the health-related lifestyle behaviors of the students were evaluated, a significant difference was found between the students of both departments ($p<0.05$, Table 1).

The findings of students' internet media times, e-health, DLS scores, and health literacy characteristics are given in Table 2. A significant difference was found between the internet time, and the social media time of PT and FEAS students ($p<0.05$, Table 2). There was no significant difference between the e-health, and DLS scores of the students in both groups ($p>0.05$, Table 2). There was no significant difference between the groups' HLS-EU-Q47 scores ($p>0.05$, Table 2). 70.1% of all students did not have enough HL.

A statistically significant difference was found between the students of both departments in terms of walking, vigorous physical activity, and total physical activity values ($p<0.05$, Table 3). There was no significant difference between IPAQ-SF moderate-intensity physical activity and sitting times of PT and FEAS students ($p>0.05$, Table 3). A significant difference was found between the low, moderate, and high physical activity levels of the students from both departments ($p<0.05$, Table 3). The activity level of the students of the FEAS department was statistically significantly higher ($p<0.05$). 79.6% of all students did not have sufficient physical activity levels (PALs).

The evaluation of the correlations between the scales in all students is given in Table 4. There was a positive correlation between the e-HEALS with the HLS-EU-Q47 (rho=0.351, $p<0.001$) and DLS (rho=0.476, $p<0.001$). A significant correlation was found between the HLS-EU-Q47 and DLS (rho=0.288, $p<0.001$). There was a positive correlation between IPAQ-SF with the HLS-EU-Q47 (rho=0.104, $p=0.016$) and DLS (rho=0.111, $p=0.010$). No correlation was found between the IPAQ-SF and e-HEALS.

DISCUSSION

This study found that university students studying in health and social fields had lower levels of e-health literacy and physical activity compared to the normal population. However, the physical activity levels of Physical Therapy (PT) students were higher than those of students in non-health fields.

PT students also had lower BMI compared to other health fields and non-health fields. Similarly, the mean BMI of the students from the health-related department was found to be lower among university students studying in Italy than those from the non-health department (15). In addition, the participation of FEAS students more than male students may explain the high BMI values. In terms of smoking and alcohol habits, students of the Faculty of Education and Applied Sciences (FEAS) department reported higher rates of use than PT students. However, according to another study in the literature, health science students expressed more smoking habits than social science students (24). According to the results of studies run with university students in different countries, the rate of physical activity for more than 4 hours a week is stated as 33% in the USA, 69.6% in Spain, and 55% in Turkey (25). In this study, 52% of the students had regular exercise habits and FEAS department students reported higher exercise habits than PT department students. The choice of healthy lifestyle behaviors may vary depending on the individual's sociocultural support and characteristics, and available resources (26). Health-related behaviors that continue in adulthood become more permanent when acquired during university years (27).

According to a study conducted in Turkey in 2017, the average daily internet time was found to be 2-3 hours (28). With the development of technology and the formation of pandemic conditions, the time people spend on the internet and social media has increased. During the pandemic period, the average time allocated by university students on social media and the internet is stated as 4-6 hours (29). In our study, the internet use of university students was found to be over 4 hours per day.

The digital literacy levels of university students studying in 10 different departments in South Korea in 2019 were compared, and it was stated that there was no significant difference (30). In our study, it was

specified that the DLS scores of the students studying outside the field of health and health were similar due to their close age in terms of both department and class levels and due to the electronic systems they met at an early age.

We determined that the average e-health literacy scores of university students, which we evaluated with E-HEALS, were found to be 27.78. In a study sample conducted in our country, no difference was observed between the e-health literacy levels

Table 3. Categorized classification of IPAQ-SF and IPAQ-SF scores of students studying in different fields

	PT (n=307)			FEAS (n=228)			Statistical Value		
IPAQ- SF Scores	**Median (IQR)**	**Min**	**Max**	**Median (IQR)**	**Min**	**Max**	**z**	**p**	**Effect size**
IPAQ-Vigorous activity (MET a week)	0.00 (0.00-480.00)	0	6720	240.00 (0.00-1440.00)	0	8640	-4.232	<0.001	-0.183
IPAQ Moderate activity (MET min. a week)	160.00 (0.00-480.00)	0	4200	200.00 (0.00-690.00)	0	4200	-1.279	0.20	-0.055
IPAQ Walking (MET min a week)	495.00 (198.00-800.00)	0	4158	693.00 (297.00-1386.00)	0	4158	-3.817	<0.001*	-0.165
IPAQ Total (MET min. a week	980.00 (495.00-1884.00)	0	9439	1784.50 (658.75-4142.25)	0	11250	-4.749	<0.001*	-0.205
Sitting time (min.)	450.00 (300.00-600.00)	40	900	450.00 (240.00-600.00)	30	900	-1.183	0.23	-0.051

	PT (n=307)		FEAS (n=228)		Statistical Value	
IPAQ-SF Categorized Classification	**n**	**%**	**n**	**%**	**χ2**	**p**
Low PA (<600 MET-minutes per week)	98	31.9	55	24.1		
Moderate PA (600-3000 MET-minutes per week)	174	56.7	99	43.4	35.758	<0.001*
High PA (>3000 MET-minutes per week)	35	11.4	74	32.5		

*χ2: Chi-Square value. Mann-Whitney U test.*p<0.05. PT: Department of Physiotherapy and Rehabilitation; FEAS: Faculty of Economics and Administrative Sciences. PA: Physical Activity. IPAQ-SF: International Physical Activity Questionnaire Short Form*

Table 4. Correlations between the scales of students studying in different fields

Scales		**E-Heals**	**HLS-EU-Q-47**	**DLS**	**IPAQ-SF**
E-Heals	rho	-	0.351*	0.476*	0.040
	p	-	<0.001	<0.001	0.352
HLS-EU-Q-47	rho		-	0.288*	0.104*
	p		-	<0.001	0.016
DLS	rho			-	0.111*
	p			-	0.010

E-Heals: E-Health Literacy Scale, HLS-EUQ47: European Health Literacy Scale. DLS: Digital Literacy Scale, IPAQ-SF: International Physical Activity Questionnaire Short Form. rho: Spearman correlation coefficient. *p<0.05

evaluated by E-HEALS among students studying in health and non-health fields. And the mean E-HEALS score of all students was expressed as 25.5 (12). In our study, there was no significant difference between the PT department students in the health field and the non-health FEAS department students, in line with this study. Unlike our study, there are studies in the literature that state that students studying in the field of health have higher e-health literacy. As an example, it was stated that the average E-HEALS score in Japan and the mean score of the 12-item e-health literacy scale in Taiwan were higher in health department students (14). When our findings are compared with the studies conducted on the students of the Faculty of Health Sciences in our country, the e-health scores are below the stated average (28). These data show that university students studying especially in the field of health in Turkey do not have a sufficient level of knowledge on the subject. Differences in the results of studies conducted between countries may be due to the scales used in the assessment and the different socio-demographic and cultural characteristics of the populations taken. It is recommended that university students be given the training to increase their level of literacy in the field of computer and e-health, encouraging them to read periodicals and articles about health, and informing them about the accuracy/reliability of the information they obtain from the internet (12). It is also important for public health that students studying in the field of health have sufficient e-health literacy levels (31).

According to the results of the research that compared the levels of HL between departments; a study using the Health Literacy Questionnaire (HLQ) scale in Australia showed that medical school students had the highest mean score when comparing allied health, nursing, and medical school students (32). In a study in Italy in which Newest Vital Sign (NVS) and Health Literacy Assessment Tool (HLAT-8) scales were used, it was stated that the HL level was higher in nursing department students than in movement sciences and economics departments (15), and in the study in which the HLQ was used in Denmark, the students studying in the field of public health had a higher level of HL than the students of molecular biomedicine. In another study using the HLS-EU-Q16 scale, while the adequate HL level of social science students varies between 25-30%, this range of 70% of the students studying in the nursing department (33). In another study conducted in Turkey using EHLS, it was stated that university students had similar results (34). There was no significant difference between the HL total score and sub-dimensions of the students included in our study and studying outside the field of health and health. The reason for this can be thought that the behavior of university students seeking and accessing health-related information is similar to the effect of the epidemic process we are in. The difference between the results in studies evaluating HL is remarkable. The results may vary depending on the differences between the measurement methods used in the studies and the socio-cultural and demographic characteristics of the population. Despite this, the fact that university students mostly have insufficient health literacy levels, together with the literatüre, is an issue that should also be taken into consideration.

We determined that 28.6% of the students were found to be inactive, only 20.4% of students have sufficient activity levels and the sitting time was 445 minutes. In Portugal, 70% of the young population follows the recommended 30 minutes of moderate or vigorous-intensity physical activity daily. According to studies conducted with university students are sufficient activity levels; 44.7% of 4193 university students in Germany (35), and 62.9% in Switzerland (36). The average residence time of university students is 44% over 8 hours in Germany (35), 420 minutes in Switzerland (36) 525 minutes in Italy (37)

Similar to the literature, it is noteworthy that most of the students have insufficient physical activity levels and an increase in the time they spend inactive. The restrictions we have encountered with the Covid-19 pandemic in the current period have increased the effects of the physical inactivity pandemic, which is already a problem, to an alarming level (38). In our study, the fact that students continue their education process remotely may be another reason for the increase in sitting time. While technological developments make our lives easier, the disadvantages of our activity levels and the isolation measures taken within the scope of the pandemic conditions we are in also lay the groundwork for an inactive lifestyle (36).

Having a sufficient level of health literacy can provide to individuals make conscious choices regarding their physical activities and thus contribute to the prevention of many non-communicable chronic diseases. According to the systematic review, 15 of 19 study contents showed a positive relationship between health literacy and physical activity level in adults (39). In a study conducted with university

students, it is stated that a higher level of e-health literacy enables them to adopt more than one behavior that is positive for their health, including physical activity (40). In our study, in line with the literature, a significant relationship was found between all students' digital literacy, physical activity, and health literacy levels. As the level of physical activity increases, both digital and health literacy levels increase. We think that pandemic conditions and distance education process may also affect this situation.

A positive correlation was found between the HLS-EU-Q47, DLS, and E-HEALS scales used in our study. A moderate correlation was found between the E-HEALS score averages of all students and DLS and HLS-EU-Q47 and a low correlation between HLS-EU-Q47 and DLS. There are a very limited number of correlational studies between the related scales in the literature. To reach a clear view, studies that examine the relation between the scales in different populations with larger sample groups are needed in the future.

The strength of our study is that it is the first study to investigate the relationship between e-health literacy and physical activity level in PT students. The limitation of this study is that our study was conducted during the Covid period and it creates a disadvantage in terms of PALs. On the other hand, it may have provided an advantage in terms of evaluation of e-health.

CONCLUSION

Consequently, the study found that e-health literacy and physical activity levels of university students in health and social fields were similarly low. There was a positive correlation between e-HEALS with DLS and HL, and a significant correlation was found between HL and DLS. The study highlights the need for education and training programs to increase health literacy and physical activity levels in higher education. It is suggested that appropriate environments should be created in universities to address this issue. Additionally, identifying the level of health literacy and physical activity of physiotherapists is important for improving the quality of service they provide to patients and society. The results of this study can ensure insight for future research on evaluating methods for improving health literacy in university students.

Acknowledgments: Thank you to all volunteer university students who participated.

Author contribution: Conception: Sema Savci, Ayse Kardelen Acar. Design: Sema Savci, Ayse Kardelen Acar, Buse Ozcan Kahraman, Aylin Tanriverdi. Supervision: Sema Savci. Data collection: Ayse Kardelen Acar. Analysis: Sema Savci, Ayse Kardelen Acar, Buse Ozcan Kahraman, Aylin Tanriverdi. Writing: Ayse Kardelen Acar. Critical review: Sema Savci, Buse Ozcan Kahraman, Aylin Tanriverdi.

Conflict of interests: The authors declare that they have no conflict of interest.

Ethical approval: The study was accepted by Dokuz Eylul University University Non-Interventional Clinical Research Ethics Committee (Decision Date: 05.10.2020, Number: 2020/24-17).

Funding: The authors declare that they have no conflict of interest.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Sørensen K, Pelikan JM, Röthlin F, Ganahl K, Slonska Z, Doyle G, et al. Health literacy in Europe: comparative results of the European health literacy survey (HLS-EU). Eur J Public Health 2015;25(6):1053–8.
2. Norman CD, Skinner HA. eHEALS: The eHealth literacy scale. J Med Internet Res. 2006;8(4):1–7.
3. Anwar A, Malik M, Raees V, Anwar A. Role of Mass Media and Public Health Communications in the COVID-19 Pandemic. Cureus 2020;12(9):e10453.
4. Beleigoli AM, Maeder A, Button D, Lange B, Tiemann J. The Care Informatics and Technologies Project - Enhancing Capability, Motivation and Opportunities in Digital Health Among Health Professionals and Students. Stud Health Technol Inform 2019;266:25–9.
5. Conard S. Best practices in digital health literacy. Int J Cardiol. 2019;292:277–9.
6. Austin EW, Austin BW, Willoughby JF, Amram O, Domgaard S. How Media Literacy and Science Media Literacy Predicted the Adoption of Protective Behaviors Amidst the COVID-19 Pandemic. J Health Commun 2021;26(4):239–52.
7. Mattioli A V, Sciomer S, Cocchi C, Maffei S. Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information. 2020;(January). Available from: https://doi.org/10/1016/j/numecd.2020.05.020
8. World Health Organization. Global action plan on physical activity 2018–2030: more active people

for a healthier world. Geneva: World Health Organization; 2018. 2018.
9. Saglam M, Arikan H, Savci S, Inal-Ince D, Bosnak-Guclu M, Karabulut E, et al. International physical activity questionnaire: Reliability and validity of the Turkish version. Percept Mot Skills 2010;111(1):278–84.
10. Hudson, S., Rikard, R.V., Staiculescu, L., Edison K. Improving Health and The Bottom Line: The Case for Health Literacy, Building the Case for Health Literacy Proceedings of a Workshop [Internet]. Alper J, editor. Washington, DC: The National Academies Press; 2018. 15–28 p. Available from: https://www.nap.edu/catalog/25068/building-the-case-for-health-literacy-proceedings-of-a-workshop
11. Kobayashi R, Ishizaki M. Examining the Interaction Between Medical Information Seeking Online and Understanding: Exploratory Study. JMIR Cancer 2019;5(2):e13240.
12. Nakas D. e-Health Literacy Levels of University Students in Turkey and Affecting Factors 2020;13(3):2149–59.
13. Yilmaz A, Meltem S, Kaya M. Determining of E-Health Literacy Levels of Students of The Faculty of Health Sciences. Mehmet Akif Ersoy University Journal of Social Sciences Institute 2020;(May):148–57.
14. Tsukahara S, Yamaguchi S, Igarashi F, Uruma R, Ikuina N, Iwakura K, et al. Association of eHealth Literacy With Lifestyle Behaviors in University Students: Questionnaire-Based Cross-Sectional Study. J Med Internet Res. 2020;22(6):e18155.
15. Gallè F, Calella P, Napoli C, Liguori F, Parisi EA, Orsi GB, et al. Are health literacy and lifestyle of undergraduates related to the educational field? An italian survey. Int J Environ Res Public Health 2020;17(18):1–9.
16. Abacigil F, Harlak H, Okyay P, Kiraz DE, Turan SG, Saruhan G, et al. Validity and reliability of the Turkish version of the European Health Literacy Survey Questionnaire. Health Promot Int. 2019;34(4):658–67.
17. Sørensen K, Van den Broucke S, Fullam J, Doyle G, Pelikan J, Slonska Z, et al. Health literacy and public health: A systematic review and integration of definitions and models. BMC Public Health 2012;12(1):80.
18. Norman CD, Skinner HA. eHealth Literacy: Essential Skills for Consumer Health in a Networked World. J Med Internet Res 2006;16;8(2):e9.
19. Coskun S, Bebis H. E-health literacy scale for adolescents: Validity and reliability study. Gulhane Medical Journal. 2015;57:378–84.
20. Ng W. Can we teach digital natives digital literacy? Comput Educ 2012;59(3):1065–78.
21. Hamutoglu, N., Gungoren, O. C., Uyanik, G. K., Erdogan DG. Digital Literacy Scale: Adaptation Study to Turkish. Journal of Ege Education. 2017;7(18):408–29.
22. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-Country reliability and validity. Med Sci Sports Exerc 2003;35(8):1381–95.
23. Fritz CO, Morris PE, Richler JJ. Effect size estimates: Current use, calculations, and interpretation. J Exp Psychol Gen 2012;141(1):2–18.
24. Suka M, Odajima T, Okamoto M, Sumitani M, Igarashi A, Ishikawa H, et al. Relationship between health literacy, health information access, health behavior, and health status in Japanese people. Patient Educ Couns 2015;98(5):660–8.
25. Gunal A, Demirturk F, Arikan H, Inal B. Exercise Behavior, Smoking Addiction and General Health Status of Nursing and Midwifery Students. Journal of Health Sciences and Professions. 2018;5(2):169–78.
26. Vyas CM, Ogata S, Reynolds CF, Mischoulon D, Chang G, Cook NR, et al. Telomere length and its relationships with lifestyle and behavioural factors: variations by sex and race/ethnicity. Age Ageing 202;50(3):838–46.
27. Essiet IA, Baharom A, Shahar HK, Uzochukwu B. Application of the Socio-Ecological Model to predict physical activity behaviour among Nigerian University students. Pan Afr Med J 2017;26:110.
28. Sengul H, Cınar F, Capar;H. E-Health Literacy Knowledge Levels of the Health Sciences Faculty Students and Attitudes to Use the Internet: A Foundation University Sample. Journal of Socıal And Humanıtıes Sciences Research 2017;4(5):1277–88.
29. Rahaman MS. Use of Internet by the undergraduate and postgraduate students at the University of Gour Banga, Malda, West Bengal. Library Philosophy and Practice 2021;4859:1–11.

30. Kim KT. The structural relationship among digital literacy, learning strategies, and core competencies among south korean college students. Educational Sciences: Theory and Practice 2019;19(2):3–21.
31. Tubaishat A, Habiballah L. eHealth literacy among undergraduate nursing students. Nurse Educ Today 2016;42:47–52.
32. Mullan J, Burns P, Weston K, McLennan P, Rich W, Crowther S, et al. Health literacy amongst health professional university students: A study using the health literacy questionnaire. Educ Sci (Basel) 2017;7(2).
33. Juvinyà-Canal D, Suñer-Soler R, Porquet AB, Vernay M, Blanchard H, Bertran-Noguer C. Health literacy among health and social care university students. Int J Environ Res Public Health 2020;17(7):1–10.
34. İnkaya B, Tüzer H. Investigation of Health Literacy of Reading Students in Social and Health Sciences of a University. Kocaeli Med J 2018;7(3):124–9.
35. Tan SL, Jetzke M, Vergeld V, Müller C. Independent and Combined Associations of Physical Activity, Sedentary Time, and Activity Intensities With Perceived Stress Among University Students: Internet-Based Cross-Sectional Study. JMIR Public Health Surveill 2020;6(4):e20119.
36. Taeymans J, Luijckx E, Rogan S, Haas K, Baur H. Physical Activity, Nutritional Habits, and Sleeping Behavior in Students and Employees of a Swiss University During the COVID-19 Lockdown Period: Questionnaire Survey Study. JMIR Public Health Surveill 2021;7(4):e26330.
37. Barkley JE, Lepp A, Glickman E, Farnell G, Beiting J, Wiet R, et al. The Acute Effects of the COVID-19 Pandemic on Physical Activity and Sedentary Behavior in University Students and Employees. Int J Exerc Sci 2020;13(5):1326–39.
38. Ercan S, Keklicek H. Investigation of the Change in Physical Activity Levels of University Students Due to COVID-19 Pandemic. Journal of Izmir Katip Celebi University Faculty of Health Sciences 2020;5(2):69–74.
39. Buja A, Rabensteiner A, Sperotto M, Grotto G, Bertoncello C, Cocchio S, et al. Health Literacy and Physical Activity: A Systematic Review. J Phys Act Health. 2020;17(12):1–16.
40. Hsu W, Chiang C, Yang S. The effect of individual factors on health behaviors among college students: the mediating effects of eHealth literacy. J Med Internet Res 2014;16(12):e287.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 390-401
https://doi.org/10.30621/jbachs.1340729
RESEARCH ARTICLE

QUALITY AND COMPLIANCE OF VIDEO-BASED INFORMATION WITH KNEE OSTEOARTHRITIS TREATMENT GUIDELINES

Ozlem Feyzioglu[1], Ozgul Ozturk[1]

[1] Acibadem Mehmet Ali Aydinlar University, Department of Physiotherapy and Rehabilitation, Istanbul, Turkey

ORCID: O.F. 0000-0002-7479-4128; O.O. 0000-0002-5207-1893

Corresponding author: Ozlem Feyzioglu, **E-mail:** ozlem.feyzioglu@acibadem.edu.tr
Received: 10.08.2023; **Accepted:** 14.11.2023; **Available Online Date:** 31.05.2024

Cite this article as: Feyzioglu O. Ozturk O. Quality and Compliance of Video-Based Information with Knee Osteoarthritis Treatment Guidelines. J Basic Clin Health Sci 2024; 8: 390-401.

ABSTRACT

Purpose: This study aimed to evaluate the current knee osteoarthritis (OA) information available on YouTube and to evaluate if these videos report information about core treatment methods in the current guidelines.
Material and Methods: We searched for the keyword as “knee osteoarthritis” on YouTube. A total of 61 videos were evaluated and their quality, reliability and knee OA specific content were analyzed. Popularity of the videos and the number and kind of treatment recommendations were recorded. The videos were dichotomized into two groups according to their content if they were including core non-drug treatment methods or not.
Results: The majority of the content was uploaded by health-care professionals (37.8 %) and exercise was the most recommended treatment method. Reliability and quality of the videos uploaded by health-care professionals, academic and health-care organizations were higher than other sources ($p<0.05$). The academic and health-care organizations had the highest knee OA content score and health-care professionals had the highest popularity ($p<0.05$). Videos uploaded by physicians and physical therapists mostly included evidence-based non-drug treatment recommendations.
Conclusion: Exercise and patient education were the main topics in knee OA-related videos. Patients can be referred to the videos uploaded by academic and healthcare organizations to obtain comprehensive information about knee OA.

Keywords: Video analysis; knee osteoarthritis; exercise; guideline

INTRODUCTION

Osteoarthritis (OA) is a major contributor to disability and healthcare costs worldwide. (1) OA causes pain, stiffness, loss of function, and a diminished quality of life, leading to increased mortality and morbidity (2, 3). Various guidelines recommend pharmacological and non-pharmacological treatment options to manage pain, enhance functionality, and prevent further complications. Evidence-based recommendations encompass exercise, patient education, and weight management as core non-pharmacological approaches for patients with knee OA (4, 5). Implementing these methods into the treatment programs yields cost-effectiveness (6). However, individuals with knee OA may be less likely to utilize exercise and weight management as part of their treatment plan (7). Rehabilitation interventions are necessary to maintain, develop, and restore physical capacity and movement since these are critical components of optimal general health and quality of life (8). Although the benefits of rehabilitation and physical therapy are well-recognized, these services may be underutilized. Inadequate services or patient resources and high

demand to physiotherapy access may result in long waiting lists. Thus, restricting access to treatment becomes necessary (9, 10).

In cases where rehabilitation is necessary but not adequately implemented, alternative rehabilitation models have been created to improve coverage using new resources such as digital health tools (9). Thus, telerehabilitation, considered as a branch of telehealth can be used to increase treatment adherence, satisfaction and overall health by enabling participants to take an active role in disease management and decision-making process. Telerehabilitation can replace the traditional treatment approach, allowing individuals to access treatment remotely (10, 11).

Digital health applications include web-based digital intervenions, smartphone applications, and social media platforms such as Facebook, Twitter, Instagram, YouTube and patients can have a direct access to disease-related exercise and education using these platforms(12) . Gürler et al. compared social media platforms and found that the videos with the highest information content were on the YouTube platform. Additionally, the medical quality of Instagram and twitter videos was found to be quite low (13). However, the applicability of YouTube in telerehabilitation has some limitations, not allowing direct and real-time interaction between patient and clinician. Patients can also access therapy videos on YouTube that may be inappropriate or dangerous for their diseases. Therefore, the quality and reliability of the information on YouTube videos should be investigated for each disease(14).

A video-based program delivering information about knee OA, incorporating behavioral change strategies, proves to be a cost-effective solution (15, 16). Since OA means more than just the “wear and tear” theory and not all patients undergo surgical interventions (17), poor or incorrect online content can induce fear in patients, negatively impacting their health or health-related behaviors.

An increasing number of patients search the internet for healthcare information about diseases and treatment methods (18). YouTube, as the third most visited website and a video-sharing platform, has become a valuable resource for healthcare information. However, the reliability of the videos on YouTube is not regulated, as they do not undergo an editorial process (19). Consequently, this platform may contain misleading and inaccurate information, potentially influencing decision-making process (20). Nevertheless, it is important to note that patients may access accurate information easily by producing appropriate content due to the accessibility and free use of YouTube. Therefore, it is crucial to assess the alignment of information on social media platforms with current scientific recommendations (21).

Several studies have evaluated the reliability, quality and content of Youtube videos on various diseases and have found it to be a poor or important source of information regarding diseases and treatment methods (18,20,22-24). YouTube has been characterized as an inadequate resource for patients with knee OA (20). However, this video platform has been served as a reliable source for knee OA exercises (25). To date, no study has investigated the compatibility of the videos with current treatment guidelines.

Therefore, the aim of this study was to assess the current information available on knee OA and determine whether these videos include information about core non-drug treatment methods recommended in the current knee OA guidelines.

MATERIAL AND METHODS.

Search strategy

The present study was designed as a cross-sectional observational study. Two independent researchers both of whom have clinical experience with knee OA patients, conducted a search on YouTube (www.youtube.com) using the keywords “knee osteoarthritis” and “knee arthritis”. The videos that appeared for each search term were sorted by applying the “view count” filter which enables to identify the most viewed videos on this platform. The researchers logged out their personal Google accounts, deleted the cookies and cleared their search history. A pilot search was carried out on 10 August 2021, to identify potential discrepancies between the researchers. The final search was conducted on September 10, 2021, at the same time, and each observer independently selected the first 200 videos. The search results were compared, and the final selection of videos was determined. Only videos in the English language were included. Exclusion criteria were as follows; 1) duplicate videos, 2) videos in languages other than English, 3) videos without or with inappropriate audio, and 4) advertisements. Additonally, educational videos designed to demonstrate interventional procedures such as surgery and intra-articular injection were

excluded. The Universal Resource Locator (URL) links were saved by the researchers.

This study obtained ethical approval and the present study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guideline. (26) Study was approved by Acıbadem Mehmet Ali Aydınlar University, Medical Research Ethics Committee (Decision Date: 24.02.2023, Number: ATADEK 2023-03/75).

Video features

The following information was recorded for each video; i) the type of the video (program, videoconference, animation), ii) duration (in minutes), iii) time elapsed since the upload date (days), iv) the category of the speaker (physician, physical therapist, trainer, massage therapist, chiropractor, layperson), v) the source of the content (healthcare professionals including physicians and allied health professionals such as physical therapists, exercise trainers, academic and health-related organizations, and other sources (health-related websites and commercials)), vi) intention (general information about the disease, general information about the disease and treatment recommendations, information on diagnosis, exercise demonstrations, other treatment methods, manual therapy). Additionally, the number of likes and dislikes, the number of comments, and the number of views were recorded. The view ratio (views/days) and the like ratio (number of likes*100)/(number of likes + number of dislikes), as well as the Video Power Index (VPI) were calculated using the following formula: [(number of likes*100)/(number of likes + dislikes)]* [views per day]/100. (24)

Video content

The quality and reliability of the included videos were evaluated by two independent physical therapists (authors) both of whom are asisstant professors at the university and have a minimum of 10 years of clinical experience in orthopeadic physiotherapy. Items with differences were discussed among the researchers, and a consensus was reached. The educational value of the videos was evaluated using the Global Quality Score (GQS) which was developed by Bernard et al. (27) The GQS assesses the flow, the quality of the web-related information, and ease of use by the patient, using a five-item scale to determine whether the videos are useful for patients. If a video is scored 4 or 5 points, it is considered high quality, 3 points indicate moderate quality, and 1 or 2 indicate poor quality (Table 1). (27) The reliability of YouTube videos was assessed using the modified DISCERN tool, which is a shortened version of the DISCERN tool adapted by Singh et al (28). The modified DISCERN consists of 5 questions and evaluates video content in terms of clarity, bias, uncertainty of the content, and resources used and addressed. Each “yes” response is scored as 1 point with a maximum score of 5 (Table 1).

The content of the videos was independently reviewed by the two researchers to verify the accuracy of information pertaining to important issues in knee OA. To better assess the accuracy of information within the videos, a knee OA content scoring system was employed, as previously established in similar study designs (20, 29). This scoring system comprises 9 items and evaluates aspectes such as the definition, diagnosis of knee OA, and information about the disease based on available literature (30). Videos scoring between 7 to 10 points were categorized as high content, those scoring between 4 to 6 were classified as moderate content and, scores of 0 to 3 were labeled as poor content (Table 1).

Furthermore, the videos were examined for compliance with current treatment guidelines for knee OA, utilizing a checklist prepared by combining treatment approaches recommended in guidelines (4, 5, 31-33). The number of videos included treatment recommendations, as well as the type and quantity of treatment recommendations included in each video, were recorded (Table 1). The evaluated videos were categorized into three groups based on the source of their content; health-care professionals (physicians, physical therapists, exercise trainers, personal trainers and chiropractors), academic and healthcare organizations (university personel and research groups) and other sources (health-related websites, healthcare organization, commercials). Healthcare organization included foundations and patient organizations aiming to give information about knee osteoarthritis.” Additionally, the videos were compared based on the speaker’s qualifications (physician, physical therapist, massage therapist, chiropractor, layperson, athletic trainer).

Statistical Analysis

The Statistical Package for the Social Sciences version 22.0 package program (SPSS Inc., Chicago, IL, USA) was used for data analysis. Median

Table 1. Assessment tools for quality, reliability and content of the videos

Quality (Global Quality Score)	
1. Poor quality, poor flow, most information is missing, not helpful for patients	
2. Poor quality, some information is present, but of very limited use to patients	
3. Moderate quality, some informaton is adequately discussed	
4. High quality and flow, most important information is covered, useful for patients	
5. Excellent quality and flow, very useful for patients.	
Reliability (Modified DISCERN Tool)	
1. Is the video clear and understandable?	
2. Are valid sources cited?	
3. Is the information in the video unbiased and balanced?	
4. Are additional sources of information given from which the reviewer can benefit?	
5. Does the video address areas of controversial or uncertain?	
Knee Osteoarthritis Specific Content Score	
• Definition of the knee OA	1 point
• Risk factors	1 point
• Symptoms	1 point
• Prevention	1 point
• Diagnosis of knee OA	1 point
• Statistics and Epidemiology	1 point
• Prognosis	1 point
• Treatment methods (non-surgical) (if partially mentioned 1, fully mentioned 2)	2 points
• Treatment methods (surgical)	1 point
List of non-surgical treatment recommendations	
A. Patient education including information about disease, joint protection, self-management	
B. Structured exercise therapy (strengthening, aerobic, aquatic)	
C. Weight reduction / weight management	
D. Appropriate footwear, use of insoles and braces	
E. Use of NSAIDs or paracetamol for pain	
F. Use of chrondroitin sulfate or glucosamine	
G. Use of modalities (electrotherapy devices, manual therapy, acupuncture, cold and heat)	
H. Gait aids or assistive devices	
I. Intra-articular injection	

(minimum-maximum), number, and percentage were used to express descriptive data. The videos were dichotomized based on their content, determining if they included evidence-based non-drug core treatment methods (exercise, patient education, and weight management) or other treatment methods. The chi-squared test was used to compare these groups with the speaker of the videos.

The distribution of the data was assessed using the Shapiro-Wilk test. Continuous variables were compared using the Kruskal-Wallis test, followed by pairwise comparisons using Dunn-Bonferonni post-hoc method after significance was established. The agreement between the two researchers was measured using the Kappa coefficient. P values less than 0.05 were considered significant.

RESULTS

Among the 200 videos, 139 videos were excluded, leaving a total of 61 videos for analysis (Fig 1). The Kappa values for the two observers were 0.91 for the GQS, 0.91 for the modified DISCERN score, 0.92 for the knee OA specific content score. When we analyzed the type and intention of the videos, 78.7 %

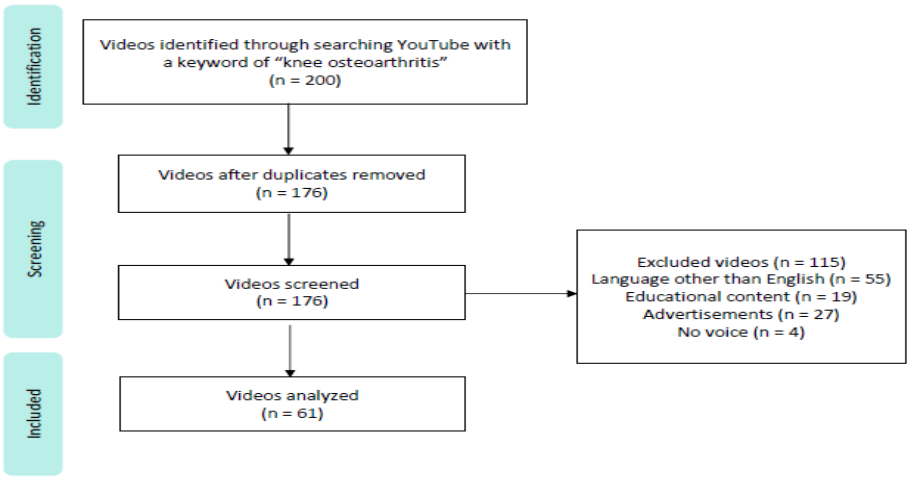


Figure 1. Flow chart

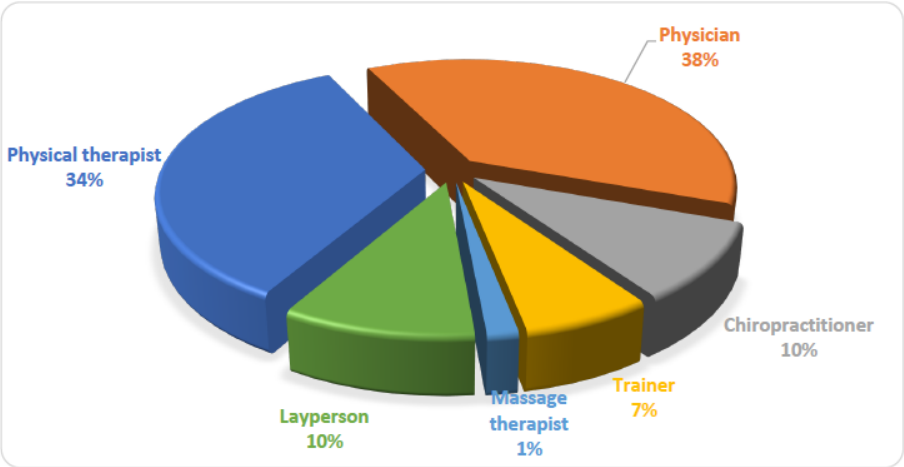


Figure 2. Videos according to the speaker

of them were categorized as programs, with exercise demonstration being the most common intention (Table 2). Additional characteristics of the YouTube videos can be found in Table 2. Figure 2 illustrates the distribution of speakers, with physicians presenting 38 % of the uploaded videos. A total of 41 (67.2 %) videos included evidence-based core treatment methods, while 20 (32.8 %) videos included other treatment methods.

General features of the videos and total values for GQS, DISCERN, and knee OA content score are summarized in Table 2. According to the GQS, of the 61 videos evaluated 44.2 % (n=27) were of high quality, 36.1 (n=22) were of moderate quality, and 19.7 (n=12) were of poor quality. When analyzed by the source of content, 44 % (n=11) of the videos uploaded by healthcare professionals were of high quality, 40 % (n=10) were of moderate quality, and 16 % (n=4) were of poor quality. Among the 20 videos uploaded by academic and healthcare organizations, 60 % (n=12) were of high quality, 35 % (n=7) were of moderate quality, and only 5% (n=1) were of poor quality. Finally, 25 % (n=4) of the videos uploaded by other sources were of high quality, 31.3 % (n=5) were of moderate quality, and 43.8 % (n=7) were of poor quality.

Based on the speaker of the videos, physical therapists uploaded 13 (61.9 %) high quality videos, 5 (23.8 %) moderate quality videos, and 3 (14.3 %) poor quality videos. Physicians uploaded 12 (52.1 %) high quality videos, 8 (34.8 %) moderate quality videos, and 3 (13 %) poor quality videos. Among 6 videos uploaded by chiropractors, 1 (16.7 %) video

Table 2. Characteristics of YouTube videos

Type of video	
Program	48 (78.7 %)
Animation	10 (16.4 %)
Videoconference	2 (3.3 %)
Videoclass	1 (1.6 %)
Treatment recommendations	
No treatment recommendations	7 (11.4 %)
At least one treatment recommendation	54 (88.5 %)
Intention	
General information about the disease	9 (14.8 %)
General information about the disease and treatment methods	17 (27.9 %)
Information on diagnosis	4 (6.6 %)
Exercise demonstration	23 (37.8 %)
Other treatment methods (taping, injection, stem cell treatment, nutritional support)	5 (8.1 %)
Manual therapy	3 (4.9 %)
Video features	
Duration (minutes)	7.08 (1.2-122)
Number of views	71 556 (9520-3 202 204)
Number of likes	783 (0-88 000)
Number of dislikes	34 (0-1200)
Number of comments	47 (0-3508)
View ratio	72.4 (0 – 2160.7)
Like ratio	94.4 (0 – 99.1)
VPI	56.6 (0 – 1983.1)
GQS	3 (1 – 5)
DISCERN	3 (1 – 5)
Knee OA content score	3 (1 – 9)

Data are presented as median (minimum-maximum) and frequency (proportion).
GQS, Global Quality Score; VPI, Video Power Index.

was of high quality, and 3 (50.0 %) videos were of moderate quality. Athletic trainers uploaded 2 (50.0 %) moderate quality videos and 2 (50.0 %) poor quality videos. Among the 6 videos uploaded by laypersons, 1 (16.7 %) of was of high quality, 4 (66.7 %) were of moderate quality, and 1 (16.7 %) was of poor quality. A video uploaded by a massage therapist was of poor quality.

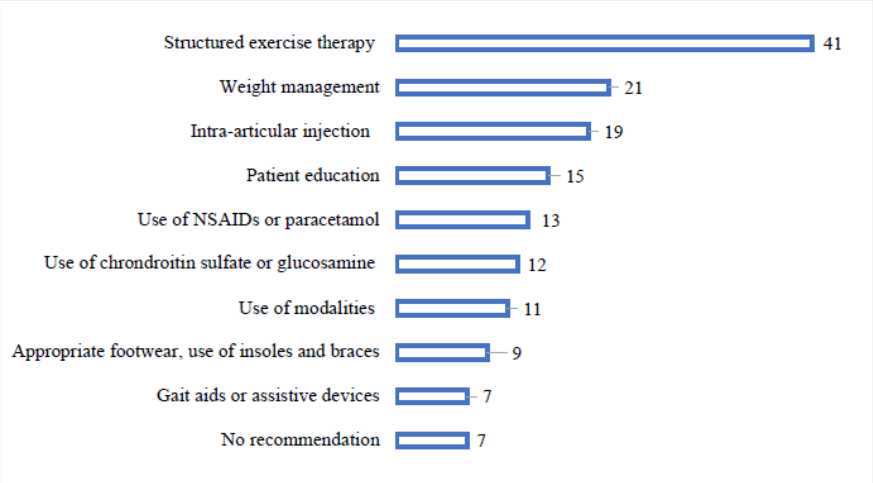


Figure 3. Number of videos including treatment recommendations

When the features, quality, reliability, and content score of the videos were compared among the groups, no significant differences were found in views, like ratio, and dislikes ($p>0.05$). However, significant differences were observed in likes, the number of comments, view ratio, VPI, GQS, DISCERN, and knee OA content score between the groups ($p<0.05$) (Table 3). According to the results of the Dunn-Bonferonni post-hoc method, both the GQS and DISCERN scores of the academic and healthcare organization group and healthcare professionals were significantly higher than those of other sources. No difference was found between the videos uploaded by academic and healthcare organizations and healthcare professionals in terms of GQS and DISCERN scores ($p>0.05$). Additionally, the knee OA content score of the videos uploaded by academic and healthcare organizations was significantly higher than that of videos uploaded by healthcare professionals and other sources. The view ratio, number of comments, number of likes, and VPI were significantly higher for videos uploaded by healthcare professionals compared to the other two groups (Table 3).

Comparisons among the groups based on the video speaker revealed that physicians and physical therapists uploaded more videos containing core treatment methods ($p=0.04$). Additionally, DISCERN, GQS, and knee OA content scores differed among the groups. While GQS, DISCERN, and knee OA scores for videos uploaded by physical therapists and physicians did not differ significantly, their quality surpassed that of videos uploaded by other speakers, with the exception of massage therapists (Table 4).

Figure 3 displays the number of treatment recommendations in the evaluated videos. Out of the 148 recommendations, 27.7 % of them pertained to structured exercise therapy. Of the treatment recommendations, 47.3 % originated from healthcare professional sources, 33.7 % from academic and healthcare organizations, and 18.9 % from commercial and health-related websites.

DISCUSSION

This study aimed to evaluate the current information related to knee OA and determine if these videos include core non-drug treatment methods recommended in knee OA current guidelines. Most videos on the management of knee OA align with the evidence-based recommendations and include core treatment methods such as exercise, patient education, and weight management. Exercise was the most frequently recommended method among the analyzed videos. Additionally, we found that videos uploaded by academic and healthcare organizations had the highest quality, and their knee OA content score was higher than that of the two groups. However, healthcare Professional-sourced videos were more popular than the other evaluated videos. More than half of the uploaded videos included evidence-based core non-drug treatment methods presented by physicians and physical therapists.

Patients are increasingly using online platforms as a source of information to learn about their diseases and treatment methods (34). Therefore, the quality, reliability, and accuracy of information in online resources are becoming more critical over time. The average number of views in our study was 349 910,

Table 3. Analysis of the videos according to the source of upload.

Variables	Healthcare professionals (n=25)	Academic and healthcare organization (n=20)	Other sources (Commercial and health-related website) (n=16)	P value
View	285 518 (10 636 – 2 217 828)	105 588 (9520 – 743 225)	42 373 (12 281 – 3 202 204)	0.20
Like	2400 (0 – 88 000)	386.5 (0 - 5200)	414.5 (0 – 22 000)	**0.01**
Dislike	70 (0 – 1200)	30.5 (0 - 333)	20.5 (0 – 737)	0.10
Number of comments	143 (2 – 3508)	23 (0 – 534)	28 (0 – 769)	**0.00**
View ratio	145.3 (3.2 – 2014)	49.7 (0 – 340)	26 (4.4 – 210.7)	**0.02**
Like ratio	95.8 (0 - 99.1)	93.2 (0 – 96.1)	95.5 (0 – 99.1)	0.07
VPI	90.2 (0 – 1983.1)	29.6 (0 – 320.7)	22.3 (0 – 1423.6)	**0.04**
GQS	3 (2-5)	4.5 (2 – 5)	3 (1 – 5)	**0.01**
DISCERN	3 (2-5)	4 (1 – 5)	2 (1 – 5)	**0.02**
Knee OA content score	2 (1-9)	4.5 (1 – 9)	3 (1 – 5)	**0.00**

Values are presented as median (minimum – maximum).

GQS Global Quality Score, **VPI** Video Power Index, **DISCERN** Quality Criteria for Consumer Health Information

Table 4. Evaluation of the videos according to the speaker

Speaker of the video					
	Core non-drug treatment methods N (%)	**Other treatment methods N (%)**	**DISCERN score Mean (Median)**	**GQS score Mean (Median)**	**Knee OA content score Mean (Median)**
Physical therapist	19	2	3.5 (4)	4 (5)	3.4 (3)
Physician	14	9	3.3 (3)	3.7 (4)	4.4 (4)
Chiropractitioner	2	4	2.1 (2)	2.8 (3)	1.8 (1.5)
Athletic trainer	3	1	2.5 (2.5)	2.2 (2.5)	2 (1.5)
Massage therapist	0	1	2 (2)	2 (2)	4 (4)
Layperson	3	3	1.6 (2)	3 (3)	1 (1)
P value	**0.04****		**0.001***	**0.021***	**0.042***

consistent with previous studies reporting increased viewership among patients seeking information about medical conditions (20, 35). YouTube is a free video content platform availabe to everyone, and even non-evidence-based or non-useful treatment approaches can spread easily due to the lack of a content control mechanism and reliability of the uploaded videos. In this study, the overall mean GQS was 3.5, and

DISCERN was 3.1, indicating moderate quality and reliability. Most published studies have found YouTube videos to be of low quality and unreliable (24, 36). However, some studies have reported that YouTube videos include accurate and reliable information that can be helpful for patients (18, 22). These differing results may reflect the subjective experience of independent evaluators. To minimize minimize the differences between assessors, GQS and DISCERN scores were defined in detail before video analysis, and meetings were conducted to ensure a consistent perspective. Inter-rater kappa scores were calculated based on randomly selected videos related to the topic, and our study's kappa value was above 0.70, indicating strong agreement.

Without classifying videos based on their publishing source, the knee OA content score in our study was 3.5, indicating poor content quality. This result is in line with previous studies on YouTube videos evaluating the medical information. (20, 24) Videos created by academic and healthcare organizations had the highest knee OA content score (median:4.5/10), surpassing videos from healthcare professionals or other sources. The 47.3 % of the 148 treatment recommendations were published by healthcare professionals, mostly featuring exercise demonstrations. The low knee OA content score may be related to the fact that non-surgical treatment recommendations were scored with 1 or 2 points. Academicians and healthcare organizations prepared videos covering a broader range of topics according to the content checklist, contributing to their higher content score.

The quality and reliability of videos uploaded by healthcare professionals, academics, or healthcare organizations have been found to be higher than those from medical advertisements, health-related websites, or independent users (18, 23, 37). However, Culha et al. reported no significant difference in GQS and DISCERN scores based on the source of the content (22). Our study revealed that when the source is an academician or healthcare organization, YouTube can provide valuable information about knee OA and its treatment methods. We also believe that healthcare professionals, academicians, or individuals working in healthcare organizations should be encouraged to produce unbiased and informative videos about diseases and evidence-based treatment recommendations (22). In line with this recommendation, patients should be educated on how to find more useful and accurate content within these platforms.

Previous studies have investigated the reliability and quality of YouTube videos prepared for different diseases or conditions such as ankylosing spondylitis, sarcopenia, fibromyalgia, and rheumatoid arthritis (18, 23, 28, 38). Wong et al. evaluated YouTube content using the keyword "knee osteoarthritis" and concluded that YouTube is a poor educational source for knee OA information. However, their study did not investigate the reliability and quality of the videos using widely accepted tools, also they did not record the treatment approaches in detail. Their study reported that 82.14 % of the 56 videos included information about non-operative treatment approaches (20). Consistent with this study, 78.6 % of the videos in our study contained information about treatment methods or demonstrated some of them, such as exercise or manual therapy. Bağcıer et al. analyzed videos using a keyword "exercise for knee OA" and suggested that YouTube can be a reliable source for obtaining information (25).

Exercise and patient education have been identified as core treatment methods in several guidelines. In accordance with these guidelines, exercise is the most recommended treatment method (67.2%) in our study and is typically demonstrated by physical therapists. This suggests that YouTube videos can serve as an informative tool for patients who have limited or no access to physical therapy services. Furthermore, evidence-based non-drug core treatment methods (exercise, physical education, and weight management) were presented in 67.2 % of the analyzed videos. However, the viewed videos on knee OA prioritized treatment methods and did not mostly include disease-related information, as mentioned earlier (21). Therefore, we can propose that informative videos not only focus on treatment approaches but also encompass the disease process, may better help patients to manage their condition.

Our results indicate that videos sourced from healthcare professionals were more popular, as evidenced by the view ratio, the number of comments, the number of likes, and the VPI compared to academic, healthcare organization, and other sources. Erdem et al. found that videos uploaded by academicians had the lowest VPI (24). In contrast, some studies reported no difference in popularity based on content source (22, 23). Ayoub

et al. suggested that low-quality videos tend to be more attractive (29). Our study showed that despite being less popular, videos uploaded by academic and healthcare organizations were rated as high quality and more comprehensive. Consistent with our results, Kocyigit et al. concluded that popularity does not predict video quality (18). The high popularity of healthcare professionals should motivate them to produce high-quality, comprehensive videos that cover both disease-related information and treatment methods. Patients diagnosed with knee OA should consider accessing videos produced by academic and healthcare organizations first, followed by those created by health professionals, to maximize the benefits of the YouTube platform. This approach can raise awareness of various treatment modalities for both the disease and its progression.

This study has several limitations. Similar to published studies, we have evaluated the videos using subjective and unvalidated tools (GQS, knee OA scoring system, modified DISCERN) which may be influenced by the evaluators' perspective. This limitation arises from the lack of valid and disease-specific metrics for assessing online or video-based information. To mitigate this, two independent authors evaluated each video twice. Additionally, the viewed videos were only in English which may limit the generalizability of our results. Another limitation is the sample size; we have evaluated 61 videos, which is consistent with the existing literature. Most internet users typically view the first two pages of their search results (39). Furthermore, this study is a "snapshot" of the content on YouTube, and the platform is dynamic affecting search results. In future studies, analyzing videos in the native languages of the countries may provide more useful information for patients and contribute more to the literature. Moreover, YouTube may promote videos uploaded by academicians and healthcare professionnals through its embeded algorithm to serve more qualified information for the patients.

CONCLUSION

The popularity of YouTube is increasing among knee OA patients for health information. Exercise and patient education, core treatment methods in several guidelines, were the most prevalent content in line with the guideline recommendations. Videos uploaded by academic and healthcare organizations can be recommended to patients seeking comprehensive information about knee OA and its treatment methods. Despite being less popular, healthcare professionals should provide informative videos to ensure that patients can access well-prepared healthcare information. Additionally, patients should be guided in selecting the right content while checking the video sources.

Acknowledgments: None.
Author contribution: Study concept and design: Ö.Ö; acquisition of data: Ö.Ö, Ö.F; analysis and interpretation of data: Ö.Ö, Ö.F; drafting of the manuscript: Ö.Ö; critical revision of the manuscript for important intellectual content: Ö.Ö, Ö.F.
Conflict of interests: Ö. Öztürk and Ö. Feyzioğlu declare that they have no competing interests.
Ethical approval: This study was approved by Acıbadem Mehmet Ali Aydınlar University, Medical Research Ethics Committee (Decision Date: 24.02.2023, Number: ATADEK 2023-03/75)
Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Vina ER, Kwoh CK. Epidemiology of osteoarthritis: literature update. Curr Opin Rheumatol 2018;30(2):160-7.
2. Wang Y, Nguyen USD, Lane NE, Lu N, Wei J, Lei G, et al. Knee Osteoarthritis, Potential Mediators, and Risk of All-Cause Mortality: Data From the Osteoarthritis Initiative. Arthritis Care Res (Hoboken) 2021;73(4):566-73.
3. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 2014;73(7):1323-30.
4. Bannuru RR, Osani M, Vaysbrot E, Arden N, Bennell K, Bierma-Zeinstra S, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. Osteoarthritis Cartilage 2019;27(11):1578-1589.
5. Kolasinski SL, Neogi T, Hochberg MC, Oatis C, Guyatt G, Block J, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. Arthritis & Rheumatology 2020;72(2):220-33.
6. Davis A, Davis K, Skou S, Roos E. Why Is Exercise Effective in Reducing Pain in People with Osteoarthritis? Current Treatment Options in Rheumatology 2020;6;149-156.
7. Hinman R, Nicolson P, Dobson F, Bennell K. Use of nondrug, nonoperative interventions by community-dwelling people with hip and knee

osteoarthritis. Arthritis Care Res (Hoboken) 2015;67(2):305-9.
8. Seron P, Oliveros MJ, Gutierrez-Arias R, et al. Effectiveness of Telerehabilitation in Physical Therapy: A Rapid Overview. Phys Ther 2021;101(6):pzab053.
9. Rogante M, Grigioni M, Cordella D, Giacomozzi C. Ten years of telerehabilitation: A literature overview of technologies and clinical applications. NeuroRehabilitation 2010;27(4):287-304.
10. Winters JM. Telerehabilitation research: emerging opportunities. Annu Rev Biomed Eng 2002;4(1):287-320.
11. Suso-Martí L, La Touche R, Herranz-Gómez A, Angulo-Díaz-Parreño S, Paris-Alemany A, Cuenca-Martínez F. Effectiveness of telerehabilitation in physical therapist practice: An umbrella and mapping review with meta–meta-analysis. Phys Ther 2021;101(5):pzab075.
12. Devine KA, Viola AS, Coups EJ, Wu YP. Digital health interventions for adolescent and young adult cancer survivors. JCO Clin Cancer Inform 2018;2:1-15.
13. Gurler D, Buyukceran I, editors. Assessment of the Medical Reliability of Videos on Social Media: Detailed Analysis of the Quality and Usability of Four Social Media Platforms (Facebook, Instagram, Twitter, and YouTube). Healthcare; 2022;10(10):1836.
14. Manasco MH, Barone N, Brown A. A role for YouTube in telerehabilitation. Int J Telerehabil 2010;2(2):15.
15. Egerton T, McLachlan L, Graham B, Bolton J, Setchell J, Short CE, et al. How do people with knee pain from osteoarthritis respond to a brief video delivering empowering education about the condition and its management? Patient Educ Couns 2021;104(8):2018-2027.
16. Egerton T, Bolton J, Short CE, Bennell KL. Exploring changes, and factors associated with changes, in behavioural determinants from a low-cost, scalable education intervention about knee osteoarthritis: An observational cohort study. BMC Musculoskelet Disord 2021;22(1):1-13.
17. Bunzli S, BHealthSci POB, Ayton D, Dowsey M, Gunn J, Choong P, et al. Misconceptions and the acceptance of evidence-based nonsurgical interventions for knee osteoarthritis. A qualitative study. Clin Orthop Relat Res. 2019;477(9):1975.
18. Kocyigit BF, Nacitarhan V, Koca TT, Berk E. YouTube as a source of patient information for ankylosing spondylitis exercises. Clin Rheumatol 2019;38(6):1747-51.
19. Madathil KC, Rivera-Rodriguez AJ, Greenstein JS, Gramopadhye AK. Healthcare information on YouTube: a systematic review. Health informatics Journal 2015;21(3):173-94.
20. Wong M, Desai B, Bautista M, Kwon O, Kolodychuk N, Chimento G. YouTube is a poor source of patient information for knee arthroplasty and knee osteoarthritis. Arthroplasty Today 2019;5(1):78-82.
21. Maia LB, Silva JP, Souza MB, Henschke N, Oliveira VC. Popular videos related to low back pain on YouTube™ do not reflect current clinical guidelines: a cross-sectional study. Braz J Phys Ther 2021;25(6):803-810.
22. Culha Y, Ak ES, Merder E, Ariman A, Culha MG. Analysis of the YouTube videos on pelvic floor muscle exercise training in terms of their reliability and quality. Int Urol Nephrol 2021;53(1):1-6.
23. Akyol A, Karahan İ. Is YouTube a quality source of information on sarcopenia? Eur Geriatr Med 2020;11(4):693-7.
24. Erdem MN, Karaca S. Evaluating the accuracy and quality of the information in kyphosis videos shared on YouTube. Spine (Phila Pa 1976). 2018;43(22):E1334-E9.
25. Bağcıer F, Yorulmaz E, Temel MH. YouTube as a source of patient information for knee osteoarthritis exercises. 2021. Turk J Osteoporos 2021;27:133-139.
26. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. International journal of Surgery 2014;12(12):1495-9.
27. Bernard A, Langille M, Hughes S, Rose C, Leddin D, Van Zanten SV. A systematic review of patient inflammatory bowel disease information resources on the World Wide Web. Official journal of the American College of Gastroenterology| ACG 2007;102(9):2070-7.
28. Singh AG, Singh S, Singh PP. YouTube for information on rheumatoid arthritis—a wakeup call? The Journal of Rheumatology 2012;39(5):899-903.

29. Ayoub G, Chalhoub E, Sleilaty G, Kourie HR. YouTube as a source of information on breast cancer in the Arab world. Support Care Cancer 2021:1-9.
30. Roos EM, Arden NK. Strategies for the prevention of knee osteoarthritis. Nature Reviews Rheumatology 2016;12(2):92.
31. Bruyère O, Honvo G, Veronese N, Arden NK, Branco J, Curtis EM, et al., editors. An updated algorithm recommendation for the management of knee osteoarthritis from the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO). Semin Arthritis Rheum 2019;49(3):337-350.
32. Bichsel D, Liechti FD, Schlapbach JM, Wertli MM. Cross-sectional analysis of recommendations for the treatment of hip and knee osteoarthritis in clinical guidelines. Arch Phys Med Rehabil 2022;103(3):559-569.e5.
33. Fernandes L, Hagen KB, Bijlsma JW, Andreassen O, Christensen P, Conaghan PG, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. Ann Rheum Dis 2013;72(7):1125-35.
34. Wang X, Shi J, Kong H. Online health information seeking: A review and meta-analysis. Health Communication 2021;36(10):1163-75.
35. Ng MK, Emara AK, Molloy RM, Krebs VE, Mont M, Piuzzi NS. YouTube as a source of patient information for total knee/hip arthroplasty: quantitative analysis of video reliability, quality, and content. JAAOS-Journal of the American Academy of Orthopaedic Surgeons 2021;10:5435.
36. Yildiz S, Toros SZ. The Quality, Reliability, and Popularity of YouTube Education Videos for Vestibular Rehabilitation: A Cross-sectional Study. Otol Neurotol 2021;42(8):e1077-e83.
37. Delli K, Livas C, Vissink A, Spijkervet FK. Is YouTube useful as a source of information for Sjögren's syndrome? Oral Dis 2016;22(3):196-201.
38. Ozsoy-Unubol T, Alanbay-Yagci E. YouTube as a source of information on fibromyalgia. Int J Rheum Dis 2021;24(2):197-202.
39. Morahan-Martin JM. How internet users find, evaluate, and use online health information: a cross-cultural review. CyberPsychology & Behavior 2004;7(5):497-510.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 402-412
https://doi.org/10.30621/jbachs.1357214
RESEARCH ARTICLE

INVESTIGATION OF THE CORRELATION BETWEEN PAIN, PROPRIOCEPTION AND RANGE OF MOTION IN PATIENTS WITH TEMPOROMANDIBULAR JOINT DYSFUNCTION

Sercan Akdag[1], Gamze Aydin[2]

[1] Istanbul Okan University, Institute of Graduate Education, Department of Physiotherapy and Rehabilitation, Istanbul, Turkey
[2] Istanbul Okan University, Faculty of Health Sciences, Division of Physiotherapy and Rehabilitation, Istanbul, Turkey

ORCID: S.A. 0000-0001-9126-8085; G.A. 0000-0002-4952-2825

Corresponding author: Gamze Aydin, **E-mail:** gmzetsn@gmail.com
Received: 08.09.2023; **Accepted:** 08.03.2024; **Available Online Date:** 31.05.2024

Cite this article as: Akdag S. Aydın G. Investigation of The Correlation Between Pain, Proprioception and Range of Motion in Patients With Temporomandibular Joint Dysfunction. J Basic Clin Health Sci 2024; 8: 402-412.

ABSTRACT

Purpose: The aim of study was to investigate the relationship between pain, proprioception and range of motion in patients with temporomandibular joint dysfunction (TMD).
Material and Methods: The study was completed with 45 participants diagnosed with TMD and 45 healthy controls. Visual analog scale and graded chronic pain scale were used to assess pain intensity, dolorimeter was used for pain pressure threshold (PPT) assessment. Evaluation of cervical proprioception by cervical joint position error test (JPET), cervical joint range of motion assessment by digital goniometer, mouth opening measurements were made with a ruler.
Results: In the study, pain intensity was high and PPT was low in the TMD group. In the JPET, the right-left rotation and left lateral flexion values in the TMD group had higher mean values than the control group (p=0.028, p=0.003, p=0.004, respectively). There was a significant difference between the groups in digital goniometer measurement in right-left rotation, right-left lateral flexion movements(p=0.008, p=0.001, p=0.041, p=0.005, respectively). The TMD group had a lower mean than the control group in painless, maximum assisted and unassisted mouth opening measurements(p=0.001, p=0.001, p=0.001, respectively).
Conclusion: TMD patients presented a lower PPT, less accurate head repositioning, and some impairment in cervical range of motion.

Keywords: temporomandibular joint, pain, proprioception, range of motion

INTRODUCTION

Temporomandibular joint dysfunction (TMD) is a musculoskeletal disorder involving the temporomandibular joint (TMJ), masticatory muscles, ligaments, and surrounding tissues (1). Conditions characterized by tenderness, pain, clicking sound during movement, or functional limitations in the TMJ or surrounding tissues are included under TMD (2). Although few patients seek treatment, the prevalence of TMD is between 3% and 15% in developed societies (2). TMD increases in the population mostly between the ages of 20–40 years and is more common in women than in men (3).

Pain is the most common sign of degenerative changes in TMD. A clicking sound felt in the joint and associated with uncomfortable jaw movement, neck pain, or headache is indicative of muscle issues in TMJ disorders. When people with TMD have discomfort, joint issues, and restricted jaw movements, it affects their ability to eat, chew, swallow, and talk, which lowers their quality of life as the disease progresses (4,5).

TMD is associated with problems in the cervical region, and dysfunctions in the cervical region affect the masticatory region (5,6,7). According to Silveira et al., high degrees of muscle tenderness in the upper trapezius and temporalis muscles were associated with high levels of jaw and neck dysfunction. Furthermore, severe neck disability was associated with severe jaw dysfunction (5). Another study by von Piekartz et al. investigated whether subjects with acute/subacute temporomandibular disorders exhibit associated cervical impairments and indicated that the greater the dysfunction and pain in the temporomandibular region, the greater the dysfunction on a number of cervical musculoskeletal function assessments (6). Additionally, Cuenca-Martnez et al. performed a systematic review and meta-analysis of observational studies to examine craniocervical and cervical spine features in TMD patients and discovered statistically significant variations in the relationship between neck impairment and jaw disability (7). Because of the close relationship between these two regions, cervical region functionality and proprioception can be expected to be affected in individuals with TMD. It has been demonstrated that movement limitation or functional impairment in the cervical region may affect the TMJ as well as the cervical fascia and masticatory muscles, and it is recommended that programs prepared for the evaluation and treatment of patients with TMD should include the cervical region.

The purpose of the current study was to compare measurements between patients with TMD and healthy controls by examining the pain intensity, pain pressure threshold (PPT), cervical proprioception, cervical range of motion (ROM), and mouth opening.

MATERIAL AND METHODS

Participants

Ethical approval was obtained from the Health Sciences Research Ethics Committee of Istanbul Okan University (Decision Date: 24.11.2021, Number: 8) and the study was conducted in accordance with the Declaration of Helsinki. Healthy individuals (control group (CG)) and participants with TMD (TMD group) who matched the inclusion criteria were included in the study. After the participants were given thorough information regarding the assessments to be conducted, informed consent for the study was acquired. The inclusion criteria were patients have the appropriate diagnostic criteria for TMD (DC-TMD) a result of evaluation by a dentist, be in arthrogenic, myogenic, mixed type according to the DC/TMD classification, TMJ pain for at least 3 months, and age more than 18 years, while the exclusion criteria were the presence of an orthopedic or neurological problem that would prevent the evaluations from being performed; the presence of any psychiatric disease; and a history of surgical operations involving the face, jaw, and cervical region, rheumatoid arthritis, fracture, and malignant conditions.

Sample Size

The sample size for this study was calculated using the G*POWER program. Yıldırım et al. obtained a moderate effect size (Eta squared ($\eta 2$) = 0.49) using the mean and standard deviation values of the pain intensity in patients with TMD. For this effect size, it was determined that there should be at least 45 observations for each group in the sample with a statistical power level of 81.7% and a significance level of 5%. In line with these results, the study was planned to include a minimum of 90 participants (8).

Evaluation Methods

The demographic information of the study participants was obtained using the sociodemographic form (age, gender, body weight, height, educational status, occupation, complaints, pain duration, and pain type). Within the scope of the present study, pain intensity, pain pressure threshold, cervical region proprioception sensation, cervical region range of motion, and mouth opening were measured. All assessments were done face-to-face by two physiotherapists who are blinded to groups.

Assessment of Pain İntensity

The pain intensity was assessed using the Visual Analog Scale (VAS) and Graded Chronic Pain Scale (GCPS). For the VAS, two points on a 100 mm line, with markings from “0”, indicating no pain, to “10”, indicating excruciating pain, were determined.

Between 0 and 10, patients were asked to mark the severity of their pain during three different actions (rest, activity, night (9). The GCPS Version 2.0 is a scale that assesses pain intensity, overall chronic pain severity, and pain-related disability in two dimensions over the previous 1 month. The GCPS consists of eight items in total, six of which are scored from 0 (no pain) to 10 (highest pain), and the results are calculated by adding the number of days for the remaining two items (10).

Assessment of Pain Pressure Threshold

The PPT was evaluated using a dolorimeter. Before using the dolorimeter for measurement, it was tested by pushing it on the pulp of the thumb. The algometer was then pressed vertically on the masseter, temporalis, trapezius, sternocleidomastoid, and lateral to the TMJ muscles while the patient sat until pain was felt. The pressure was applied in 1kg/cm2 increments. The patient was asked to raise his/her hand when he/she first felt pain. This technique was carried out three times and mean values was calculated (11).

Evaluation of Proprioception Sensation in the Cervical Region

A participant sits in a chair, 90 cm distant from a target on a wall. A laser pointer is put on top of the participant's head, and the subject is blindfolded. The participant is told to move their head away from the target while starting with the laser pointer exactly in the middle of the target. After returning to the center, the difference between the initial and final positions is calculated. The final laser location is measured in centimeters in relation to the initial position. The test was repeated ten times and the arithmetic mean of the results was used. The active neck movements (flexion, extension, right and left rotation, right and left lateral flexion, and right and left lateral flexion) were assessed (12,13).

Evaluation of Range of Motion in the Cervical Region

Flexion, extension, lateral flexion, and rotation angles of motion were measured using a digital goniometer for the ROM assessment of the cervical region. Cervical flexion and extension measurements were

Table 1. Evaluation and comparison of demographic characteristics of the participants

		Groups		Test Statistics	P
		TMD (n = 45)	Control (n = 45)		
		Mean ± SD Median (IQR)	Mean ± SD Median (IQR)		
Age (years)		29.11 ± 7.90 29 (11)	28.93 ± 6.07 29 (9)	-0.120	0.905 [1]
Height (cm)		169.51 ± 9.06 169 (12)	172.02 ± 11.44 171 (13)	1.153	0.252 [1]
Body Weight (kg)		69 ± 11.05 67 (15)	73.36 ± 10.16 73 (15)	1.945	0.055 [1]
BMI (kg/m^2)		24.05 ± 3.56 23 (5)	25.14 ± 5.15 24 (6)	1.170	0.245 [1]
		n (%)	n (%)		
Gender	Male	4 (%9)	4 (%9)	0.001	0.999 [2]
	Female	41 (%91)	41 (%91)		

SD: Standard deviation, TMD: Temporomandibular Joint Dysfunction, BMI: Body Mass Index,[1]: Independent t test (t); [2]: Chi-Square test-Fisher's Exact test (χ^2); summary statistics are given as mean ± standard deviation for continuous data; Median (IQR) and Number (percentage) for categorical data.

Table 2. Comparison of pain pressure threshold, proprioception and range of motion of cervical region, measurements of mouth opening

			TMD	Control		
			Mean ± SD Median (IQR)	Mean ± SD Median (IQR)	Test Ist.	p
Pain pressure threshold	Masseter muscle		1.56 ± 0.59 1.3 (0.9)	2.5 ± 0.74 2.3 (1.45)	-5.425	0.001 **
	Temporalis muscle		2.27 ± 0.90 2.1 (1.8)	3.03 ± 0.53 3.2 (1)	-4.183	0.001 **
	Sternocleidomastoid muscle		1.5 ± 0.74 1.3 (1.03)	2.52 ± 0.85 2.8 (1.5)	-5.146	0.001 **
	Trapezius muscle		2.18 ± 0.79 2.1 (1.4)	3 ± 0.59 3.1 (0.7)	-4.702	0.001 **
	TMJ lateral		2.47 ± 0.81 2.3 (1.6)	3.35 ± 0.38 3.5 (0.35)	-5.271	0.001 **
Proprioception of the cervical region	Flexion		12.47 ± 6.80 12 (7.35)	11.63 ± 2.48 12 (2.4)	-0.008	0.993
	Extension		13.57 ± 6.77 14 (6.5)	12.06 ± 2.35 12 (2.75)	-1.331	0.183
	Rotation	R	14.28 ± 8.88 13 (7.25)	10.99 ± 2.76 10 (4.5)	-2.200	0.028 *
		L	14.24 ± 8.60 13 (7.25)	10.18 ± 3.39 9 (4)	-2.994	0.003 **
	Lateral Flexion	R	12.61 ± 6.73 12 (6.75)	9.32 ± 3.59 8 (5.5)	-2.898	0.004 **
		L	12.36 ± 6.53 10.33 (5.5)	10.55 ± 3.83 9.5 (4.75)	-1.423	0.155
Cervical region joint movements (°)	Flexion		43.54 ± 5.91 43.2 (3)	43.58 ± 1.84 43.5 (2.65)	-0.146	0.884
	Extension		44.09 ± 4.53 44.1 (3.35)	44.16 ± 1.73 44.3 (2.3)	-0.747	0.455
	Rotation	R	55.66 ± 5.69 56.9 (7.15)	58.22 ± 3.96 59.4 (4.5)	-2.632	0.008 **
		L	55.74 ± 5.45 57.1 (5.75)	58.75 ± 3.28 59.4 (3.35)	-3.217	0.001 **
	Lateral Flexion	R	41.46 ± 3.68 42.3 (3.95)	42.9 ± 1.98 42.9 (2.9)	-2.043	0.041 *
		L	41.21 ± 4.10 41.8 (4.65)	43.39 ± 2.47 43.8 (3.5)	-2.793	0.005 **
Mouth Opening (mm)	PMO		16.87 ± 3.71 17 (5)	19.69 ± 1.90 20 (2)	-4.647	0.001 **
	MMO		40.96 ± 6.04 42 (8.5)	46.44 ± 4.33 48 (6)	-4.679	0.001 **
	MAMO		49.49 ± 5.59 51 (7.5)	53.47 ± 3.81 54 (4)	-3.625	0.001 **
	Lateral	R	12.67 ± 2.02 13 (2)	12.73 ± 1.28 13 (1.5)	-0.650	0.516
		L	12.2 ± 2.10 12 (3)	12.84 ± 1.41 13 (2)	-1.660	0.097

**p < 0.05; **p < 0.01 [1]: Mann–Whitney U Test (z); mean ± standard deviation for summary statistics ; Median (IQR) is given as value. SD: Standard deviation, TMD: Temporomandibular Joint Dysfunction, R; Right, L; Left, PMO: Painless mouth opening, MMO: Maximum Mouth Opening, MAMO: Maximum Assisted Mouth Opening*

performed in the sitting position. The pivot point of the goniometer was set as the acromion. The fixed arm was parallel to the floor and the moving arm followed the midline of the ear.14 During the rotation movement measurement, the participants were seated and the physiotherapist stood behind the patient. The pivot point of the goniometer was placed at the center of the head, the fixed arm was kept parallel to the ground, and the moving arm followed the head movement. During lateral flexion movement, the patient was seated, the pivot point of the goniometer was placed at the spinal process of C7 and the fixed arm was parallel to the floor. The moving arm followed the spinal processes of the cervical vertebrae and it was ensured that there was no head rotation during the measurement (14).

Assessment of Mouth Opening

In the assessment of painless mouth opening (PMO), the patient was seated with the head in the neutral position and asked to open his/her mouth without straining until they felt pain and the distance between the upper and lower incisors was measured using a ruler. Care was taken to avoid any slippage in the jaw. In the maximum mouth opening (MMO), the patient was asked to open the mouth as wide as possible in the same position and the distance between the upper and lower incisors was measured. In the maximum assisted mouth opening (MAMO), the patient was asked to open the mouth as wide as possible in the same position and the lower jaw was supported to increase mouth opening (15). For the lateral mouth opening, the patient was seated and the mouth was slightly open and the upper and lower teeth were not in contact. The distance between the midpoint of the anterior incisors during right lateral and left lateral movements was measured (16).

Statistical Analysis

The SPPS 25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) statistical package program was used in the analysis of the data. Descriptive statistics were used as categorical and continuous variables. The normality assumption was checked using the Shapiro–Wilk test; the Student t test was used to examine differences between two groups when the conditions for parametric testing were met, and the Mann-Whitney U test was used when they were not. When the conditions for a parametric test were not met, the correlation between two continuous variables was assessed using the

Table 3. The relationship between pain intensity and pain pressure threshold in TMD group

			VAS			GCPS
			Rest	Activity	Night	
Pain pressure threshold	Masseter muscle	r	-0.235	-0.409	-0.296	-0.452
		p	0.121	0.005 **	0.048 *	0.002 **
	Temporalis muscle	r	-0.325	-0.289	-0.358	-0.508
		p	0.029 *	0.054	0.016 *	0.000 **
	Sternocleidomastoid muscle	r	-0.232	-0.482	-0.244	-0.313
		p	0.130	0.001 **	0.110	0.039 *
	Trapezius muscle	r	-0.433	-0.317	-0.273	-0.304
		p	0.003 **	0.034 *	0.069	0.042 *
	TMJ lateral	r	-0.191	-0.408	-0.366	-0.139
		p	0.208	0.005 **	0.013 *	0.363

*p < 0.05; **p < 0.01 [1]: Spearman Correlation Coefficient (r); TMD: Temporomandibular Joint Dysfunction, VAS: Visual Analog Scale, GCPS: Graded Chronic Pain Scale

Pearson and Spearman correlation coefficients. Statistical significance was set at $p < 0.05$.

RESULTS

The mean age were 29.11±7.90 and 28.93±6.07 years in the TMD and CG, respectively. There were no significant differences in the demographic characteristics between the groups ($p>0.05$) (Table 1) In the TMD group, all PPT assessments and proprioception in right and left cervical rotation, and right lateral cervical flexion had higher mean compared to the CG ($p<0.05$). Proprioception in the cervical region flexion, extension, and left lateral flexion did not differ between the groups ($p>0.05$) (Table 2). In the TMD group, right-left rotation, and right-left lateral flexion ROM of the cervical region had lower compared to the CG ($p<0.05$). Flexion and extension ROM in the cervical region also did not differ between the groups ($p>0.05$). In PMO, MMO, MAMO measurements, the TMD group had lower mean values than the CG ($p<0.05$). Right-left lateral mouth opening did not differ between the groups ($p>0.05$) (Table 2).

VAS-rest was negatively correlated with PPT in the temporalis and trapezius muscles, while VAS-activity was negatively correlated with PPT in all regions except the temporalis muscle, and VAS-night was negatively correlated with PPT in all regions except the sternocleidomastoid and trapezius muscles ($p<0.05$) (Table 3).

In the TMD group, there was a positive correlation between only the cervical left rotation proprioception measurement and VAS-activity and night ($p<0.05$). In addition, a negative correlation was present between VAS-activity and MAMO and unassisted mouth opening ($p<0.05$) (Table 4).

DISCUSSION

In the present study, the TMD group had higher pain intensity and lower PPT values, had decreased proprioception during right-left rotation and right lateral flexion compared to CG. Cervical ROM (excluding flexion and extension ROM) and mouth opening (excluding right-left lateral) of the TMD group were limited compared to the CG. Mostly, the source of pain in temporal and the angle of the mandible is effected cervical and occipital region. Tenderness on trapezius, cervical, occipital (specially deep small muscles) and masseter muscles, neck pain and spasm in cervical region may limit the proprioceptive inputs during especially rotation movements and also limit the range of motion with increasing pain intensity.

In studies, TMD is more common in women than in men (17,18). Kuttila et al. suggested that higher levels of stress perception in women cause visible TMD symptoms, and therefore, the prevalence is higher in women (18). Eraslan et al. found that TMD is more common in women (19). In the present study, in agreement with the literature, 91% of the participants in the TMD group were female. Arıkan et al. reported that joint involvement was unilateral in patients with TMD, while Sahin et al. reported that bilateral joint involvement was more common (20,21). In the present study, 71% of the participants in the TMD group had bilateral joint involvement. We believe that can be attributed to the overloading of the painless side during speaking, chewing, and swallowing activities after the onset of unilateral pain, leading to bilateral dysfunction.

Pain intensity, multidimensional assessment of pain, and measurement of pain pressure threshold play an important role in comprehensive patient assessment. In study on the effect of trigger point therapy on pain and functionality in TMD, VAS score was found to be 5.48 ± 2.76 before treatment (21). Pihut et al. examined masseter muscle pain in TMD and found that the VAS was 4.86 ± 1.84 (22). In the present study, the scores of pain intensity were 6.11 ± 2.55, 6.20 ± 2.91, 5.91 ± 2.86, and 4.80 ± 1.841 (VAS-rest, VAS-activity, VAS-night, GCPS, respectively). In line with published literature, the participants also reported more intense pain during exercise. We believe that this is because activity puts more stress on the TMJ, which is subjected to strong forces when opening and closing.

Wanman et al. reported that the PPT was lower in both masticatory muscles and neck and shoulder muscles in individuals with TMD compared to healthy individuals (23). De Laat et al. found that the PPT was lower in the sternocleidomastoid and trapezius muscles in patients with TMD (24). Benli et al. found that TMD-induced pain and PPT were lower in the neck and masticatory muscles of patients with TMD compared to controls (25). In present study, we found that the PPT was lower and sensitivity to pain was higher in individuals with TMD than CG. This can be attributed to psychological factors, such as deterioration in the quality of daily life of individuals with TMD, increased stress factors, decreased belief that the pain will subside, and decreased pain tolerance of tissues and surrounding structures, due

Table 4. The relationship between pain intensity and cervical region proprioception sensation, cervical region range of motion and mouth opening in TMD group

				VAS			GCPS
				Rest	Activity	Night	
Cervical Proprioception Measurement	Flexion		r	0.244	0.024	0.031	0.151
			p	0.107	0.877	0.839	0.323
	Extension		r	0.245	0.169	0.132	0.214
			p	0.105	0.268	0.389	0.158
	Rotation	R	r	0.116	0.102	0.139	0.086
			p	0.446	0.507	0.363	0.574
		L	r	0.176	0.303	0.296	0.165
			p	0.246	0.043 *	0.049 *	0.279
	Lateral Flexion	R	r	0.076	0.056	0.063	-0.092
			p	0.618	0.714	0.682	0.549
		L	r	0.113	0.246	0.092	0.119
			p	0.460	0.104	0.550	0.435
Cervical region joint movements (°)	Flexion		r	-0.192	-0.143	-0.081	0.065
			p	0.207	0.350	0.595	0.673
	Extension		r	-0.009	0.077	0.030	-0.078
			p	0.955	0.615	0.847	0.611
	Rotation	R	r	0.132	0.094	-0.034	-0.083
			p	0.389	0.539	0.826	0.589
		L	r	0.000	-0.175	-0.218	-0.216
			p	0.998	0.251	0.150	0.153
	Lateral Flexion	R	r	0.095	0.096	0.099	0.136
			p	0.534	0.530	0.518	0.371
		L	r	0.125	0.055	-0.076	0.005
			p	0.413	0.720	0.622	0.975
Mouth opening (mm)	PMO		r	-0.147	-0.063	-0.089	-0.131
			p	0.336	0.683	0.561	0.391
	MMO		r	-0.014	-0.466	-0.212	-0.103
			p	0.926	0.001 **	0.161	0.501
	MAMO		r	0.008	-0.400	-0.246	-0.079
			p	0.958	0.007 **	0.103	0.606
	Right-Lateral		r	-0.126	-0.180	-0.128	-0.025
			p	0.408	0.236	0.402	0.871
	Left-Lateral		r	0.079	-0.289	0.099	0.128
			p	0.608	0.055	0.517	0.401

*p < 0.05; **p < 0.01 [1]: Spearman Correlation Coefficient (r); TMD: Temporomandibular Joint Dysfunction, R; Right, L; Left, VAS: Visual Analog Scale, GCPS: Graded Chronic Pain Scale PMO: Painless mouth opening, MMO: Maximum Mouth Opening, MAMO: Maximum Assisted Mouth Opening

to physiological factors, such as the chronicization of the pain-spasm-pain cycle, overuse, and faulty chewing patterns.

Cervical proprioception is defined as the awareness of the head or neck's location in space, explaining the interaction between efferent and afferent receptors to track position with movement. Bevilaqua-Grossi et al. found that cervical joint problems accompanied TMJ symptoms (26). Matheus et al. reported that patients with TMD had symptoms of cervical region problems, and stated that the cervical vertebrae are directly connected to the structures related to the head and mastication through muscles, fascia, joints, and neurovascular structures, therefore, changes seen in either region may affect the other region (27). Cervical spine problems may affect the cervical region as well as the cranium, TMJ, and shoulder (28). We hypothesized that cervical region dysfunction can directly affect proprioception due to the aforementioned structural relationships, and TMD can indirectly affect proprioception in the long term through the relationships between the TMJ and

cervical structures. Receptors in the cervical spine are connected to various regions of the central nervous system and vestibular and visual inputs. Cervical dysfunction differentiates afferent input and may subsequently alter sensorimotor control. Measurable changes in cervical joint proprioception, postural stability, and reports of imbalance in patients with neck conditions can be associated with changes in sensorimotor control. Abnormal cervical somatosensory input and sensorimotor control should be evaluated in patients with cervical pain. Trauma, functional impairment of receptors, changes in muscle spindle sensitivity, and the broad impacts of pain at many levels of the nervous system can all modify afferent information from cervical receptors. Based on the evidence to date, recommendations for the clinical assessment and management of such sensorimotor control deficits in difficulties involving the cervical region are offered (29). Some studies that have evaluated the proprioception in the cervical area in patients with neck pain have been published, but there are none that do so for patients with TMD (30,31). Ozgoren et al. evaluated proprioception in patients with chronic neck pain and found significant results in favor of the healthy group in all directions except left lateral flexion (32). Treleaven et al. found that participants with chronic neck pain had higher joint position error values than healthy individuals (33). In a study with 64 female participants with chronic neck pain, Jull et al. reported that cervical joint proprioception was low in patients with neck pain (34). De Vries et al. examined cervical proprioception in people with neck pain using the SEPT test and reported that proprioception in those with neck pain was worse than in healthy individuals (35). Civelek et al. stated that cervical proprioception and head-eye coordination disorder due to receptor dysfunction in patients with cervical region problems should be evaluated after the patients exercise and that increasing sensorimotor input is beneficial for these patients; other recent studies also support these results (36). If we consider TMD problems to be a part of cervical problems, the results of the present study are similar to those of previous studies. Lendraitiene et al. and De Laat et al. found that cervical joint ROM was lower in patients with TMD compared to healthy individuals (29, 24). In the present study, except for the flexion and extension ROM measurements in the cervical region, the TMD group had less ROM than healthy controls. Because of unilateral mastication and occlusion problems in individuals with TMD, the masticatory and as well cervical muscles and joint structures are overloaded, and joint movement limitation may develop accordingly. In addition, muscular connection between the head, neck and jaw, forward head posture, and changes in the activity of masticatory muscles also influence the vertical and horizontal position of the mandible and vice versa. However, the present study found no limitation of sagittal plane movement (flexion-extension), despite other cervical movement loss. This may be due to individual disease related differences such as duration of dysfunction, unilateral or bilateral involvement, painful areas.There is a need for studies that will evaluate jaw, head, neck posture and joint range of motion in detail by increasing the number of samples.

Studies have shown that TMD-related pain, psychological problems, and limitation of jaw movements may negatively affect the patients' QoL. Patients have difficulty in performing basic tasks, such as speaking and chewing, especially due to the limitation of mandibular movements (37). Armijo-Olivo et al. reported that cervical joint restriction affects the limitation of jaw joint movement in patients with TMD (38). Shiozaki et al. reported that the ROM in the cervical region and mouth was lower in individuals with TMD compared to healthy individuals (39). La Touche et al. examined the effect of cervical posture on mouth opening and pain pressure threshold in TMD (40). It concluded that worsen cervical posture reduces the mouth opening of the TMJ and surrounding muscles. In the present study as well, mouth opening measurements were evaluated in the study groups and similar results were obtained.

To the best of our knowledge, this study is the first to evaluate proprioception during cervical movements in individuals with TMD. One of the limitations was we did not the subclassifications (arthrogenic, myogenic, mixed) according to the DC/TMD classification because of clinical conditions did not allow it. In addition, postural evaluations of the head, neck, and spine could have increased the quality of the present study, especially considering that it may affect the participants' perception of body schema. And also, disease related or jaw-specific questionnaires for assessment of pain or functionality could be beneficial.

CONCLUSION

In summary, this case-control study compared functional and sensory variables of the cervical region between healthy participants and patients with TMD. TMD patients presented a lower PPT, less accurate head repositioning, and some impairment in cervical range of motion. These findings emphasize the importance of considering functional and sensory variables of the neck when evaluating and treating patients with TMD.

Acknowledgments: We thank to Enago (https://www.enago.com.tr/ceviri/) for their assistance in manuscript translation and editing.

Author contribution: GA and SA had made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted.

Conflict of interests: With regard to the work, no conflict of interest exists.

Ethical approval: The study was approved by Social and Non-Interventional Health Sciences Research Ethics Committee of Istanbul Okan University (Decision Date: 24.11.2021, Number: 8).

Funding: No financial support or other benefits from commercial sources has been provided for this study.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Durham J, Newton-John, TR, Zakrzewska, JM. Temporomandibular Disorders. BMJ 2015;350(9):1-9.
2. Fujita Y, Motegi E, Nomura M, Kawamura S, Yamaguchi D, Yamaguchi H. Oral habits of temporomandibular disorder patients with malocclusion. Bull Tokyo Dent Coll 2003;44(4):201-207.
3. Bonjardim LR, Gavião MBD, Pereira LJ, Castelo PM, Garcia RCMR. Signs and symptoms of temporomandibular disorders in adolescents. Braz Oral Res 2005;19:93-98.
4. Yadav S, Yang Y, Dutra EH, Robinson JL, Wadhwa S. Temporomandibular Joint Disorders in Older Adults. J Am Geriatr Soc 2018;66(6):1213-1217.
5. Silveira A, Gadotti IC, Armijo-Olivo S, Biasotto-Gonzalez DA, Magee D. Jaw dysfunction is associated with neck disability and muscle tenderness in subjects with and without chronic temporomandibular disorders. Biomed Res Int 2015;2015:512792.
6. von Piekartz H, Pudelko A, Danzeisen M, Hall T, Ballenberger N. Do subjects with acute/subacute temporomandibular disorder have associated cervical impairments: A cross-sectional study. Man Ther 2016;26:208-215.
7. Cuenca-Martínez F, Herranz-Gómez A, Madroñero-Miguel B, et al. Craniocervical and Cervical Spine Features of Patients with Temporomandibular Disorders: A Systematic Review and Meta-Analysis of Observational Studies. J Clin Med 2020;9(9):2806.
8. Yıldırım NK, Özkan M, Dıraçoğlu D, Saral İ, Karan A, Aksoy C, Özkan S. Psychopathological and Clinical Features in Patients With Temporomandibular Joint Dysfunction Syndrome. Turk J Phys Med Rehabil 2012;58(1):9-15.
9. Myles PS. The pain visual analog scale: linear or nonlinear?. Anesthesiology. 2004;100(3):744-745.
10. Von Korff M, DeBar LL, Krebs EE, Kerns RD, Deyo RA, Keefe FJ. Graded chronic pain scale revised: mild, bothersome, and high-impact chronic pain. Pain 2020;161(3):651-661.
11. Mailloux C, Beaulieu LD, Wideman TH, Massé-Alarie H. Within-session test-retest reliability of pressure pain threshold and mechanical temporal summation in healthy subjects. PLoS One 2021;16(1):e0245278.
12. Treleaven J. Sensorimotor disturbances in neck disorders affecting postural stability, head and eye movement control. Man Ther. 2008;13(1):2-11.
13. Palmgren PJ, Andreasson D, Eriksson M, Hägglund A. Cervicocephalic kinesthetic sensibility and postural balance in patients with nontraumatic chronic neck pain-a pilot study. Chiropr Osteopat 2009;17(1):1-10.
14. Sukari AAA, Singh S, Bohari MH, Idris Z, Ghani ARI, Abdullah JM. Examining the Range of Motion of the Cervical Spine: Utilising Different Bedside Instruments. Malays J Med Sci 2021;28(2):100-105.
15. Gomes CA, Dibai-Filho AV, Silva JR, Oliveira PM, Politti F, Biasotto-Gonzalez DA. Correlation between severity of temporomandibular disorder and mandibular range of motion. J Bodyw Mov Ther 2014;16:306-310.
16. Alajbeg I, Giki M, Valentić PM. Mandibular range of movement and pain intensity in patients with anterior disc displacement without reduction. Acta Stomatol Croat 2015;49:119-127.
17. Yekkalam N, Wänman A. Associations between craniomandibular disorders, sociodemographic

factors and self-perceived general and oral health in an adult population. Acta Odontol Scand 2014;72(8):1054-1065.
18. Kuttila M, Niemi PM, Kuttila S, Alanen P, Le Bell Y. TMD treatment need in relation to age, gender, stress, and diagnostic subgroup. J Orofac Pain 199;12(1):67-74.
19. Eraslan R, Kilic K. Examining the relationship of temporomandibular joint internal derangement with gender, age, educational status, job status and marital status. Selcuk Dent J 2020;7(2):246-251.
20. Arıkan H, Sertel M, Akkor BB. Investigation the Fatigue of Temporomandibular Joint, Functionality of Neck and Headache in Individuals With Temporomandibular Disorders. J Health Soc 2018;28(3):39-46.
21. Şahin D, Kaya Mutlu E, Şakar O, Ateş G, İnan Ş, Taşkıran H. The effect of the ischaemic compression technique on pain and functionality in temporomandibular disorders: A randomised clinical trial. J Oral Rehabil 2021;48(5):531-541.
22. Pihut M, Ferendiuk E, Szewczyk M, Kasprzyk K, Wieckiewicz M. The efficiency of botulinum toxin type A for the treatment of masseter muscle pain in patients with temporomandibular joint dysfunction and tension-type headache. J Headache Pain 2016;17(1):1-6.
23. Wänman A, Marklund S. Treatment outcome of supervised exercise, home exercise and bite splint therapy, respectively, in patients with symptomatic disc displacement with reduction: A randomised clinical trial. J Oral Rehabil 2020;47(2):143-149.
24. De Laat A, Meuleman H, Stevens A, Verbeke G. Correlation between cervical spine and temporomandibular disorders. Clin Oral Investig 1998;2(2):54-57.
25. Benli M, Gökçen-Röhlig B. Evaluation of pressure pain thresholds and limits of mandibular movements in selected neck and masticatory muscles in healthy and idiopathic scoliotic adolescents. Journal of Ege University Faculty of Dentistry 2018;39(3):184-191.
26. Bevilaqua-Grossi D, Chaves TC, Oliveira ASD. Cervical spine signs and symptoms: perpetuating rather than predisposing factors for temporomandibular disorders in women. J Appl Oral Sci 2007;15(4):259-264.
27. Matheus RA, Ramos-Perez FMM, Menezes AV, Ambrosano GMB, Haiter-Neto F, Bóscolo FN, Almeida SM. The relationship between temporomandibular dysfunction and head and cervical posture. J Appl Oral Sci 2009;17(3):204-208.
28. De Wijer A, Steenks MH, Bosman F, Helders PJM, Faber J. Symptoms of the stomatognathic system in temporomandibular and cervical spine disorders. J Oral Rehabil 1996;23(11):733-741.
29. Lendraitiene E, Smilgiene L, Petruseviciene D, Savickas R. Changes and associations between cervical range of motion, pain, temporomandibular joint range of motion and quality of life in individuals with migraine applying physiotherapy: a pilot study, Medicina 2021;57(6):630.
30. Strimpakos N, Sakellari V, Gioftsos G, Kapreli E, Oldham J. Cervical joint position sense: an intra- and inter-examiner reliability study. Gait Posture 2006;23(1):22-31.
31. Treleaven J, Jull G, LowChoy N. The relationship of cervical joint position error to balance and eye movement disturbances in persistent whiplash. Man Ther 2006;11(2):99-106.
32. Özgören Ç, Ciddi PK, Sahin M. Joint position sense and its relationship with pain, range of motion, muscle strength, fear of movement, functionality, and quality of life parameters in chronic neck pain. J Exerc Ther Rehabil 2022;9(1):48-58.
33. Treleaven J, Jull G, Sterling M. Dizziness and unsteadiness following whiplash injury: characteristic features and relationship with cervical joint position error. J Rehabil Med 2003;35(1):36-43.
34. Jull G, Falla D, Treleaven J, Hodges P, Vicenzino B. Retraining cervical joint position sense: the effect of two exercise regimes. J Orthop Res 2007;25(3):404-412.
35. De Vries J, Ischebeck BK, Voogt LP, Van Der Geest JN, Janssen M, Frens MA, Kleinrensink GJ. Joint position sense error in people with neck pain: a systematic review. Man Ther 2015;20(6):736-744.
36. Civelek FÖ, Nacir B, Erdem HR. Importance of Cervical Spine in Sensorimotor Control and Clinical Evaluation Methods of Sensorimotor Disturbances Due to Neck Disorders: Review. J Phys Med Rehabil Sci 2017;20(1):37-43.
37. Resende CM, Alves AC, Coelho LT, Alchieri JC, Roncalli AG, Barbosa GA. Quality of life and general health in patients with

temporomandibular disorders. Brazilian Oral Research, 201;27(2):116–121.
38. Armijo-Olivo S, Pitance L, Singh V, Neto F, Thie N, Michelotti A. Effectiveness of manual therapy and therapeutic exercise for temporomandibular disorders: systematic review and meta-analysis. Phys Ther 2016;96(1):9-25.
39. Shiozaki M, Terao Y, Taniguchi K. Evaluation of temporomandibular joint movement after mandibular reconstruction. J Craniofac Surg 2019;30(1):154-157.
40. La Touche R, París-Alemany A, Von Piekartz H, Mannheimer JS, Fernández-Carnero J, Rocabado M. The influence of cranio-cervical posture on maximal mouth opening and pressure pain threshold in patients with myofascial temporomandibular pain disorders. Clin J Pain 2011;27(1):48-55.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 413-422
https://doi.org/10.30621/jbachs.1374244
RESEARCH ARTICLE

PHANTOM LIMB PAIN RATING SCALE: A SCALE DEVELOPMENT STUDY

Hamdiye Banu Katran[1], Nuray Akyuz[2]

[1] Marmara University, Faculty of Health Sciences, Department of Surgical Diseases Nursing, Istanbul,Türkiye.
[2] Istanbul University-Cerrahpasa Florence Nightingale Faculty of Nursing, Department of Surgical Diseases Nursing, Istanbul,Türkiye.

ORCID: H.B.K. 0000-0001-5095-6316; N.A. 0000-0002-1552-4136

Corresponding author: Hamdiye Banu KATRAN, **E-mail:** banu.katran@marmara.edu.tr
Received: 11.10.2023; **Accepted:** 16.03.2024; **Available Online Date:** 31.05.2024

Cite this article as: Katran HB. Akyuz N. Phantom Limb Pain Rating Scale: A Scale Development Study. J Basic Clin Health Sci 2024; 8: 413-422.

ABSTRACT

Purpose: The aim of this study was to develop a valid and reliable scale to evaluate and measure phantom limb pain.
Material and Methods: This study, which was designed in a methodological type, was conducted with a total of 258 patients. A demographics form and a draft scale developed by the research authors were used to collect the study data. Kuder-Richardson Formula 20 was used to provide descriptive statistics and reliability analyses for the study data. Exploratory Factor Analysis was used in the development of the phantom limb pain rating scale, and Reliability and Confirmatory Factor Analysis were used for the study's validity and reliability evaluations.
Results: The Kuder-Richardson 20 value, which shows the internal consistency of the questions of the 16-item the rating scale, was found to be 0.921. The total score of the rating scale ranged from 1 to 16, with an average of 11.19±4.94. It was determined that the fit criterias and corrected chi-square values showed acceptable fit, and that the scale was both statistically significant and valid ($p=0.001$; $p<0.01$).
Conclusion: The self-reported scale developed in this study was found to be a reliable and valid measurement tool for evaluating phantom limb pain in affected patients.

Keywords: Amputation, Pain Measurement, Phantom limb pain, Scale, Pain.

INTRODUCTION

Problems following limb amputation can result in insufficiencies that impact the daily living activities of affected patients across different dimensions, potentially causing these individuals to become completely or partially physically, economically, and socially dependent Phantom Limb Pain (PLP) is a common chronic problem following amputation (1). PLP is defined as the experience of pain in a non-existing extremity and the sensation that an amputated extremity is still in place following amputation. The incidence of PLP following amputation is reported to be 49–83%. This subject is worth examining since post-amputation pain can result in functional limitations due to limb loss and can reduce quality of life among affected patients (2-4).

The severity of pain resulting from PLP is based on believing the severity of pain reported by the affected patient. However, patients may not be able to express their pain objectively due to various social and psychological factors. Therefore, the level of severity of the pain should be evaluated using objective pain scales whenever possible. This indicates the importance of using objective pain scales when evaluating the level of pain experienced as a result of PLP (4).

Pain perception, diagnoses, and reactions to pain vary from person to person. For this reason, the patient's pain assessment should be undertaken by taking a detailed anamnesis, continuous close observation, and the use of appropriate measurement tools. Pain is a difficult phenomenon to evaluate and

manage due to its subjective nature (1). The first step in pain management, which is one of the most important components of a holistic approach to nursing care in surgical nursing, is to increase the quality of care through accurate diagnosis, the continuous evaluation of pain, and to offer a systematic approach to relieve the individual's pain through successful pain management. The management of PLP poses a challenge for nurses, patients, and the patient's relatives when evaluated together with the psychosocial adjustment problems experienced by the patient following limb amputation (1,2,5). As there is no validated and reliable scale for the diagnosis of PLP in particular, previous studies on PLP use general pain-rating scales.

MATERIAL AND METHODS.

This study was designed and conducted as a methodological study to develop a valid and reliable scale to evaluate PLP in patients who underwent limb amputation for any reason.

Study data were collected between 29 March and 10 May 2021 in a training and research hospital. Before starting the research, ethics committee approval (Decision Date: 07.01.2021, No: 2019/158) was obtained from the Social and Humanities Studies Ethics Committee of Istanbul University-Cerrahpaşa Rectorate. Patients were informed that participation in this research was voluntary, and informed consent was obtained.

Inclusion criteria for patients were as follows: aged 18 years or over; without communication problems; had undergone major limb amputation within the past 1–5 years to exclude stump pain and incision pain; experienced PLP of a severity of at least 3 out of 10 according to the Numeric Rating Scale (NRS), and voluntarily agreed to participate in this study. Patients who met these inclusion criteria participated in this research. Those without PLP, those with an NRS score below 3, and those with incision and stump pain (n=83) were excluded.

The study population consisted of 442 patients who underwent amputation between January 1, 2015 and December 31, 2020 in the Orthopedics and Traumatology Clinic of a training and research hospital in Istanbul. The study sample was determined to be at least ten times the number of items, considering the number of items in the scale and since this number of items should be determined as 5-10 times. Of the 442 patients, 23 could not be reached due to incorrect phone numbers, and 48 people could not be interviewed because they had died. 30 people who experienced phantom limb pain were not included in the sample because a pre-study was made and the questions were modified as a result of the pre-study. 83 of 341 people were excluded from the study because they did not have phantom limb pain. 258 patients, who experienced PLP and whose pain severity was 3 or above out of 10 according to NRS (scores from 3 to 4 indicate mild pain), comprised the study sample.

Research data were collected using the demographics form and the revised Phantom Limb Pain Rating Scale, which was developed by the authors of the present study based on previous studies in the literature.

Demographics Form: The Demographics Form consists of 26 questions created in line with the literature (1,3,5-10).

Phantom Limb Pain Rating Draft Scale: The statements in the draft scale were designed as a 36-question form evaluating PLP by using information from the literature and the opinions of expert academics who were expert in their field. First, a question pool was created within the scope of the related literature, after which the opinions of the researchers and their colleagues were used to determine the surface validity of those question pool items. The content validity of the 36-item draft scale was determined through examination and evaluation by the faculty members of the nursing faculty and those related branches of the institution with which the researchers were involved (1-10). Subsequently, Turkish grammar experts were consulted and the Davis technique was used to correct any language and spelling errors in the prepared version. The resulting version was sent via e-mail to five experts for evaluation. A value of 0.80 was accepted as a criterion for Content Validity Index (CVI) (11). The 16th question, the CVI value of which was found to be 0.60, was therefore removed from the draft scale. Consequently, the final draft scale comprised as 35 items and included those corrections suggested in the expert evaluation.

Before determining the validity of the scale, a preliminary study of the scale was undertaken by the researcher who distributed the scale to 30 participants. In this preliminary study, those scale questions participants had difficulty understanding were corrected (11 items out of a total of 26–36

items), thereby improving and ensuring the clarity of all scale questions. The wording of several questions were changed; for instance, “the pain in my amputated limb lasts for hours”, “the pain in my amputated limb lasts for days”, “my pain in my amputated limb lasts for weeks”, “the pain in my amputated limb lasts for months”, and “the pain in my amputated limb lasts for years” were changed and amalgamated into a single item: “the pain in my amputated limb is constant”. With this arrangement, the number of scale items was reduced from 35 to 24. After the pre-study had been repeated through test–retest, the 24-item draft scale was then applied to the study sample (11) The test-retest reliability coefficient was determined to be 0.83 and acceptable (Figure 1). The Number Cruncher Statistical System Utah, USA, 2007 (NCSS) program was used to conduct the study’s statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, lowest value, highest value) were used to evaluate the study data. The conformity of the quantitative data to the normal distribution was tested using the Kolmogorov–Smirnov test, the Shapiro–Wilk test, and graphical evaluations. The Mann–Whitney U test was then used to compare two groups of data that did not show normal distribution, the

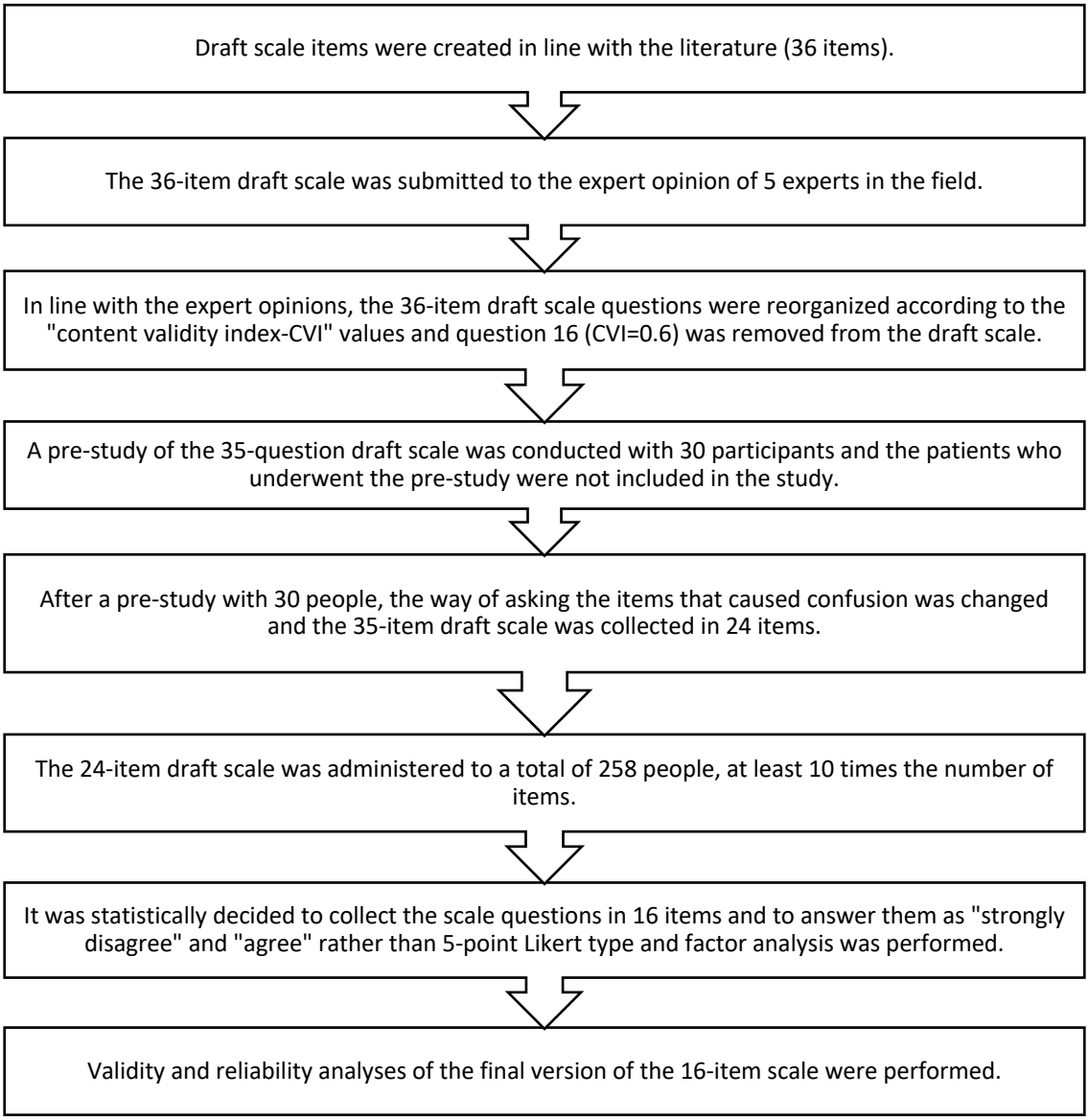


Figure 1. Implementation of the Research

Kruskal–Wallis test was used to compare groups of three or more groups that did not show normal distribution, and the Bonferroni–Dunn test was used for pairwise comparisons. Spearman's correlation analysis was used to evaluate the relationships between the variables that did not show normal distribution; the Wilcoxon signed-ranks test was used for in-group comparisons of parameters that did not show normal distribution. Exploratory factor analysis was used in the development of the phantom-limb pain rating scale, and Reliability Analysis and Confirmatory Factor Analysis (AMOS) were used for the validity and reliability evaluations of the study data. Statistical significance was evaluated at the $p<0.05$ level.

RESULTS

The sociodemographic characteristics of the patients participating in the study are presented in Table 1.

Phantom Limb Pain Rating Scale Factor Analysis Results

There are 16 items in the PLP rating scale. Data obtained from the scale were analyzed using exploratory factor analysis (EFA). The results of the PLP rating scale Kaiser–Meyer–Olkin (KMO) and Bartlett's test are presented in Table 2. This single

Table 1. Demographic characteristics of patients (N=258)

Socio-Demographic Characteristics		n	%
Gender	Female	82	31,8
	Male	176	68,2
Age (years)	18-35 years	19	7,3
	36-55 years	70	27,1
	56-75 years	143	55,4
	≥ 76 years	26	10,1
Cause of Amputation	Vascular Diseases	32	12,4
	Diabetes Mellitus	128	49,6
	Traffic accident	40	15,5
	Other	58	22,6
Amputated Limb	Under the knees	152	58,9
	Above knee	47	18,2
	Below the elbow	35	13,6
	Above elbow	12	4,6
	Multiple limbs	12	4,7
Postoperative Phantom Pain Intensity	Median (Lowest-Top)	7 (3-10)	
	Mean±SD	6,95±2,12	

SD: Standard Deviation

Table 2. Phantom limb pain rating scale Kaiser-Meyer-Olkin and Bartlett Sphericity Test results and factor analysis Eigen Values and announced total variance results

Kaiser-Meyer-Olkin Sample Adequacy Measurement			**0,894**
Bartlett Test of Sphericity		**Chi square**	**2238,085**
		Degrees of freedom	**120**
		Significance	**0,001**
	Sum of Eigen values	**Variance %**	**Total Variance %**
Factor 1	7,395	46,217	46,217

factor explains 46.217% of the variance of the PLPRS. When the factor weights related to the factor analysis of the PLP rating scale were examined it was found that the lowest value was 0.483 and the highest value was 0.815.

Phantom Limb Pain Rating Scale Validity and Reliability Analysis Results

The Kuder–Richardson 20 (KR-20) value was used to test the reliability of the scale. The "Alpha if Item Deleted" value was then calculated to determine the extent and direction of the effect questions had on this value (11,12). Alpha if Item Deleted values show the internal consistency of the remaining variables when any variable is deleted. When the KR-20 values of the table were examined, it was determined that removing any item from the factor would not increase the reliability. In this framework, the single factor structure was preserved (Table 3).

The KR-20 value, which indicates the internal consistency of the questions of the PLP rating scale, was found to be 0.921. Accordingly, the scale was determined to be highly reliable. The total score of the PLP assessment scale was 1–16, with a mean score of 11.19±4.94 (Table 4).

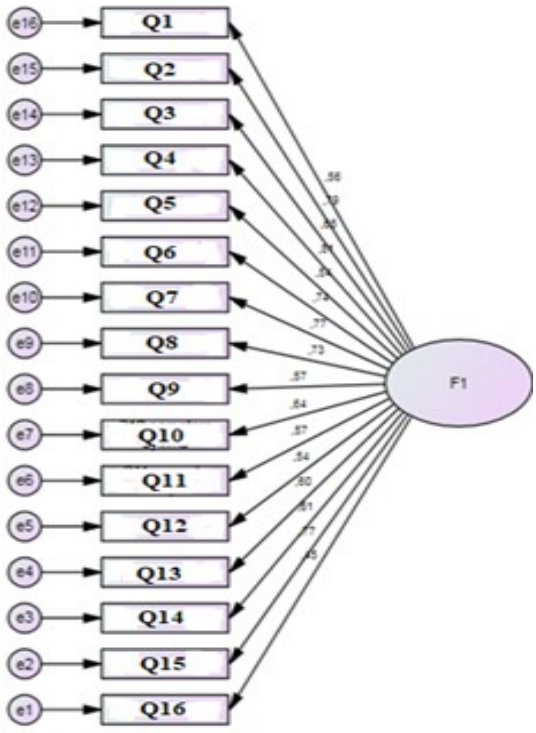


Figure 2. Confirmatory factor analysis of the phantom limb pain rating scale (Q: Question)

Phantom Limb Pain Rating Scale Confirmatory Factor Analysis Results

Figure 2 presents the standardized loads of questions comprising the single dimension of the PLP rating scale resulting from the confirmatory factor analysis.

On examination of the model results, it was revealed that the Root Mean Square Error of Approximation (RMSEA) fit criterion was 0.089, showing an acceptable fit. Among the other fit criteria, Normed Fit Index (NFI) was found to be 0.90, Relative Fit Index (RFI) 0.85, Standardized Root Mean Square Residual (SRMR) 0.055, Goodness of Fit Index (GFI) 0.90, and Adjusted Goodness of Fit Index (AGFI) 0.85; accordingly, acceptable fit was determined for all the results. In addition, it was determined that the corrected chi-square value (3.0) showed acceptable fit, the PLP rating scale had an acceptable fit, and that the scale was statistically significant and valid ($p<0.01$).

DISCUSSION

PLP is known to be difficult to assess and treat. The major challenge in the management of a PLP is the difficulty in assessing PLP symptoms due to the physical absence of the affected body part (12). Therefore, good observation and anamnesis should first be taken after amputation and/or nerve injury to identify phantom pain and evaluate how it occurs and what affects this pain (13,14). Other studies in the literature show that patients who are being treated for a chronic disease do not express their pain unless explicitly asked about its severity (15,16). Scales have been developed for the assessment of pain in critically ill patients; however, these have not been validated for use in patients with phantom pain. Accordingly, the scale designed in the present study was developed with the aim of creating a pain assessment system through which patients with PLP could clearly and easily describe their pain for the improvement of pain management.

The experience of PLP is expressed differently in each individual and a patient may experience more than one type of PLP. All PLP complaints are expressed as one of the following sensations: a stabbing pain, a burning-like stabbing pain, pins and needles, tingling, cramps, itching, contraction, compression, an electric shock, a stinging, a temperature increase, or a cold throbbing and sensation. It is difficult to state which of these is the most commonly experienced (1,5,15,16). In the present study, it was found that "as if someone is

Table 3. The Effects of the Items Forming the Factors of the Phantom Limb Pain Rating Scale on Reliability

	Scale mean when the item is deleted	Scale variance when item deleted	Corrected item-total correlation	KR-20 when item deleted
My pain in my amputated limb is throbbing (Q1)	10.438	22.037	0.534	0.919
My pain in my amputated limb is a feeling of pulling (Q2)	10.558	20.808	0.761	0.912
I have pain in my amputated limb as if stabbing with a knife (Q3)	10.492	21.488	0.632	0.916
The pain in my amputated limb seems to have become stiff (blunt) (Q4)	10.574	20.736	0.771	0.912
I have pain like electric shock in my amputated limb (Q5)	10.430	22.114	0.521	0.919
The pain in my amputated limb is like burning (Q6)	10.562	21.002	0.712	0.914
I have pain like crushing in my amputated limb (Q7)	10.566	20.924	0.729	0.913
I have pain like someone is drilling my amputated limb (Q8)	10.512	21.208	0.689	0.914
My pain in my amputated limb is aching (Q9)	10.465	21.931	0.540	0.919
I'm in pain like my amputated limb is torn into pieces (Q10)	10.512	21.457	0.627	0.916
I have pain as if my amputated limb is cutting right now (Q11)	10.419	22.058	0.547	0.918
I feel sharp pain in my amputated limb (Q12)	10.426	22.152	0.515	0.919
In my amputated limb, my pain is in the form of cold/coldness/freezing (Q13)	10.457	21.782	0.584	0.917
I have pain as if my amputated limb is cramped (Q14)	10.446	21.859	0.574	0.918
I have pain like my amputated limb is stuck somewhere (Q15)	10.547	20.887	0.747	0.912
I have pain in my amputated limb as if ants are lurking (Q16)	10,446	22,427	0,429	0,922

Q: Question

Table 4. Distribution of Phantom Limb Pain Rating Scale Internal Consistency Value and Scores

	Number of Items	Top-bottom (Median)	Mean±SD	KR-20
Phantom limb pain assessment scale total score	16	1-16 (14)	11.19±4.94	0.921

SD: Standart Deviation KR-20: Kuder-Richardson 20

cutting right now" was most frequently reported among patients' expressions of PLP experiences, which support the results of existing studies in the literature.

It is important that both healthcare professionals and patients have knowledge about the assessment tool used to measure PLP, that they understand PLP measurement scales, and that they can easily and practically use these scales. In particular, the patient's knowledge of how to use one-dimensional scales determining the severity of their pain, and their perceptions and responses to these measurement tools, depend on the selection of the correct scale (12).

Since there is no specific scale to evaluate PLP in the literature, general pain assessment scales were used in the studies (1-4). It was designed with the thought that it would be easier to design a pain scale in the evaluation of phantom pain in clinical practice than with existing pain scales and that patients would be successful in pain management. It is stated in the literature that applying a draft scale prepared for use with a small representative sample group will be beneficial; therefore, it will be beneficial to conduct a preliminary study (17). In the present study, the preliminary application of the 35-question draft scale was carried out with 30 patients before the validity application of the scale commenced. With this pre-application, corrections were made to those questions that were difficult to understand and, as a result, the clarity of the questions was improved and ensured. Test–retest was performed on the same patients with an interval of 2 weeks, and surface validity was ensured by testing the comprehensibility of the draft scale, with 24 items evaluating PLP; this 24-item scale was also prepared by consulting the opinions of expert academics. The test-retest reliability coefficient was determined to be 0.83 and acceptable.

Two prerequisites were determined regarding the use of the draft scale: first, that the patient evaluated the PLP according to a NRS evaluation, ranging from 0 (no pain) to 10 (unbearable pain), with values of 3 or above (mild pain) indicting PLP; second, that the patient was able to clearly express their experience of PLP while differentiating it from other pain. When pain becomes chronic, after three to six months of acute pain, the pain can become centralized. A lower threshold for experiencing pain is required for centralized pain. Lowered thresholds are problematic. Pain is an adaptive response to a stimulus that is painful. A lower threshold for pain subjectively means that pain can be experienced from non-painful stimuli (allodynia), or mildly painful stimuli can be experienced as severe pain (hyperalgesia). Central pain is the maladaptive type of pain. Neuropathic pain is a disorder of the somatosensory pathway of the nervous system, not the spinothalamic pathway (18,19). Central and neuropathic pain often occur together but are not mutually exclusive. Neuropathic pain may be both peripheral and central. Centralized and neuropathic pain are both considered functional (pain) gains. Both play a role in the development of chronic pain (20,21). Incongruence between motor intention and sensory feedback and corresponding activation of parietal and frontal brain areas may be involved in painful sensations such as PLP (22). Therefore, the physiopathology of pain perception does not show major differences, and the Phantom limb pain rating scale in its current form does not focus on the type of pain (nociceptive, nociceptive, nociciplastic or neuropathic), but allows for a unidimensional assessment of pain through self-report. It was also analyzed that it would be appropriate to answer only as "agree" or "strongly disagree" instead of a 5-point Likert-type rating, since the prerequisite for the scale was that the current pain was at least 3 according to the NRS.

It is recommended that a study sample size should be 5–10 times greater than the number of items used in the data-collection scale or tool as this will ensure validity and reliability of the study data and the analysis of those data (23,24). In the present study, the number of items in the draft scale was 24; accordingly, the study sample size should comprise 240 participants. The number of patients in the present study who experienced PLP with a severity of 3 or above was 258, thereby corroborating their reliability and validity.

The factor analysis method is mostly used to evaluate whether items in the scale will be grouped under different dimensions; it is divided into two groups: explanatory factor analysis and confirmatory factor analysis (23,24). EFA was used in the statistical analysis of the PLP rating scale. When varimax rotation was applied in the exploratory factor analysis, it was determined that the questions were gathered under a single factor and the explanatory coefficient was 46.22%.

The KMO value is normally between 0–1 and should be close to 1 for factor analysis to be performed. Although it is considered sufficient for the KMO

coefficient to be above 0.60, values of 0.80 or above are more desirable (11,24). The KMO sample adequacy measurement value of the present study was determined to be 0.894, a very good value for analyzing the study's sample.

Bartlett's sphericity test is used to evaluate the universal significance of the correlation matrix found by the exploratory factor analysis. Bartlett's test revealed a p value of less than 0.05, indicating that the correlation matrix is suitable for factor analysis (11). Bartlett's sphericity test was used to determine if the correlation matrix is a similar matrix. This value was rejected at the $p<0.001$ level, thereby demonstrating the existence of a relationship between the items and the suitability of the data for factor analysis (12).

Eigen values and total variance were then analyzed according to the scale analysis results. This single factor explains 46.217% of the variance of the PLP rating scale. Higher variance rates obtained as a result of the analysis reflect a stronger factor structure of the scale (17,23,24). For the present study, the variance rate was found to be 46.2%. According to the eigenvalues it was determined that the factors would be collected in one dimension. In health sciences, a higher variance ratio may be more appropriate due to the potential for greater heterogeneity in patient populations and treatment outcomes. However, it is essential to note that there is no universally accepted threshold for a strong factor structure in health sciences, and the appropriate variance ratio will depend on the specific context and the nature of the data being analyzed. In summary, while a variance ratio between 40% and 60% is often considered sufficient in social sciences, a higher threshold may be more appropriate in health sciences. The specific threshold should be determined based on the nature of the data and the context of the analysis (25-27). This suggests that no generally accepted threshold for a strong factor structure exists in the health sciences, and that the appropriate proportion of variance is dependent on the specific context and nature of the data under analysis.

The KR-20 reliability coefficient is expressed as a weighted standard variation obtained by dividing the sum of the variances of all items in the scale by the general variance. A KR-20 value of 0.90 or above is considered "highly reliable" (24). One of the fit criteria, RMSEA, represents the approximate square root of the means "It takes a value between zero and 1". An RMSEA below 0.05 indicates a good fit, an RMSEA value below 0.08 indicates a fair value, and an RMSEA value of 0.08–0.10 indicates a moderate fit. RMSEA values above 0.10 are not acceptable. "In addition, factor loads are required to be above 0.30. Factor load values of 0.60 and above are high; load values of 0.30–0.59 can be defined as of medium magnitude" (11,24). The RMSEA fit criterion in the study was 0.089, which showed acceptable fit. Acceptable fit was also determined in NFI (0.90), RFI (0.85), SRMR (0.055), GFI (0.90), and AGFI (0.85), among other fit criteria.

For a model to be acceptable, the fit criteria chi-square value should not be statistically significant. This is due to the fact that the chi-square value is sensitive to the sample size. Instead, the chi-square value were evaluated by dividing it by degrees of discretion. Values of 2 or less show that the model is good; values of 5 or less show that the model has an acceptable fit (24). In the present study, the corrected chi-square value was determined as 3 and therefore showed an acceptable fit. According to the fit criteria, the PLP rating scale was found to have an acceptable fit, and the scale was found to be statistically significant and valid ($p<0.01$).

Pain rating scales can help healthcare providers gain a better understanding of certain aspects of a person's pain, such as the duration, severity, and type of pain. Pain rating scales can also help healthcare providers with accurate diagnosis, treatment planning, and measurement of treatment effectiveness. By consistently using a pain scale to monitor symptoms, feelings, and sensations, people can explain the nature, severity, and duration of their pain when communicating with healthcare providers, which helps them receive the best possible treatment. Pain scales also help healthcare providers assess how each person feels on an individual, case-by-case basis (12-16,28).

CONCLUSION

This self-report-based scale, which was developed to evaluate the PLP of individuals who experienced PLP after amputation, was determined as a valid and reliable measurement tool. It is recommended that the scale is used by nurses employed in surgical units for the evaluation of the pain of patients with PLP.

Limitations

The limitations of the study include the inability to conduct face-to-face interviews with patients due to

the Covid-19 pandemic, thus the stump area of the limb could not be examined by the researcher, and the inability to compare this scale with other similar pain scales due to the lack of a pain assessment scale to evaluate phantom limb pain before.

Acknowledgments: This original article was produced from the doctoral thesis (Katran, H.B. 2021. Phantom Limb Pain Rating Scale: A Scale Development Study. Istanbul University, Institute of Graduate Education, Department of Surgical Nursing. PhD Thesis. Istanbul.)
Author contribution: Conception: HBK, NA Design: HBK, NA. Supervision: NA. Fundings: HBK, NA. Materials: HBK, NA Data collection or processing: HBK, NA. Analysis: HBK, NA .Literature review: HBK. Writing: HBK. Critical review: NA. (HBK: Hamdiye Banu KATRAN, NA: Nuray AKYÜZ)
Conflict of interests: There is no conflict of interest between the authors.
Ethical approval: Ethics committee approval (Decision Date: 07.01.2021, No: 2019/158) was obtained from the Social and Humanities Studies Ethics Committee of Istanbul University-Cerrahpaşa Rectorate.
Funding: No financial support was received for the research.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Yıldırım M, Kanan N. The effect of mirror therapy on the management of phantom limb pain. Agri 2016;28(3):127-34.
2. Kern U, Busch V, Rockland M, Kohl M, Birklein F. Prevalence and risk factors of phantom limb pain and phantom limb sensations in Germany: A nationwide field survey. Der Schmerz 2009;23:479-88.
3. Foell J, Bekrater-Bodmann R, Flor H, Cole J. Phantom limb pain after lower limb trauma: Origins and treatments. The International Journal of Lower Extremity Wounds 2011;10(4):224-235.
4. Richardson C, Crawford K, Milnes K, Bouch E, Kulkarni J. A clinical evaluation of postamputation phenomena including phantom limb pain after lower limb amputation in dysvascular patients. Pain Management Nursing 2015;16(4):561-569.
5. Ephraim PL, Wegener ST, MacKenzie EJ, Dillingham TR, Pezzin LE. Phantom pain, residual limb pain, and back pain in amputees: Results of a national survey. Archives of Physical Medicine and Rehabilitation 2005;86(10):1910-1919.
6. Sato K, Fukumori S, Matsusaki T, Maruo T, Ishikawa S, Nishie H, et al. Nonimmersive virtual reality mirror visual feedback therapy and its application for the treatment of complex regional pain syndrome: an open-label pilot study. Pain Medicine 2010;11(4):622-629.
7. Weeks SR, Anderson-Barnes VC, Tsao JW. Phantom limb pain: Theories and therapies. The Neurologist 2010;16(5):277-286.
8. Rothgangel AS, Braun S, Schulz RJ, Kraemer M, de Witte L, Beurskens A, Smeets RJ. The PACT trial: PAtient Centered Telerehabilitation: Effectiveness of software-supported and traditional mirror therapy in patients with phantom limb pain following lower limb amputation: protocol of a multicentre randomised controlled trial. Journal of Physiotherapy 2015;61(1):42.
9. Richardson C, Kulkarni J. A review of the management of phantom limb pain: Challenges and solutions. Journal of Pain Research 2017;10:1861-1870.
10. Limakatso K, Bedwell GJ, Madden VJ, Parker R. The prevalence and risk factors for phantom limb pain in people with amputations: A systematic review and meta-analysis. PloS One 2020;15(10):e0240431.
11. Yeşilyurt S, Çapraz C. Ölçek geliştirme çalışmalarında kullanılan kapsam geçerliği için bir yol haritası. Erzincan Üniversitesi Eğitim Fakültesi Dergisi 2018;20(1):251-264.
12. Yeşilyurt M, Faydalı S. Ağrı değerlendirmesinde tek boyutlu ölçeklerin kullanımı. Anadolu Hemşirelik ve Sağlık Bilimleri Dergisi 2020;23(3):444-451.
13. Kikkert S, Mezue M, Slater DH, Johansen-Berg H, Tracey I, Makin TR. Motor correlates of phantom limb pain. Cortex 2017;95:29-36.
14. Kaur A, Guan Y. Phantom limb pain: A literature review. Chinese Journal of Traumatology 2018;21(6):366-368.
15. Casale R, Ceccherelli F, Labeeb AAEM, Biella GE. Phantom limb pain relief by contralateral myofascial injection with local anaesthetic in a placebo-controlled study: preliminary results. Journal of Rehabilitation Medicine 2009;41(6):418-422.
16. Cole J, Crowle S, Austwick G, Henderson Slater D. Exploratory findings with virtual reality for phantom limb pain; from stump motion to agency and analgesia. Disability and Rehabilitation 2009;31(10):846-854.
17. Saczynski JS, McManus DD, Goldberg RJ. Commonly used data-collection approaches in clinical research. The American Journal of Medicine 2013;126(11):946-950.
18. Colloca L, Ludman T, Bouhassira D, Baron R, Dickenson AH, Yarnitsky D, Freeman R, Truini A,

Attal N, Finnerup NB, Eccleston C, Kalso E, Bennett DL, Dworkin RH, Raja SN. Neuropathic pain. Nat Rev Dis Primers 2017;3:17002.
19. Kucyi A, Davis KD. The Neural Code for Pain: From Single-Cell Electrophysiology to the Dynamic Pain Connectome. Neuroscientist 2017;23(4):397-414.
20. Olesen AE, Andresen T, Staahl C, Drewes AM. Human experimental pain models for assessing the therapeutic efficacy of analgesic drugs. Pharmacol Rev 2012;64(3):722-779.
21. Ossipov MH, Morimura K, Porreca F. Descending pain modulation and chronification of pain. Curr Opin Support Palliat Care 2014;8(2):143-151.
22. Diers M, Christmann C, Koeppe C, Ruf M, Flor H. Mirrored, imagined and executed movements differentially activate sensorimotor cortex in amputees with and without phantom limb pain. Pain 2010;149(2):296-304.
23. Clark LA, Watson D. Constructing validity: New developments in creating objective measuring instruments. Psychological Assessment 2019;31(12):1412.
24. Brown TA. Confirmatory factor analysis for applied research. Guilford publications, 2015.
25. Blanca MJ, Alarcón R, Arnau J, Bono R, Bendayan R. Effect of variance ratio on ANOVA robustness: Might 1.5 be the limit? Behav Res Methods 2018;50(3):937-962.
26. Plöderl M, Hengartner MP. What are the chances for personalised treatment with antidepressants? Detection of patient-by-treatment interaction with a variance ratio meta-analysis. BMJ Open 2019;9(12):e034816.
27. Güvendir MA, Özkan YÖ. Item removal strategies conducted in exploratory factor analysis: A comparative study. International Journal of Assessment Tools in Education 2022;9(1):165-180.
28. Kisa EP, Cavlak U, Mercan D. (2024). Pain assessment preferences in healthcare providers: A survey from Turkey. İzmir Katip Çelebi Üniversitesi Sağlık Bilimleri Fakültesi Dergisi 2024;9(1):101-104.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 423-432
https://doi.org/10.30621/jbachs.1374685
RESEARCH ARTICLE

THE IDENTIFICATION OF HIGH SCHOOL STUDENTS' ATTITUDES TOWARDS AGEISM AND RELATED FACTORS

Kamil Kocak[1], Hatice Simsek Keskin[2]

[1] Dokuz Eylül University, Institute of Health Sciences, Department of Public Health, Izmir, Turkey
[2] Dokuz Eylül University, Faculty of Medicine, Department of Public Health, Izmir, Turkey

ORCID: K.K. 0000-0002-1942-8192; H.S.K. 0000-0001-7209-485X

Corresponding author: Kamil KOCAK, **E-mail:** kamilkocak45@gmail.com
Received: 11.10.2023; **Accepted:** 29.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Kocak K. Keskin HS. The Identification of High School Students' Attitudes Towards Ageism and Related Factors. J Basic Clin Health Sci 2024; 8: 423-432.

ABSTRACT

Purpose: The aim of this study was to determine the attitudes of students towards the elderly and the associated factors.
Material and Methods: The population of this cross-sectional study consisted of 660 students attending a high school during the 2021-2022 academic year. No sample was selected; it was aimed to reach the entire population. The dependent variable in the study is the attitude towards the elderly, determined using the Positive and Negative Ageism Scale. The independent variables consist of socio-demographic characteristics and experiences related to the elderly. Data was collected through a self-administered questionnaire and analyzed using the Mann Whitney U test and Kruskal Wallis Analysis of Variance.
Results: A total of 509 students participated in the study. The mean Positive and Negative Ageism Scale scores of the students were found to be 44.3±6.7 and 36.6±5.9, respectively. The Positive and Negative Ageism Scale scores were found to be significantly higher among students involved in projects related to elderly health ($p=0.034$, $p=0.049$), those who intend to live with their parents ($p=0.010$, $p<0.001$), and those who wish to work with elderly individuals in the future ($p<0.001$, $p<0.001$).
Conclusion: To mitigate students' ageism attitudes, it is recommended to organize projects and educational activities.

Keywords: Ageism, aged, attitude, discrimination

INTRODUCTION

Aging is a complex process encompassing biological, psychological, and social changes. As a consequence of alterations occurring during the aging process, both physical and mental capacities tend to decline (1). The ability to adapt to environmental factors diminishes with aging, increasing the susceptibility to various illnesses (2). The global population is rapidly aging due to the substantial increase in the number of elderly individuals (3,4). This demographic shift on a global scale is attributed to factors such as the extended life expectancy, reduced fertility rates, and lowered mortality rates (5). Presently, the proportion of the population aged 65 and above is 9.8% worldwide and 9.7% in Turkey. It is projected that by 2050, this proportion will reach approximately 22% globally (6). Societies undergoing changes due to aging find it difficult to adapt to this demographic structure (4). As the proportion of elderly individuals in the population rises, issues like ageism are expected to escalate (7). The presence of marginalized attitudes towards elderly individuals within society, the perception that elderly individuals should live separate from the broader community, and the lack of respect for their values and attitudes are labeled as ageism (8). Ageism leads individuals

to have stereotypical and prejudiced thoughts and attitudes solely based on age. (9,10). Ageism adversely impacts the health, well-being, access to healthcare services, and the quality of care received by elderly individuals (11).

Considering the impending increase in the elderly population in Turkey, identifying ageism attitudes among particularly young individuals and discerning the factors behind these attitudes are of paramount importance. In this way, positive attitudes towards the elderly can be fostered among young individuals, thus enhancing interactions and cohesion between the young and the elderly (8-12). The majority of ageism studies in the literature have centered around undergraduate students in health sciences, such as medical and nursing students, who are expected to play a role in healthcare service delivery, as well as students in programs related to elderly care at the associate degree level (13-20). There is a lack of research assessing the attitudes of secondary school students towards the elderly. The evaluation of attitudes towards the elderly among high school students having education in healthcare services is particularly crucial since a considerable portion of them are expected to pursue degrees in health sciences at the undergraduate and associate degree levels in the future. Thus, this study has been designed to reveal the attitudes of high school students having education in healthcare services towards the elderly and the factors influencing these attitudes.

MATERIAL AND METHODS

Research Type, Setting, and Time

This cross-sectional study was conducted during the academic year 2021-2022 at a high school in the Meram District of Konya Province, where healthcare education is given.

Research Population and Sample

The population of the study comprised 660 students attending a high school in the Meram District of Konya Province during the academic year 2021-2022. No sampling was conducted for the research since the aim was to reach the entire population. The school offers programs in the field of healthcare services, specifically in the areas of nursing assistantship, midwifery assistantship, and health care technician training.

Data Collection Process

The data was collected using a pre-prepared questionnaire administered through the self-administration method. The independent variables of the study were the socio-demographic characteristics of both students and their parents, the status of living with elderly individuals, students' future preferences regarding living or working with elderly individuals, and their prior involvement in projects related to elderly health. The dependent variable of the research was students' attitudes towards the elderly, assessed using the Positive and Negative Ageism Scale (PNAS), developed by Yurttaş and Sarıkoca (21). The PNAS comprises two subscales consisting of a total of 23 items, rated on a 5-point Likert type scale. The Positive Ageism (PA) subscale comprises 13 items, with higher scores indicating higher levels of positive attitudes. Conversely, the Negative Ageism (NA) subscale consists of 10 items, where higher scores signify lower levels of negative attitudes. The Cronbach's alpha of the PNAS was found to be 0.80 in the original study. It was found to be 0.79 in this study.

Data Analysis

The SPSS version 25.00 was employed for data analysis. Descriptive statistics were presented in the form of means, standard deviations, and percentage distributions. The Kolmogorov-Smirnov test was employed to assess the normality of the data distribution. For data that did not conform to a normal distribution ($p=0.006$), non-parametric tests including the Mann Whitney U test and the Kruskal Wallis Analysis of Variance were utilized. The Bonferroni correction Mann Whitney U test was performed as a post-hoc test. Spearman's correlation analysis was employed to assess the linear relationship between parental age and the mean PNAS scores.

Ethical Considerations

Permission for the use of the PNAS scale was obtained from the author. Ethical approval was obtained from Dokuz Eylül University Non-Invasive Research Ethics Board (Decision Date: 06.04.2022, No: 2022/13-11), and institutional permission was obtained from the Konya Provincial Directorate of National Education (Date: 29/04/2022, Number: E-83688308-605.99-48873873). Furthermore, the students and their parents were informed about the purpose of the study, and written informed consent was obtained from them.

Table 1. Socio-demographic characteristics of the students

Characteristics		n	%
Gender (n=509)	Female	380	74.7
	Male	129	25.3
Grade (n=509)	9th	121	23.8
	10th	158	31.0
	11th	141	27.7
	12th	89	17.5
Place of residence (n=509)	With family	503	98.8
	Dormitory	6	1.2
Longest place of residence (n=509)	City	470	92.3
	Rural area	39	7.7
Family type (n=509)	Nuclear family	427	83.9
	Extended family	57	11.2
	Split/single-parent family	25	4.9
Family's Perception of Income-Expenditure (n=509)	Income more than expenses	80	15.7
	Income equal to expenses	304	59.7
	Income less than expenses	125	24.6
Mother's level of education (n=509)	Illiterate	7	1.4
	Literate	6	1.2
	Primary school	281	55.2
	Middle school	123	24.2
	High school	71	13.9
	University	21	4.1
Father's level of education (n=509)	Illiterate	1	0.2
	Literate	4	0.8
	Primary school	179	35.2
	Middle school	127	25.0
	High school	139	27.3
	University	59	11.6
Mother's occupation (n=509)	Not Working and Not Seeking Employment (Housewife)	402	79.0
	Wage-earning worker	62	12.2
	Daily laborer	14	2.8
	Civil servant	8	1.6
	Not Working and Seeking Employment	7	1.4
	Self-Employed (Does not employ workers)	6	1.2
	Employer	5	1.0
	Other (Passed away)	3	0.6
	Retired	2	0.4
Father's occupation (n=509)	Wage-earning worker	274	53.8
	Employer	61	12.0
	Self-Employed (Does not employ workers)	56	11.0
	Retired	35	6.9
	Civil servant	29	5.7
	Daily laborer	25	4.9
	Other (Passed away)	12	2.4
	Not Working and Not Seeking Employment	8	1.6
	Not Working and Seeking Employment	5	1.0
	Other (Farmer)	4	0.8
Participation in the eTwinning Project titled "Geriatric Aspects of Patient Care" (n=509)	Yes	16	3.1
	No	493	96.9
Having Lived with an Elderly Family Member (n=509)	Yes	236	46.4
	No	273	53.6
Desire to Live with Parents in the Future (n=508)	Yes	248	48.7
	No	260	51.1
Desire to Work in a Nursing Home or Elderly Care Facility in the Future (n=509)	Yes	297	58.3
	No	212	41.7
Desire to Work with Elderly Individuals as a Colleague (n=509)	Yes	319	62.7
	No	190	37.3

RESULTS

In this study, the data of 509 students were presented, which accounted for 77.1% of the total population. About 31% of the sample consisted of 11th graders, and approximately 75% were female students. The vast majority of the participants (92.3%) resided in urban areas. The average age of the students' mothers was 42.1±5.3 (32.0-60.0), and the average age of their fathers was 45.5±5.9 (34.0-70.0). The socio-demographic characteristics are presented in Table 1.

The ways the participants define old age, reasons for not wanting to work in nursing homes or elderly care facilities in the future, and reasons for not wanting to work as colleagues with elderly individuals in the future are presented in Table 2. Among the students in the sample, 53.6% expressed negative connotations in their definitions of old age, and 13.4% characterized it as illness. The mean score of the students on the Positive Ageism (PA) subscale was 44.3±6.7, while their mean score on the Negative Ageism (NA) subscale was 36.6±5.9 (Table 3).

Table 2. Students' views on aging

Characteristics		n	%
Definition of old age (n=453)	Illness*	68	13.4
	People over 65	64	12.6
	People in need of care*	59	11.6
	End of life/ death*	53	10.4
	Grandparents	39	7.7
	Experience	30	5.9
	Being weak and exhausted*	24	4.7
	Retirement	18	3.5
	Having a difficult life*	16	3.1
	Graying hair / wrinkled skin *	16	3.1
	Moodiness*	15	2.9
	Loneliness*	11	2.2
	Nursing home	10	2.0
	Sweet/lovable people	8	1.6
	Peace	7	1.4
	Narrow-minded people*	4	0.8
	Advisors	4	0.8
	Weakening of the body*	3	0.6
	People behaving like children*	2	0.4
	Regret*	1	0.2
	Stingy people*	1	0.2
Reasons for Not Wanting to Work in Nursing Homes or Elderly Care Facilities in the Future (n=177)	Thinking that they will not be able to get along with the elderly	79	15.5
	Having different goals	59	11.6
	Thinking it would be exhausting	39	7.6
Reasons for Not Wanting to Work with Elderly Individuals as Colleagues in the Future (n=160)	Thinking that they will not be able to get along with the elderly	107	21.0
	Preferring to work with younger individuals	43	8.4
	Thinking they would be more exhausted	10	2.0

*** Negative Expressions Used in Defining Old Age**

Table 3. Students' scores on the positive and negative ageism

	X±SD	**Median**	**Min-Max**
Positive ageism	44.3±6.7	44.0	20-62
Negative ageism	36.6±5.9	37.0	18-50

Table 4. Positive and negative ageism scores according to students' sociodemographic characteristics -1

Characteristics		Positive Ageism			Negative Ageism		
		X±SS	Median (Min-Max)	P	X±SS	Median (Min-Max)	p
Gender	Female	43.9±6.8	44.0 (20-62)	0.051	36.9±5.9	38.0 (18-50)	0.016
	Male	45.4±6.5	45.0 (29-60)		35.4±6.0	36.0 (18-48)	
Place of residence	With family	44.4±6.7	45.0 (20-62)	0.160	36.6±5.9	37.0 (18-50)	0.889
	Dormitory	41.5±5.5	40.0 (36-52)		36.5±4.8	35.5 (30-43)	
Longest place of residence	City	44.1±6.6	44.0 (20-62)	0.037	36.5±5.9	37.0 (18-50)	0.726
	Rural area	46.8±7.9	47.0 (24-60)		37.0±5.7	37.0 (22-48)	
Participation in the eTwinning Project titled “Geriatric Aspects of Patient Care”	Yes	47.1±8.9	49.0 (24-59)	0.034	39.4±3.7	39.0 (32-45)	0.049
	No	44.2±6.6	44.0 (20-62)		36.5±6.0	37.0 (18-50)	
Having Lived with an Elderly Family Member	Yes	44.8±6.9	45.0 (24-62)	0.839	36.5±6.2	37.0 (18-50)	0.194
	No	44.0±6.6	44.0 (20-59)		36.6±5.7	37.0 (18-49)	
Having Lived with an Elderly Family Member for 5 years or more	Yes	46.2±6.6	47.0 (32-59)	0.041	36.0±6.2	36.0 (18-48)	0.356
	No	44.1±7.0	44.0 (24-62)		36.7±6.2	38.0 (21-50)	
Desire to Live with Parents in the Future	Yes	45.9±6.1	46.0 (24-62)	0.010	37.2±5.9	38.0 (18-50)	<0.001
	No	42.8±7.0	43.0 (20-60)		35.9±5.8	36.0 (20-50)	
Desire to Work in a Nursing Home or Elderly Care Facility in the Future	Yes	45.7±6.7	46.0 (20-62)	<0.001	37.8±5.8	38.0 (18-50)	<0.001
	No	42.4±6.3	42.0 (25-60)		34.8±5.6	35.0 (18-48)	
Desire to Work with Elderly Individuals as a Colleague	Yes	45.3±6.8	45.0 (20-62)	<0.001	37.3±6.1	38.0 (18-50)	<0.001
	No	42.7±6.4	42.5 (25-59)		35.2±5.4	35.0 (18-50)	
Defining Old Age with Negative Expressions	Yes	44.5±6.3	44.5 (27-60)	0.864	36.4±5.8	37.0 (21-50)	0.545
	No	44.3±7.0	44.0 (20-62)		36.6±6.0	37.0 (18-50)	

The median PA scores of those residing in rural areas (p=0.037), who participated in the eTwinning project (p=0.034), those who have lived with an elderly individual for 5 years or more (p=0.041), those who want to live with their parents in the future (p=0.010), those interested in working in nursing homes/elderly care facilities, and those aspiring to work as colleagues with elderly individuals (p<0.001) were found to be significantly higher. Furthermore, female students (p=0.016), those who participated in the eTwinning project (p=0.049), those interested in living with their parents in the future, those who want to work in nursing homes/elderly care facilities, and those who want to work as colleagues with elderly individuals (p<0.001) exhibited significantly higher NA median scores (Table 4).

Table 5. Positive and negative ageism scores according to students' sociodemographic characteristics -2

Characteristics		Positive ageism			Negative ageism		
		X±SD	Median (Min-Max)	P	X±SD	Median (Min-Max)	p
Grade	9th	44.8±6.9	45.0 (27-59)	0.010	35.7±6.1	36.0 (18-48)	0.016
	10th	44.2±5.8	44.0 (26-57)		36.4±5.6	37.0 (21-49)	
	11th*	45.2±6.9	45.0 (25-62)		37.7±6.2	39.0 (18-50)	
	12th	42.4±7.4	42.0 (20-60)		36.2±5.6	38.0 (21-50)	
Mother's level of education	Illiterate	46.1±4.0	45.0 (40-52)	0.139	37.6±3.7	37.0 (32-43)	0.029
	Literate-Primary school	44.5±6.6	45.0 (20-60)		36.9±5.8	38.0 (18-50)	
	High school and above	43.2±7.3	43.0 (25-62)		34.9±6.4	36.0 (18-48)	
Father's level of education	Illiterate	44.0±0.0	44.0 (44-44)	0.751	39.0±0.0	39.0 (39-39)	0.444
	Literate-Primary school	44.5±6.7	44.0 (20-60)		36.8±5.9	37.0 (18-50)	
	High school and above	44.0±6.8	45.0 (25-62)		36.1±5.9	37.0 (20-50)	
Mother's occupation	Working	44.3±7.6	45.0 (24-62)	0.856	36.7±6.4	36.0 (20-50)	0.913
	Not working	44.4±6.5	44.0 (20-60)		36.5±5.8	37.0 (18-50)	
	Retired/ Passed away	41.2±11.1	42.0 (29-53)		34.6±7.6	38.0 (23-41)	
Father's occupation	Working	44.2±6.8	44.0 (20-62)	0.548	36.5±5.9	37.0 (18-50)	0.718
	Not working	46.5±6.1	44.0 (40-56)		37.5±6.0	38.0 (26-48)	
	Retired/ Passed away	44.9±5.8	45.0 (29-57)		37.0±5.8	38.0 (26-46)	
Family type	Nuclear family	44.3±6.4	44.0 (20-60)	0.940	36.7±5.7	37.0 (18-50)	0.101
	Extended family	44.2±8.0	45.0 (24-62)		35.0±6.6	35.0 (23-50)	
	Split/single-parent family	44.5±8.9	44.0 (25-59)		36.7±7.1	37.0 (21-48)	
Family's Perception of Income-Expenditure	Income more than expenses	45.4±6.7	46.0 (26-59)	0.144	37.2±6.1	38.0 (18-50)	0.489
	Income equal to expenses	44.4±6.7	44.0 (20-62)		36.6±5.7	37.0 (18-49)	
	Income less than expenses	43.5±6.7	44.0 (24-59)		36.1±6.3	37.0 (20-50)	

The median PA and NA scores were compared based on the characteristics of the sample and are presented in Table 5. The PA median scores of the 9th and 11th graders are significantly higher compared to the 12th graders (p=0.010). Additionally, the NA median score of the 11th graders is significantly higher than that of the 9th graders (p=0.016). The NA median score of students whose mothers have an education level of high school or above is significantly lower compared to those whose mothers are illiterate (p=0.029). However, no significant differences were observed in PA and NA scores based on variables such as fathers' educational levels, parents' occupations, family type, and family's perception of income-expenditure (Table 5).

A weak, non-significant negative relationship was found between the ages of students' mothers and the PA and NA scores (r values: -0.057, -0.033; p values: 0.204, 0.462, respectively). Similarly, a weak, non-significant negative relationship was found between the ages of students' fathers and the PA and NA scores (r values: -0.029, -0.016; p values: 0.521, 0.726, respectively).

DISCUSSION

In this study, the participants' mean PA and NA scores were found to be lower than in the literature. In two studies conducted on students of health services vocational school using the same scale, the mean PA and NA scores were found to be approximately 3-5 points higher than our study (14,15). In other two studies conducted with nursing undergraduate students using the same scale, the mean PA and NA scores were also found to be approximately 1-3 points higher than the scores found in our study (19,20). When compared to the literature, the mean PA and NA scores in this study are generally slightly lower, indicating that the students in this study have a slightly more negative attitude. This might be attributed to the fact that the students in our study are at the high school level and there might be differences in their educational curricula. The lower scores could also be due to the fact that the study group consists of high school students who are still in their adolescence and living with their families.

When PA scores were compared based on gender, no significant difference was found. However, when NA scores were compared based on gender, a significant difference was observed as female students were found to have significantly lower levels of negative ageism compared to male students. Similar to this study, research conducted with nursing students, medical faculty students, and young individuals have shown that, in the NA subscale, females exhibit more positive ageism attitudes compared to males (13,19,20,22). This outcome might be influenced by the caregiving role that women often hold within the traditional family structure in Turkish society. Some studies in the literature conducted with university students indicate that, contrary to this study, gender does not influence attitudes towards the elderly (14,15,23). However, other studies suggest that males have more positive ageism attitudes compared to females (24, 25). Among the studies in the literature, differences in ageism attitudes based on gender are believed to be influenced by factors such as the location and time of the study, characteristics of the research sample, cultural aspects, and differences in the scale used.

When the place of longest residence was compared with the PA scores of the students, it was found that those living in rural areas exhibit more positive attitudes. Similarly, some studies in the literature demonstrated that individuals living in rural areas display more positive attitudes (26,27,28). While traditional family structures can be preserved in rural areas, urban areas tend to have more nuclear family structures. Factors such as the emergence of the option to place the elderly in nursing homes due to urbanization and changes in family structure might lead to a decrease in positive attitudes towards the elderly. No significant relationship was found between the place of longest residence and NA attitude in this study. Similar to our study, some studies report no relationship between the place of residence and attitudes towards the elderly (15,17,24,29). However, a study conducted with medical faculty students indicates that individuals living in urban areas have more positive ageism attitudes (13). It is stated in the literature, that differences in ageism attitudes based on the place of residence may be influenced by factors such as socio-cultural characteristics, research population attributes, and features of the variable categories.

Our study revealed that the attitudes of students who participated in the "Geriatric Aspects of Elderly Care" eTwinning project are more positive compared to other students. The students who participated in the project received education on elderly health and care from academics. Additionally, nursing home visits were conducted with these students. Similar findings were reported in the literature, where factors such as nursing home visits and participation in education related to elderly health and care have been shown to enhance positive ageism attitudes (16,24,30). Education is considered an effective mechanism in fostering new approaches and positive attitudes among young individuals towards the elderly.

In this study, no significant relationship was found between having lived with an elderly family member and PA and NA attitudes. Similar results have been observed in studies conducted with university and high school students (14,17,20,24,31,32). Studies conducted with medical and nursing students suggest that individuals who have lived with an elderly family member exhibit more positive PA attitudes (13,26). Our study revealed that individuals who have lived

with an elderly family member for 5 years or more show more positive PA attitudes compared to others. A study conducted with healthcare vocational school students similarly indicates that individuals who have lived with elderly individuals for 5 years or more exhibit more positive attitudes (15). In addition to having lived with an elderly family member, factors such as the identity of the family member, duration of cohabitation, and the nature of the relationship are also believed to influence PA attitudes.

In our study, the students who expressed a desire to live with their parents in the future, work in nursing homes or retirement homes, and work as colleagues with elderly individuals were found to exhibit more positive PA and NA attitudes. This finding is consistent with those in the literature (13-16,19,20,22,33). Accordingly, it is thought that students who have a willingness to live or work with the elderly demonstrate more positive attitudes towards aging and the elderly. Additionally, reverse causality may also be at play; that is, a positive view towards the elderly could encourage students to aspire to work with or care for the elderly in their professional lives, or to live with their parents in the future. These results underscore how positive intergenerational relationships can contribute to fostering positive attitudes.

In this study, 53.6% of the students defined aging using negative expressions. However, no significant relationship was found between making positive or negative references to aging and ageism attitudes. Studies involving nursing students, doctors, and nurses working in intensive care units also show that a majority of participants tend to define aging using negative expressions. Nevertheless, no significant relationship was found between the way aging is defined and ageism attitudes (34,35). The formation of ageism attitudes is influenced not only by knowledge about aging but also by emotions, thoughts, and behaviors (17). It is believed that students' incomplete or inaccurate knowledge about aging and the elderly might impact their attitudes towards age discrimination.

In this study, when ageism attitudes were analyzed according to grade level, it was observed that 11th graders exhibited more positive attitudes compared to others. It is believed that topics related to aging and elderly neglect and abuse covered in the courses of the 11th-grade in healthcare services education might contribute to this difference. Some studies in the literature indicate that as grade level increases, ageism attitudes become more positive (16,19,36). However, in some studies, no significant relationship was found between grade level and ageism attitudes (15,17,24). Differences in the curricula of schools are thought to contribute to this variation. Studies in the literature suggest that students who are enrolled in programs or courses related to aging tend to have more positive ageism attitudes compared to their peers (14,17).

In this study, no significant relationship was found between ageism attitudes and the occupations of students' parents and fathers' education levels. Many studies in the literature similarly suggest that parents' education levels and occupations do not significantly influence ageism attitudes (17,23,31,35). However, in this study, it was found that students whose mothers had a high school diploma or higher education level exhibited more negative ageism attitudes. This finding is consistent with another study that examined ageism attitudes among high school students. It is suggested that an increase in maternal education level might weaken family bonds, enhance tendency towards nuclear families, and lead to discriminatory attitudes towards the elderly (32).

The present study found that family type and perception of income and expenditure did not significantly influence ageism attitudes. Similar findings have been reported in the literature (13,16,17,20,22,24,31,32,35). In contrast to this study, research conducted with nursing students revealed that students from extended families exhibited less ageism compared to those from nuclear families. It was suggested that the presence of elderly individuals within extended families might contribute to more positive attitudes towards the elderly among students (19,37).

No significant relationship was found between parents' age and ageism attitudes in this study. Similarly, a study conducted with medical faculty students also reported no significant relationship between parents' age and ageism attitudes (13).

One strength of this study is that it is one of the first conducted at the high school level on this topic. However, one limitation is that it was conducted only in one high school, limiting the generalizability of its results to all the population. Another limitation is its cross-sectional nature, which makes it difficult to determine the direction of causality. Additionally, the possibility of social desirability bias in responses to some questions should not be overlooked.

CONCLUSION

In conclusion, this research has identified that a significant portion of students exhibit a negative attitude towards the elderly. Those who participated in projects related to the elderly, received education on elderly health, and expressed a desire to live and work with the elderly demonstrated more positive and less negative ageism attitudes. In terms of positive ageism, it was found that students living in rural areas and those who have lived with an elderly individual for 5 years or more displayed more positive attitudes compared to others. Female students and those whose mothers are illiterate exhibited less negative ageism. Curriculum for all students, particularly those expected to be involved in healthcare services, should be designed to address all forms of discrimination, including ageism. The education provided to students should not only be theoretical but also supported by activities that actively engage students in the learning process, allowing them to spend quality time with the elderly, develop empathy, and participate in activities such as nursing home visits, drama, theater, and role-playing. To improve students' attitudes towards the elderly, projects focusing on the elderly and aging should be developed, and students should be actively engaged in these projects. In order to identify groups with negative attitudes towards the elderly, studies should be conducted with different groups, and interventions to minimize negative ageism attitudes should be implemented for these groups.

Acknowledgments: The authors would like to thank students who participated in the study. This manuscript was presented as an oral presentation in 4th International 15th Academic Geriatrics Society Congress (14-18 September 2022).

Author contribution: Conceptualization: Kamil Koçak; Methodology: Kamil Koçak, Hatice Şimşek Keskin; Formal analysis and investigation: Kamil Koçak; Writing - original draft preparation: Kamil Koçak; Writing - review and editing: Hatice Şimşek Keskin; Supervision: Hatice Şimşek Keskin. All authors contributed to the study conception and design.

Conflict of interests: No conflict of interests.

Ethical approval: Ethical approval was obtained from Dokuz Eylül University Non-Invasive Research Ethics Board (Decision Date: 06.04.2022, No: 2022/13-11).

Funding: No funding was used in this study.

Peer-review: Externally peer-reviewed.

REFERENCES

1. World Health Organization. Global strategy and action plan on ageing and health 2017. [Accessed date: 25.07.2023]. Available from: https://www.who.int/publications/i/item/9789241513500
2. World Health Organization. Ageing and health 2022. [Accessed date: 27.07.2023]. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health
3. Bilir N, Paksoy Erbaydar N. Yaşlılık sorunları. In: Güler Ç, Akın L, editors. Halk Sağlığı Temel Bilgiler. Ankara; Hacettepe Üniversitesi Yayınları; 2015.p.1528-1538.
4. Mitchell E, Walker R. Global ageing: successes, challenges and opportunities. Br J Hosp Med 2020; 81(2):1-9.
5. Şimşek Keskin H, Yeşil Kuru HK. Toplum yaşlanması. In: Uçku ŞR, Şimşek Keskin H, editors. Yaşlı Sağlığı ve Sorunları. Ankara: Türkiye Klinikleri; 2021.p.1-5.
6. Türkiye İstatistik Kurumu. İstatistiklerle Yaşlılar, 2021. [Accessed date: 28.07.2023]. Available from: https://data.tuik.gov.tr/Bulten/Index?p=Istatistiklerle-Yaslilar-2021-45636
7. Burnes D, Sheppard C, Henderson CR, et al. Am J Public Health 2019; 109(8):1-9.
8. Altun A, Demirel B. Üniversite öğrencilerinin yaşlı ayrımcılığıyla ilgili tutumları: Keskin MYO örneği. Manas Sosyal Araştırmalar Dergisi 2020;9(1):423-434.
9. Butler RN. Age-ism: Another form of bigotry. Gerontologist 1969;9(4):243-246. https://doi.org/10.1093/geront/9.4_Part_1.243
10. Chang ES, Kannoth S, Levy S, et al. Global reach of ageism on older persons' health: A systematic review. PloS One 2020; 15(1):e0220857.
11. Silva MF, Silva DSMD, Bacurau AGDM, et al. Ageism against older adults in the context of the COVID-19 pandemic: an integrative review. Rev Saude Publica 2021; 55(4):1-13.
12. Bratt C, Abrams D, Swift HJ. Supporting the old but neglecting the young? The two faces of ageism. Dev Psychol 2020; 56(5):1029.
13. Alıumuerova Z, Şimşek Sekreter Ö, Şimşek H. Tıp fakültesi 6. Sınıf öğrencilerinin yaş ayrımcılığına ilişkin tutumları ve ilişkili etmenler. Dokuz Eylül Üniversitesi Tıp Fakültesi Dergisi 2021; 35(3):363-375.
14. Güngör S, Borazan NG. Yaşlı bakım ve paramedik öğrencilerinin yaşlı ayrımcılığına yönelik tutumları. EIRJ 2021; 14(1):19-26.

15. Dikmen RD, Yildiz EAB. Yaşlı bakımı teknikerliği öğrencilerinin yaşlı ayrımcılığına yönelik tutumları. JSOAH 2022; 2(2):101-108.
16. Pekesen M, Akdeniz Ş, Sinan A. Üniversite öğrencilerinin yaşlı ayrımcılığına ilişkin tutumlarının belirlenmesi. TSHD 2021; (18):82-103.
17. Tuna S. Sağlık hizmetleri meslek yüksekokulu'ndaki öğrencilerin yaşlı ayrımcılığına ilişkin tutumlarının değerlendirilmesi: Köyceğiz Örneği. IDUHeS 2020; 3(2):145-156.
18. Tosunöz İK, Güngör S. Yaşlı ayrımcılığı: hemşirelik ve yaşlı bakım teknikeri öğrencileri örneği. İnönü Üniversitesi Sağlık Hizmetleri Meslek Yüksek Okulu Dergisi 2021; 9(1):176-190.
19. Kırca K, Sözeri Öztürk E, Bayrak Kahraman B. Nursing students' attitudes towards the elderly: positive and negative ageism. BSJ Health Sci 2023; 6(2):293-300.
20. Köse Tosunöz İ. Yaşlı ayrımcılığı ve mesleki değerler arasındaki ilişki: Hemşirelik öğrencileri örneği. SAK 2022; 7(3):426-440.
21. Yurttaş S, Sarıkoca E. Pozitif ve negatif yaşlı ayrımcılığı ölçeği (PNYAÖ) geçerlilik ve güvenirlik çalışması. Atatürk Üniversitesi Sosyal Bilimler Enstitüsü Dergisi 2018; 22(2):1977-1991.
22. Güzel B. Genç nüfusun yaşlı ayrımcılığı tutum düzeyinin sosyodemografik değişkenler açısından incelenmesi: Manisa örneği. Gençlik Araştırmaları Dergisi 2021; 9(25):109-134.
23. Ucun Y, Mersin S, Öksüz E. Gençlerin yaşlı bireylere karşı tutumu. Journal Of International Social Research 2015; 8(37):1143-1149.
24. Ayyıldız Nİ, Evcimen H. Yaşlı bakım programı öğrencilerinin yaşlı ayrımcılığına ilişkin tutumlarının belirlenmesi. İnönü Üniversitesi Sağlık Hizmetleri Meslek Yüksek Okulu Dergisi 2018; 6(2):14-24.
25. Cinar D, Karadakovan A, Sivrikaya SK. Investigation of the attitudes of university students to discrimination of the elderly. North Clin Istanb 2018; 5(1):25.
26. Alquwez N, Cruz JP, Almazan JU, Alamri MS, Mesde JJ. The Arabic version of the Kogan Attitudes toward Older People Scale among Saudi nursing students: a psychometric analysis. Ann Saudi Med 2018; 38(6):399-407.
27. Marquet M, Missotten P, Schroyen S, Nindaba D, Adam S. Ageism in Belgium and Burundi: a comparative analysis. Clin Interv Aging 2016; 11: 1129-1139.
28. Vauclair CM, Marques S, Lima ML, et al. Subjective social status of older people across countries: The role of modernization and employment. J Gerontol B Psychol Sci Soc Sci 2014; 70(4):650–660.
29. Uzuntarla Y, Ceyhan S. Ageism and altruism among students in the department of health technician training, J Clın Med Kaz 2020; 4(58):67-72
30. Veronek J, Bajs Janović M, Janović Š, et al. Attitudes Towards Older People in Croatian and Slovenian Nursing Students. Psychiatr Danub 2020; 32(4):484-490.
31. Olak A, Tümer A. Hemşirelik 1. ve 4. sınıf öğrencilerinin yaşlı ayrımcılığına ilişkin tutumları. OPUS International Journal of Society Researches 2018; 8(14):53-67.
32. Ercan FZ, Ercan M, Koçak O. Lise öğrencilerinin yaşlı ayrımcılığına ilişkin tutumlarının belirlenmesi. Toplum ve Sosyal Hizmet 2023; 34(2):361-380.
33. Can R., Tambağ H, Hüzmeli ED, Duman F. Öğrencilerin yaşlı ayrımcılığına ilişkin tutumları: bir üniversite örneği. ADYÜ Sağlık Bilimleri Derg. 2020; 6(1):68-76.
34. Naldan ME, Kara D, Soyalp C, Gürol A. Evaluation of healthcare workers at intensive care units towards aging. Med J Bakirkoy. 2018; 14(1):8-16.
35. Altay B, Aydın T. Hemşirelik öğrencilerinin yaşlı ayrımcılığına ilişkin tutumlarının değerlendirilmesi. Hemşirelikte Eğitim ve Araştırma Dergisi 2015; 12(1):11-18.
36. Turan E, Yanardag M, Metintas S. Attitudes of students of health sciences towards the older persons. Nurse Educ Today 2016; 36:53-57.
37. Salman M, Gülçek E, Aylaz R, Polat F. Hemşirelik öğrencilerinin yaşlılara karşı tutumlarının değerlendirilmesi. EIRJ 2018; 11(2):1-7.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 433-440
https://doi.org/10.30621/jbachs.1378649
RESEARCH ARTICLE

THE ASSOCIATION BETWEEN LUMBAR LORDOSIS AND FUNCTIONAL PERFORMANCE IN CHILDREN WITH DUCHENNE MUSCULAR DYSTROPHY

Numan Bulut[1], Ipek Gurbuz[1], Oznur Yilmaz[1]

[1] Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Department of Physiotherapy and Rehabilitation, Ankara, Turkey

ORCID: N.B. 0000-0001-5427-1103; I.G. 0000-0001-5556-6608; O.Y. 0000-0002-0855-9541

Corresponding author: Numan BULUT, **E-mail:** nmn60_90@hotmail.com
Received: 19.10.2023; **Accepted:** 18.04.2024; **Available Online Date:** 31.05.2024

Cite this article as: Bulut N. Gurbuz I. Yilmaz O. The Association Between Lumbar Lordosis and Functional Performance in Children with Duchenne Muscular Dystrophy. J Basic Clin Health Sci 2024; 8: 433-440.

ABSTRACT

Purpose: The aims of this study were to compare the lumbar lordosis values measured with flexible ruler between healthy peers and children with Duchenne Muscular Dystrophy (DMD) and to investigate the relationship between lumbar lordosis values and functional performance in children with DMD.
Material and Methods: The study included 20 children with DMD (median age: 8.29 years) and 10 healthy peers (median age: 7.96 years). Lumbar lordosis values and postural alignment were assessed using a flexible ruler and New York Posture Rating (NYPR). Functional performance was evaluated with the 32-item Motor Function Measure and timed performance tests.
Results: The demographic characteristics such as age and body mass index were similar for both the children with DMD and the healthy peer group ($p>0.05$). A higher degree of lumbar lordosis was determined in the children with DMD compared to the healthy peers (median angle: 46.58° vs. 36.10°) ($p<0.001$). The children with DMD had greater disturbance according to the NYPR ($p=0.002$). Both the degree of lumbar lordosis and NYPR scores were moderately to strongly related to the functional performance parameters ($p<0.05$, rs:0.5 - 0.8 and -0.5 - -0.8).
Conclusion: Assessment of lumbar lordosis using a flexible ruler in DMD may be an alternative method to differentiate between children with DMD and healthy peers, and between children with DMD at different functional levels. This study may provide additional evidence regarding the possible relationships between postural alignment and motor function parameters.

Keywords: Duchenne muscular dystrophy, spine, lordosis, posture, physical functional performance

INTRODUCTION

Duchenne muscular dystrophy (DMD) is one of the most prevalent (7.1 per 100000 males) fatal diseases of childhood with X-linked recessive inheritance (1). The disease is caused by a mutation in the DMD gene responsible for the production of dystrophin protein (2). Although DMD is characterized by more prominent muscle weakness in proximal muscles, the disease affects all muscles in the body (3, 4). The first symptoms of the disease generally emerge around the age of 3 years, and include delay in motor milestones, frequent falls, fatigue, and difficulty in getting up from the floor. Functional performance parameters tend to improve until the age of 7 years (5, 6) while symptoms become more pronounced from this age onwards and children lose their walking ability around the ages of 10-12 years (7). Cardiac

and respiratory complications can be the cause of death for these children (8, 9).

Muscle weakness in DMD results in not only decreased physical performance but also joint contractures and postural changes. Ankle contractures, which usually appear as a primary deformity, have serious side effects on functional performance (9). In a study on this subject, increased ankle contractures were found to be associated with decreased functional performance in DMD (10). However, postural alignment disturbances such as scoliosis, kyphosis and lordosis are observed at different frequencies in neuromuscular diseases (11). Increased lumbar lordosis is a compensatory mechanism in response to the pelvic girdle muscle weakness. This weakness leads to deterioration in pelvis stability, and the compensatory shortness of the iliotibial band often forces the pelvis into anterior tilt. The lumbar lordosis automatically increases to balance the compensations in the pelvis and lower limbs (12). Baptista et al. evaluated the postural alignment of children with DMD using digital photogrammetry and found a relationship between forward displacement of the centre of mass and pelvic anteversion with balance deficit (3). Increased lumbar lordosis has also been reported to negatively affect gait quality in addition to balance (12).

There is currently no cure for DMD. Disease management generally consists of symptomatic treatments such as rehabilitation, and cardiac and respiratory drugs (8, 9). It is well known that to increase the efficacy of these treatments, the symptoms should be detected at an early age while physical performance is still preserved (13). Therefore, to be able to detect symptoms as early as possible, it is crucial to select outcome measures that are practical, low-cost, provide rapid results and are relevant to the disease (14). Thus, early detection of postural changes including lumbar lordosis due to muscle weakness in the early period of DMD is one of the factors that increase the effectiveness of the treatment. In a recent study in which lumbar lordosis values were determined using a digital inclinometer, it was found that the lumbar lordosis of children with DMD was high and these values were associated with gait and balance parameters (12). However, it remains unclear whether the flexible ruler, which is valid and reliable in the measurement of lumbar lordosis in children, is an alternative to a digital inclinometer and whether lumbar lordosis is related to functional performance other than gait and balance.

The aims of this study were to compare the lumbar lordosis values assessed with a flexible ruler between healthy peers and children with DMD and to investigate the relationship between the severity of lumbar lordosis and functional performance.

MATERIAL AND METHODS.

Design and Participants

This cross-sectional observational study was conducted at Hacettepe University, Faculty of Physical Therapy and Rehabilitation between October 2022 and May 2023. Approval for the study was obtained from the Hacettepe University Non-Interventional Clinical Studies Ethics Board (Decision Date: 18.10.2022, Number: 2022/16-27). Written informed consent was obtained from children and their families, and the study was conducted in accordance with the Declaration of Helsinki.

The study included children aged 5-12 years, who were genetically confirmed, Level 1-3 on the Vignos scale, and using steroids regularly for at least six months. Children with an additional chronic disease, severe joint contractures and shortness, inadequate co-operation, or history of an injury or surgery in the last 6 months were excluded from the study. The control group was formed of healthy peers with no history of any chronic diseases and injuries or surgery in the last 6 months. A total of 22 children with DMD and 11 healthy peers were initially enrolled in the study. Two children with DMD were excluded because of a history of lower extremity fracture and insufficient co-operation, and one of the healthy children was excluded because of regular use of immunosuppressive medication. The study was completed with a total of 30 children (20 DMD and 10 healthy subjects).

Outcome measures

The demographic characteristics of all the children such as age, height, weight, and dominant side were recorded.

Functional Level

The Vignos Scale was used to determine the functional level of the children with DMD (15). The Vignos scale classifies children with DMD into different levels, ranging from 1 to 10. Level 1 indicates that the patient can walk independently and climb stairs without assistance, while Level 10 indicates that the patient is confined to bed. The children with DMD who were included in this study were those who

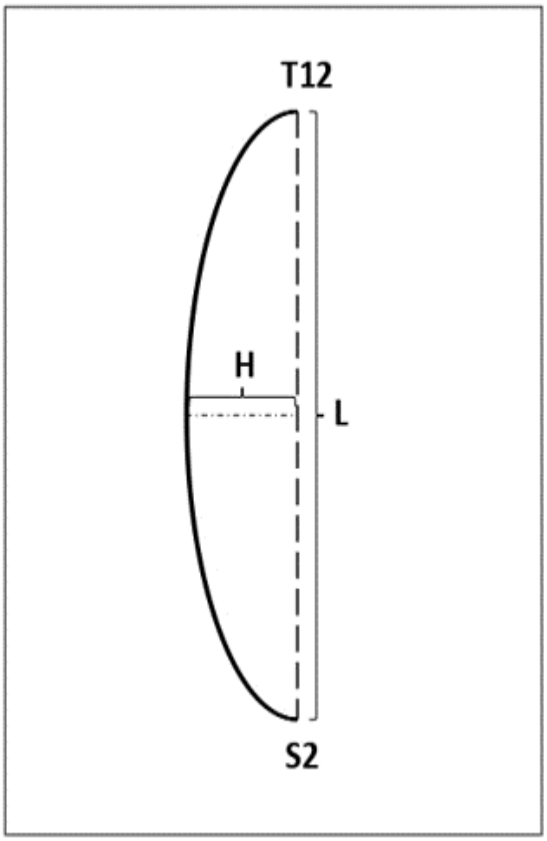


Figure 1. The measurement of lumbar lordosis with the flexible ruler

could climb stairs with or without support (Levels 1-3). This scale has been shown to have high ICC in the assessment of DMD children (16).

Lumbar Lordosis

A flexible ruler was used to assess lumbar lordosis in the children in this study (17, 18). The children were asked to stand barefoot between two parallel bands with the feet 15 cm apart, and their weight evenly distributed on both legs, their arms at the sides of the trunk and facing the opposite wall in a comfortable position for the assessment. In this position, a removable mark was placed on the children's spinous processes of T12 and S2. The flexible ruler was placed between these two marked points in the lumbar region and the obtained shape was transferred onto paper without distortion. The T12 and S2 points on the paper were connected vertically (L), and the distance between this vertical line and the maximum curvature was calculated (H) (Figure 1). The lumbar lordosis angle (θ) was calculated according to the following formula (19); θ=4X[Arctan2H/L]. Although this method has been shown to be highly reliable in children, as it was being used for the first time in the DMD population, reliability was tested in a preliminary study.

Postural Alignment

Postural characteristics were assessed with the New York Posture Rating Scale (NYPR) modified by Howly and Franks (20). Postural changes in 10 different parts of the body such as the head, trunk and hips were observed either lateral or posterior, and scored. Each body part of each child was evaluated by giving a score of good posture (10 points), fair (5 points), or poor posture (0 points). The NYPR was determined to have moderate ICC (0.70) value (21).

Functional Performance

Timed performance tests consisting of (a) supine to stand (Gowers' maneuver), (b) ascending and descending four steps of 25 cm width and 17 cm height with handrails, and (c) 10-m walk/run test were used to determine the functional performance of the children with DMD (22). Each timed performance test score was recorded in seconds.

Motor Function

The 32-item Motor Function Measure (MFM-32), which has been shown to be valid and reliable in neuromuscular diseases in the age range of 6-60 years, was used to assess motor function in the children with DMD. This outcome measure assesses function in 3 different dimensions [sitting and transfers (D1), proximal/axial (D2) and distal (D3)] over a total of 32 items. Items are generally scored on a four-point Likert scale; (0) cannot initiate any task and cannot maintain the starting position, (1) partially completes the task, (2) performs the task slowly, with some help and compensations, and (3) performs the task in a standardized pattern. Each sub-dimension and the total score are converted into a percentage score. Higher scores indicate better motor functioning (23, 24). This assessment was performed by a certified physiotherapist (NB).

Assessment Procedure

The assessments of functional level, motor function and functional performance were only applied to the children with DMD, while all other assessments were performed on all children. One physiotherapist carried out the postural assessments and the other performed the motor performance tests. Short resting periods were allowed after each assessment to avoid

Table 1. Demographic and postural characteristics of children with Duchenne muscular dystrophy at different functional levels and healthy peers.

Variables	Children with DMD[a]		*p (comparison between DMD groups)*	Healthy peers (n=10)	*p (comparison between groups)*
	Level 1 (n=10)	Level 2 (n=10)			
Age (years)	8.04 (7.19-9.04)	8.29 (7.52-10.12)	0.4	7.96 (7.23-8.92)	0.6
Height (m)	1.23 (1.17-1.33)	1.28 (1.20-1.35)	0.4	1.31 (1.27-1.40)	0.06
Body weight (kg)	23.50 (20.5-29.37)	30.75 (22.62-35.12)	0.2	28.80 (22.25-34.50)	0.5
Body Mass Index (percentiles)	45.50 (15.75-76.00)	84.50 (65.25-91.25)	0.06	62.50 (35.50-80.50)	0.5
Lumbar Lordosis (°)	43.15 (37.23-46.40)	53.89 (47.62-63.01)	0.005*	36.10 (33.36-38.91)	<0.001*
NYPR (points)	75.00 (70.00-90.00)	65.00 (60.00-75.00)	0.01*	95.00 (90.00-100.00)	0.002*

a According to Vignos Scale. Data expressed as median (25th and 75th percentiles).*Mann Whitney-U Test DMD: Duchenne Muscular Dystrophy, NYPR: New York Posture Rating

Table 2. The results of functional assessments of children with Duchenne Muscular Dystrophy.

Functional Assessments	Children with DMD[a]		*p*
	Level 1 (n=10)	Level 2 (n=10)	
Motor Function Measure			
Total Score (%)	85.42 (82.03-91.93)	80.21 (69.53-84.64)	0.02*
Dimension 1 (%)	73.08 (66.03-82.69)	57.69 (44.87-90.97)	0.004*
Dimension 2 (%)	97.22 (94.44-100.00)	94.44 (90.97-97.92)	0.1
Dimension 3 (%)	90.48 (89.29-96.43)	95.24 (90.48-95.24)	0.7
Supine to stand (sec)	4.80 (2.81-8.59)	7.12 (4.91-17.61)	0.09
Ascending four stairs (sec)	2.41 (2.18-2.91)	3.79 (2.99-9.49)	0.01*
Descending four stairs (sec)	2.22 (1.80-3.23)	3.50 (2.00-5.09)	0.2
10 meter walk/run test (sec)	4.70 (4.24-5.02)	5.91 (4.82-8.40)	0.03*

a According to Vignos Scale. Data expressed as median (25th and 75th percentiles).*Mann Whitney-U Test, DMD: Duchenne Muscular Dystrophy.

fatigue in the children. The assessments lasted about 50 minutes in total for the children with DMD and 10 minutes for the healthy children.

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS vn 23.0 software (SPSS Inc., Chicago, IL, USA). Conformity of the data to normal distribution was evaluated with the Shapiro-Wilk test and it was determined that the data did not fit normal distribution. Scores were expressed as median and percentiles (25th and 75th percentiles). The Mann-Whitney U test was used to compare the lumbar lordosis and postural alignment scores of both children with DMD at different levels and children with DMD and their healthy peers. The relationship between postural alignment parameters and motor performance scores in children with DMD was analyzed using Spearman rank correlation coefficient (rs). The strength of correlations were determined as; rs = 0.7–0.99 strong; rs = 0.4–0.69 moderate; and rs =0.01-0.39 weak (25). A value of $p<0.05$ was accepted as statistical significance level.

In the post-hoc power analysis performed with G*Power 3.1 using the lumbar lordosis values of DMD and healthy peers, the effect size (Cohen's *d*) was 1.38 and the power of the study was 93.0%.

RESULTS

The demographic and postural characteristics of the children with DMD at different functional levels and their healthy peers are shown in Table 1. The demographic characteristics were similar in both the children with DMD (median age: 8.29 years) and their

Table 3. The correlations between postural alignment parameters and functional assessments (n=20).

	Lumbar Lordosis		New York Posture Rating	
	r_s	*p*	r_s	*p*
Motor Function Measure				
Total Score	-0.5*	0.01	0.6*	0.002
Dimension 1	-0.6*	0.002	0.8*	<0.001
Dimension 2	-0.3	0.1	0.3	0.1
Dimension 3	-0.08	0.7	0.01	>0.9
Supine to stand	0.6*	0.002	-0.6*	0.006
Ascending four stairs	0.7*	<0.001	-0.7*	0.001
Descending four stairs	0.3	0.1	-0.4	0.09
10 meter walk/run test	0.8*	<0.001	-0.5*	0.01

*Spearmann Correlation Coefficient.

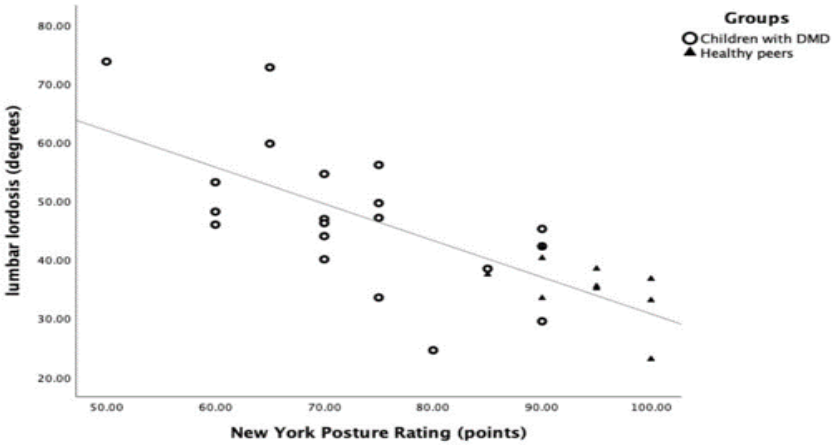


Figure 2. The results of postural alignment of children with Duchenne muscular dystrophy and healthy peers (DMD: Duchenne muscular dystrophy)

healthy peers (median age: 7.96 years) (p>0.05). All the children included in the study were right-handed.

The degree of lumbar lordosis was determined to be statistically significantly higher in the children with DMD compared to the healthy peers (median angle: 46.58° vs. 36.10°) (p<0.001). The flexible ruler was found to have high inter-rater reliability (ICC: 0.925; p<0.001) in a preliminary study involving 14 children with DMD. The lumbar lordosis values measured with the flexible ruler and the NYPR scores of each child are shown in Figure 2. A strong positive correlation was determined between the NYPR scores and lumbar lordosis in the children with DMD (rs= 0.8, p<0.001).

The functional assessment results of the children with DMD are presented in Table 2. The MFM total score, MFM D1, ascending four stairs and 10 m walk/run test results were significantly better in the children with Level 1 DMD (p<0.05).

Moderate to strong relationships were determined between postural alignment and motor performance test parameters, as shown in Table 3 (p<0.05).

DISCUSSION

The results of this study, which assessed lumbar lordosis in children with DMD using a flexible ruler, showed that children with DMD had increased lumbar lordosis in the ambulatory period compared to their

healthy peers. It was determined that with the worsening of functional ability, the lumbar lordosis increased, and postural alignment disturbances might be associated with the worsening functional performance. Considering the studies in the literature in which different methods have been used in the evaluation of lumbar lordosis (3, 12), it can be stated that the evaluation of lumbar lordosis with the flexible ruler reveals similar results in differentiating healthy children and those with DMD and provides information about physical performance.

Muscle weakness and imbalance, which are the main symptoms in children with DMD, cause joint contractures, postural deviations and deterioration in functional ability (3). Ankle contractures have been reported to occur in about half of children with DMD, even in the ambulatory phase, followed by hip and knee contractures (26). In addition to contractures, postural alignment disturbances such as an increased anterior position of the centre of mass and significant pelvic anteversion have been observed (3). Scoliosis and lordosis are also part of the postural alignment disturbances in DMD (11). Filiz et al. (12) reported that lumbar lordosis became more pronounced compared to healthy children, even at a stage that can be considered the early ambulatory phase according to the age of the children (mean age: 8.0 years). Similarly, it was seen in the current study that children with DMD had higher lumbar lordosis values and worse posture. This shows that the postural change is not only in the proximal region such as lumbar lordosis but also in the whole body. However, the lumbar lordosis values of both the healthy and DMD children in the current study were numerically different from those reported in other studies (12, 18). This may be due to differences in methodology and the age range of participants.

Due to the progressive nature of DMD, there are many reports of worsening symptoms such as contractures and gait. (27, 28). In other words, as performance decreases so the functional level worsens. Alkan et al. (29) stated that balance parameters deteriorated as the functional level worsened in children with DMD. The current study results showed that the lumbar lordosis values of children with Level 1 DMD, which is functionally better, were 10 degrees lower and their postural scores were 10 points higher than those of children with Level 2 DMD. From these results, it can be concluded that when functional loss occurs, it leads to holistic changes in the whole body.

In children who maintain their functional level until the age of 6-8 years, there are losses in both muscle strength and functional performance after this age, and children may be later confined to a wheelchair (30). In an 18-month follow-up study of steroid-using DMD children with a mean age of 7.6 years, it was reported that the MFM D1 sub-dimension and MFM total scores tended to decrease (31). Another DMD cohort study reported deterioration after 7 years of age in timed performance tests such as supine to stand, ascending four steps and 10 m walk/run test (22). The fact that the median age of the children with DMD in the current study was above 6-8 years, which is the critical threshold, may explain the difference in assessment parameters between the DMD and healthy peer groups. The age of children with DMD provides important information, but not all of it. Although the age of the children at two different functional levels was similar, the difference in proximal and axial motor function and in timed performance tests such as ascending four stairs and the 10-meter walk test can be explained by the holistic change mentioned above rather than by age.

Physical symptoms are expected to interact because many of the problems in DMD are related to muscle weakness. In this regard, there are studies showing a relationship between muscle strength and motor functions in children with DMD (32, 33). In addition, both proximal and distal postural alignment have been shown to be associated with balance and gait in children with DMD (3, 34). A study that focussed on lumbar lordosis reported a correlation between the lumbar lordosis values and gait quality and balance (12). The results of the current study showed an association of both lumbar lordosis values and postural alignment scores with proximal and functional performance parameters in the children with DMD. Thus, in addition to the information in the literature on the relationship between postural alignment and balance and gait, this study provides further evidence that postural alignment may be related to functional performance. This supports the view that problems which occur secondary to muscle weakness may influence each other. The main limitation of this study was the relatively low number of participants.

CONCLUSION

In conclusion, the assessment of lumbar lordosis using a flexible ruler can be used to differentiate between both children with DMD and healthy peers,

and children with DMD at different functional levels. In the light of these results, flexible ruler measurements may be an alternative option to the methods used for the assessment of lumbar lordosis in children with DMD. In addition to the existing knowledge about the relationships between postural alignment and gait and balance, this study may provide additional evidence in respect of the possible relationships between postural alignment and motor function parameters. To be able to confirm these results, there is a need for a cohort study including a wider spectrum of children. The use of flexible ruler measurements in future studies may be of guidance to researchers and clinicians for the determination of the cut-off value for lumbar lordosis.

Acknowledgments: We would like to thank the children and their families who agreed to participate in the study.

Author contribution: Numan Bulut: Conceptualization, Design, Data Collection, Literature Review Writing-Original Draft and Critical Review. İpek Gürbüz: Conceptualization, Design, Materials, Analysis, Writing Original Draft and Review. Öznur Yılmaz: Conceptualization, Design, Supervision, Interpretation, Writing Original Draft and Review. All authors approve the submitted and final version.

Conflict of interests: Approval for the study was obtained from the Hacettepe University Non-Interventional Clinical Studies Ethics Board (Decision Date: 18.10.2022, Number: 2022/16-27). Written informed consent was obtained from children and their families, and the study was conducted in accordance with the Declaration of Helsinki.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Peer-review: Externally peer-reviewed.

REFERENCES

1. C Crisafulli S, Sultana J, Fontana A, Salvo F, Messina S, Trifirò G. Global epidemiology of Duchenne muscular dystrophy: an updated systematic review and meta-analysis. Orphanet J Rare Dis 2020;15(1):1-20.

2. Hainsey T, Senapati S, Kuhn D, Rafael J. Cardiomyopathic features associated with muscular dystrophy are independent of dystrophin absence in cardiovasculature. Neuromuscul Disord 2003;13(4):294-302.

3. Baptista CR, Costa AA, Pizzato TM, Souza FB, Mattiello-Sverzut AC. Postural alignment in children with Duchenne muscular dystrophy and its relationship with balance. Braz J Phys Ther 2014;18(2):119-126.

4. Sá CdSCd, Fagundes IK, Araújo TB, Oliveira ASB, Fávero FM. The relevance of trunk evaluation in Duchenne muscular dystrophy: the segmental assessment of trunk control. Arq Neuro-Psiquiatr 2016;74(10):791-795.

5. Mazzone E, Vasco G, Sormani M, et al. Functional changes in Duchenne muscular dystrophy: a 12-month longitudinal cohort study. Neurology 2011;77(3):250-256.

6. MCDonald CM, Henricson EK, Han JJ, et al. The 6-minute walk test in Duchenne/Becker muscular dystrophy: longitudinal observations. Muscle Nerve 2010;42(6):966-974.

7. P Parreira SLS, Resende MBD, Zanoteli E, Carvalho MS, Marie SK, Reed UC. Comparison of motor strength and function in patients with Duchenne muscular dystrophy with or without steroid therapy. Arq Neuro-Psiquiatr 2010;68(5):683-688.

8. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol 2018;17(3):251-267.

9. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol 2018;17(4):347-361.

10. Kiefer M, Bonarrigo K, Quatman-Yates C, Fowler A, Horn PS, Wong BL. Progression of ankle plantarflexion contractures and functional decline in Duchenne muscular dystrophy: implications for physical therapy management. Pediatr Phys Ther 2019;31(1):61-66.

11. Kinali M, Main M, Mercuri E, Muntoni F. Evolution of abnormal postures in Duchenne muscular dystrophy. Ann Indian Acad Neurol 2007;10(5):44-54.

12. Filiz MB, Toraman NF, Kutluk MG, et al. Effects of lumbar lordosis increment on gait deteriorations in ambulant boys with Duchenne Muscular Dystrophy: A cross-sectional study. Braz J Phys Ther 2021;25:749-755.

13. Case LE, Apkon SD, Eagle M, et al. Rehabilitation management of the patient with Duchenne muscular dystrophy. Pediatrics 2018;142(Supplement_2):17-33.

14. Govoni A, Magri F, Brajkovic S, et al. Ongoing therapeutic trials and outcome measures for Duchenne muscular dystrophy. Cell Mol Life Sci 2013;70:4585-602.

15. Jung I-Y, Chae JH, Park SK, et al. The correlation analysis of functional factors and age with duchenne muscular dystrophy. Ann Rehabil Med 2012;36(1):22-32.

16. Florence JM, Pandya S, King WM, et al. Clinical trials in Duchenne dystrophy: standardization and reliability of evaluation procedures. Phys Ther 1984;64(1):41-45. https://doi.org/10.1093/ptj/64.1.41.
17. Lovell FW, Rothstein JM, Personius WJ. Reliability of clinical measurements of lumbar lordosis taken with a flexible rule. Phys Ther 1989;69(2):96-102.
18. Reshma, Sirajudeen MS, Chinnakalai T, Suhail M, al-Hussinan NM, Pillai SP. Reliability of the flexible ruler in measuring lumbar lordosis among children. J Clin Diagnostic Res 2020;14:01-04.
19. Youdas JW, Garrett TR, Harmsen S, Suman VJ, Carey JR. Lumbar lordosis and pelvic inclination of asymptomatic adults. Phys Ther 1996;76(10):1066-1081.
20. Howley ET, Franks BD. Health/Fitness Instructor's Handbook. ERIC, 1986.
21. McRoberts LB, Cloud RM, Black CM. Evaluation of the New York Posture Rating Chart for assessing changes in postural alignment in a garment study. Cloth Text Res J 2013;31(2):81-96.
22. Arora H, Willcocks RJ, Lott DJ, et al. Longitudinal timed function tests in Duchenne muscular dystrophy: ImagingDMD cohort natural history. Muscle Nerve 2018;58:631-638.
23. Bérard C, Payan C, Hodgkinson I, Fermanian J, Group MCS. A motor function measure scale for neuromuscular diseases. Construction and validation study. Neuromuscul Disord 2005;15:463-470.
24. İnal HS, Tarakci E, Tarakci D, et al. Turkish version of the Motor Function Measure Scale (MFM-32) forneuromuscular diseases: a cross-cultural adaptation, reliability, and validity study. Turk J Med Sci 2017;47:1826-1833.
25. Akoglu H. User's guide to correlation coefficients. Turk J Emerg Med 2018;18(3):91-93.
26. Choi Y-A, Chun S-M, Kim Y, Shin H-I. Lower extremity joint contracture according to ambulatory status in children with Duchenne muscular dystrophy. BMC Musculoskelet Disord 2018;19(1):1-6.
27. Hsu JD, Furumasu J. Gait and posture changes in the Duchenne muscular dystrophy child. Clin Orthop Relat Res 1993;288:122-125.
28. Vuillerot C, Girardot F, Payan C, et al. Monitoring changes and predicting loss of ambulation in Duchenne muscular dystrophy with the Motor Function Measure. Dev Med Child Neurol 2010;52(1):60-5.
29. Alkan H, Mutlu A, Fırat T, Bulut N, Karaduman AA, Yılmaz ÖT. Effects of functional level on balance in children with Duchenne Muscular Dystrophy. Eur J Paediatr Neurol 2017;21(4):635-8.
30. Fowler EG, Staudt LA, Heberer KR, et al. Longitudinal community walking activity in Duchenne muscular dystrophy. Muscle Nerve 2018;57(3):401-6.
31. Silva ECd, Machado DL, Resende MB, Silva RF, Zanoteli E, Reed UC. Motor function measure scale, steroid therapy and patients with Duchenne muscular dystrophy. Arq Neuro-Psiquiatr 2012;70(3):191-195.
32. Beenakker EA, Maurits NM, Fock JM, Brouwer OF, van der Hoeven JH. Functional ability and muscle force in healthy children and ambulant Duchenne muscular dystrophy patients. Eur J Paediatr Neurol. 2005;9(6):387-93.
33. Nunes MF, Hukuda ME, Favero FM, Oliveira AB, Voos MC, Caromano FA. Relationship between muscle strength and motor function in Duchenne muscular dystrophy. Arq Neuro-Psiquiatr 2016;74:530-5.
34. Aydın Yağcıoğlu G, Yılmaz Ö, Alemdaroğlu Gürbüz İ, et al. Examination of the relationship between foot-body posture and balance and gait in Duchenne muscular dystrophy. Ir J Med Sci 2023;192(4):1883-1888.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 441-447
https://doi.org/10.30621/jbachs.1387268
RESEARCH ARTICLE

KNOWLEDGE AND AWARENESS OF SPINAL MUSCULAR ATROPHY IN PRE-MARITAL HEALTH SCREENINGS: A CROSS-SECTIONAL STUDY

Gadime Yanmaz[1], Ersan Gürsoy[1]

[1]Erzincan Binali Yıldırım University Faculty Of Medicine, Department Of Family Medicine, Erzincan

ORCID: G.D. 0000-0003-0722-5053; E.G. 0000-0002-5020-412X

Corresponding author: Ersan Gürsoy, **E-mail:** ersangursoy@gmail.com
Received: 07.11.2023; **Accepted:** 29.03.2024; **Available Online Date:** 31.05.2024

Cite this article as: Yanmaz G, Ersoy G. Knowledge and Awareness of Spinal Muscular Atrophy in Pre-Marital Health Screenings: A Cross-Sectional Study. J Basic Clin Health Sci 2024; 8: 441-447.

ABSTRACT

Purpose: Early diagnosis of Spinal Muscular Atrophy (SMA) is crucial. This study assesses the awareness and attitudes toward SMA screening among individuals preparing for marriage.
Material and Methods: This cross-sectional study was conducted in three family health centers in the central district of Erzincan from June to September 2023. A researcher-designed 15-item instrument was utilized to collect demographic data and assess knowledge and attitudes regarding SMA among participants.
Results: The study was participated in by 197 individuals, with an average age determined to be 29.45±7.48. The proportion of those supporting the implementation of SMA screening was 84.8% (n=167), while the intention to undergo the test was identified at 72.6% (n=143).
A significant relationship was found between the willingness to be tested and variables such as the level of education, the absence of disabled close relatives, not considering SMA to be genetically inherited, finding screenings appropriate, the perceived impact of test results on marriage, and the belief that screening could not be conducted after marriage.
Conclusion: While most recognized SMA's severity, there's a notable deficit in understanding its preventability, suggesting the need for targeted educational interventions to enhance genetic screening uptake.

Keywords: Spinal Muscular Atrophy, Genetic Screening, Diagnostic Screening Programs, Secondary Prevention

INTRODUCTION

Spinal Muscular Atrophy (SMA) is a genetic and progressive neuromuscular disorder characterized by the loss of motor neuron function due to mutations in the SMN1 (survival motor neuron 1) gene (1). This condition results in a progressive weakening and atrophy of the muscles. The clinical spectrum of SMA exhibits significant variability in terms of the onset and severity of symptoms, which presents considerable challenges in the diagnosis and treatment of the disease(2).

The disease has four main types: Type I (Werdnig-Hoffmann disease) is the most severe form, beginning in infancy with limited life expectancy due to respiratory failure. Type II (Intermediate SMA) manifests in infancy or early childhood, where children can sit but are unable to stand or walk unassisted. Type III (Kugelberg-Welander disease)

starts after early childhood; individuals can walk but may lose this ability over time, yet they have a normal life expectancy. Type IV begins in adulthood and is the mildest form, progressing slowly with a normal life expectancy. Each type of SMA is associated with mutations in the SMN1 gene, which leads to a deficiency in the SMN protein critical for motor neuron survival, and the copy number of the SMN2 gene can influence the severity of the disease (3). SMA is a genetic disorder that exhibits varying incidence rates across different populations. These rates can fluctuate depending on factors such as genetic diversity, diagnostic methods, and characteristics of the population (4). Nevertheless, it can be stated that SMA occurs at an approximate rate of 7.8-10 per 100,000 live births worldwide (5-7).

SMA is a genetic condition where early diagnosis is particularly crucial. In the early stages of SMA, non-neuromuscular symptoms can be detected prior to the clinical signs of neuromuscular degeneration, potentially offering a sequence for the progression of the disease (8). Early diagnosis enables the timely initiation of interventions to slow disease progression and improve quality of life. As knowledge of the pathophysiology of SMA increases, promising strides in its treatment are also emerging (9). Therefore, early diagnosis of SMA is of critical importance in the management of the disease and the development of treatment strategies.

In Turkey, with the directive issued by the Ministry of Health on December 27, 2021, SMA screening has become mandatory nationwide during the pre-marital and newborn periods. Through this program, couples who are carriers for SMA can be identified, allowing for the provision of genetic counseling and treatment options before or after pregnancy. SMA screening is conducted free of charge at Family Health Centers. Nevertheless, comprehensive studies on the societal acceptance of screening programs and the challenges encountered in this process have not been conducted.

The purpose of our study is to assess the knowledge levels and attitudes towards SMA screening among individuals applying for a marriage certificate at family health centers in the central district of Erzincan, thereby contributing to the more effective shaping of relevant health policies and educational programs.

MATERIAL AND METHODS

Study design and execution

This descriptive and cross-sectional study was conducted at three different family health centers affiliated with the central district of Erzincan between June and September 2023.

Study population

The research population consisted of adults aged 18-65 years residing in the central district of Erzincan who applied for a health report for marriage purposes. Individuals without a diagnosis of mental retardation who voluntarily agreed to participate were included in the study.

Data collection instrument

Table 1 and Figure 1 present items from a 15-item questionnaire developed by researchers following a literature review, which was employed to measure participants' demographic characteristics and their knowledge and attitudes about SMA. The survey was designed using a five-point Likert scale for attitude scales and was converted to a three-point Likert scale for analysis. The scale does not have a total score, and the surveys were administered via face-to-face interviews.

Sample size and sampling method

According to TUIK 2022 population data, the number of marriages in Erzincan was recorded as 1309. It was projected that approximately 350 marriages would occur in the central district during the study period. The sample size was calculated to be a minimum of 184 with a 5% sampling error and p=0.5, q=0.5 values, and interviews were conducted with 197 individuals within the scope of the study.

Ethical approval

The research received ethical approval from the Erzincan Binali Yıldırım University Clinical Research Ethics Committee (Decision Date: 13.04.2023, Number: 2023-08/4). Both verbal and written consent were obtained from participants, and the principles of the revised Declaration of Helsinki were adhered to throughout the study.

Table 1. Demographic Data of Participants

		n	%
Gender	Female	103	52.3
	Male	94	47.7
Education	Illiterate - primary school	9	4.6
	Middle school	21	10.7
	High school	65	33
	University	102	51.8
Profession	Employee	64	32.5
	Officer	53	26.9
	Retired	5	2.5
	Housewife	22	11.2
	Self-employment	26	13.2
	Not working	27	13.7
Is there a consanguineous marriage (2nd and 3rd degree)	Yes	26	13.2
	No	171	86.8
Do you have any chronic diseases	Yes	4	2
	No	193	98
Do you have a disabled person in your 1st and 2nd degree relatives?	Yes	12	6.1
	No	185	93.9
Have you ever heard of SMA disease?	Yes	178	90.4
	No	19	9.6
Resource	Television-social media	142	72.1
	Physician and other healthcare personnel	12	6.1
	Friend-other	24	12.2

Data analysis

Data analysis was performed using IBM SPSS Statistics 23 (SPSS Inc., Chicago, IL, USA). The normal distribution of data was tested with the Kolmogorov-Smirnov test, numerical data were reported as mean ± standard deviation or median (min-max), and categorical variables were reported as frequency and percentage.

Statistical methods

Descriptive statistical analyses were conducted. The relationship between two categorical variables was examined with Chi-Square and Fisher's Exact tests, and the means of two independent samples were compared using the Independent Samples t-test. The level of statistical significance was set at $p<0.05$.

RESULTS

A total of 197 individuals were included in the study. The average age of the participants was 29.45±7.48 years, and 178 individuals who had previously heard of SMA had been aware of the disease for an average of 4.37 years (max=10, min=1). The demographic data of the participants are presented in Table 1.

A total of 84.8% (n=167) of the participants agreed with the implementation of SMA screening, while 45.2% (n=89) responded with "I don't know" to the statement "SMA is a preventable disease." On the other hand, the response rate for "Will you get tested for SMA?" with "Yes" was 72.6% (n=143). The responses to the attitude and knowledge questions by the participants are illustrated in Figure 1.

No significant relationship was found between the duration of awareness about SMA in years and the desire to undergo SMA testing (p=0.376). Similarly, no significant relationship was detected between age and the desire to be tested (p=0.148).

The desire to be tested and its association with various variables were evaluated using Chi-Square analysis, as presented in Table 2. Accordingly, a significant relationship was found between the desire to be tested and factors such as increased education level, absence of disabled individuals among close relatives, not considering SMA to be a genetically inherited disease, approving of SMA screenings, believing that a negative screening test would be a barrier to marriage, and the belief that screening could not be performed after marriage.

DISCUSSION

In this study, the knowledge levels and attitudes towards SMA screening among individuals applying for a marriage certificate at family health centers in the central district of Erzincan were investigated. The

Table 2. Comparison of variables with desire to have SMA screening

		Will you have an SMA screening test? Yes		No		
		n	%	n	%	p
Gender	Male	72	76.6	22	23.4	0.228
	Female	71	68.9	32	31.1	
Education	Illiterate-primary school	6	67.7	3	33.3	**0.017**
	Middle school	13	61.9	8	38.1	
	High school	40	61.5	25	38.5	
	University	84	82.4	18	17.6	
Do you have a consanguineous marriage?	Yes	21	80.8	5	19.2	0.316
	No	122	71.3	49	28.7	
Do you have a disabled person in your 1st and 2nd degree relatives?	Yes	5	41.7	7	58.3	**0.020***
	No	138	74.6	47	25.4	
Have you ever heard of SMA** disease?	Yes	132	74.2	46	25.8	0.131
	No	11	57.9	8	42.1	
SMA is a genetically inherited disease	I totally agree - I agree	63	78.8	17	21.3	**0.039**
	No idea	65	65	35	35	
	Disagree - completely disagree	15	88.2	2	11.8	
SMA is a preventable disease	I totally agree - I agree	72	77.4	21	22.6	0.133
	No idea	63	70.8	26	29.2	
	Disagree - completely disagree	8	53.3	7	46.7	
I find SMA campaigns correct	I totally agree - I agree	108	78.3	30	21.7	**0.024**
	No idea	24	58.5	17	41.5	
	Disagree - completely disagree	11	61.1	7	38.9	
I think it is correct to perform an SMA screening	I totally agree - I agree	130	77.8	37	22.2	**<0.001**
	No idea	10	43.5	13	56.5	
	Disagree - completely disagree	3	42.9	4	51.7	
If the SMA test is positive, it is an obstacle to marriage	I totally agree - I agree	27	87.1	4	12.9	**0.001**
	No idea	50	59.5	34	40.5	
	Disagree - completely disagree	66	80.5	16	19.5	
SMA test can also be done after marriage	I totally agree - I agree	76	77.6	22	22.4	**0.005**
	No idea	38	58.5	27	41.5	
	Disagree - completely disagree	29	85.3	5	14.7	

findings indicate that a significant portion of the participants lacks adequate awareness about the importance of SMA screening, perceiving it as a mandatory or routine procedure in the pre-marital process. This can be considered a significant deficiency in terms of preventing genetic diseases and promoting the birth of healthy generations.

Without asking for detailed knowledge, participants were only queried whether they had heard of SMA before and for how long. Out of 197 individuals, 178 (90.4%) acknowledged prior awareness of SMA, averaging 4.37 years of knowledge about the disease (min=1, max=10).

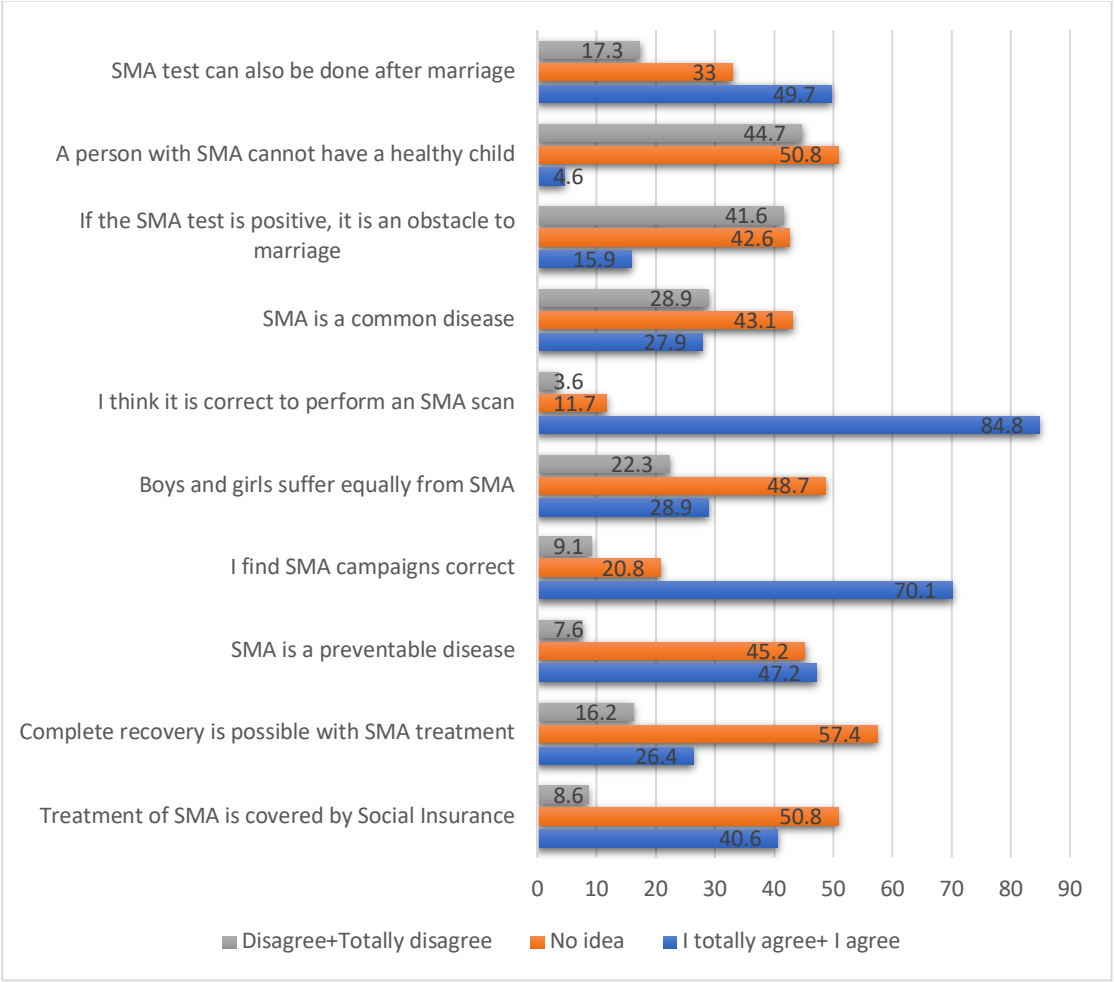


Figure 1. Participants' answers to attitude and knowledge questions

Conversely, 19 individuals (9.6%)reported never having heard of SMA before. It is also noteworthy that TV and social media were the primary sources of information. These findings suggest that while there is a general awareness of SMA in the population, this awareness is still not at a sufficient level. Previous studies have highlighted the critical importance of the public's knowledge level in the early diagnosis and treatment of genetic diseases(10). Additionally, research on the effectiveness of genetic counseling and screening programs has revealed that the level of knowledge within the community is a decisive factor in the success of these programs(11). On the other hand, no significant relationship was found between the duration of awareness of the disease and the desire to undergo SMA screening. This may suggest that the knowledge held is superficial. In this context, the results of our study underscore the importance of increasing public awareness regarding the prevention and management of genetic diseases, highlighting the significant responsibility that falls on health professionals.

While 84.8% (n=167) of participants supported SMA screening, 45.2% (n=89) were unsure about the preventability of SMA. However, 72.6% (n=143) indicated they would consider getting tested. This high level of support could be interpreted as a result of mandatory pre-marital screening procedures, despite participants not having sufficient knowledge about the disease. Factors influencing participation in health screenings include perceived risk, physician recommendations, personal vulnerability, concerns about receiving adverse results, and belief in the benefits of early detection(12, 13). However, it is understood from this study that the participation of the participants in the screening programs stems from the mandatory nature of these programs as part of the marriage process. While this situation has the potential to increase the effectiveness of screening programs and encourage participation, it also

indicates the need for greater efforts to enhance the community's level of knowledge and awareness about the disease.

Public health campaigns and informative programs in the field of SMA screenings are crucial for enhancing societal awareness. Increasing awareness toward the early diagnosis and treatment of genetic diseases can prevent the spread of these conditions and significantly improve individuals' quality of life in the future. Health professionals play a central role in the prevention and management of genetic diseases(14). They must accurately inform patients and emphasize the importance of genetic screenings so that patients view these programs not as obligations but as necessities.

As expected, the desire to undergo testing increased with the participants' level of education. Studies in the literature indicate that the level of education is a significant factor in the desire to undergo genetic testing, with a higher level of education often associated with a greater understanding and a more cautious approach towards genetic tests(15, 16). This situation leads to implications for the need for targeted educational programs to facilitate informed decision-making across different educational strata and public health policy.

The absence of disabled individuals among close relatives and disbelief in the genetic transmission of SMA were seen to increase the willingness to undergo screening. This could be a phenomenon known as "fear of the unknown" or "anxiety about a bad outcome." People may want to detect and manage a potential health issue in advance, thinking that genetic diseases not seen in their families could pose a "hidden" risk to themselves. This trend is reinforced by increasing public awareness of the carrier status and transmission of genetic diseases and the growing accessibility of genetic tests.

Research indicates that individuals' beliefs about the accuracy of health screenings and the validity of these tests can influence their willingness to participate in screening tests(17, 18). The belief in the accuracy of SMA screenings, the perception that a negative screening result could impede marriage, and the belief that screenings cannot be conducted after marriage are significantly associated with the desire to undergo testing. Such beliefs can influence individuals' participation in screening tests and their preference for the timing of these tests. Notably, the belief in the importance of pre-marital screening tests can lead to a higher willingness to undergo such tests before marriage. Health professionals and policymakers should consider these beliefs and perceptions when developing and implementing screening programs.

Study limitations

Limitations of this study include its execution in only three family health centers in the central district of Erzincan, which may limit the generalizability of the findings to the broader population of Erzincan or other regions. Additionally, the use of a researcher-developed questionnaire due to the lack of a standardized measurement tool in the literature may limit the validity and reliability of the survey. Lastly, the assumption that every individual applying for a pre-marital health certificate may potentially have children does not take into account fertility and the desire to have children as independent variables. However, this methodological choice is due to the fact that women's fertility status cannot be biochemically verified and would only be based on self-report. Moreover, even a young woman may not be fertile. Nonetheless, the relatively low average age of the participants included in our study minimizes this limitation.

CONCLUSION

In conclusion, the study conducted among individuals applying for a marriage certificate in the central district of Erzincan reveals a notable gap in awareness and understanding of SMA and the importance of SMA screening. While a majority of the participants are aware of SMA, their knowledge often stems from less formal sources such as TV and social media, which may not provide comprehensive or accurate information. This superficial awareness, coupled with the mandatory nature of pre-marital screening programs, suggests that individuals might not fully grasp the significance of these screenings beyond a bureaucratic requirement. The study underscores the crucial role of health professionals in bridging this knowledge gap, emphasizing the necessity for targeted educational campaigns and personal counseling to foster a deeper understanding of genetic diseases, their prevention, and management.

Moreover, the study highlights the influence of education level, familial history, and personal beliefs on the willingness to undergo SMA screening, pointing to the need for public health strategies that cater to diverse segments of the population. By

enhancing public awareness and understanding of genetic conditions and the benefits of early detection, health authorities can encourage more informed participation in screening programs, thus improving the overall effectiveness of genetic disease prevention efforts.

Acknowledgements: None
Author(s) contribution(s): Concept: GY, EG. Design: GY, EG. Supervision: EG. Data Collection and/or Processing: GY. Analysis and/or Interpretation: EG. Literature Search: GY, EG. Writing Manuscript: GY, EG. Critical Review: EG.
Conflict of interest: The authors declare that they have no financial or non-financial competing interests in relation to this manuscript
Ethical approval: The research received ethical approval from the Erzincan Binali Yıldırım University Clinical Research Ethics Committee (Decision Date: 13.04.2023, Number: 2023-08/4).
Funding: None.
Peer-Review: Externally peer-reviewed.

REFERENCES

1. Mercuri E, Sumner CJ, Muntoni F, Darras BT, Finkel RS. Spinal muscular atrophy. Nature Reviews Disease Primers 2022;8(1):52.
2. Lipnick SL, Agniel DM, Aggarwal R, Makhortova NR, Finlayson SG, Brocato A, et al. Systemic nature of spinal muscular atrophy revealed by studying insurance claims. PLoS One 2019;14(3):e0213680.
3. Kolb SJ, Kissel JT. Spinal muscular atrophy. Neurologic Clinics 2015;33(4):831-46.
4. Wijngaarde CA, Stam M, Otto LA, van Eijk RP, Cuppen I, Veldhoen ES, et al. Population-based analysis of survival in spinal muscular atrophy. Neurology 2020;94(15):e1634-e44.
5. Sugarman EA, Nagan N, Zhu H, Akmaev VR, Zhou Z, Rohlfs EM, et al. Pan-ethnic carrier screening and prenatal diagnosis for spinal muscular atrophy: clinical laboratory analysis of> 72 400 specimens. European journal of human Genetics 2012;20(1):27-32.
6. Mailman MD, Heinz JW, Papp AC, Snyder PJ, Sedra MS, Wirth B, et al. Molecular analysis of spinal muscular atrophy and modification of the phenotype by SMN2. Genetics in Medicine 2002;4(1):20-6.
7. Ogino S, Leonard DG, Rennert H, Ewens WJ, Wilson RB. Genetic risk assessment in carrier testing for spinal muscular atrophy. American journal of Medical Genetics 2002;110(4):301-7.
8. Lipnick SL, Agniel DM, Aggarwal R, Makhortova NR, Finlayson SG, Brocato A, et al. Systemic nature of spinal muscular atrophy revealed by studying insurance claims. PLoS One 2019;14(3):e0213680.
9. Monani UR. Spinal muscular atrophy: a deficiency in a ubiquitous protein; a motor neuron-specific disease. Neuron 2005;48(6):885-95.
10. Meldrum C, Scott C, Swoboda KJ. Spinal muscular atrophy genetic counseling access and genetic knowledge: parents' perspectives. Journal of Child Neurology 2007;22(8):1019-26.
11. Madlensky L, Trepanier AM, Cragun D, Lerner B, Shannon KM, Zierhut H. A rapid systematic review of outcomes studies in genetic counseling. Journal of Genetic Counseling 2017;26(3):361-78.
12. Teo CH, Ng CJ, White A. Factors influencing young men's decision to undergo health screening in Malaysia: a qualitative study. BMJ Open 2017;7(3):e014364.
13. McCaul KD, Tulloch HE. Cancer screening decisions. JNCI Monographs. 1999;1999(25):52-8.
14. Prior TW. Spinal muscular atrophy: a time for screening. Current Opinion In Pediatrics 2010;22(6):696-702.
15. Aro AR, Hakonen A, Hietala M, Lönnqvist J, Niemelä P, Peltonen L, et al. Acceptance of genetic testing in a general population: age, education and gender differences. Patient Education Counseling 1997;32(1-2):41-9.
16. Hafertepen L, Pastorino A, Morman N, Snow J, Halaharvi D, Byrne L, et al. Barriers to genetic testing in newly diagnosed breast cancer patients: Do surgeons limit testing? The American Journal of Surgery 2017;214(1):105-10.
17. Gaugler JE, Pavlik E, Salsman JM, Andrykowski MA. Psychological and behavioral impact of receipt of a “normal” ovarian cancer screening test. Preventive Medicine 2006;42(6):463-70.
18. Tacken MA, Braspenning JC, Hermens RP, Spreeuwenberg PM, Van Den Hoogen HJ, De Bakker DH, et al. Uptake of cervical cancer screening in The Netherlands is mainly influenced by women's beliefs about the screening and by the inviting organization. The European Journal of Public Health 2007;17(2):178-85.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 448-455
https://doi.org/10.30621/jbachs.1390156
RESEARCH ARTICLE

KALLISTATIN LEVELS IN CHILDREN DIAGNOSED WITH BRONCHITIS

Kamile Yucel[1], Sekibe Isik Disci[2], Tugce Duran[3]

[1]KTO Karatay University, Faculty of Medicine, Department of Medical Biochemistry, Konya Türkiye
[2]Seydişehir Public Hospital, Department of Pediatrics, Konya, Türkiye
[3]KTO Karatay University, Faculty of Medicine, Department of Medical Genetics, Konya, Türkiye

ORCID: K.Y. 0000-0003-4088-8932; S.I.D. 0000-0002-8857-9875; T.D. 0000-0002-7353-4527

Corresponding author: Kamile Yucel, **E-mail:** kamile_yucel@hotmail.com
Received: 13.11.2023; **Accepted:** 30.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Yucel K, Isik-Disci S, Duran T. Kallistatin Levels in Children Diagnosed with Bronchitis o J Basic Clin Health Sci 2024; 8: 448-455.

ABSTRACT

Purpose: The aim of this study is to evaluate the levels of kallistatin in the plasma of children diagnosed with bronchitis and to compare them with healthy control subjects.
Material and Methods: A total of 89 participants, including 16 patients diagnosed with bronchitis and taking medication with the diagnosis of tonsillitis (BT), 26 patients diagnosed with bronchitis only (B), and 47 healthy controls who attended the same outpatient clinic for routine control, were included in the study.
Results: When we looked at the differences by dividing the patient group into 2 groups (B, BT), we found that the kallistatin levels in the BT group were significantly higher than both the B group and the healthy control groups. There was no significant difference in kallistatin levels between the healthy controls and the B group. We found that the AUC for kallistatin was 0.631 in the ROC analysis performed between the patient (B+BT) and control groups.
Conclusion: Kallistatin levels were significantly higher in the patient group than in the control group. More comprehensive studies with repeated kallistatin measurements are needed to understand whether kallistatin levels are important in the diagnosis and management of patients with bronchitis and to confirm our findings.

Keywords: Bronchitis, enzyme-linked immunosorbent assay, kallistatin

INTRODUCTION

Bronchitis is an inflammation of the trachea and large airways characterised by coughing. While acute bronchitis is usually caused by upper respiratory tract infections, chronic bronchitis is the result of long-term exposure to irritants such as smoking. Acute bronchitis is a important reason of hospitalization among infectious diseases in children (1,2). Although viruses play a major role in the etiology of acute bronchitis at a high rate (about 90%), it is known that bacteria rarely (about 10%) also play a role. In general, as a result of inflammation caused by microbes such as viruses or bacteria, edema in the mucosa, thickening of the bronchial walls, and increase in bronchial secretion occur. The basis of treating acute bronchitis is symptomatic treatment. The incidence of the disease varies with age and season (1,3,4).

Kallistatin is an endogenous serine proteinase inhibitor that is naturally produced in the body and has many biological functions. Kallistatin has two structural domains, the active site and the heparin binding site. Through these domains, kallistatin exerts vasodilator, anti-angiogenic, antioxidant and anti-inflammatory effects (5,6). It regulates oxidative stress, cell apoptosis, the expression of several genes, and controls the activation of several signalling pathways (5,7). The active site of kallistatin stimulates the expression of endothelial nitric oxide synthase (eNOS) and sirtuin1 (SIRT1), thereby

inhibiting tissue kallikrein activity. Kallistatin forms a covalent complex with its heparin binding site to specifically inhibit human tissue kallikrein. The heparin-binding domain is required to inhibit vascular endothelial growth factor (VEGF)-induced angiogenesis and tumour necrosis factor-α (TNF-α)-induced inflammation (Figure 1) (6,7). Most studies have mentioned the protective effect of increasing kallistatin levels against disease. Studies have shown that the levels of kallistatin are reduced in patients with liver disease, septic shock, severe pneumonia, and acute respiratory distress syndrome also support this information (5,6,8,9). There are also studies reporting that plasma kallistatin levels decrease in sepsis and severe inflammation, and that low kallistatin levels are linked to mortality in community-acquired pneumonia (10,11).

Based on the information in the literature, we set out to evaluate the plasma kallistatin levels at the time of initial diagnosis in children with bronchitis and to compare the data we obtained with the kallistatin levels and other biomarkers of the healthy control group. We do not know of any other published in the literature evaluating kallistatin levels in children diagnosed with bronchitis. Thus, our study is original and contributes to the literatüre.

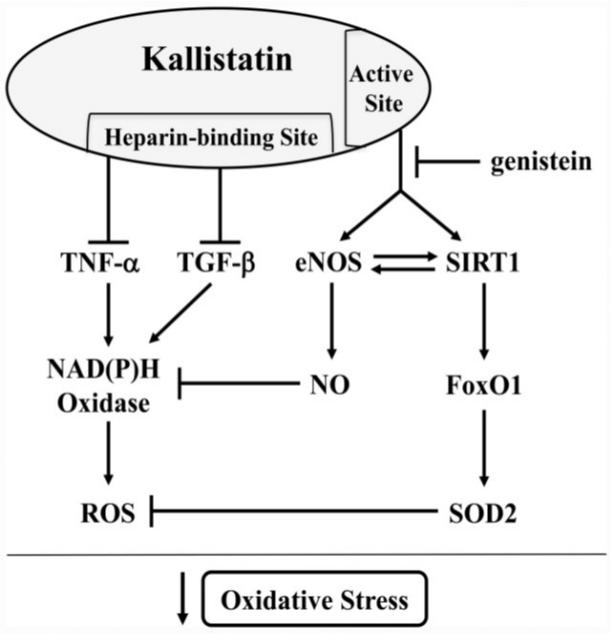


Figure 1. Structure and activity of kallistatin

MATERIAL AND METHODS

Study population

This study was conducted at Seydişehir State Hospital between 10 April 2023 and 10 July 2023. After obtaining the informed consent, the approval of the Ethics Committee and the institutional approval of the hospital, the sample collection procedures were performed. No invasive procedure were performed during the study. A total of 89 participants, including 16 patients diagnosed with bronchitis and taking medication with the diagnosis of tonsillitis (BT), 26 patients diagnosed with bronchitis only (B), and 47 healthy controls without any disease who attended the same outpatient clinic for routine control, were included in the study (Figure 2). The plasma samples of the patient and control groups were obtained from the blood that was taken during the routine analyses of these patients. Plasma samples processed in the laboratory were collected in Eppendorf tubes. It was kept at -80°C until kallistatin measurement. Age, gender, presence of additional diseases, medications and other laboratory information for the patient and control groups were obtained from the hospital's automated system and by interviewing the patients.

Patient group exclusion criteria: >18 years of age, presence of chronic diseases and any other disease (asthma, pneumonia, allergy, influenza, etc.).

Control group exclusion criteria: >18 years of age, presence of any disease such as asthma, pneumonia, allergy, influenza, bronchitis, tonsillitis, drug use etc.

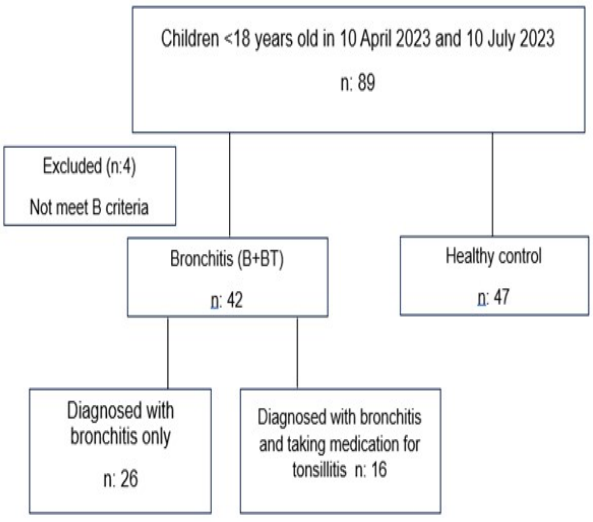


Figure 2. Flowchart used to select groups.

Table 1. Comparison of age and laboratory parameters between patient and control groups.

Variables	Patient (B+BT= n: 42)	Control (n: 47)	P value
[a]Age	2.43 (1.00-3.00)	2.9 (2.00-3.90)	0.71
[b]WBC ($10^3/mm^3$)	9.33±3.33	8.23±2.41	0.08
[b]HGB (g/dL)	12.01±1.33	13.12±1.16	0.00*
[b]RBC ($10^6/mm^3$)	4.65±0.56	4.91±0.46	0.01*
[b]MPV (fL)	9.34±0.79	9.49±0.75	0.34
[b]PDW (fL)	9.85±1.45	10.34±1.52	0.13
[b]PLT ($10^3/mm^3$)	337.07±112.74	329.12±74.35	0.70
[a]MCV (fL)	78.75 (76.27-83.22)	80.90 (78.30-86.60	0.02*
[a]MCH (pg)	26.15 (24.80- 27.70)	27.20 (26.00-28.40)	0.04*
[a]MON ($10^3/mm^3$)	0.77 (0.55-1.07)	0.59 (0.46-0.73)	0.00*
[a]EOS ($10^3/mm^3$)	0.14 (0.05-0.32)	0.18 (0.09-0.30)	0.31
[a]BAS ($10^3/mm^3$)	0.03 (0.02-0.05)	0.04 (0.03-0.05)	0.47
[a]Neutrophil ($10^3/mm^3$)	3.26 (1.39-4.38)	3.19 (2.22-4.04)	0.42
[a]Fasting glucose (mg/dL)	88.00 (85.00-93.00)	85.00 (80.00-89.00	0.07
[a]AST (U/L)	36.50 (30.75-41.25)	26.00 (20.00-32.02)	0.00**
[a]ALT (U/L)	16.00 (12.00-20.50)	15.00 (11.00-18.00)	0.18
[a]CRP (mg/L)	4.10 (1.00-7.50)	1.00 (1.00-3.00)	0.00*
[a]Albumin (g/L)	44.30 (42.54-45.36)	46.32 (44.52-47.22)	0.00**
[b]Urea (mg/dL)	18.13±6.78	19.26±5.70	0.13
[b]Creatinine (mg/dL)	0.39±0.10	0.46±0.12	0.06
[b]Na (mmol/L)	137.60±2.25	138.66±1.79	0.06
[b]K (mmol/L)	4.71±0.49	4.42±0.29	0.00*
[b]Ca (mg/dL)	9.88±0.52	9.95±0.51	0.57
[b]Mg (mg/dL)	2.21±0.20	2.15±0.21	0.06

*a: Mann-Whitney U test, b: Independent samples t-test, *p<0.05, **p<0.01*

Biochemical analysis

Enzyme-linked immunosorbent assay (ELISA) was used to measure plasma kallistatin levels. BT LAB brand Human Kallistatin, SERPINA4 ELISA Kit Catalog No: E3392Hu, Shanghai, China) was used. The manufacturer's instructions were followed for the ELISA study. The results of this study were read using a Multiskan Sky Thermo (A.B.D.) device. A Combi Wash (Human) washer was used in the study. Intra- and inter-assay variation were <5.5% and <10%, respectively. The minimum detectable concentration of kallistatin was 0.022 ng/mL, and the diagnostic interval of the assay was 0.05-20 ng/mL.

Table 2. Comparison of the groups with regard to the kallistatin levels.

Laboratory findings	**Patient (B+BT = n: 42)**		**Control (n: 47)**	**p value**
Kallistatin (ng/mL)	7.20 (4.45-17.10)		4.20 (3.10-8.90)	0.03*
	Patient (B, n: 26)	**Patient (BT, n: 16)**	**Control (n: 47)**	
Kallistatin (ng/mL)	[a, c] 5.45 (2.78-7.10)	[a, b] 19.50 (11.30-22.10)	[b, c] 4.20 (3.10-8.80)	a:<0.01** b: <0.01** c: >0.05

Data are expressed as median-IQR, Statistics for two groups: Mann-Whitney U, Statistics for three groups: Kruskal Wa Test, *p<0.05, **p<0.01

Statistical analysis

SPSS for Windows version 18.0 was used for data entry and statistical analysis (SPSS Inc. Chicago, IL, USA). The conformity of the data to the normal distribution was tested using visual and analytical methods. Arithmetic mean, standard deviation (SD), and median (1st quartile-3rd quartile (IQR)) were used to evaluate numerical data. Categorical data were summarised using frequencies and percentages. To compare categorical data, the chi-square test ($\chi 2$) was used. Non-normally distributed numerical data were compared using the Man-Whitney U test. The Kruskal-Wallis test was used for the evaluation of three or more groups with numerical data that were not normally distributed. Pairwise comparisons between groups with significant Kruskal-Wallis test results were post-hoc Man-Whitney U test with Bonferroni correction. The Spearman correlation coefficient has been used to analyse the correlations between numerical variables that are not normally distributed. Spearman correlation coefficients were considered to be highly correlated if they were less than 0.19, low if they were 0.20-0.39, moderate if they were 0.40-0.69, high if they were 0.70-0.89, and very high if they were greater than 0.90. The diagnostic decision-making properties of kallistatin levels in predicting disease were assessed using receiver operating characteristics (ROC) curves. Statistical significance has been defined as $p < 0.05$.

Ethical Approval

The KTO Karatay University, Faculty of Medicine, Ethics Committee for Non-Drug and Medical Device Research, has approved this study (Date: 31.03.2023, Number: 2023/011) in accordance with the tenets of the Declaration of Helsinki. The article complied with research and publication ethics.

RESULTS

Twenty-six (12F, 14M) patients diagnosed with bronchitis (B), 16 (10F, 6M) patients diagnosed with bronchitis and tonsillitis (BT), 47 (26F, 21M) healthy controls were included in this study. Among the patients diagnosed with bronchitis (n: 42), there were also patients (n: 16) who used drugs to treat tonsillitis. There were no other comorbidities in the patient group. Mean age of patients (B+BT) was 2.43 years, mean age of controls was 2.9 years. Between patient (B+BT) and control group there was no difference in age and gender ($p>0.05$).

When comparing the patient (B+BT) and control groups in terms of laboratory parameters, HGB, RBC, MCV, MCH, albumin were significantly lower, AST, CRP, K, monocytes, and kallistatin were significantly higher in the patient group compared to the control group ($p<0.05$). The kallistatin levels were 7.20 ng/mL (4.45 - 17.10) in the patient group and 4.20 ng/mL (3.10 - 8.90) in the control group. Table 1 and Table 2 show the laboratory data of the patient and control groups. When we compared the laboratory parameters of the patient group within themselves, there was no statistically significant difference between the B and BT patient groups in terms of any other parameter except kallistatin ($p>0.05$). The kallistatin levels in group B were 5.45 ng/mL (2.78-7.10), and kallistatin levels in group BT were 19.50 ng/mL (11.30-22.10).

Comparing the laboratory parameters of the 3 groups (B, BT and control), AST and CRP levels were significantly higher in both the B and BT groups than in the healthy control. In addition, kallistatin levels were significantly higher in the BT group than in the B

Table 3. Spearman's correlation coefficients of patient and control groups

	Correlations	Correlation coefficient (r)	Level	P value
Patient (B+BT= n: 42)	Age - Creatinine	0.740	High	p<0.01
	Age - Urea	0.710	High	
	Kallistatin - Creatinine	-0.469	Moderate	
	Kallistatin - Age	-0.397	Low	
Control (n: 47)	Kallistatin - Creatinine	-0.538	Moderate	
	Kallistatin - D vit	0.457	Moderate	
	Kallistatin - Mg	0.446	Moderate	
	Kallistatin - Age	-0.440	Moderate	
	Age - Creatinine	0.409	Moderate	

Statistics: Spearman's correlation test, p < 0.05 statistical significance

and control groups (p<0.01). There was no statistically significant difference in kallistatin between the B and control groups (p>0.05) (Table 2). When all participants' data were analysed for correlations, there was a moderately significant negative correlation between kallistatin and age (r: -0.554, p: 0.00), kallistatin and creatinine (r: -0.581, p: 0.00), a moderately significant positive correlation weakly significant positive correlation between kallistatin and vitamin D (r: 0.381, p: 0.009), kallistatin and WBC (r: 0.360, p: 0.001). Table 3 shows the significant correlation values of the patient and control groups.

We performed ROC curves and AUC analyses to investigate the predictive power of kallistatin. We found that the AUC for kallistatin was 0.631 (p=0.033, CI=0.512- 0.751) in the ROC analysis performed between the patient (B+BT) and control groups. Figure 3 shows the ROC analysis graph.

DISCUSSION

In this study, healthy controls and patients diagnosed with bronchitis were compared for kallistatin levels. Our findings showed that kallistatin levels were significantly higher in the patient groups than in the control groups.

Bronchitis is among the lower respiratory tract infections that are frequently seen at early ages. There is no specific laboratory parameter that can be used to diagnose bronchitis (3,12). There are studies that suggest a significant association between low hemoglobin levels and lower respiratory tract infections (13-15). In a 2021 study of 101 infants diagnosed with acute bronchiolitis and 62 healthy controls, HGB levels were found to be lower in the patient group and it has been reported that HGB levels and the severity of bronchiolitis have a significantly negative correlation (16). In our study, there was no patient diagnosed with anemia, but HGB, RBC, MCV and MCH levels were significantly lower in the patient group than in the healthy control group. When we compared the patient group as B and the BT group, there was no significant difference in laboratory parameters between the groups.

CRP is an acute phase reactant that increases in the blood during inflammatory reactions. CRP elevation is seen in most inflammatory diseases. In a study of 149 infants diagnosed with bronchiolitis, increased plasma CRP levels and the CRP/albumin ratio were associated with the need for advanced respiratory support in infants with acute bronchiolitis. Plasma albumin is a well-known negative acute phase reactant and its low level may indicate a poor prognosis. A study showing that hypoalbuminemia increases the risk of apnea in bronchiolitis supports this information. Another study showed an association between hypoalbuminemia and the need for neonatal intensive care (17). In our study, we found that the levels of CRP were higher and the levels of albumin were lower in the group of patients compared to the control group, which supports the literature.

Kallistatin is a protein produced naturally in the body and has many biological functions. Kallistatin is known to play an important role in the prevention of several diseases, through anti-angiogenic, anti-

inflammatory, anti-apoptotic and antioxidant effects. (6,7,18,19). Kallistatin levels are reduced in animal models of hypertension, septic shock, diabetes mellitus and liver neoplasia (20-23). However, in patients with diabetic vascular complications and rheumatoid disease, kallistatin levels have been shown to be elevated (24-26). Kallistatin has been studied in various diseases, but there is no literature investigating the relationship between bronchitis and kallistatin. If we look at the studies that have investigated kallistatin levels in community-acquired pneumonia, there are data that kallistatin levels are lower in such diseases than in the control group. A 2013 study of 54 patients with community-acquired pneumonia and 17 healthy controls reported that lower kallistatin levels were associated with more severe disease risk and increased mortality. A study investigating kallistatin in community-acquired pneumonia (CAP) found that kallistatin was significantly depleted in CAP patients (8.3 µg/mL) compared to healthy subjects (17.2 µg/mL). In the study, they found an AUC value of 0.683 for kallistatin levels measured on the first day of ICU admission between the surviving and non-surviving groups. In the study, low plasma kallistatin levels on day 1 were associated with the development of septic shock and acute respiratory distress syndrome in patients with severe CAP. In addition, it was stated in the study that there was a negative significant correlation between kallistatin levels and CRP levels (10). The results of another study, conducted in 2018 on 53 children and 55 healthy controls diagnosed with community-acquired pneumonia, reported that the kallistatin levels in the patient group at admission were significantly higher than in the control group. When this study made a comparison by dividing the patient group into 3 subgroups (hospitalised, those requiring mechanical ventilation and ex) according to their complications, it also reported that the kallistatin levels in these groups were significantly higher than in the healthy control group (27). The results of the study by Hangül M. et al. (27) are contrary to other information and expectations in the literature. To the best of our knowledge, this is the first study to show the role of kallistatin in children who have been diagnosed with bronchitis. Kallistatin levels were significantly higher in the patient group than in the control group in our study. In the ROC analysis performed between the patient (B+BT) and control groups, we found that the AUC for kallistatin was 0.631. When we looked at the differences by dividing

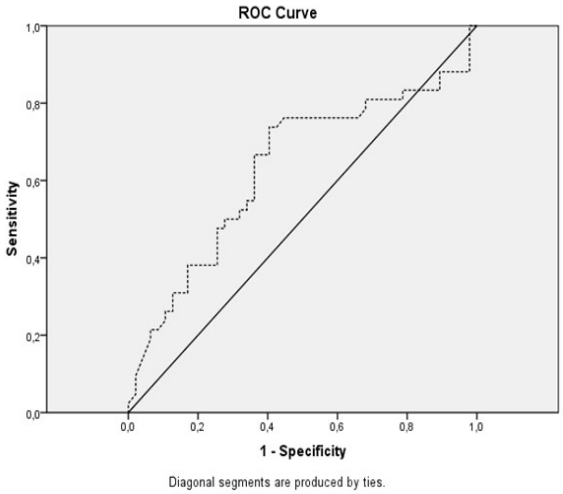


Figure 3. The ROC analysis for kallistatin (AUC: 0.631).

the patient group into 2 groups (B, BT), we found that the kallistatin levels in the BT group were significantly higher than both the B group and the healthy control groups. Between the healthy controls and the B group, there was no significant difference in kallistatin levels. We believe that the significantly higher kallistatin levels in the BT group compared to the other two groups may be due to the use of antibiotics to treat tonsillitis in patients in the BT group, or that kallistatin levels may have increased during the recovery period. We could not find any information in the literature on the effect of antibiotic use on kallistatin levels to compare with our study.

Study limitations

The low number of patients in the study and the fact that some patients diagnosed with bronchitis were treated for tonsillitis are important limitations. Most studies have emphasised the need for repeated measurements for kallistatin. Another limitation of our study is the use of plasma samples taken at the time of initial diagnosis and the inability to perform repeated measurements of kallistatin.

CONCLUSION

We designed this study expecting kallistatin levels to be lower in the group of patients with bronchitis, but the fact that kallistatin levels were not statistically different in the patient group compared to the healthy control group showed that kallistatin measurement was not useful for the diagnosis and follow-up of bronchitis. As a result, kallistatin levels were significantly higher in the patient group than in the

control group. The high kallistatin levels in the patient group were due to the high kallistatin levels in the group of 16 patients (BT) with bronchitis who were treated for tonsillitis. There was no difference in kallistatin levels between the group diagnosed with bronchitis only and the healthy control group. More comprehensive studies with repeated kallistatin measurements are needed to understand whether kallistatin levels are important in the diagnosis and management of bronchitis and to confirm our findings.

Author Contributions: KY, SID planned to work. KY, TD did ELISA's work of plasma. KY, SID, TD designed the study and wrote the paper. SID obtained clinical data. KY performed statistical analysis. KY sent the article to the journal. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Conflict of Interests: No competing interests declared.

Ethical Approval: The Ethics Committee for Non-Drug and Medical Device Research of KTO Karatay University, Faculty of Medicine, has approved this study in accordance with the tenets of the Declaration of Helsinki (Decision Date: 31.03.2023, Number: 2023/011). The article complied with research and publication ethics. Informed consent was obtained from all of the individuals who participated in this study.

Funding: None

REFERENCES

1. Kinkade S, Long NA. Acute bronchitis. Am Fam Physician 2016;1;94(7):560-5.
2. Clark TW, Medina MJ, Batham S, Curran MD, Parmar S, Nicholson KG. Adults hospitalised with acute respiratory illness rarely have detectable bacteria in the absence of COPD or pneumonia; viral infection predominates in a large prospective UK sample. J Infect 2014;69(5):507-15.
3. Fretzayas A, Moustaki M. Etiology and clinical features of viral bronchiolitis in infancy. World J Pediatr 2017;13(4):293-9.
4. Sung FC, Wei CC, Muo CH, et al. Acute bronchitis and bronchiolitis infection in children with asthma and allergic rhinitis: A retrospective cohort study based on 5,027,486 children in taiwan. Viruses 2023;15(3):1-10.
5. Lin WC, Chen CW, Chao L, Chao J, Lin YS. Plasma kallistatin in critically ill patients with severe sepsis and septic shock. PLoS One 2017;12(5):1-15.
6. Wang G, Zou J, Yu X, Yin S, Tang C. The antiatherogenic function of kallistatin and its potential mechanism. Acta Biochim Biophys Sin (Shanghai) 2020;52(6):583-9.
7. 7. Chao J, Li P, Chao L. Kallistatin: double-edged role in angiogenesis, apoptosis and oxidative stress. Biol Chem 2017;398(12):1309-17.
8. Lin WC, Chen CW, Huang YW, et al. Kallistatin protects against sepsis-related acute lung injury via inhibiting inflammation and apoptosis. Sci Rep 2015;12463:1-16.
9. Liu Y, Bledsoe G, Hagiwara M, Shen B, Chao L, Chao J. Depletion of endogenous kallistatin exacerbates renal and cardiovascular oxidative stress, inflammation, and organ remodeling. Am J Physiol Renal Physiol 2012;303(8):1230-8.
10. Lin WC, Lu SL, Lin CF, et al. Plasma kallistatin levels in patients with severe community-acquired pneumonia. Crit Care 2013;17(1):1-10.
11. Kim T, Suh GJ, Kwon WY, Kim KS, Jung YS, Shin SM. Lower serum kallistatin level is associated with 28-day mortality in patients with septic shock. J Crit Care 2018;48:328-33.
12. Mahowald M, Shahan B, Forbes D. Respiratory conditions: Lower respiratory tract infections. FP Essent 2019;486:19-25.
13. Behairy O, Mohammad O, Elshaer O. Iron-deficiency anemia as a risk factor for acute lower respiratory tract infections in children younger than 5 years. Egypt J Bronchol 2018;12(3):352-7.
14. Mourad S, Rajab M, Alameddine A, Fares M, Ziade F, Abou MB. Hemoglobin level as a risk factor for lower respiratory tract infections in Lebanese children. N Am J Med Sci 2010;2(10):461-6.
15. Ramakrishnan K, Harish PS. Hemoglobin level as a risk factor for lower respiratory tract infections. Indian J Pediatr 2006;73(10):881-3.
16. Celik E, Celik SF, Güngör S, Dursun A. Impact of anaemia on the severity of acute bronchiolitis in infants. Journal of Nepal Paediatric Society 2021; 41(1): 73-9.
17. Rodriguez-Gonzalez M, Estepa-Pedregosa L, Estalella-Mendoza A, et al. Routine laboratory test to assess the need of respiratory support in acute bronchiolitis. Pediatr Pulmonol 2022;57(5):1339-47.
18. Gao L, Yin HS, Smith RJ, Chao L, Chao J. Role of kallistatin in prevention of cardiac remodeling after chronic myocardial infarction. Lab Invest 2008;88:1157-66.
19. Miao RQ, Agata J, Chao L, Chao J. Kallistatin is a new inhibitor of angiogenesis and tumor growth. Blood 2002;100:3245-52.

20. Chao J, Chai KX, Chen LM, et al. Tissue kallikrein-binding protein is a serpin. I. Purification, characterization, and distribution in normotensive and spontaneously hypertensive Shen B, Hagiwara M, Yao YY, Chao L, Chao J. Salutary effect of kallistatin in salt-induced renal injury, inflammation, and fibrosis via antioxidative stress. Hypertension 2008;51:1358-1365.
21. Chao J, Chen LM, Chai KX, Chao L. Expression of kallikrein-binding protein and alpha 1-antitrypsin genes in response to sex hormones, growth, inflammation and hypertension. Agents Actions Suppl 1992;38(1):174-181.
22. Luo Q, Siconolfi-Baez L, Annamaneni P, Bielawski MT, Novikoff PM, Angeletti RH. Altered protein expression at early-stage rat hepatic neoplasia. Am J Physiol Gastrointest Liver Physiol 2007;292:1272-1282.
23. McBride JD, Jenkins AJ, Liu X, et al. Elevated circulation levels of an antiangiogenic SERPIN in patients with diabetic microvascular complications impair wound healing through suppression of Wnt signaling. J Invest Dermatol 2014;134:1725-1734.
24. Jenkins AJ, McBride JD, Januszewski AS, et al. Increased serum kallistatin levels in type 1 diabetes patients with vascular complications. J Angiogenes Res 2010;2:19:1-8.
25. Wang CR, Chen SY, Shiau AL, et al. Upregulation of kallistatin expression in rheumatoid joints. J Rheumatol 2007;34:2171-2176.
26. Hangul M, Ozturk D, Keti DB, Demirkan FG, Kose M. Plasma kallistatin levels in children with community-acquired pneumonia. Pediatr Allergy Immunol Pulmonol 2018;31(3):146-50.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 456-463
https://doi.org/10.30621/jbachs.1401258
RESEARCH ARTICLE

ANGIOGENIC REGULATORS DURING ALPINE SKIING TRAINING

Metin Polat[1], Inayet Gunturk[2], Duran Demiryurek[3]

[1] Sivas Cumhuriyet University, Faculty of Sport Sciences, Sivas, Turkey
[2] Nigde Omer Halisdemir University, Faculty of Health Sciences, Department of Midwifery, Nigde, Turkey
[3] Erciyes University, Institute of Health Sciences, Kayseri, Turkey

ORCID: M.P. 0000-0001-7299-0531; I.G. 0000-0002-8299-1359; D.D. 0000-0003-3545-1082

Corresponding author: Metin Polat, **E-mail:** polat.metin@gmail.com
Received: 07.12.2023; **Accepted:** 20.01.2024; **Available Online Date:** 31.05.2024

Cite this article as: Polat M, Gunturk I, Demiryurek D. Angiogenic Regulators During Alpine Skiing Training. J Basic Clin Health Sci 2024; 8: 456-463.

ABSTRACT

Purpose: The present study evaluates angiogenesis response through the determination of acute changes in hypoxia inducible factor 1 alpha, vascular endothelial growth factor, erythropoietin and endostatin levels measured after a single-session slalom and giant slalom trainings.
Material and Methods: A total of 20 volunteer male athletes average age of 22.16 ± 4.86 years with no health problems, and with international alpine skiing competition experience were included in the study. At the outset, the height, body weight and VO_2max values of the volunteers was measured, and a giant slalom training lasting 2.5 hours was performed after a week on a giant slalom course. The volunteers were then asked not to exercise for a week, and slalom training was performed lasting 2.5 hours on a slalom course. The endostatin, erythropoietin, hypoxia inducible factor 1 alpha, and vascular endothelial growth factor levels of the volunteers were examined from 5 ml venous blood samples drawn into biochemistry tubes 20 minutes before and as soon as trainings over both the giant slalom and slalom trainings.
Results: A significant increase was determined in the hypoxia inducible factor 1 alpha, vascular endothelial growth factor, erythropoietin and endostatin levels after both the giant slalom and slalom trainings ($p < 0.05$).
Conclusion: These increases observed in the angiogenesis markers suggests that a single-session giant slalom and slalom trainings induces angiogenesis responses.

Keywords: Capillarization, Alpine Skiing, Performance, Ischemia

INTRODUCTION

Alpine Skiing competitions comprise two speed and two technical categories, differentiated by the turning radius, speed and course length. The speed category includes downhill and super giant slalom (super G) (1), while the technique category includes slalom (SL) and giant slalom (GS) (2). Although a high level of anaerobic power is required, aerobic power is also substantially important in alpine skiing (3). In addition, the use of explosive power has also been reported during skiing activities (4), and eccentric movements have been reported to be widely used during alpine skiing competitions (5). Significant intramuscular pressure increases have been reported during the turning phase, resulting in a more anaerobic load (2). All such activities result in metabolic processes, including muscle ischemia, hypoxia and changes in ion concentrations in the body (6). In addition, the high degree of knee flexion and the continuous muscle contractions, typically experienced during skiing competitions contribute to a decrease in oxygen delivery to the active muscles. In conclusion, the blood perfusion of active muscle is decreased due to a greater decrease in the blood volume, increased lactate accumulation and an unproportionally high heartbeat (7). Hereby, muscle ischemia and a greater

dependency on the anaerobic metabolism is experienced (2).

Capillarization resulting from adaptation due to training can help the athlete cope with the metabolic and mechanical conditions that cause fatigue resulting from eccentric contractions, while providing an increase in the amount of blood delivered to the active muscles during exercise and a positive effect on performance (8). Muscle capillarization is important for the delivery of nutrients and oxygen to the exercise muscles. A higher capillary density may increase the muscle-blood exchange surface and decrease the oxygen diffusion distance and increase the erythrocyte mean transit time (9).

Hypoxic conditions trigger a series of physiological and pathophysiological responses and adaptations such as vasculogenesis, angiogenesis and erythropoiesis to protect the organism (10). Angiogenesis refers to the growth of new capillary vessels from the previously present vessels (11) and is stimulated by the metabolic cycle and hypoxia (12) as well as by the mechanical factors such as shear stress and the passive stretching of muscle fiber (13,14). High-intensity training has been considered a powerful stimulus for angiogenesis, since metabolic demand, blood deoxygenation and blood flow are increased together with the increased workload (15). High-intensity interval training and low intensity endurance training have been shown to exert equal effects on angiogenesis in those who are untrained (16).

Regulating proteins such as hypoxia inducible factor 1 alpha (HIF-1α), vascular endothelial growth factor (VEGF), erythropoietin (EPO) and endostatin are known to play a key role in the proangiogenetic process. HIF-1α, VEGF and EPO support angiogenesis, while endostatin has a tendency to halt the angiogenetic process (17). Previous studies have investigated the chronic angiogenesis response to training, while studies of acute angiogenesis response are limited. To our best of our knowledge, there has been no study to date on angiogenesis as a response to alpine skiing competition or training.

The present study, therefore, investigates the acute changes in HIF-1α, VEGF, EPO and endostatin levels in post-training for both slalom and giant slalom, which are included in the alpine skiing technical category, and also to evaluate the angiogenesis response that is considered to have a positive effect on skiing performance.

MATERIAL AND METHODS

Volunteer groups and ethical approval

Included in the study were 20 volunteers male athletes average age of 22.16 ± 4.86 years with no health problems, and with international alpine skiing competition experience. Approval for the study was obtained from the Clinical Investigations Ethics Board of Erciyes University (Decision Date: 20.01.2017, Number: 2017/32) prior to the start of the study. All testing and training procedures were fully explained, and written informed consent was obtained for each participant. The study was supported by the Erciyes University Scientific Research Projects Coordination Unit, project number TYL-2017-7493.

Experimental Design

At the outset of the study the height, body weight and VO_2max values of the volunteers were measured. A giant slalom training session lasting 2.5 hours was completed a week later on a giant slalom course homologated by the International Ski Federation (FIS). The volunteers were then asked not to exercise for a week, and a further slalom training session was performed lasting 2.5 hours on a slalom course that was also homologated by the FIS. The study participants all provided a 5 ml venous blood sample 20 minutes before and as soon as trainings over both the giant slalom and slalom training sessions, drawn into biochemistry tubes, and the obtained samples were sent immediately to the Department of Medical Biochemistry of the Faculty of Medicine of the Erciyes University.

Measurements

The height of the volunteers was measured while standing against the wall using a height scale with 0.01 cm sensitivity, and the body weight was measured using an electronic scale with 0.1 kg sensitivity. An exercise protocol with incremental running test was applied on a motorized treadmill (h/p/Cosmos Quasar med, Nussdorf-Traunstein, Germany) to determine the VO_2max of the athletes. Throughout the VO_2max test, breath-by-breath gas measurements were taken using an indirect calorimetric system (Quark PFT Ergo, Cosmed Srl, Rome, Italy) which was calibrated before the test to the manufacturer's instructions. The test started with running at a 0% incline at a speed of 7 km/hour, and the speed was increased by 1 km/hour every minute. The athletes were asked to continue the exercise until they were exhausted. The criteria for having reached

the VO_2max for the athletes were accepted as reaching the maximal heart rate (220-age), a respiratory exchange ratio (RER) greater than 1.10 and a plateauing of oxygen intake despite increased exercise intensity (18). The highest 15 second oxygen intake value at the time when at least these two of the criteria were met was accepted as the VO_2max value (ml/kg/min).

Blood Analyses

The blood samples sent to the biochemistry laboratory were centrifuged at +4°C at 1500 g for 15 minutes, and the separated serum samples were stored at -80 °C in small pieces until the study date. The levels of HIF-1α (Cusabio Technology LLC, Cat No: CSB-E12112h), VEGF (ThermoFisher Scientific, Cat No: KHG0111), EPO (ThermoFisher Scientific, Cat No: BMS2035-2) and endostatin (Cusabio Technology LLC, Cat No: CSB-E07973h) in the serum samples were determined using the ELISA technique.

Training Applications for Giant Slalom and Slalom

The giant slalom training course was prepared by the national Turkish alpine skiing team coach using a giant slalom course that was homologated by the FIS. A total of 36 giant slalom gates, 28 meters apart were laid out on the course, which had a 300-meter altitude difference. The volunteers trained for 2.5 hours on the prepared giant slalom course.

The slalom training course was also prepared by the national Turkish alpine skiing team coach on a slalom course homologated by the FIS. A total of 42 slalom gates, 10 meters apart were laid out on the course, which had a 120-meter altitude difference. The volunteers trained for 2.5 hours on the prepared slalom course.

Table 1. Descriptive Information of the Volunteers

	n	$\overline{X}$ ±SD	Min.	Max.
Age (years)	20	22.16±4.86	18	27
Height (cm)		178.07±3.42	169	182
Body weight (kg)		80.69±8.46	67	98
VO_2max ($ml/kg^{1}/min^{-1}$)		50.71±2.87	45.41	54.22

Statistical Analysis

The data obtained in the study were analyzed using IBM SPSS Statistics (Version 25.0. Armonk, NY: IBM Corp.). After conducting descriptive analyses, the data were evaluated to determine the normality of distribution using a Shapiro-Wilk test, skewness and kurtosis levels and histogram and Q-Q and P-P graphics and were found to be non-normally distributed. A Wilcoxon Signed Ranks Test was used to compare the blood analyses before and after the training sessions. The level of significance was set at $p < 0.05$.

RESULTS

The age, height, body weight and VO_2max levels of the volunteers participating in the study are presented in Table 1.

The pre- and post-giant slalom training Endostatin, EPO, HIF-1α and VEGF levels are presented in Table 2, in which the Endostatin, EPO, HIF-1α and VEGF levels can be seen to be significantly increased following giant slalom training ($p<0.05$).

The pre- and post-slalom training Endostatin, EPO, HIF-1α , and VEGF levels are presented in Table 3, where Endostatin, EPO, HIF-1α and VEGF levels can be seen to be significantly increased after slalom training ($p<0.05$).

Table 2. Comparison of the Pre-and Post- Giant Slalom Training Values

		n	Median (25-75%)	z	p
Endostatin (ng/mL)	Pre-training	20	15.33 (9.92-21.25)	-2.156	0.031*
	Post-training		17.49 (10.63-25.40)		
EPO (mIU/mL)	Pre-training		6.07 (5.40-6.85)	-3.288	0.001*
	Post-training		8.95 (7.13-10.25)		
HIF-1α (pg/mL)	Pre-training		292.39 (203.57-372.55)	-3.724	< 0.001*
	Post-training		331.84 (251.11-415.24)		
VEGF (pg/mL)	Pre-training		125.09 (94.23-155.32)	-2.373	0.018*
	Post-training		130.39 (96.15-172.20)		

*$p < 0.05$

DISCUSSION

HIF-1α has been reported to be a transcription factor mediating adaptive responses to low cellular oxygen levels (19) and has also been reported to transcriptionally activate hundreds of genes associated with angiogenesis in cancer, exercise and ischemia, energy metabolism, nutrient transport and cell migration (20). Furthermore, HIF-1α gene transfer has been demonstrated to increase muscle perfusion and collateral vessel formation in the ischemic rabbit hind limbs (21). Decreased arterial O2 saturation and PiO2 of exercise origin has been reported to activate HIF-1, and HIF-1α to independently stimulate angiogenesis and thus facilitate muscle oxygen extraction (22).

The increased O2 consumption during exercise leads to a decrease in PiO2 levels, while the addition of environmental hypoxia to exercise further decreases the already lowered PiO2 (22). Exercise in hypoxia or normoxia has been reported to increase muscle HIF-1α mRNA (23), protein content, and also the degree of nucleus translocation of HIF-1α and DNA binding activity (24). These observations, independent of the arterial O2 saturation, suggest that any decrease in PiO2 of exercise origin is likely sufficient to completely activate HIF-1α (22).

The increased intramuscular pressure resulting from the high intensity contractions during alpine skiing may limit blood flow to the working skeletal muscle and may even stop it altogether (25). This condition results in decreased tissue oxygenation and the muscle becomes ischemic due to the decrease in oxygen supplied to the functioning muscles. A decrease in oxygen saturation in the quadriceps muscle has been reported in young well-trained skiers during GS and SL (2).

HIF-1α levels were found to be significantly increased after both slalom and giant slalom training in the present study ($p < 0.05$), suggesting that the level of hypoxemia to which skeletal muscles are exposed during a single unit alpine skiing training session increases HIF-1α production and triggers angiogenesis.

HIF-1 activation has been reported to be important in VEGF release in skeletal muscle angiogenesis upon exercise (26), and VEGF release has also been reported to occur through HIF-1α transcription (19). Additionally, VEGF has been reported to be of vital importance for training originated angiogenesis (27).

VEGF has been identified as a key regulator of physiological angiogenesis (11,28), and has been shown to increase during exercise (29). An inadequate level of O2 in skeletal muscle tissue has been shown during exercise, and this has been demonstrated to cause an increase in VEGF mRNA and protein levels in skeletal muscle tissue (30,31). Such an increase in VEGF mRNA and protein levels, it has been suggested, may cause new capillary vessels along the chemical gradient of VEGF (32). On the other hand, increased physical exercise has been reported to increase total skeletal muscle blood flow, while emergent mechanical stress has been reported to play a very important role in angiogenesis through increased VEGF production (33).

Nevertheless, interval training has been suggested to be as equally effective as endurance training in increasing capillarization (16). Repeated exercise is reported to have the potential to complicate muscle oxygen homeostasis, since a single exercise session is associated with muscle hypoxia (34). Increased VEGF levels have been recorded after a single unit of exercise (35). It has also been reported that higher intensity exercise produces a higher venous plasma VEGF level than lower intensity exercise (36).

Loading intensity may be high during alpine skiing training. Heartrate, VO2 and blood lactate levels have been recorded at 201.7 + 2 bpm, 38.50 + 2.34 ml/kg/min, and 10.13 + 0.43 mmol/L, respectively

Table 3. Comparison of the Pre-and Post- Slalom Training Values

		n	Median (25-75%)	z	p
Endostatin (ng/mL)	Pre-training	20	24.71 (15.20-37.07)	-3.527	< 0.001*
	Post-training		33.35 (26.15-44.46)		
EPO (mIU/mL)	Pre-training		6.97 (5.40-8.62)	-3.516	< 0.001*
	Post-training		10.47 (7.63-12.50)		
HIF-1α (pg/mL)	Pre-training		328.18 (213.92-399.96)	-2.722	0.006*
	Post-training		365.74 (328.91-447.85)		
VEGF (pg/mL)	Pre-training		118.01 (94.69-172.80)	-3.154	0.002*
	Post-training		137.40 (99.51-196.32)		

*$p < 0.05$

during a single giant slalom running (37). In addition, alpine skiing training sessions include consecutive interval loadings. Athletes reach the start point using the mechanical plant after completing the training run on a course, and approximately 15 minutes pass between the two loading periods.

The present study also revealed significantly increased VEGF levels after both GS and SL, concurring with the results of the studies mentioned above ($p < 0.05$). The obtained data suggest that a single unit alpine skiing training increases VEGF release and stimulates angiogenesis.

One of genes that HIF-1α regulates its transcriptions to produce cellular adaptation against low PO2 is EPO (38). It is well known that the primary function of EPO is to stimulate erythropoiesis and to increase the oxygen transfer to working muscles during exercise (39). Furthermore, it has been suggested that EPO leads to a decrease in lactate production during submaximal exercise (40), affecting also local vascular and skeletal muscle properties by stimulating localized angiogenesis and slow oxidative fibril-type changes, respectively (41,42).

There is evidence that EPO may stimulate an increase in mitochondrial activity, and thus increase the oxidative metabolic properties of human muscle fibers (43). EPO may possibly stimulate, whether directly or indirectly, an increase in muscle oxidative capacity, although this has yet to be confirmed. Erythropoietin also has been suggested to exert angiogenic effects on growing or repairing tissues (41). Taking these findings in consideration together, it can be suggested that EPO has an effect similar to endurance training, which is known to induce muscle mitochondrial biogenesis and growth, and to increase oxidative enzymatic activity, angiogenesis induction and the transition to muscle fiber type (39).

After the GS and SL trainings EPO levels were found to be significantly increased in the present study ($p < 0.05$). In the light of the above information, the elevated EPO levels after skiing training suggest that EPO induces the physiological adaptations required by both angiogenesis and alpine skiing.

Endostatin has been shown to inhibit angiogenesis by preventing the proliferation and migration of endothelial cells (10). Endostatin prevents the progression of atherosclerosis (44), and the primary growth of tumors and metastasis (45) by inhibiting angiogenesis. A significant increase was observed in endostatin levels after both giant slalom and slalom training in the present study ($p<0.05$), and this increase is thought to be an anti-angiogenic effect against the angiogenic effect originating from the increased HIF-1α, VEGF and EPO levels.

That said, several authors have reported that endostatin may function as an angiogenic modulator rather than an anti-angiogenic agent (46,47). Schmidt et al. (46,48) determined both the proangiogenic and anti-angiogenic dose-dependent effects of endostatin, although further studies are required to definitively determine the angiogenic modulator effect of endostatin.

In parallel to the findings of the present study, Gu et al. (49) reported an increase in plasma endostatin levels in circulation after a treadmill exercise test due to exercise proportionate to the intensity of the exercise. Suhr et al. (10) reported a significant increase in the plasma concentration of endostatin following physical exercise, independent of such exogenously induced stimuli as normobaric hypoxia and mechanical loading. Sponder et al. (50), in their study of healthy young male and female volunteers, reported a significant increase in serum endostatin levels, by 23.6% and 26.92% in females and males, respectively during a maximal cycling exercise test.

In addition, endostatin has been reported to lead to vasorelaxation by increasing in vitro cytosolic nitric oxide (NO) production (47), and it is therefore considered to be one of the mechanisms regulating blood flow during high intensity physical activity (10). It has been stated that vasorelaxation provides more O2 and metabolites to the tissue, which is an advantage during exercise (50). The increase in endostatin levels reported in the present study suggests that endostatin release may be induced due to the increased requirement for vasodilation in the active tissues during exercise, in addition to the anti-angiogenic effects of endostatin.

CONCLUSION

In conclusion, a significant increase was observed in HIF-1α, VEGF, EPO and Endostatin levels after a single-session slalom and giant slalom trainings in the present study. This increase observed in angiogenesis markers supports that a single unit alpine skiing training induces the production of angiogenesis. An increase in the amount of capillarization in response to alpine skiing training will result in an increased capacity of blood flow in the active muscles. Thus, it will be possible to contribute to optimal performance by providing more oxygen and substrates to the active muscles during loading

and more efficient removal of accumulated metabolic wastes.

Acknowledgements: The authors thank to Erciyes University Scientific Research Projects Coordination Unit (project number TYL-2017-7493) for the support this study.
Author Contributions: Conception: Metin Polat, İnayet Güntürk, Duran Demiryürek. Design: Metin Polat, İnayet Güntürk. Supervision: Metin Polat. Fundings: Metin Polat. Materials: İnayet Güntürk. Data Collection: Metin Polat, İnayet Güntürk, Duran Demiryürek. Analysis: Metin Polat, İnayet Güntürk. Literature Review: Metin Polat, İnayet Güntürk, Duran Demiryürek. Writing: Metin Polat. Critical Review: Metin Polat, İnayet Güntürk
Conflict of interest: The authors declare no conflict of interest
Ethical approval: The study was approved by Clinical Investigations Ethics Board of Erciyes University (Decision Date: 20.01.2017, Number: 2017/32).
Funding: Erciyes University Scientific Research Projects Coordination Unit (project number TYL-2017-7493).

REFERENCES

1. White AT, Johnson SC. Physiological Aspects and Injury in Elite Alpine Skiers. Sport Med Eval Res Exerc Sci Sport Med 1993;15(3):170-178.
2. Szmedra L, Im J, Nioka S, Chance B, Rundell KW. Hemoglobin/myoglobin oxygen desaturation during Alpine skiing. Med Sci Sports Exerc 2001;33(2):232-236.
3. Andersen RE, Montgomery DL. Physiology of Alpine Skiing. Sport Med An Int J Appl Med Sci Sport Exerc 1988;6(4):210-221.
4. Tesch PA. Aspects on muscle properties and use in competitive Alpine skiing. Med Sci Sports Exerc. 1995;27(3):310-314.
5. Berg HE, Eiken O, Tesch PA. Involvement of eccentric muscle actions in giant slalom racing. Med Sci Sports Exerc 1995;27(12):1666-1670.
6. Seifert JG, Kipp RW, Amann M, Gazal O. Muscle damage, fluid ingestion, and energy supplementation during recreational alpine skiing. Int J Sport Nutr Exerc Metab 2005;15(5):528-536.
7. Petrofsky JS, Hendershot DM. The interrelationship between blood pressure, intramuscular pressure, and isometric endurance in fast and slow twitch skeletal muscle in the cat. Eur J Appl Physiol Occup Physiol 1984;53(2):106-111.
8. Kyröläinen H, Takala TES, Komi P V. Muscle damage induced by stretch-shortening cycle exercise. Med Sci Sports Exerc 1998;30(3):415-420.
9. Egginton S. Invited review: activity-induced angiogenesis. Pflugers Arch 2009;457(5):963-977.
10. Suhr F, Brixius K, De Marées M, et al. Effects of short-term vibration and hypoxia during high-intensity cycling exercise on circulating levels of angiogenic regulators in humans. J Appl Physiol 2007;103(2):474-483.
11. Prior BM, Yang HT, Terjung RL. What makes vessels grow with exercise training? J Appl Physiol 2004;97(3):1119-1128.
12. Hudlicka O, Milkiewicz M, Cotter MA, Brown MD. Hypoxia and expression of VEGF-A protein in relation to capillary growth in electrically stimulated rat and rabbit skeletal muscles. Exp Physiol 2002;87(3):373-381.
13. Høier B, Rufener N, Bojsen-Møller J, Bangsbo J, Hellsten Y. The effect of passive movement training on angiogenic factors and capillary growth in human skeletal muscle. J Physiol 2010;588(19):3833-3845.
14. Gliemann L, Gunnarsson TP, Hellsten Y, Bangsbo J. 10-20-30 training increases performance and lowers blood pressure and VEGF in runners. Scand J Med Sci Sports 2015;25(5):e479-e489.
15. Jensen L, Bangsbo J, Hellsten Y. Effect of high intensity training on capillarization and presence of angiogenic factors in human skeletal muscle. J Physiol 2004;557(Pt 2):571-582.
16. Cocks M, Shaw CS, Shepherd SO, et al. Sprint interval and endurance training are equally effective in increasing muscle microvascular density and eNOS content in sedentary males. J Physiol 2013;591(3):641-656.
17. Shah I, Malik MO, Khan MJ, Fatima S, Baxendale RH, Habib SH. Endostatin Concentration In Plasma Of Healthy Human Volunteers. J Ayub Med Coll Abbottabad 2017;29(2):200-206.
18. Howley ET, Bassett DR, Welch HG. Criteria for maximal oxygen uptake: review and commentary. Med Sci Sports Exerc 1995;27(9):1292-1301.
19. Niemi H, Honkonen K, Korpisalo P, et al. HIF-1α and HIF-2α induce angiogenesis and improve muscle energy recovery. Eur J Clin Invest 2014;44(10):989-999.
20. Qutub AA, Popel AS. A computational model of intracellular oxygen sensing by hypoxia-inducible factor HIF1α. J Cell Sci 2006;119(16):3467-3480.

21. Patel TH, Kimura H, Weiss CR, Semenza GL, Hofmann L V. Constitutively active HIF-1alpha improves perfusion and arterial remodeling in an endovascular model of limb ischemia. Cardiovasc Res 2005;68(1):144-154.
22. De Smet S, D'Hulst G, Poffé C, Van Thienen R, Berardi E, Hespel P. High-intensity interval training in hypoxia does not affect muscle HIF responses to acute hypoxia in humans. Eur J Appl Physiol 2018;118(4):847-862.
23. Slivka DR, Heesch MWS, Dumke CL, Cuddy JS, Hailes WS, Ruby BC. Human skeletal muscle mRNAResponse to a single hypoxic exercise bout. Wilderness Environ Med 2014;25(4):462-465.
24. Ameln H, Gustafsson T, Carl ‡, et al. Physiological activation of hypoxia inducible factor-1 in human skeletal muscle. FASEB J 2005;19(8):1009-1011.
25. Sjøgaard G, Savard G, Juel C. Muscle blood flow during isometric activity and its relation to muscle fatigue. Eur J Appl Physiol Occup Physiol 1988;57(3):327-335.
26. Lindholm ME, Rundqvist H. Skeletal muscle hypoxia-inducible factor-1 and exercise. Exp Physiol 2016;101(1):28-32.
27. Hoier B, Hellsten Y. Exercise-induced capillary growth in human skeletal muscle and the dynamics of VEGF. Microcirculation 2014;21(4):301-314.
28. Ferrara N, Gerber HP, LeCouter J. The biology of VEGF and its receptors. Nat Med 2003;9(6):669-676.
29. Gu JW, Shparago M, Tan W, Bailey AP. Tissue endostatin correlates inversely with capillary network in rat heart and skeletal muscles. Angiogenesis 2006;9(2):93-99.
30. Laufs U, Werner N, Link A, et al. Physical training increases endothelial progenitor cells, inhibits neointima formation, and enhances angiogenesis. Circulation 2004;109(2):220-226.
31. Tang K, Breen EC, Gerber HP, Ferrara NMA, Wagner PD. Capillary regression in vascular endothelial growth factor-deficient skeletal muscle. Physiol Genomics 2004;18(1):63-69.
32. Adair TH. Growth regulation of the vascular system: an emerging role for adenosine. Am J Physiol Regul Integr Comp Physiol 2005;289(2).
33. Brown MD, Hudlicka O. Modulation of physiological angiogenesis in skeletal muscle by mechanical forces: involvement of VEGF and metalloproteinases. Angiogenesis 2003;6(1):1-14.
34. Lundby C, Calbet JAL, Robach P. The response of human skeletal muscle tissue to hypoxia. Cell Mol Life Sci 2009;66(22):3615-3623.
35. Hiscock N, Fischer CP, Pilegaard H, Pedersen BK. Vascular endothelial growth factor mRNA expression and arteriovenous balance in response to prolonged, submaximal exercise in humans. Am J Physiol Heart Circ Physiol 2003;285(4).
36. Wahl P, Jansen F, Achtzehn S, et al. Effects of high intensity training and high volume training on endothelial microparticles and angiogenic growth factors. PLoS One 2014;9(4).
37. Polat M. An examination of respiratory and metabolic demands of alpine skiing. J Exerc Sci Fit 2016;14(2).
38. Mounier R, Pialoux V, Schmitt L, et al. Effects of acute hypoxia tests on blood markers in high-level endurance athletes. Eur J Appl Physiol 2009;106(5):713-720.
39. Larsen MS, Vissing K, Thams L, et al. Erythropoietin administration alone or in combination with endurance training affects neither skeletal muscle morphology nor angiogenesis in healthy young men. Exp Physiol 2014;99(10):1409-1420.
40. Thomsen JJ, Rentsch RL, Robach P, et al. Prolonged administration of recombinant human erythropoietin increases submaximal performance more than maximal aerobic capacity. Eur J Appl Physiol 2007;101(4):481-486.
41. Ribatti D. Erythropoietin and tumor angiogenesis. Stem Cells Dev 2010;19(1):1-4.
42. Wang L, Jia Y, Rogers H, et al. Erythropoietin contributes to slow oxidative muscle fiber specification via PGC-1α and AMPK activation. Int J Biochem Cell Biol 2013;45(7):1155-1164.
43. Plenge U, Belhage B, Guadalupe-Grau A, et al. Erythropoietin treatment enhances muscle mitochondrial capacity in humans. Front Physiol. 2012;3.
44. Zeng X, Chen J, Miller YI, Javaherian K, Moulton KS. Endostatin binds biglycan and LDL and interferes with LDL retention to the subendothelial matrix during atherosclerosis. J Lipid Res 2005;46(9):1849-1859.

45. O'Reilly MS, Boehm T, Shing Y, et al. Endostatin: an endogenous inhibitor of angiogenesis and tumor growth. Cell 1997;88(2):277-285.
46. Schmidt A, Wenzel D, Ferring I, et al. Influence of endostatin on embryonic vasculo- and angiogenesis. Dev Dyn 2004;230(3):468-480.
47. Wenzel D, Schmidt A, Reimann K, et al. Endostatin, the proteolytic fragment of collagen XVIII, induces vasorelaxation. Circ Res 2006;98(9):1203-1211.
48. Schmidt A, Addicks K, Bloch W. Opposite effects of endostatin on different endothelial cells. Cancer Biol Ther 2004;3(11):1162-1166.
49. Gu J-W, Gadonski G, Wang J, Makey I, Adair TH. Exercise increases endostatin in circulation of healthy volunteers. BMC Physiol 2004;4(1):2.
50. Sponder M, Sepiol K, Lankisch S, et al. Endostatin and physical exercise in young female and male athletes and controls. Int J Sports Med 2014;35(13):1138-1142.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 464-473
https://doi.org/10.30621/jbachs.1404333
RESEARCH ARTICLE

DETERMINING THE RELATIONSHIP BETWEEN PERCEIVED GENDER ROLES AND MENOPAUSAL SYMPTOMS IN WOMEN

Fatma Nur Duman[1], Didem Simsek Kucukkelepce[2], Zehra Golbasi[3]

[1]Faculty of Health Sciences, Department of Obstetrics and Gynecology Nursing, Lokman Hekim University, Ankara, Turkey
[2]Faculty of Health Sciences, Midwifery Department, Lokman Hekim University, Ankara, Turkey
[3]Faculty of Health Sciences, Department of Obstetrics and Gynecology Nursing, Lokman Hekim University, Ankara, Turkey

ORCID: F.N.D. 0000-0001-9736-2769; D.S.K. 0000-0003-0001-2581; Z.G. 0000-0002-0410-7433

Corresponding author: Fatma Nur DUMAN, **E-mail:** fatmanurduman8@gmail.com
Received: 13.12.2023; **Accepted:** 21.04.2024; **Available Online Date:** 31.05.2024

Cite this article as: Duman FN, Simsek-Kucukkelepce D, Golbası Z. Determining the Relationship Between Perceived Gender Roles and Menopausal Symptoms in Women. J Basic Clin Health Sci 2024; 8: 464-473.

ABSTRACT

Purpose: This research was directed to determine the connection betwixt perceived gender roles and menopausal symptoms experienced in women.
Material and Methods: The research was designed in descriptive type and was made in family centers in Turkey. The study group of the research consists of 465 women. “Personal Information Form”, “Menopause Rating Scale” “BEM Gender Roles Inventory” were used to collect the data. Research data were evaluated with SPSS 27 and descriptive statistics, Kolmogorov-Smirnov, Kruskal Wallis, Mann Whitney U test were used.
Results: Women's MRS total mean score was 17.45±8.37, somatic complaints mean score was 6.39±3.50, psychological complaints mean score was 7.31±3.75, urogenital complaints mean score was 3,74±2,77. It was detected that 48.2% of the women adopted the androgynous role. A statistically discernible difference was detected betwixt the mean scores of MRS urogenital complaints according to the gender roles adopted by the women participating in the study ($p=0.024<0.05$). The mean urogenital complaints sub-dimension score of women who perceive themselves as masculine was found to be statistically significantly lower than the other gender role groups.
Conclusion: It has been determined that women who describe themselves as masculine experience less urogenital complaints from menopausal symptoms than women who describe themselves as feminine, androgynous and ambiguous.

Keywords: Gender role, gender role inventory, menopause, menopausal symptoms, nursing.

INTRODUCTION

The climacteric period, which includes premenopause, menopause, and postmenopause stages, represents the transition from the reproductive age to the post-reproductive age (1). Premenopausal period; it is the late reproductive period when fertility begins to decline and a woman begins to see changes in her menstrual cycles. Menopausal period; it is the period in which bleeding does not occur for at least 12 months after the last menstrual bleeding. The postmenopausal period, is defined as the period of time that starts after menopause and lasts until the beginning of the old age period (2-4). Although dynamic changes in physical, mental and social health are experienced during the climacteric period, these changes can negatively affect women's quality of life (5,6). The age at menopause differs according to many factors, and the average age at menopause in Turkey is 47 (7). Considering that the average life expectancy at birth

in our country is 81 years, it is seen that women expend a significant part of their lives in the menopause period. Menopausal women experience complaints about many different body systems, from vasomotor complaints to emotional symptoms, from sexual function changes to musculoskeletal problems (8,9). These complaints can cause negative changes in women's well-being, body image perception and self-esteem (9-11). Although the severity of these complaints varies from person to person, they are affected by many factors. Factors affecting this process include the age and type of menopause, perception of social support, socio-cultural and socio-economic conditions, and gender perception. It has been reported that one of the factors affecting menopausal complaints is personality traits (12,13). Sex is a feature related to reproductive functions that explains the biological aspect of being male or female. Gender identity is the way individuals define themselves in terms of their feminine or masculine personality traits. Gender role, is when individuals perceive their own identity as male or female and reveal the behaviors and attitudes required by their gender (14). Traditionally, assumptions about gender have suggested that the development of knowledge, skills, interests, behaviors and social roles will be different according to the gender of individuals (15). Contrary to the traditional approach, it is emphasized that it is possible for individuals to be psychologically healthy by turning to gender roles that are satisfying, appropriate and allow for self-actualization (16,17). In the light of this information, it is thought that women's being psychologically healthy and compatible can only be achieved by turning to gender roles that are suitable for them, and that the complaints they experience during menopause may be related to their gender role. In the literature, there is no research examining the effect of women's perceptions of gender roles on menopausal complaints. Therefore, this research was conducted to determine the connection betwixt women's perceptions of gender roles and menopausal symptoms.

MATERIAL AND METHODS

Design

The study was approved by the Non-Interventional Ethics Committee of Lokman Hekim University (Date: 27.05.2021 Decision No: 2021/056) and permission from the family center coordinator where the research was conducted. The research is planned as a descriptive study. It was conducted between April 2022 and June 2022 in family centers working under a metropolitan municipality in Turkey. In family centers, there are physical development courses, various social activities such as music and painting, and children's clubs.

Sample

The target group of the study be made up of women aged 45 and over who applied to family centers for any reason. The sampling calculation of the study was based on the study conducted by Pérez-Herrezuelo et al. (2020). Accordingly, it was aimed to reach 400 women as a result of the sampling calculation made with an effect size of 0.254, a margin of error of 0.05, and a power of 99%. The study was completed with 465 women (18). G Power 3.1.9.2 Package program was used to calculate the sample size.

Inclusion Criteria

- Being between the ages of 45-65,
- Being in the menopausal or postmenopausal period,
- Not having undergone surgical menopause,
- Absence of a diagnosed psychiatric illness.

Dependent Variables of the Study

Scores obtained from the Menopause Rating Scale

Independent Variables of the Study

Women's perceived gender roles and their descriptive characteristics.

Measurement

Data in the study were collected using the “Personal Information Form”, “Menopause Rating Scale” (MRS) and “BEM Sex-Role Inventory” (BSRI).

- Personal Information Form

The 9-question questionnaire was developed by the researchers and included questions about identifying characteristics (age, employment status, marital status, educational status, income status, menopause-specific and gender perception characteristics).

- Menopause Rating Scale

The validity and reliability study of the scale developed by Schneider, Heinemann et al. measuring the severity of menopausal symptoms in the Turkish population was evaluated by Can Gürkan (2005) (19). The four-point Likert-type and 11-item scale has 3 sub-dimensions: “somatic complaints, psychological complaints and urogenital complaints”. Somatic complaints sub-dimension consists of 1st, 2nd, 3rd and 11th items and the highest score that can be obtained from this sub-dimension is 16. Psychological

complaints sub-dimension includes 4th, 5th, 6th and 7th items and the highest score that can be obtained from this sub-dimension is 16. Urogenital complaints sub-dimension consists of 8th, 9th and 10th items and the highest score that can be obtained from this sub-dimension is 12. The lowest score that can be obtained from the scale is 0 and the highest score is 44. An increase in the total score indicates that menopausal symptoms increase and quality of life decreases. While the total Cronbach's alpha internal consistency coefficient of the scale was 0.84, it was found to be 0.65 for the somatic symptom, 0.79 for the psychological symptoms, and 0.72 for the urogenital symptoms.[19] In this study, Cronbach's alpha coefficient was determined to be 0.85 for the total score of the scale, 0.68 for the somatic symptoms, 0.82 for the psychological symptoms, and 0.65 for the urogenital symptoms.

• BEM Sex-Role Inventory

Dökmen (1999) conducted the validity and reliability study of the BEM Gender Role Inventory developed by Bem in 1974 in Turkish culture (20). The seven-point Likert scale, consisting of 40 items, consists of two sub-dimensions: femininity and masculinity. The median values of the scores obtained from the sub-dimensions describe the gender role of the participants. The cut-off score for the femininity sub-dimension in the original scale was 111; The cut-off point for the masculinity sub-dimension was determined as 104. Femininity sub-dimension items in the scale: 1, 3, 5, 6, 7, 9, 11, 14, 16, 19, 22, 23, 24, 30, 31, 34, 36, 37, 39.40 while masculinity sub-dimension items It is 2, 4, 8, 10, 12, 13, 15, 17, 18, 20, 21, 25, 26, 27, 28, 29, 32, 33, 35, 38.

- If the femininity score, which is calculated by calculating the total score of the femininity and masculinity sub-dimensions separately for each individual, is below the median of the femininity score (≤111), and the masculinity score is above the median of the masculinity score (>104), the individual is considered "***masculine***".
- If the femininity score is above the median of femininity (> 111) and the masculinity score is below the median of masculinity (≤104), the individual is considered "***feminine***".
- If the femininity score is above the median of femininity (>111), and the masculinity score is above the median of masculinity (>104), the individual is defined as "***androgynous (both feminine and masculine)***".
- If the femininity score is below the median of femininity (≤111), and the masculinity score is below the median of masculinity (≤104), the individual is described as "***ambiguous***".

While the total Cronbach's alpha internal consistency coefficient of the scale was 0.79, it was 0.73 for the femininity and 0.75 for the masculinity (20). In this study, Cronbach's alpha value was 0.88 for the total score, 0.84 for femininity and 0.85 for masculinity.

Data Collection and Analysis

The data were collected through face-to-face interviews with women. SPSS 27.0 (SPSS Inc., Chicago, IL, USA) program was used for data evaluation. The homogeneity of the data set was evaluated using the Kolmogorov-Smirnov Test and Kurtosis-Skewness values. As a result, it was determined that the data did not show normal distribution. Numerical variables that do not fit the normal distribution are given as mean, standard deviation, median, minimum and maximum values, while categorical variables are given as frequencies (percentiles). Kruskal Wallis Analysis of Variance and Mann Whitney U Test were used for numerical variables that did not show normal distribution for the difference between groups.

Since the data were non-parametric, Permanova analysis, which is a non-parametric multivariate analysis of variance, was used to compare the mean MRS scores of women according to independent variables and Bray-Curtis method was used as the similarity index in this analysis. Statistically discernible level was accepted as $p<0.05$.

RESULTS

Table 1 shows the distribution of some demographic, menopausal, and gender-related characteristics of the participants. The mean age of the women was 51.13±5.53 and the mean age of the last menstrual period was 46.65±3.92. Among the women who participated in our research, 84.7% are unemployed, 87.5% are married and 38.3% are primary school graduates. It was set up that 42.6% of women perceived the menopause period as stress or depression, 53.8% were satisfied with having a female gender identity, and 18.7% would prefer to be a male gender (Table 1).

Table 1. Distribution of Some Demographic, Menopausal-Specific and Gender Perception Characteristics (n=465)

Features		X±SD	Median	Min-Max
Age		51,13±5,53	50	45-65
Last Menstrual Age		46,65±3,92	46	37-59
			n	**%**
Working Status	Working		71	15,3
	Not working		394	84,7
Marital Status	Single		58	12,5
	Married		407	87,5
Educational Status	Uneducated		22	4,7
	Primary school		178	38,3
	Secondary school		74	15,9
	High school		127	27,3
	University		64	13,8
Income status	Income less than expenses		206	44,3
	Income equal to expenses		211	45,5
	Income more than expenses		48	10,3
Perception of Menopause Period	Relaxation		74	15,9
	Inability to bear children		45	9,7
	Loss		34	7,3
	Stress/Depression		198	42,6
	Aging		104	22,4
	A natural process		10	2,2
Satisfaction with Having a Female Gender Identity	Very satisfied		134	28,8
	Satisfied		250	53,8
	Indecisive		44	8,6
	Not glad		22	4,7
	Not satisfied at all		19	4,1
Gender She Would Prefer If He Had The Chance	Female		378	81,3
	Male		87	18,7

Table 2 shows the distribution of women's MRS total and sub-dimension mean scores. In our study, the mean MRS total score of women was 17.45±8.37, and it was found to be at a moderate level. When we look at the MRS sub-dimensions, it was set up that the mean score of the sub-dimension of somatic complaints was 6.39±3.50, the mean score of the sub-dimension of psychological complaints was 7.31±3.75, and the mean score of urogenital complaints was 3.74±2.77 (Table 2).

Table 3 shows the comparison of women's mean MRS scores according to independent variables. The mean MRS total and sub-dimension scores of women show a significant difference according to marital status, educational status, income level, perception of menopause period and level of satisfaction with the gender they have ($p<0.05$) (Table 3).

The distribution of gender roles adopted by women is presented in Table 4. In our study, it was determined that 48.2% of women adopted androgynous role, 30.1% adopted feminine role, 12.7% adopted ambiguous role and 9.0% adopted masculine role (Table 4).

Table 5 shows the comparison of the MRS sub-dimension and total score averages according to the gender roles adopted by women. In our study, no statistically discernible difference was found between the mean MRS total score, somatic complaints and psychological complaints sub-dimension scores according to the gender roles adopted by women ($p>0.05$). A statistically discernible was detected betwixt the mean MRS urogenital complaints sub-dimension scores according to the gender roles adopted by women ($p=0.024<0.05$). Statistical difference in which the group performed in order to

Table 2. Distribution of Women's MRS Total and Sub-Dimensional Scores (n=465)

Features	X±SD	Median	Min-Max
MRS Total Score	17,45±8,37	18	0-43
Somatic Complaints	6,39±3,50	6	0-16
Psychological Complaints	7,31±3,75	7	0-16
Urogenital Complaints	3,74±2,77	3	0-12

determine where this originates from Mann-Whitney U test, as a result of self-describing as masculine women urogenital complaints sub-dimension points on average self-management from an average of points describing women as feminine as it was found to be significantly lower. At the same time, the mean urogenital complaint sub-dimension score of women who feel androgynous (3.50±2.89) was found to be significantly lower than the score of women who feel feminine.

DISCUSSION

In our study, women's MRS mean total score was 17.45±8.37, somatic complaints mean score was 6.39±3.50, psychological complaints mean score was 7.31±3.75, and urogenital complaints mean score was 3,74±2,77 (Table 2). In the study conducted by Tümer and Kartal (2018) to determine the relationship betwixt menopausal attitudes and menopausal complaints in women, the mean MRS total score was 14.65±7.62, the mean score of the somatic complaints 2.85±1.99, the mean score of the psychological complaints 8.96±4.94, and the urogenital score average of 5.35±3.09 (21). In the study of Khatoon et al. (2018) to evaluate menopausal symptoms of women in North India, it was reported that the most common symptom reported was joint and muscle disorders, followed by depressive mood symptoms (22). In the study of Zhang et al. (2021) to compare the severity of menopausal symptoms experienced by perimenopausal and postmenopausal women and included 4063 women, it was reported that women, regardless of group, most frequently experienced urogenital complaints including sexual problems (23). In the study of Ji et al. (2021), it was found that women experienced physical symptoms most frequently (24). The reason why our research results differ from the results of other studies may be that the severity and frequency of menopausal complaints differ from culture to culture, person to person, region to region and country to country. Sociodemographic status, cultural characteristics, and differences in lifestyle also change the frequency and perception of menopausal symptoms (9).

As a result of multivariate analysis, a significant difference was determined in the mean score of urogenital complaints sub-dimension according to the marital status of the women and it was found that the mean score of urogenital complaints sub-dimension was higher in married women (Table 3). In other studies in the literature, similar to our results, married women were reported to experience urogenital symptoms more (25-27). The reason for this may be active sexual life, fertility and physical deformations seen due to advancing age.

A significant difference was found between the mean scores of somatic complaints, psychosocial complaints and MRS total score according to the educational level of the women and it was determined that the severity of menopausal symptoms decreased with increasing educational level (Table 3). In a study similar to our results, it was reported that symptoms were felt milder with increasing educational level (22). The reason for this may be the increase in the level of awareness of the subject as the level of education increases. At the same time, considering that the level of health literacy increases as the level of education increases, women with a high level of education can learn and apply methods of coping with menopausal symptoms.

In our study, it was found that as the income level of women increased, their experience of menopausal symptoms decreased (Table 3). In one study, it was reported that women with low income levels experienced more menopausal symptoms (28); in another study, it was reported that as women's economic status improved, their knowledge and attitudes towards menopause increased and thus they experienced fewer menopausal symptoms (29). they experienced fewer menopausal symptoms (29). The reason for this situation is thought to be the increase in the perceived income level of women, which increases their access to health services and thus their level of awareness about menopausal symptoms.

In our study, it was determined that the mean total and subscale scores of MRS showed a significant difference according to women's perceptions of menopause and that women who perceived the menopause period negatively experienced

Table 3. Comparison of Women's MRS Total and Sub-Dimension Mean Scores According to Independent Variables (n=465)

Independent Variables			**MRS**			
			Somatic Complaints	**Psychological Complaints**	**Urogenital Complaints**	**Total Score**
		n	**X±SD**	**X±SD**	**X±SD**	**X±SD**
Working Status	Working	71	6,26±3,94	6,67±3,66	3,16±2,78	16,11±8,47
	Not working	394	6,41±3,42	7,43±3,76	3,84±2,76	17,69±8,34
F=1,934 η^2=0,012	p=0,123	**Test and p Value**	F=0,104 p=0,747	F=2,462 p=0,117	F=3,611 p=0,058	F=2,153 p=0,143
Marital Status	Single	58	5,93±3,56	7,55±4,05	2,36±2,19	15,84±8,21
	Married	407	6,45±3,50	7,28±3,71	3,94±2,79	17,68±8,38
F=8,496 η^2=0,052	**p=0,000***	**Test and p Value**	F=1,141 p=0,286	F=0,256 p=0,613	F=16,966 **p=0,000**	F=2,452 p=0,118
Educational Status	Uneducated(1)	22	7,86±2,47	8,04±2,38	4,22±2,63	20,13±5,89
	Primary school(2)	178	6,75±3,66	7,52±3,97	3,74±2,85	18,03±8,96
	Secondary school(3)	74	6,74±3,49	7,66±3,44	4,37±2,72	18,78±7,87
	High school(4)	127	5,96±3,42	7,46±3,60	3,62±2,81	17,06±8,05
	University(5)	64	5,29±3,24	5,79±3,87	3,06±2,45	14,15±7,82
F=2,184 η^2=0,019	**p=0,011***	**Test and p Value**	F=3,744 **p=0,005**	F=3,240 **p=0,012**	F=2,170 p=0,071	F=3,887 **p=0,004**
		Significant Difference	1>4 2>5 1>5 3>5	1>5 3>5 2>5 4>5		1>5 3>5 2>5 4>5
Income status	Income less than expenses(1)	206	6,93±3,45	8,04±3,75	4,05±2,84	19,03±8,21
	Income equal to expenses(2)	211	5,78±3,46	6,63±3,71	3,31±2,67	15,74±8,18
	Income more than expenses(3)	48	6,72±3,06	7,16±3,41	4,29±2,70	18,18±8,63
F=3,443 η^2=0,022	**p=0,002***	**Test and p Value**	F=5,922 **p=0,003**	F=7,598 **p=0,001**	F=4,773 **p=0,009**	F=8,511 **p=0,000**
		Significant Difference	1>2	1>2	1>2 2>3	1>2
Perception of Menopause Period	Relaxation(1)	74	5,00±3,79	5,44±8,80	2,72±2,66	13,17±8,50
	Inability to bear children(2)	45	4,51±2,89	6,37±3,56	3,68±3,21	14,57±7,93
	Loss(3)	34	6,58±3,20	6,52±2,69	4,20±2,44	17,32±7,02
	Stress/Depression(4)	198	7,64±3,29	8,53±3,68	4,20±2,81	20,38±8,22
	Aging(5)	104	6,08±3,15	7,40±3,33	3,54±2,49	17,03±6,96
	A natural process(6)	10	2,90±2,37	3,10±2,68	2,80±2,78	8,80±6,37
F=6,346 η^2=0,022	**p=0,000***	**Test and p Value**	F=13,753 **p=0,000**	F=12,667 **p=0,000**	F=3,704 **p=0,003**	F=13,573 **p=0,000**
		Significant Difference	3>1 5>2 4>1 3>6 5>1 4>5 3>2 4>6 4>2 5>6	4>1 3>6 5>1 4>5 4>2 4>6 2>6 5>6 4>3	3>1 4>1 4>5	3>1 4>3 4>1 3>6 5>1 4>5 4>2 4>6 2>6 5>6
Satisfaction with Having a Female Gender Identity	Very satisfied(1)	134	5,46±3,33	6,42±3,63	3,29±2,49	15,18±7,60
	Satisfied(2)	250	6,60±3,44	7,25±3,61	3,74±2,80	17,60±8,30
	Indecisive(3)	44	5,82±3,55	8,22±3,73	3,82±2,43	17,87±7,59
	Not glad(4)	22	8,68±2,35	9,86±3,90	5,18±3,51	23,72±8,52
	Not satisfied at all(5)	19	8,63±4,19	9,63±3,89	5,10±3,28	23,36±6,69
F=3,695 η^2=0,031	**p=0,000***	**Test and p Value**	F=7,523 **p=0,000**	F=7,200 **p=0,000**	F=3,561 **p=0,007**	F=8,463 **p=0,000**
		Significant Difference	2>1 4>2 3>1 5>2 4>1 4>3 5>1 5>3	2>1 5>1 3>1 4>2 4>1 5>2	4>1 5>1 4>2 5>2	2>1 5>2 4>1 4>3 5>1 5>3 4>2
Gender She Would Prefer If He Had The Chance	Female	378	6,26±3,47	7,09±3,75	3,64±2,70	17,00±8,35
	Male	87	6,91±3,64	8,29±3,58	4,17±3,03	19,39±8,23
F=2,511 η^2=0,016	p=0,058	**Test and p Value**	F=2,431 p=0,120	F=7,408 p=0,070	F=2,553 p=0,111	F=5,782 p=0,071

**Permanova Analysis*

Table 4. Distribution of Gender Roles Adopted by Women (n=465)

Gender Roles	n	%
Masculine	42	9,0
Feminine	140	30,1
Androgynous	224	48,2
Ambiguous	59	12,7
Total	**465**	**100,0**

menopausal symptoms more severely (Table 3). In a study similar to our results, it was reported that women who perceived the menopause period negatively experienced more symptoms (30). The reason for this may be that the positive attitude towards menopause helps to accept menopause as a part of the developmental process and raises awareness about coping with symptoms.

In our study, it was found that women who were dissatisfied with having a female gender experienced menopausal symptoms at a higher severity than women who were satisfied (Table 3). Although there is no study examining this variable in the literature, it is thought that it is normal for women who are dissatisfied with their gender to perceive menopause negatively and therefore experience more menopausal symptoms.

The frequency and severity of menopausal symptoms vary according to the socio-cultural and personality characteristics of the individual (31). Gender identity is when individuals define themselves according to their masculine or feminine personality traits (14). In our study, it was determined that 30.1% of women adopted the feminine role, 12.7% adopted the ambiguous role, 9.0% adopted the masculine role, and nearly half (48.2%) adopted the androgynous role according to the BSRI score ranges (Table 4). In Ghiasi's (2019) study to determine the effect of gender role adopted in university students on attitudes towards menstruation, 16.6% of the participants were female gender role, 16.6% masculine gender role, 33.7% androgynous gender role. It was determined that 33% of the participants adopted an ambiguous gender role, and most of the participants were reported to be in the androgynous gender role group (32). In a study conducted by García Vega et al. (2017) to determine the relationship between gender, gender roles and sexual attitudes in university students, it was determined that 27% of the participants adopted the androgynous role (33). Our research result is similar to the results of studies conducted in different sample groups in the literature.

In our study, no statistically discernible was detected betwixt the MRS total score, somatic complaints and psychological complaints sub-dimension mean scores according to the gender roles adopted by women, while a statistically discernible difference was found between the MRS urogenital complaints sub-dimension mean scores (p=0.024<0.05). The mean urogenital complaints sub-dimension score of women who describe themselves as masculine (3,10±2,38) was found to be statistically discernible lower than the other gender role groups (Table 5). No study has been determined in the national and international literature examining the effect of women's perception

Table 5. Comparison of MRS Sub-Dimension and Total Scores According to Women's Adopted Gender Roles (n=465)

		MRS Sub-Dimensions			
		Somatic Complaints X±SD	**Psychological Complaints X±SD**	**Urogenital Complaints X±SD**	**Scale Total X±SD**
Gender Roles	**Masculine (1)**	6,07±3,37	6,93±3,92	**3,10±2,38***	16,10±7,94
	Feminine (2)	6,43±3,16	7,28±3,64	4,14±2,60	17,84±7,35
	Androgynous (3)	6,38±3,73	7,34±3,82	3,50±2,89	17,22±8,91
	Ambiguous (4)	6,58±3,61	7,61±3,71	4,19±2,89	18,37±8,90
Test and p Value		KW=0,558 p=0,906	KW=1,255 p=0,740	KW=9,457 **p=0,024** 2>1** 2>3**	KW=2,257 p=0,521

*Kruskal Wallis analysis of variance, **Mann Whitney U test

of gender roles on menopausal complaints. Women during menopause; ürogenital complaints, including dryness in the genitals, atrophy, vulvar itching, discharge, low sexual desire, dyspareunia and urinary tract infections, are frequently experienced (12,34). These problems reduce the quality of life of women. At the same time, women may perceive all these problems experienced with menopause as a threat to their femininity (35). The reason why women who describe themselves as masculine in our research experience less urogenital complaints may be that they do not fully adopt their feminine identity, therefore, their feminine identity will not be harmed.

This study has some limitations. The research was conducted in family centers affiliated with a metropolitan municipality and women who prefer to apply to the relevant family center may have common socioeconomic characteristics that affect perceived gender roles. Therefore, our results are limited to the centers where the research was conducted. It is important to study a larger sample group in terms of generalizability of the results. The study provides information about the current situation of the participants. In addition, participants' responses to menopausal symptoms were based on self-report. Considering that depression may increase during menopause, the results of the study cannot be generalized to women with any psychiatric disorder.

CONCLUSION

As a result of our research, it was found that the average score of menopausal symptoms of the women participating in our study was below the moderate level, and women experienced the most psychological complaints. It was found that the womens in our research mostly adopted the androgynous role and the women who described themselves as masculine experienced less urogenital complaints from menopausal symptoms. In order to generalize the results of the research, it can be recommended to work with larger sample groups and to consider the menopause and gender perceptions of women while giving care to women in the climacteric period. In addition, only women who entered menopause naturally were included in our study. Our results cannot be generalized to women with surgical menopause and early menopause.

Acknowledgements: The authors thank Mamak Municipality Family Centers Coordination Office for their contribution to the data collection phase of the research, and all the participants.

Author Contributions: Concept: ZG, DSK, FND.Design: ZG, DSK. Supervision: ZG, DSK. Data Collection and/or Processing: FND. Analysis and/or Interpretation: ZG, DSK, FND. Literature Research: FND. Writing: ZG, DSK, FND. Critical Review: ZG, DSK, FND.

Conflict of interest: The authors have no conflicts of interest to declare.

Ethical approval: The study was approved by the Non-Interventional Ethics Committee of Lokman Hekim University (Date: 27.05.2021 Decision No: 2021/056) and permission from the family center coordinator where the research was conducted.

Funding: The authors declare that this study received no funding.

Peer-Review: Externally peer-reviewed.

REFERENCES

1. Kurugodiyavar MD, Gajula M, Bant DD, Bathija G. Climacteric syndrome: symptom prevalence and quality of life assessment, a proxy of health care services. Int J Community Med Public Health 2017; 4(7):2377-2382.
2. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, Sherman S, Sluss PM, De Villiers TJ. Straw + 10 Collaborative Group. Executive Summary Of The Stages Of Reproductive Aging Workshop + 10: Addressing The Unfinished Agenda Of Ataging Reproductive Aging. Climacteric 2012;97(1):105–114.
3. Gürler M, Kızılırmak A, Baser M. The effect of aromatherapy on sleep and quality of life in menopausal women with sleeping problems: a non-randomized, placebo-controlled trial. Complementary Medicine Research 2020;27(6):421-430.
4. Ulusoy MN, Kukulu K. The Relationship of Sleep Problems in Women with Menopause. Gümüşhane University Journal Of Health Sciences 2013;2(2):206–213.
5. Potter B, Schrager S, Dalby J, Torell E, Hampton A. Menopause. Prim Care 2018;45(4):625-41.
6. Mceniery CM. Transitioning The Menopause: A Stiff Challenge. Arteriosclerosis, Thrombosis And Vascular Biology 2020;40(4):850-852.
7. Turkey Demographic and Health Survey 2018. Hacettepe University Institute of Population Studies, Ankara, Turkey. Available at: http://www.hips.hacettepe.edu.tr/ Accessed October 12, 2022.
8. Yağcı N, Şimşek Ş, Şenel A. Attitudes of women in climacteric period towards menopause and the role of psychological symptoms: The case of Denizli. Turkish Journal of Public Health 2022;20(1):80-89.
9. Çakıl NA. Evaluation of Menopausal Complaints and Perceptions of Self-Efficacy in Middle Age

Women. Sted/Journal of Continuing Medical Education 2020;29(4):267-275.
10. Erkin Ö, Ardahan M, Aslı K. The Effect of Menopause Period on Women's Quality of Life. Gümüşhane University Journal Of Health Sciences 2014;3(4):1095-1113.
11. Abay H, Kaplan S. Validation And Reliability Of The Turkish Utian Quality-Of-Life Scale İn Postmenopausal Women. Menopause 2016;23(4):425-432.
12. Zhang L, Ruan X, Cui Y, Gu M, Mueck AO. Menopausal Symptoms And Associated Social And Environmental Factors İn Midlife Chinese Women. Clinical İnterventions In Aging 2020;15:2195.
13. Zou P, Waliwitiya T, Luo Y, Sun W, Shao J, Zhang H, Huang Y. Factors influencing healthy menopause among immigrant women: a scoping review. BMC women's health 2021;21(1):1-11.
14. Zeren F, Köşgeroğlu N. Reflections of Gender Inequality on Nursing Profession. Gümüşhane University Journal Of Health Sciences 2020;9(3):293-299.
15. Redlick MH. Traditional gender roles and their connections to relational uncertainty and relational satisfaction. Psychology & Sexuality 2019;10(1):1-16.
16. Bem SL. The Measurement Of Psychological Androgyny. Journal Of Consulting And Clinical Psychology 1974;42(2):155-162.
17. Çelik AS, Bayrakçeken E, Kılınç T. Individual Innovation Characteristics of Nurses According to Gender Roles and Affecting Factors. Anatolian Journal of Nursing and Health Sciences 2020;23(3):397-409.
18. Pérez-Herrezuelo I, Aibar-Almazán A, Martínez-Amat A, Fábrega-Cuadros R, Díaz-Mohedo E, Wangensteen R, Hita-Contreras F. Female sexual function and its association with the severity of menopause-related symptoms. International Journal of Environmental Research and Public Health 2020;17(19):7235.
19. Can Gürkan Ö. Reliability and Validity of the Turkish Version of the Menopausal Symptoms Evaluation Scale. Journal of Nursing Forum 2005;7(2):147–173.
20. Dökmen Z. Psychometric Properties of Turkish Version of Bem Gender Role Inventory Femininity and Masculinity Scales. Ankara University Journal of Crisis 1999;7(1):27–40.
21. Tümer A, Kartal A. The Relationship between Women's Attitudes towards Menopause and their Menopausal Complaints. Pamukkale Journal of Medicine 2018;11(3): 337-346.
22. Khatoon F, Sinha P, Shahid S, Gupta U. Assessment Of Menopausal Symptoms Using Modified Menopause Rating Scale (Mrs) İn Women Of Northern India. Int J Reprod Contracept Obstet Gynecol 2018;7(3):947-51.
23. Zhang L, Ruan X, Cui Y, Gu M, Mueck AO. Menopausal Symptoms Among Chinese Peri- And Postmenopausal Women: A Large Prospective Single-Center Cohort Study. Gynecological Endocrinology 2021;37(2):185-189.
24. Ji X, Singleterry S, Kulikova A, Harrison Y, Shivakumar G, Brown ES. Association Of Menopause Symptoms With Depressive Symptom Severity İn A Diverse Community-Based Sample. Maturitas 2021;143(1):78-80.
25. Zerkinli D. Investigation of the effect of menopausal symptoms on general health status in women in the postmenopausal period. Cumhuriyet University Institute of Health Sciences, Master's Thesis, 2020.
26. Thapa R, Yang Y. Menopausal symptoms and related factors among Cambodian women. Women & Health 2019;60(4):396-411.
27. Darıcı Koçan MK, Cangöl E. Symptoms and Coping Methods Experienced by Menopausal Women. JCME 2023;32(3):256-68.
28. İkiışık H, Turan G, Kutay F, Karamanlı DC, Gülen E, Özdemir E. Awareness of menopause and strategies to cope wıth menopausal symptoms of the women aged between 40 and 65 who consulted to a tertıary care hospıtal. ESTÜDAM Journal of Public Health 2020;5(1):10-21.
29. Noroozi E, Dolatabadi NK, Eslami AA, Hassanzadeh A, Davari S. Knowledge and attitude toward menopause phenomenon among women aged 40-45 years. J Educ Health Promot 2013;2(1):25.
30. Zorlu S, Türkmenoğlu B, Budak M. Traditional Practices Applied by Menopausal Women for Menopausal Symptoms. Cumhuriyet University Journal of Institute of Health Sciences 2022;7(3):139-149.
31. Ergin O, Yağmur Y. The relationship between menopausal complaints and personality traits. Perspectives in Psychiatric Care 2018;54(3):365-370.

32. Ghiasi A. The Effect Of Gender-Role Orientation On Attitudes Towards Menstruation In A Sample Of Female University Students. Journal Of The Turkish German Gynecological Association 2019;20(3):138.
33. García Vega E, Rico Fernández R, García Fernández P. Sex, Gender Roles And Sexual Attitudes In University Students. Psicothema 2017;29(2):178-183.
34. Heidari M, Ghodusi M, Rezaei P, Abyaneh SK, Sureshjan EH, Sheikhi RA. Sexual Function And Factors Affecting Menopause: A Systematic Review. Journal Of Menopausal Medicine 2019;25(1):15-27.
35. Hardy C, Griffiths A, Hunter Ms. Development And Evaluation Of Online Menopause Awareness Training For Line Managers İn Uk Organizations. Maturitas 2019;120(2):83-9.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 474-482
https://doi.org/10.30621/jbachs.1410610
RESEARCH ARTICLE

A TURKISH-LANGUAGE VALIDATION AND RELIABILITY STUDY OF THE STORM FEAR QUESTIONNAIRE (SFQ)

Busra Parlak Somuncu[1], Irem Dilaver[2], Serdar Karakullukcu[3], Nazim Ercument Beyhun[3], Murat Topbas[3]

[1]Erzincan Community Health Center, Erzincan, Turkey
[2]Trabzon Provincial Health Directorate, Trabzon, Turkey
[3] Karadeniz Technical University, Faculty of Medicine, Department of Public Health, Trabzon, Turkey

ORCID: B.P.S. 0000-0002-0271-7019; I.D. 0000-0002-9962-7908; S.K. 0000-0001-7673-7699; N.E.B. 0000-0002-4664-9070; M.T. 0000-0003-4047-4027

Corresponding author: Busra Parlak Somuncu, **E-mail:** parlakbusra@hotmail.com
Received: 27.12.2023; **Accepted:** 13.03.2024; **Available Online Date:** 31.05.2024

Cite this article as: Parlak-Somuncu B, Dilaver I, Karakullukcu S, Beyhun N E, Topbas M. A Turkish-Language Validation and Reliability Study of the Storm Fear Questionnaire (SFQ)J Basic Clin Health Sci 2024; 8: 474-482.

ABSTRACT

Purpose: The purpose of this study is to determine the validity and reliability of the Turkish-language version of the Storm Fear Questionnaire (SFQ).
Material and Methods: The research was completed with 299 individuals. After obtaining sociodemographic information of the participants, Storm Fear Questionnaire, Eco-Anxiety Scale and Severity Measure for Specific Phobia were administered. Exploratory and confirmatory factor analysis was applied to evaluate the scale's construct validity, while Cronbach's alpha (α) reliability coefficient was used to determine its consistency, and test-retest reliability was employed to determine its stability.
Results: Scores from the SFQ scale ranged from 0 to 56, with a mean score of 13.3 ±11.4. A structure consisting of a single factor with an eigenvalue greater than 1, explaining 59.0% of the total variance emerged from the factor analysis. Factor loadings for the SFQ, the original of which consists of 15 items, ranged between 0.594 and 0.879. One item with a factor loading less than 0.30 was removed from the scale. The Cronbach alpha coefficient of the first test was 0.943.
Conclusion: We think that the 14-item scale obtained in this research can be employed as a valid and reliable tool for evaluating storm fear in adults in Türkiye.

Keywords: Phobias, fear, wind, extreme weather, factor analysis.

INTRODUCTION

Storms are defined as organized system of clouds and thunderstorms that has a closed low-level circulation (1). Approximately 2000 storms occur worldwide at any one time, the total annual number being approximately 16 million. Ten percent of these may be severe (2). An increase in the strength and frequency of storms has been predicted due to the alarming situation resulting from weather events deriving from global climate change evolving into a global climate crisis (3,4). Extreme weather events such as storms, severe rain, floods, and hail have also tended to increase in Türkiye in the last 20 years. Storms represented 21.4% of extreme weather events in the country in 2022 (5). According to Turkish State Meteorological Office data, storms can be seen in almost all regions of Türkiye, with tornadoes even being reported in the Eastern Black Sea and Northeast Anatolia regions, where they had never been observed until the last 10 years (6,7).

Several health-related effects of storms have been reported. For example, they can lead to injuries, the interruption of basic health services, infrastructure problems, material and economic losses, and

mortality, both directly and indirectly (8). Injuries, infections and parasitic diseases, cardiovascular diseases, respiratory diseases, and neuropsychiatric disorders and been shown to capable of being linked to increased mortality, even months after a storm (4). In the light of their potential to affect large numbers of people and multifaceted health impacts, storms and the weather events accompanying them represent an important public health problem (8).

Although various studies have revealed the effect of storms and the global climate crisis on human health, their impacts on human psychology have only recently become the subject of discussion. A report published in 2009 espoused the possibility of an interaction between climate change and mental health and called for greater research into the subject (3,9). This revealed the need for an examination of the effects of storms, expected to increase in line with climate change, on human psychology. Fear of storms was therefore addressed in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (10) and was classified among the natural/environmental type phobias, a specific phobia subtype.

Fear of storms is defined as a continuous and extreme fear of meteorological events such as storms and hurricanes. Individuals with storm phobia often experience a worried expectation of weather events such as storms (10). In addition, this fear can lead to physiological reactions such as tachycardia and sweating, symptoms which may emerge not only at the time of storms, but during their anticipation (11). Natural/environmental type phobias are one of the most overlooked clinical manifestations in terms of clinical studies and scientific publications. They are generally detected incidentally in patients presenting for treatment of other problems. Sufferers frequently do not present to health institutions for treatment, for reasons such as storm fear not being perceived as a disease, its being regarded as a personality trait, failure to report the development of symptoms, and their being able to continue with their lives by means of successful avoidance tactics (12,13). Westefeld (12) performed semi-structured interviews with 81 individuals in America reporting extreme fear of storms of hurricanes. Eighty-six percent of the participants reported anxiety concerning approaching storms, and that such anxiety was accompanied by countless other symptoms (such as constantly monitoring weather forecasts, security anxiety, and difficulty falling asleep). However, only 10% of that sample reported seeking treatment for those symptoms. In addition, that study reported that affected by severe weather events through experience or media were probable factors causing of storm phobia. Two percent of the total populations of the USA and Canada are thought to experience fear of storms at least once in their lives (2). However, the prevalence of fear of storms in Türkiye is unknown since no studies have been performed on the subject. The only validated scale measuring fear of storms in the literature is the Storm Fear Questionnaire (SFQ). This self reported questionnaire consists of 15-item with five point Likert type response format and measures the severity of storm fear by investigating its behavioral and cognitive characteristics. Nelson et al. (14) concluded that the SFQ exhibits powerful psychometric properties and is reliable and valid in English. That study also reported a difference in scale scores between individuals reporting high and low fear following exposure to a virtual storm. There is no personal tool measuring fear of storms in Turkish. A clinical interview performed by a specialist within the scope of DSM-5 criteria is required for disease evaluation. The development of a measurement tool based on self-reports will facilitate diagnosis and provide an opportunity to treat such patients. It will also contribute to the objective determination of the prevalence of storm fear in society by providing resources for research into such fear in adults.

The purpose of this research is to determine the validity and reliability of the Turkish-language version of the SFQ.

MATERIAL AND METHODS

Design

This research was conducted in a metadological design. The requisite permissions for the SFQ adaptation study were obtained from its developer, Martin M. Anthony. This study was approved by Scientific Research Ethics Committee of Karadeniz Technical University (Decision Date: 13.07.2023, Number: 24237859-442). All participants were explained the details of the study prior to enrolment, and verbal consent was obtained.

Participants

The research was performed among adults in the Turkish provinces of Trabzon, Gümüşhane, and Erzincan. When calculating the sample size in validity and reliability studies, it is recommended to reach participants 10 times the number of items in the scale

(15). Since the SFQ consists of 15 items, we planned to include at least 270 individuals in the research, 15 for each variable, with a 20% margin of error. The research was eventually completed with 299 individuals. In the second part of the research, a repeat test containing the SFQ was administered to 80 of the participants taking part in the first stage. The research data were collected by the authors using the face-to-face survey method. The inclusion criteria were age 18 or over, and the absence of any condition that might hinder the establishment of communication, answering the questions in the survey, or taking part in the research.

Application Stages

The English to Turkish translation was done by two translators independent of the research team with a good knowledge of both languages. The translated scale was then evaluated by three public health specialists, each item being compared with the original version. The scale finally assumed its final form in the light of the suggestions received. A pre-test was applied with 10 individuals to assess the scale's comprehensibility and clarity. Following the pre-test, the scale was once again examined by the specialist group, and any requisite amendments were made. It was then translated back into English by a Turkish-English translator. The version translated back into English was then sent to the developer of the scale, Martin M. Anthony, and feedback was received. At the end of the final corrections, the scale was translated back into Turkish by an English-Turkish translator. This final version was applied to the individuals agreeing to take part. For the purpose to test the test-retest reliability of the scale, a retest was administered to 80 participants 14 days after the survey. The final version of the scale is presented in the Appendix.

Data Collection Tools

The first part of the data collection form employed in the first stage of the research and prepared by the authors investigated sociodemographic and personal characteristics. The second part contained the Eco-Anxiety Scale (EAS) and the Severity Measure for Specific Phobia (SMSP) in addition to the SFQ. The EAS, which measures the anxiety that individuals experience when thinking about climate change and other global climate conditions, was employed since storms are a climate change event, and the SMSP since storm phobia is included under the heading of nature-environment type phobias, a specific phobia subtype. In the second stage of the research, only the SFQ was applied to participants due to be retested.

Storm Fear Questionnaire (SFQ); This 15-item self-report scale was developed by Nelson et al. (14) in 2014. Participants are asked to indicate how much each statement describes them on a five-point Likert-type scale (0 = not at all true and 4 = almost always true). The scale score is calculated by summing the scores obtained from all items in the scale. The score that can be obtained from the scale varies between 0 and 60, higher scores indicating greater storm fear. Nelson et al. (14) showed that the scale exhibited a one-dimensional factor structure, with a Cronbach α value of 0.95.

Eco-Anxiety Scale (EAS); This scale was developed by Hogg et al. (16) for the purpose of measuring anxiety in the light of experience of anxiety associated with environmental crisis and the severity thereof. The EAS consists of 13 items, four measuring emotional symptoms, three measuring rumination, three measuring behavioral symptoms, and three measuring personal effect anxiety. The participants were asked how frequently they experienced each eco-anxiety characteristics when reflecting on climate change and other environmental climate conditions (0 = never, 1 = sometimes, 2 = frequently, 3 = almost always). No items on the scale are reverse-scored, and higher scale scores indicate greater anxiety. The Turkish language validation and reliability study were done by Uzun et al. (17) in 2022. The scale structure preserved that of the original version. Reported Cronbach α values were 0.91 for the total scale, 0.83 for emotional symptoms, 0.86 for behavioral symptoms, and 0.84 for rumination and personal effect anxiety.

The Severity Measure for Specific Phobia (SMSP); This scale was developed for DSM-5 by the American Psychiatric Association (10) for measuring the severity of specific phobia in individuals aged 18 or over. It consists of 10 items. Each item asks the respondent to indicate the severity of specific phobia symptoms in the previous seven days using a five-point scale (0= Never; 1= Sometimes; 2= Half the week, 3= Most of the week, and 4= All the week). The scale score is calculated by adding the scores for the individual items. Possible scores range between 0 and 40. The internal consistency of the scale in Öztekin et al. (18) study was 0.79, with item-total score correlation coefficients ranging between 0.33

Table 1. The participants' sociodemographic characteristics of (n=299)

Characteristics		
	Mean ± SD	**Median (Min – Max)**
Age	37.7 ± 12.1	35 (18 – 70)
	Frequency (n)	**Percentage (%)**
Marital Status		
Single	85	28.4
Married	214	71.6
Education Status		
Primary school graduate	13	4.3
Secondary school graduate	9	3.0
High school graduate	67	22.4
University graduate	210	70.3
In Income-Generating Employment		
Yes	229	76.6
No	70	23.4
Presence of Chronic Disease Diagnosed		
Yes	78	26.1
No	221	73.9

and 0.78, showing that the Turkish-language version is also valid and reliable.

Statistical Analysis

IBM SPSS 23.0 software was used for statistical analyses. AMOS version 24.0 software was employed for confirmatory factor analysis. Descriptive statistics were presented as number and percentage for qualitative variables and as mean±standard deviation and median, minimum-maximum values for quantitative variables. Statistical alpha significance level was accepted as $p < 0.05$.

Validity Studies

In order for a scale to be standardized and subsequently yield accurate information, it must possess two features known as 'validity' and 'reliability.' Validity refers to the degree to which a measurement tool is capable of accurately measuring the feature it is intended to measure, without confusing it with any other characteristic (19). Construct validity and convergent-divergent validity were analyzed in the present study.

Exploratory and confirmatory factor analysis was applied to assess the structural validity of the scale. Principal component analysis (PCA) was used to perform exploratory factor analysis (EFA). To determine whether the sampling adequacy for factor analysis Kaiser-Meyer-Olkin (KMO) test and Bartlett's Test of Sphericity (BTS) were used. Root Mean Square Error of Approximation (RMSEA), Root Mean Square Residual (RMR), Chi-square ($\chi 2$), degrees of freedom (df), comparative fit index (CFI), goodness of fit index (GFI), normed fit index (NFI) and Tucker-Lewis Index (TLI) were used to assess the model fit in confirmatory factor analysis.

The Turkish versions of the Eco-Anxiety and The Severity Measure for Specific Phobia were used to analyze the convergent-divergent validity of the Turkish-language version of the SFQ, and the relationship between the scales was determined using Spearman correlation analysis.

Reliability Studies

Reliability refers to the consistency with which a measurement tool measures the desired variable, or the degree to which the measurement results are free from error (19). In the present research, stability and internal consistency tests were used to determine the reliability of the SFQ.

Cronbach's alpha (α) reliability coefficient was employed to determine the internal consistency of the SFQ. Item-total correlations were evaluated. A cut-off value of 0.7 was employed when evaluating the Cronbach alpha test results (19).

Test-retest reliability was used to determine the stability of the scale. For test-retest reliability, the scale was re-applied to 80 individuals 14 days after the first test, and the Intraclass Correlation Coefficient (ICC) test was performed between the two applications.

RESULTS

The study was completed with 299 individuals with a mean age 37.7 ± 12.1 years (min=18; max=70). The sociodemographic and descriptive characteristics of the participants are shown in Table 1.

Scores from the SFQ ranged from 0 to 56, with a mean score of 13.3 ±11.4. A summary of correlations means and standard deviations of 14 items according to the first test is shown in Table 2. A moderate and significant correlation was observed between the responses given to 14 items.

As a result of the analysis, the KMO value was 0.954 and the p value was <0.001 in Bartlett's test. In line with these data, it was decided that the sample was suitable for factor analysis. (Chi-square value = 2887.13, df = 91).

Factor analysis revealed a structure consisting of a single factor with an eigenvalue exceeding 1, explaining 59.0 of the total variance.

The model fit of the scale was determined by evaluating chi- square, degrees of freedom and Root Mean Square Error of Approximation. In terms of goodness of fit indices, RMSEA value below 0.08 is considered a good fit indicator. In this research, the mean RMSEA value was found to be 0.077. An χ2 / df ratio of 2.76 was determined (acceptable value <5). The Comparative Fit Index (CFI) value was 0.954, the Normed Fit Index (NFI) value was 0.930, and the Goodness of Fit Index (GFI) was 0.905 (Table 3).

In Table 4, the explanatory and confirmatory factor analysis results are shown. Factor loadings for the SFQ, which originally consisted of 15 items, ranged

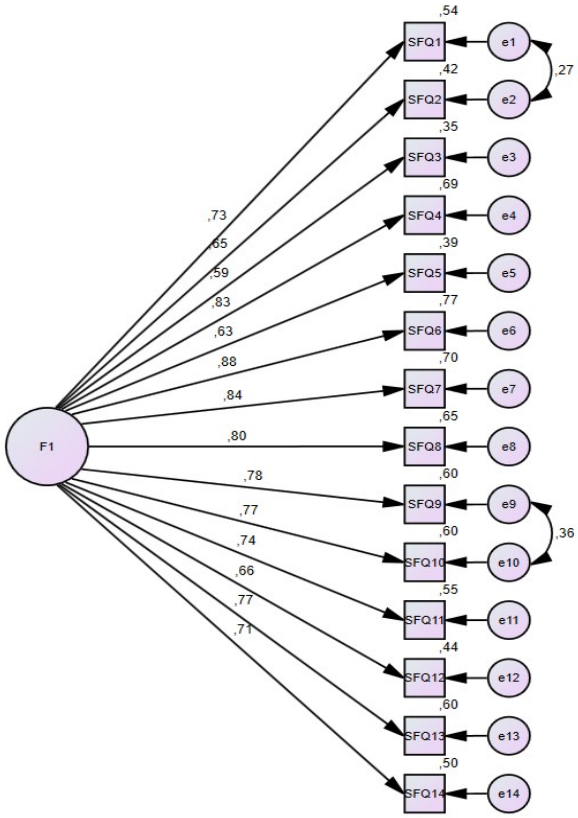


Figure 1. Standardized factor loadings in confirmatory factor analysis

Table 2. Correlations, means and standard deviations of 14 items according to the first test (n=299)

Items	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1														
2	0.615*													
3	0.406*	0.419*												
4	0.621*	0.580*	0.554*											
5	0.383*	0.475*	0.523*	0.565*										
6	0.682*	0.579*	0.519*	0.756*	0.529*									
7	0.610*	0.536*	0.474*	0.689*	0.537*	0.759*								
8	0.635*	0.520*	0.413*	0.657*	0.527*	0.687*	0.694*							
9	0.574*	0.497*	0.380*	0.616*	0.450*	0.689*	0.679*	0.650*						
10	0.550*	0.462*	0.416*	0.639*	0.420*	0.674*	0.652*	0.580*	0.742*					
11	0.549*	0.476*	0.450*	0.600*	0.491*	0.617*	0.537*	0.621*	0.594*	0.602*				
12	0.418*	0.388*	0.469*	0.536*	0.443*	0.567*	0.533*	0.526*	0.532*	0.546*	0.504*			
13	0.559*	0.447*	0.433*	0.626*	0.361*	0.697*	0.663*	0.599*	0.603*	0.687*	0.594*	0.507*		
14	0.491*	0.478*	0.446*	0.546*	0.493*	0.567*	0.587*	0.600*	0.534*	0.542*	0.639*	0.529*	0.564*	
M	0.95	1.07	1.25	0.82	1.50	0.73	0.62	0.98	0.78	0.70	1.20	0.82	0.58	1.30
SD	1.05	1.01	1.26	1.03	1.21	1.04	0.93	1.02	0.98	1.04	1.16	1.06	0.97	1.20

**p<0.001; M=mean; SD=standard deviation*

Table 3. Fit index results of confirmatory factor analysis (22,23,27–31)

Sample		**N>250**		**Calculated values**
Number of observed variables	**I≤12**	**12<I<30**	**I≥30**	
χ2	Non-significant *P*-value	Significant *P*-value even if the fit is good	Significant *P*-value	<0.001
χ2/df		**χ^2/ df<5**		2.76
RMR	<0.08	<0.08	<0.08	0.048
RMSEA	<0.08	<0.08	<0.08	0.077
GFI	>0.90	>0.90	>0.90	0.905
CFI	>0.95	>0.92	>0.90	0.954
NFI-TLI	>0.95	>0.90	>0.80	0.930-0.944

Table 4. The scale's exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) results

	EFA		**CFA**				
I	**PCA**	**ML**	**SFL**	**SE**	**T values**	**R^2**	**CA**
1	0.758	0.741	0.734	0.044	11.446	0.504	0.940
2	0.692	0.658	0.650	0.050	11.721	0.597	0.941
3	0.631	0.588	0.594	0.086	11.860	0.436	0.944
4	0.841	0.830	0.833	0.030	10.760	0.547	0.937
5	0.661	0.620	0.626	0.075	11.798	0.596	0.942
6	0.875	0.877	0.879	0.024	10.024	0.604	0.936
7	0.841	0.836	0.838	0.024	10.701	0.645	0.937
8	0.817	0.801	0.803	0.033	11.045	0.702	0.938
9	0.803	0.792	0.777	0.034	11.199	0.773	0.938
10	0.799	0.786	0.772	0.039	11.230	0.391	0.938
11	0.772	0.740	0.739	0.053	11.438	0.694	0.939
12	0.694	0.659	0.661	0.054	11.714	0.353	0.941
13	0.783	0.773	0.772	0.034	11.263	0.423	0.939
14	0.745	0.708	0.710	0.062	11.559	0.539	0.940

I=Items, PCA= principal component analysis, ML= maximum likelihood, SFL=standardized factor loadings, CA=Cronbach Alpha's if item deleted

Table 5. Correlations between the SFQ with EAS and SMSP

Scales (min-max values that can be obtained from the scales)		**1**	**2**	**Mean±SD**	**Median**	**Min-Max**
1.Storm Fear Questionnaire (0-56)	r p	1		13.3 ± 11.4	11	0-56
2. Eco-Anxiety Scale (0-39)	r p	0.568 <0.001	1	8.0 ± 7.1	7	0-39
3.The Severity Measure for Specific Phobia (0-28)	r p	0.486 <0.001	0.485 <0.001	6.6 ± 6.3	6	0-28

between 0.594 and 0.879 (Figure 1). One item with a factor loading lower than 0.30 was removed from the scale. Factor loadings were divided by the corresponding standard errors and t values were calculated for each factor. All calculated T values were greater than 1.96 (basic distribution limit). According to the modification indices, a covariance structure was suggested between e1 and e2 and

between e9 and e10. The Cronbach alpha coefficient of the first test was 0.943, and 0.913 in the final test.

In the retest the intraclass coefficient value was 0.800 ($p<0.001$), and in Spearman correlation analysis $r=0.729$ ($p<0.001$).

The correlation coefficients between the SFQ in this study and the Eco-Anxiety Scale and the Severity Measure for Specific Phobia are shown in Table 5. A correlation was found between the SFQ with Eco-Anxiety Scale ($r=0.568$, $p<0.001$) and the The Severity Measure for Specific Phobia ($r=0.486$, $p<0.001$).

DISCUSSION

The aim of this research was to establish the validity and reliability of the Turkish-language version of the SFQ. The factor structure, internal consistency, and convergent validity were therefore evaluated, and test-repeat test analysis was performed. There are no previous validity and reliability studies for the SFQ developed in English by Nelson et al. (14) in any other language. This discussion is therefore limited to the data from the present research.

In order for data to be appropriate for factor analysis, the KMO sampling adequacy must exceed 0.5, and the Bartlett sphericity test result must be significant. KMO values between 0.80-1.00 indicate that the sample is adequate. KMO values between 0.70-0.79 is considered moderate, between 0.60-0.69 is considered mediocre and below 0.50 is considered unacceptable (20). The KMO value in this research was 0.954, showing that the sampling was adequate. The Bartlett's test result was also statistically significant ($p<0.001$). These findings show that the data were suitable for factor analysis.

Construct validity was assessed using principal component analysis. Factor loadings in factor analysis must be at least 0.30 (21). The factor loading of the 15th item showed that this item was insufficient, and it was therefore decided to remove it from the scale. The 15th item contained the statement 'I use medications, alcohol, or drugs to help me cope during a storm.' The loading of this item may have been low because participants were reluctant to admit it since alcohol and drug use can result in stigmatization in Türkiye.

Exploratory factor analysis revealed a single-factor structure with an eigenvalue exceeding 1, explaining 59.0% of the total variance. Similarly to the original study, a one-dimensional factor structure was obtained (14). A moderate correlation was determined among the 14 items.

Using confirmatory factor analysis (maximum likelihood estimation), it was determined whether the SFQ could be validated in the Turkish sample. Fit indices evaluation revealed RMSEA= 0.077, $X^2/df=2.76$, CFI=0.954, NFI=0.930, and GFI=0.905. These results showed that the scale has adequate fit indices.

T value greater than 1.96 indicates significance at the 0.05 level and T value greater than 2.58 indicates significance at the 0.01 level (22,23). The value in this research was significant at the 0.05 level. This finding shows that the sample was sufficient for CFA and that no other item needed to be removed from the scale.

The reliability of the SFQ was assessed using internal consistency coefficient (Cronbach Alpha) and test-repeat test methods. The Cronbach alpha coefficient is used as a determinant of internal consistency, the closer the coefficient is to 1, the more consistent with one another the statements in the scale. Alpha coefficients of $0.00 \leq \alpha < 0.40$ are considered as meaning that 'the scale is not reliable,' values of $0.40 \leq \alpha < 0.60$ as meaning that 'the scale exhibits low reliability,' values of $0.60 \leq \alpha < 0.80$ as meaning that 'the scale is quite reliable,' and values of $0.80 \leq \alpha < 1.00$ as meaning that 'the scale is highly reliable' (24). This value needs to be at least 70 in studies evaluating psychological concepts (25). The Cronbach alpha coefficient in the present research was 0.943. This high value, similar to that of 0.95 obtained in the original study by Nelson et al. also indicated that the Turkish-language version of the form is highly reliable.

In order to evaluate the scale's test-repeat test reliability, the Turkish-language form obtained was re-applied to 80 individuals after 14 days, and a correlation coefficient of 0.800 ($p<0.001$) was determined between the two applications. At a 95% confidence interval, ICC reference values < 0.5, 0,50 to < 0.75, 0.75 to < 0.90, and > 0.90 are classified as weak, moderate, good, and perfect (26). This finding shows that the SFQ possesses good test-retest reliability and that the reliability obtained does not change over time.

The Eco-Anxiety and the Severity Measure for Specific Phobia scales were employed for similar scale validity. The SFQ was found to be moderately positively correlated with both scales.

CONCLUSION

In conclusion, in this study of the adaptation of the SFQ developed by Nelson et al. Into Turkish, the

validity and reliability findings supported those from the original study. In contrast to the original study, however, the 15th item was deleted, and a single factor structure consisting of 14 items emerged. We therefore think that the resulting 14-item scale can be used as a valid and reliable tool for evaluating storm fear in adults in Türkiye.

Acknowledgements: None.

Authors Contributions: Conception: BPS, NEB, MT; Design: BPS, ID, SK, NEB, MT; Supervision: BPS, SK, NEB; Fundings: BPS, ID; Data Collection and/or Processing: BPS, ID, SK; Analysis-Interpretation: SK, NEB, MT; Literature Review: BPS, ID, SK, NEB, MT; Writing: BPS, ID, SK; Critical Review: BPS, ID, SK, NEB, MT.

Conflict of interest: All authors declare that there is no conflict of interest.

Ethical approval: The requisite permissions for the SFQ adaptation study were obtained from its developer, Martin M. Anthony. This study was approved by Scientific Research Ethics Committee of Karadeniz Technical University (Decision Date: 13.07.2023, Number: 24237859-442). All participants were explained the details of the study prior to enrolment, and verbal consent was obtained.

Funding: All authors declare they have no financial or non-financial interests to disclose.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Pan American Health Organization. Storms. [Accessed date: 20 November 2023]. Available form: https://www.paho.org/en/topics/storms
2. NOAA National Severe Storms Laboratory. Thunderstorm basics. [Accessed date: 20 October 2023]. Available form: https://www.nssl.noaa.gov/education/svrwx101/thunderstorms/
3. Pörtner HO, Roberts DC, Tignor M, et al. IPCC, 2022: Climate Change 2022: Impacts, Adaptation and Vulnerability. Contribution of Working Group II to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change. New York: Cambridge University Press; 2022.
4. Parks RM, Benavides J, Anderson GB, et al. Association of tropical cyclones with county-level mortality in the US. JAMA 2022;327(10):946–955.
5. T.C. Çevre, Şehircilik ve İklim Değişikliği Bakanlığı Meteoroloji Genel Müdürlüğü. 2022 yılı iklim değerlendirmesi. Ankara; 2023.
6. Türkeş M. Türkiye'de hortumlar artıyor mu?. EKOIQ 2021:97-101.
7. Türkeş M, Şahin S. Türkiye'nin fırtına afeti etkilenebilirliği ve risk çözümlemesi. Kebikeç İnsan Bilim İcin Kaynak Arastirmaları Dergisi 2018;46(46):219–246.
8. World Meteorological Organization. Weather-related disasters increase over past 50 years, causing more damage but fewer deaths. [Accessed date: 2 October 2023]. Available form: https://public.wmo.int/en/media/press-release/weather-related-disasters-increase-over-past-50-years-causing-more-damage-fewer
9. American Psychological Association Task Force on the Interface between Psychology and Global Climate Change. Psychology and global climate change: Addressing a multi-faceted phenomenon and set of challenges; 2009.
10. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013.
11. Stinson FS, Dawson DA, Chou SP, et al. The epidemiology of DSM-IV specific phobia in the USA: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Psychological Medicine. 2007;37(7):1047-1059.
12. Westefeld JS. Severe weather phobia: An exploratory study. J Clin Psychol. 1996;52(5):509–515.
13. Türk Psikiyatri Derneği. Özgül fobiler. [Accessed date: 9 October 2023]. Available form:
14. Nelson AL, Vorstenbosch V, Antony MM. Assessing fear of storms and severe weather: Validation of the Storm Fear Questionnaire (SFQ). J Psychopathol Behav Assess. 2014;36:105–114.
15. Sousa VD, Rojjanasrirat W. Translation, adaptation and validation of instruments or scales for use in cross-cultural health care research: A clear and user-friendly guideline. J Eval Clin Pract. 2011;17(2):268–274.
16. Hogg TL, Stanley SK, O'Brien L V., Wilson MS, Watsford CR. The Hogg Eco-Anxiety Scale: Development and validation of a multidimensional scale. Glob Environ Chang. 2021;71:102391.
17. Uzun K, Öztürk AF, Karaman M, et al. Adaptation of the Eco-Anxiety Scale to Turkish: A validity and reliability study. Arch Heal Sci Res 2022;9(2):110–115.
18. Öztekin S, Aydin O, Aydemir Ö, et al. DSM-5 Özgül Fobi Şiddet Ölçeği Türkçe Formunun geçerliliği ve güvenilirliği. Anadolu Psikiyatr Derg 2017;18(2):31–37.
19. Messick S. Test validity and the ethics of assessment. Am Psychol. 1980;35(11):1012–

1027.
20. Shrestha N. Factor Analysis as a Tool for Survey Analysis. Am J Appl Math Stat. 2021;9(1):4–11.
21. Stevens, J. P. Applied multivariate statistics for the social sciences. 4th ed. New York: Psychology Press 2002.
22. Şimşek ÖF. Yapısal eşitlik modellemesine giriş, temel ilkeler ve LİSREL uygulamaları. Ankara: Ekinoks; 2007. p.4-22.
23. Schumacker RE, Lomax RG. A beginner's guide to structural equation modeling. 3rd ed. New York: Routledge; 2010. p.85-90.
24. Bland JM, Altman DG. Statistics notes: Cronbach's alpha. BMJ 1997;314:572.
25. Nunnally, J. C. Psychometric theory. 2nd ed. New York: McGraw-Hill; 1978.
26. Portney, L.G., & Watkins, M.P. Foundations of clinical research: Applications to practice. 3rd ed. Toronto: Prentice Hall; 2009.
27. Munro BH. Statistical methods for health care research. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2005. p.351-376.
28. Schreiber JB, Nora A, Stage FK, Barlow EA, King J. Reporting structural equation modeling and confirmatory factor analysis results: A review. The Journal of Educational Research 2006; 99(6): 323-338.
29. Hooper D, Coughlan J, Mullen MR. Structural equation modelling: Guidelines for determining model fit. Electronic Journal of Business Research Methods 2008; 6(1): 53-60.
30. Schumacker RE, Lomax RG. A beginner's guide to structural equation modeling. 2nd ed. New Jersey: Taylor & Francis; 2004. p.1-8.
31. Wang J, Wang X. Structural equation modeling: Applications using Mplus: methods and applications. Hoboken, New Jersey: John Wiley & Sons; 2012. p.5-9.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 483-489
https://doi.org/10.30621/jbachs.1416117
RESEARCH ARTICLE

EVALUATION OF SOCIO-DEMOGRAPHIC FACTORS AND COMORBIDITIES IN ADULT HEMOPHILIA PATIENTS

Fatma Keklik Karadag[1], Zuhal Demirci[2,3], Fatos Dilan Koseoglu[4], Guray Saydam[2,3], Fahri Sahin[2,3]

[1]Izmir Tepecik Research and Training Hospital, Department of Internal Medicine, Division of Hematology, Izmir, Turkey
[2]Ege University Faculty of Medicine, Department of Hematology, Izmir Turkey
[3]Ege Adult Hemophilia and Thrombosis Center, Izmir, Turkey
[4]University of Bakırcay, Cigli Research and Training Hospital, Department of Internal Medicine, Division of Hematology, Izmir, Turkey

ORCID: F.K.K. 0000-0001-6078-5944; Z.D. 0000-0001-7509-8020; F.D.K. 0000-0002-3947-0355; G.S. 0000-0001-8646-1673; F.S. 0000-0001-9315-8891

Corresponding author: Fatma KEKLIK KARADAG, **E-mail:** fatma_keklik86@hotmail.com
Received: 07.01.2024; **Accepted:** 10.05.2024; **Available Online Date:** 31.05.2024

Cite this article as: Keklik-Karadag F, Demirci Z, Koseoglu FD, Saydam G, Sahin F. Evaluation of Socio-demographic Factors and Comorbidities in Adult Hemophilia Patients. J Basic Clin Health Sci 2024; 8: 483-489.

ABSTRACT

Purpose: The association between socio-demographic factors and hemophilia status with the prevalence of comorbidities was evaluated.
Material and Methods: Patients with hemophilia A (n=111) and B (n=24) who completed the questionnaire form about their socio-demographic factors were included in our study. Factor and inhibitor levels, comorbidities, factor replacement therapies, hemophilic arthropathy, viral status and annual bleeding episodes were recorded.
Results: The median age was 39 years among 135 hemophilia patients, and 63.1% of all patients had severe hemophilia, which was significantly higher among hemophilia A (p=0.002). Most patients (74.8%) were treated with prophylactic factor replacement therapy. The inhibitor status was positive in 8.9% of all patients. The unemployment rate was found to be 33.3%. Annual bleeding episodes were higher in workers. Most patients (60%) had graduated from at least high school. Patients with severe hemophilia were significantly less educated than those with moderate to mild hemophilia (p=0.045). The prevalence of cardiovascular disease, hypertension, diabetes mellitus, and obesity was 6.7%; 17.8%, 13.3%, and 11.9% respectively. Although there was no association between obesity and annual bleeding episodes, right ankle was the most affected joint in overweight/obese patients.
Conclusion: Age-related comorbidities and the relationship between hemophilia status and social life need further investigation.

Key words: Hemophilia, comorbidity, socio-demographic, adult

INTRODUCTION

Hemophilia A and B are characterized by deficiency or complete absence of factor VIII and IX, respectively. Spontaneous bleeding episodes and/or prolonged bleeding after trauma or surgery are the main clinical manifestations of these conditions (1). Acute and chronic joint pain due to regular bleeding in joints along with progressive musculoskeletal damage, contribute to hemophilic morbidity and impair daily activities. Insufficient management of bleeding episodes increases the risk of hemophilia-

related morbidities and decreases the quality of life in patients with hemophilia (PWH) (2). Besides the negative effects on daily functioning, clinical signs and symptoms may also impact mental and social health (3). The quality of life and life expectancy of PWH significantly improved with the development and availability of clotting factor concentrates after the 1970s (4). However, during the 1980s, PWH struggled with bloodborne infections such as human immunodeficiency virus (HIV) and the hepatitis B and C viruses (HBV, HCV)) due to contaminated plasma-derived concentrates., The introduction of home treatment and prophylaxis in the 1990s allowed the long-term survival with minimal bleeding episodes (5). PWH are now living longer due to favorable factor replacement therapies, antiviral treatments, and comprehensive hemophilia care centers (6,7). Aging with hemophilia presents additional challenges beyond bleeding, such as hemophilia-related conditions (e.g., chronic arthropathy and viral infections) and aging-related comorbidities (e.g., cardiovascular diseases, cancer, osteoporosis, renal diseases, and dementia) (5,7,8).

Despite the availability of comprehensive care, the decrease in quality of life due to hemophilia and age-related comorbidities affects socio-demographic factors such as education, social, and working life in PWH. The disparity in socio-economic engagement between individuals with hemophilia and the general population has not been extensively investigated. In this study, we aim to evaluate the association between socio-demographic factors and hemophilia status. There is limited data on comorbidities of PWH due to the restricted availability of high-quality national registries worldwide. Therefore, we aim to define the prevalence of comorbidities in the associated study group.

MATERIAL AND METHODS

Study Design

135 cases (111 with hemophilia A and 24 with hemophilia B), all aged over 18, who were admitted to Ege University Adults Hemophilia and Thrombosis Center, a European Hemophilia Comprehensive Care Centre (EHCCC) certified facility, between 10 August 2016 and 30 December 2016, were included in the study. Data were collected retrospectively through an initial patient interview and a 1-year follow-up. Only patients who completed the questionnaire during the initial interview were included in the study. This questionnaire gathered data on patients' socio-demographic characteristics, including age, race, marital status (single, married, divorced/separated), education level (none, ≤ 5 years (primary school), ≤ 8 years (middle school), ≤ 12 years (high school), >12 years (university)), income, employment status divided into; full-time, part time, unemployed, student)), and insurance status (any public, private or none). Additionally, the questionnaire inquired about patients' comorbidities and joint health status over the past year. Comorbid conditions assessed included the cardiovascular disease, hypertension, diabetes mellitus, kidney disease, cancer, neurologic disorders, liver disease/hepatitis B and C, arthritis, and human immunodeficiency virus infection/acquired immunodeficiency syndrome (HIV/AIDS). Clinical chart reviews provided data on hemophilia type, severity (classified as severe (<0.01 IU/ml FVIII or FIX), moderate (0.01–0.05 IU/ml FVIII or FIX) or mild (0.05–0.40 IU/ml FVIII or FIX) hemophilia), treatment strategy (prophylaxis or on demand), inhibitor status, history of immune tolerance, hepatitis A, B, and C antibody status. Additionally, height and weight measurements were taken to calculate body mass index (BMI).

Statistical Analysis

Statistical data analysis was conducted using SPSS version 16.0 (2007, SPSS for Windows, SPSS Inc., Chicago, IL, USA). An exploratory analysis was performed to describe the study population. Categorical variables were summarized using frequency tables, while continuous variables were expressed using measures of central tendency and dispersion, such as mean ± standard deviation (SD) and median (range). Qualitative or categorical variables were described as and proportions. The chi-square test and Fisher's exact test were used to determine association between categorical variables. For quantitative data, the independent samples t-test and Mann–Whitney U test were used to analyze data with normal and skewed distributions, respectively. A p-value of < 0.05 was considered statistically significant.

Ethical Considerations

During the planning of the study, necessary permissions were obtained from Ege University Department of Hematology, where the study was conducted. The study was approved by the Ege University Clinical Research Ethics Committee (Date: 09.08.2016, Decision No: 16-7/1). Written and verbal

consent was obtained from all individuals included in the study.

RESULTS

Patients' clinical characteristics

A total of 135 patients who completed the questionnaire were included in the study. The median age was 39 years (range, 19-68). Among these, 111 patients (82.2%) had hemophilia A, and 24 patients (17.8%) had hemophilia B. The clinical and socio-demographic characteristics of patients are summarized in Table 1. A majority of the patients (n= 85, 63.1%) had severe hemophilia (plasma factor levels <1%), while those with moderate and mild hemophilia accounted for 17.7% (n=24) and 19.2 % (n=26), respectively. Among patients with hemophilia A, 71% (78/111) had severe hemophilia, compared to 29% (7/24) of patients with hemophilia B who had severe disease. Patients with mild disease were significantly more prevalent in hemophilia B than in hemophilia A (58% vs 9%, respectively; p=0.0001). Additionally, all but two of the patients with severe hemophilia (n=85) had at least one affected joint and 31.8% of them had three and more affected joints. In our cohort, 84.4% of patients had at least one joint with hemophilic arthropathy.

Prophylaxis treatment was reported by 101 (74.8%) patients and it was more commonly preferred in patients with hemophilia A than B, and in those with severe hemophilia compared to those with moderate or mild forms hemophilia patients (p=0,002 and p=0,0001, respectively). Ninety-six percent of patients on prophylaxis had at least one joint deterioration, while 52.9% of patients on on-demand treatment had at least one joint deterioration (p=0,001). The occurrence of spontaneous bleeding

Table 1. Characteristics of Patients

Variables, *N* (%)	**Total** N=135	**Hemophilia A** N= 111 (82.2)	**Hemophilia B** N= 24 (17.8)
Age in years, median (range)	39 (18-68)	40 (19-68)	38 (18-61)
Disease severity			
Severe	85 (63.1)	78 (71)	7 (24)
Moderate	24 (17.7)	23 (20)	3 (18)
Mild	26 (19.2)	10 (9)	14 (58)
Factor VIII treatment, n (%)			
Prophylactic treatment	101 (74.8)	89 (80.2)	12 (50)
On-demand treatment	34 (25.2)	22 (19.8)	12 (50)
Presence of inhibitor, n (%)			
Yes	12 (8.9)	10 (9)	2 (8.3)
No	118 (87.4)	96 (86.5)	22 (91.7)
Marital status, n (%)			
Single	43 (31.9)	32 (28.8)	11 (45.8)
Married	87 (64.4)	74 (66.7)	13 (54.2)
Divorced/separated	5 (3.7)	5 (4.5)	None
Current Occupation			
Full-time	43 (31.9)	37 (33.3)	6 (25)
Part-time	39 (28.9)	32 (28.8)	7 (29.2)
Unemployed	45 (33.3)	36 (32.4)	9 (37.5)
Student	8 (5.9)	6 (5.4)	2 (8.3)
Insurance type, n			
Any public	135	111	24
Private	3 (2.2)	2 (1.8)	1 (4.1)
No insurance	None	None	None
Education level			
No education	2 (1.5)	1 (0.9)	1 (4.2)
≤ 5 years (primary school)	39 (21.5)	27 (24.3)	2 (8.3)
≤ 8 years (middle school)	23 (17)	19 (16.7)	4 (16.7)
≤ 12 years (high school)	39 (28.9)	29 (26.1)	10 (41.7)
>12 years (university)	42 (31.1)	35 (31.5)	7 (29.2)

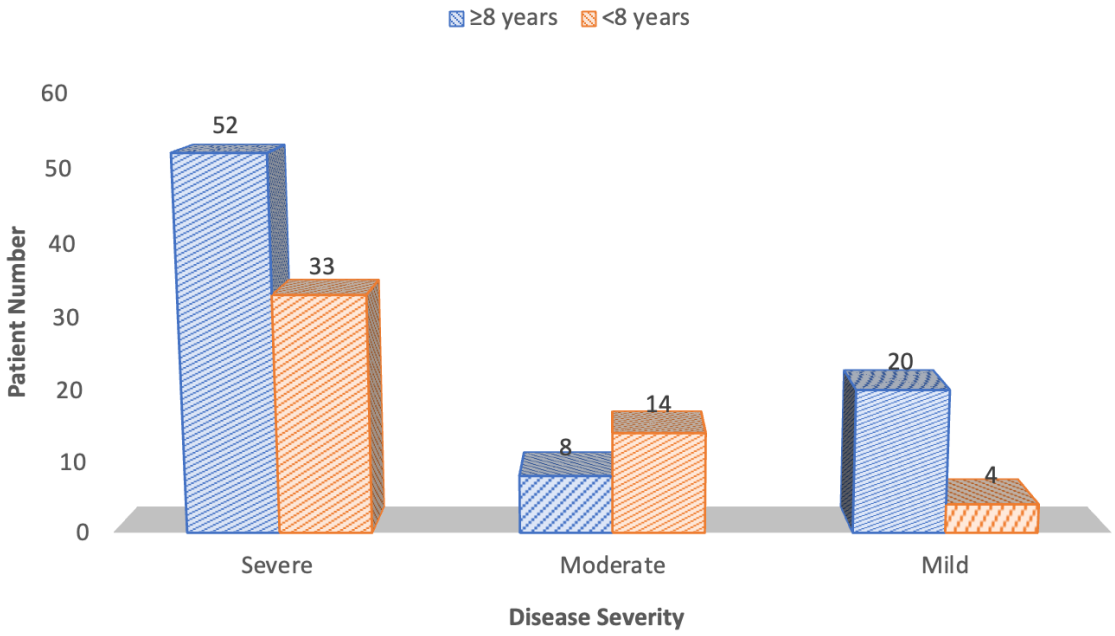


Figure 1. Association of Education Status and Hemophilia Disease Severity. Severe hemophilia patients were significantly less educated than moderate and mild hemophilia patients (p=0.045).

episodes in the previous year did not differ between patients treated with prophylaxis and those on on-demand therapy. However, bleeding episodes after trauma were significantly higher in patients on prophylaxis therapy (p=0,008). Inhibitor positivity was detected in 12 (8,9%) patients, 10 of whom had hemophilia A. Although 9 of the 12 inhibitor-positive patients had severe hemophilia, there was no association between inhibitor status and the type or severity of hemophilia.

Socio-demographic Characteristics

The marital status distribution among the patients was as follows: 64.4% (87) were married, 30.4% (41) were single, and 5.1% (7) were divorced (Table 1). There was no correlation between marital status and disease severity, hemophilia type, treatment modality, or annual bleeding episodes. All patients had public insurance. Of the participants, 5.9% (8) were students, and 60.2% (82) had a full-time or part-time job; however, 33.3% (45) were unemployed. Patients who were employed in any capacity experienced higher numbers of annual bleeding episodes and more affected joints compared to those who were unemployed (p=0.04). While only two patients were illiterate, 60% of the patients had graduated from high school and university (28.9% and 31.1%, respectively). There was no association between educational status and disease morbidity or bleeding episodes, but education status was correlated with hemophilia severity (p=0.045, data shown in Figure 1).

Comorbidities

The frequencies of comorbidities among all patients are summarized in Table 2. The mean BMI was 25,74 ±4,2 kg/m2. Among the patients, 5 had a BMI below 18.5; of these, 2 (40%) had severe disease, while the remaining 3 had mild to moderate disease. The distribution of patients within the BMI ranges of 18.5-24.9, 25-29.9, and ≥ 30 were 57, 57, and 16, respectively. There was no significant correlation between disease severity and BMI, with more than half of the patients in each BMI group having severe disease: 59% (34/57) in the 18.5-24.9 range, 66% (38/57) in the 25-29.9 range, and 68% (11/16) in the ≥30 range. Furthermore, no significant relationship was found between BMI and the number of affected joints or annual bleeding episodes. However, the frequency of affected joints varied with BMI; the right ankle was more commonly affected in patients with a BMI ≥ 25 compared to those with a BMI < 25 (p = 0.015). Hypertension was present in 17.8% (24) of the patients, all of whom were on medication, with prevalence of 17.1% (19/111) in hemophilia A and 20% (5/24) in hemophilia B. No significant correlations were found between hypertension and clinical characteristics such as disease type, severity,

Table 2. Comorbidities of Patients

	n (%)
HBV	3 (2.2)
HCV	13 (9.6)
HIV/AIDS	0
Liver Disease	2 (1.4)
Hypertension	24 (17.8)
Diabetes mellitus	18 (13.3)
Obesity [a]	16 (11.9)
Hypercholesterolemia/hyperlipidemia	8 (5.9)
Cardiovascular disease	9 (6.7)
Neurological Disease (stroke, epilepsy)	3 (2.2)
Cancer	4 (2.9)
Rheumatologic Disease	2 (1.4)
Endocrinological disease	4 (2.9)
Kidney disease	4 (2.9)

[a] Obese were calculated based on initial clinician form of height and weight; overweight is defined as BMI (=weight (kg)/height^2 (m)) ≥25 and <30; obese is defined as BMI ≥30.

inhibitor status, or bleeding episodes. Diabetes mellitus (DM) was diagnosed in 13.3% (18) of the patients, with higher annual bleeding episodes observed in patients with DM compared to those without (p=0.024). Of the patients, 61.5% (83) were smokers. Cardiovascular disease was reported in 6.7% (9) of patients; two had a history of myocardial infarction and one had undergone bypass surgery. There was no correlation between cardiovascular disease and disease type, severity, or annual bleeding episodes. Cancer history was noted in four patients, including diagnoses of acute leukemia, bone tumor, gastric cancer, and hepatocellular carcinoma. Kidney disease was observed in four patients over 40 years old, including one with membranous glomerulonephritis and three with kidney stones.

Hepatitis B and C were reported in 3 and 13 patients, respectively, with six still undergoing anti-HCV treatment. Cirrhosis due to HCV was observed in two patients, one of whom also had hepatocellular carcinoma. Among those infected with HCV, 15% of patients with severe hemophilia exhibited inhibitor positivity. Notably, none of our patients had an HIV infection.

DISCUSSION

Socio-demographic and epidemiological characteristics of adult PWH in our country are still overlooked and poorly defined. In our study group, a high proportion of patients (63.1%) had severe disease, and most were treated with prophylactic factor replacement therapy. The inhibitor positivity was reported at 8.9% among our participants. Kavaklı et al. reported inhibitor prevalence at 11.2% for hemophilia A patients and 15.8% for severe hemophilia A patients in Turkey (9). However, the prevalence of inhibitors in hemophilia patients varies widely in different studies, ranging from 6% to 27% (10-13).

PWH have a higher unemployment rate compared to the general population, largely due to joint deformities causing physical handicaps, and the inability to continue working because of bleeding episodes. The unemployment rate among all patients in our study was 33.3% while it ranges from 13% to 20% in industrialized countries and about 54% in underdeveloped countries (14,15). Our significantly higher unemployment rate is likely influenced by the overall high unemployment rate and the limited job opportunities in our country. There was a strong correlation between the patients' occupation and annual bleeding episodes; unemployed patients experienced fewer joint bleedings overall. This could be due to reduced physical activity among those not working. However, since the nature of the employed patients' jobs (whether desk-based or physically demanding) was not specifically assessed, it would be premature to attribute this trend solely to physical activity levels.

In various studies, 65% of hemophilia patients were found to have completed at least 12 years of education, equivalent to high school graduation (14). In our study, this ratio slightly lower at 60%. According to 2016 statistics, 35% of adults over 35 in Turkey had a university degree or higher, which is close to the 33.3% found in our survey. It is important to note that if this study were conducted in the eastern cities of Turkey, the proportion of university graduates among the patients might have been lower.

Previous studies have shown mixed results regarding the risk and prevalence of comorbidities in PWH compared to the general population. Few studies

have evaluated these comorbidities in PWH against an age-matched control group without hemophilia (13,16,17). Chronic viral infections and hypertension were found to be more prevalent in PWH, while cardiovascular disease (17), overweight, and hypercholesterolemia were reported less frequently (16). The incidence rates for DM and cancer were similar between cases and controls (13). Kulkarni et al. identified common risk factors for PWH, such as age, hypertension, smoking, obesity and DM, indicating that the prevalence of cardiovascular disease in PWH over 45 was comparable to that in the non-hemophilic population. However, other studies have reported lower mortality rates from cardiovascular disease in PWH. In our cohort, the prevalence of cardiovascular disease was 6.7%, slightly higher than the 6.1% reported for males over thirty in Turkey by the Turkish Statistical Committee but similar to previous retrospective studies. This underlines the importance of screening and primary prevention given the longer life expectancies of hemophilia patients. The prevalence of hypertension and DM in our study was 17.8% and 13.3%, respectively, which are lower than previously reported data (16). Interestingly, we observed that the annual bleeding rate was significantly lower in patients with DM. When reevaluating the data, we found that patients with DM were typically older and unemployed, leading to the hypothesis that reduced physical activity contributed to fewer bleeding episodes A study from Taiwan reported the prevalence of overweight and obesity was 61.8% in PWH aged 30 to 39 years, 60.6% in PWH aged 40 to 49 years, and 48% in PWH aged ≥50 years and showed that BMI and obesity also had positive correlation with annual joint bleeding rate (18). However, in our study, no correlation was found between BMI and annual bleeding episodes or disease severity. We did observe that the right ankle was the most commonly affected joint in patients with higher degrees of obesity.

HCV was the most common blood-borne virus in our study population, with an overall incidence of 11.8%. Prior to 1990, PWH were particularly susceptible to HCV and HBV infections. However, the risk significantly decreased after the implementation of mandatory serological and molecular testing; during blood donations. Currently, the expected seroprevalence of HCV infection in PWH is 3.6% (19). Hepatocellular carcinoma due to HCV infection was reported in one (1/13) patient in our cohort.

There are some limitations in our study. Firstly, it was retrospective, based on patients' recorded files, which may limit the accuracy and depth of data collected. Secondly, the correlation between socio-demographic factors and clinical features is suboptimal, as we were unable to evaluate aspects such as quality of life, physical activity, and physical and social functioning. Thirdly, while we reported the prevalence of comorbidities in our study group, these findings would be more robust if compared with an age-matched general population. Despite these limitations, to our knowledge, this is the first study in Turkey to describe the epidemiology and comorbidities of adult hemophilia patients, involving a larger number of patients than previously reported studies from other countries. Additionally, our findings indicate that the rate of university graduation and the unemployment ratio in our study group are comparable to those of the general population in our country.

CONCLUSION

Over the past seven decades, the availability of replacement factor products and new treatment strategies has significantly increased the life expectancy of the patients with hemophilia. However, treating older hemophilia patients and managing their emerging age-related diseases are still challenges for hematologists, due to relatively limited experience. Currently, there is no consensus or established guidelines for managing age-related diseases in PWH. Hemophilia caregivers and comprehensive care centers should be proactive in monitoring and managing the comorbidities in adults with hemophilia, ensuring patient well-being, and coordinating the optimal care. Moreover, further researches are essential to develop appropriate guidelines for managing older PWH.

Acknowledgements: None.
Author Contributions: Concept: FKK, FŞ. Design: FKK, GS, FŞ. Data Collection: FKK, ZD, FDK, Analysis and/or interpretation: FKK, ZD, FDK. Literature Search: FKK, FDK, FŞ, GS. Writing: FKK, ZD, FŞ, Critical Review: FKK, GS, FŞ.
Conflict of Interest: The authors declare no conflict of interest.
Ethical Approval: The study was approved by Ege University, Clinical Research Ethics Committee (Date: 09.08.2016, Decision No: 16-7/1).
Funding: None.
Peer-Review: Externally peer-reviewed.

REFERENCES

1. Nathwani AC. Gene therapy for hemophilia. Hematology Am Soc Hematol Educ Program 2019;2019(1):1-8.
2. Franchini M, Mannucci PM. Co-morbidities and quality of life in elderly persons with haemophilia. Br J Haematol 2010;148(4):522-33.
3. Aledort L, Bullinger M, von Mackensen S, et al. Why should we care about quality of life in persons with haemophilia? Haemophilia 2012;18(3):e154-7.
4. Kempton CL, Makris M, Holme PA. Management of comorbidities in haemophilia. Haemophilia 2021;27 Suppl 3:37-45.
5. Mannucci PM. Aging with Hemophilia: The Challenge of Appropriate Drug Prescription. Mediterr J Hematol Infect Dis 2019;11(1):e2019056.
6. Alam AU, Goodyear MD, Wu C, et al. Increased acute care utilisation, comorbidities and mortality in adults with haemophilia: A population-based cohort study from 2012 to 2019. Haemophilia 2023;29(1):219-229.
7. Shapiro S, Makris M. Haemophilia and ageing. Br J Haematol 2019;184(5):712-720.
8. Skjefstad K, Solberg O, Glosli H, et al. Life expectancy and cause of death in individuals with haemophilia A and B in Norway, 1986-2018. Eur J Haematol 2020;105(5):608-615.
9. Kavakli K, Aktuglu G, Kemahli S, et al. Inhibitor screening for patients with hemophilia in Turkey. Turk J Haematol 2006;23(1):25-32.
10. Ghosh K, Shetty S, Kulkarni B, et al. Development of inhibitors in patients with haemophilia from India. Haemophilia 2001;7(3):273-8.
11. Oren H, Yaprak I, Irken G. Factor VIII inhibitors in patients with hemophilia A. Acta Haematol 1999;102(1):42-6.
12. Lusher JM, Arkin S, Abildgaard CF, et al. Recombinant factor VIII for the treatment of previously untreated patients with hemophilia A. Safety, efficacy, and development of inhibitors. Kogenate Previously Untreated Patient Study Group. N Engl J Med 1993;328(7):453-9.
13. Marchesini E, Oliovecchio E, Coppola A, et al. Comorbidities in persons with haemophilia aged 60 years or more compared with age-matched people from the general population. Haemophilia 2018;24(1):e6-e10.
14. Curtis R, Baker J, Riske B, et al. Young adults with hemophilia in the U.S.: demographics, comorbidities, and health status. Am J Hematol 2015;90 Suppl 2:S11-6.
15. Sun J, Zhao Y, Yang R, et al. The demographics, treatment characteristics and quality of life of adult people with haemophilia in China - results from the HERO study. Haemophilia 2017;23(1):89-97.
16. Fransen van de Putte DE, Fischer K, Makris M, et al. Increased prevalence of hypertension in haemophilia patients. Thromb Haemost 2012;108(4):750-5.
17. Siboni SM, Mannucci PM, Gringeri A, et al. Health status and quality of life of elderly persons with severe hemophilia born before the advent of modern replacement therapy. J Thromb Haemost 2009;7(5):780-6.
18. Chang CY, Li TY, Cheng SN, et al. Obesity and overweight in patients with hemophilia: Prevalence by age, clinical correlates, and impact on joint bleeding. J Chin Med Assoc 2019 ;82(4):289-294.
19. Santos EM, Silva JM, Barbosa AN, et al. Clinico-epidemiological and sociodemographic profile of patients with hemophilia in the Brazilian Amazon: High prevalence of hepatitis C infection and its possible corrrelation with inhibitor development. Front Public Health 2022;10:963790.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 490-497
https://doi.org/10.30621/jbachs.1427464
RESEARCH ARTICLE

ITEM ANALYSIS IN MULTIPLE CHOICE QUESTIONS: A STUDY ON QUESTION DIFFICULTY AND AUTHORS' EVALUATION

Serap Konakci[1]

[1]Dokuz Eylul University, Faculty of Medicine, Department of Medical Education, Izmir-Turkey

ORCID: S.K. 0000-0002-3325-6382

Corresponding author: Serap Konakcı, **E-mail:** serapkonakci@yahoo.com
Received: 29.01.2024; **Accepted:** 10.05.2024; **Available Online Date:** 31.05.2024

Cite this article as: Konakci S. Item Analysis in Multiple Choice Questions: A Study on Question Difficulty and Authors' Evaluation. J Basic Clin Health Sci 2024; 8: 490-497.

ABSTRACT

Introduction: Multiple choice questions (MCQs) are widely used in medical education. This study aims to evaluate the quality of MCQ and the predictions of MCQ authors about the difficulty levels of their questions.

Methods: In this study, the Difficulty Index (DIF I), Discrimination Index (DI), and Distractor Efficiency (DE) values of 688 MCQs in the exams held in the first year of the 2021-2022 academic year of Dokuz Eylül University Faculty of Medicine were investigated. The data were reported as a percentage and mean ± standard deviation (SD), minimum and maximum values of items. DIF I and DI values among the groups formed according to the distractor activity were compared using the t-test, and the effect size was calculated. Estimated and actual DIF I, one-to-one matching was evaluated with Mc neamer chi-square test.

Results: The results of our research are based on the analysis of data from 688 MCQs. DIF I mean was 0.57±0.21, and 47.5% was at the ideal difficulty level. There was a significant difference between the estimated and the actual DIF I (p=0.002). The DI average was 0.31 ± 0.17, and the discrimination level of 43.6% was excellent. 36.8% of distractors were NFD. MCQ's difficulty and discriminatory ability were significantly different according to the number of NFDs (p<0.001 for all).

Discussion: It was determined that the number of NFDs significantly affected difficulty and discriminatory ability. There was a difference between the estimates of the difficulty and the actual values. Reducing the number of options in MCQs and being more careful when crafting questions can improve the quality of the questions.

Keywords: Difficulty index, Discrimination index, Functioning distractors, Item Analysis, MCQs.

INTRODUCTION

Tests consisting of multiple choice questions (MCQ) are widely used in medical education, as they allow the evaluation of high-level cognitive areas of Bloom's taxonomy and the evaluation of a large number of people simultaneously (1-5).

Item analysis allows the quality of MCQs to be evaluated. Difficulty Index (DIF I), Discrimination Index (DI), and Distractor efficiency (DE) are the most frequently used item analysis values. With these analyses, the properties of each substance can be determined separately (6). Also, item analysis helps to decide on the selection, revision, or removal of questions to create question banks. It provides data for question writers on their performance and guides them to write more effective MCQs. Guides and

studies on MCQ preparation can be easily found in the literature (1, 7-12).

DIF I takes a value between '0' and '1'; the closer it is to 1, the easier the MCQ is. DIF I value for medical education can be grouped as ≤ 0.29 too difficult, 0.30-0.70 acceptable, 0.50-0.60 ideal, and ≥ 0.70 too easy (13-15).

DI defines the extent to which the item can distinguish between students knowledgeable in the targeted field and students who are not. DI can take a value between '-1' and '+1'. As DI approaches '+1', the ability to distinguish between those who know and those who do not know increases. If the DI value of an item is 0.19 or below and does not contain an obvious error that can be corrected when examined, it is recommended that the item be removed from the test/not used again. A DI value of ≥0.35 is considered excellent in an ideal test.

DE is effective in determining the difficulty and discrimination level of an item. For someone who does not have sufficient knowledge of the subject being evaluated, distractors are expected to be the correct answer and be preferred. Arranging the appropriate distractor is as tricky as arranging the correct response (16). A distractor with a preference rate of <5% is generally considered non-functional. The more non-functional distractors (NFD) in an MCQ, the lower and easier it becomes to discriminate.

It is important in ensuring the validity and reliability of the exams that MCQ writers master the principles of question preparation and have knowledge about interpreting the results of item analysis. Besides, it is important to consider the item analysis results in creating question banks.

The questions of this research are as follows:

- What are the conditions of DIF I, DI, and DE of the evaluated MCQs?
- Does the number of NFD have an effect on DIF I and DI?
- Do question authors have a realistic foresight about the difficulty level of their questions?

In this study, the evaluation of MCQ quality and the assessment of question authors' predictions about the difficulty level of their questions are aimed to find answers to the research questions mentioned above.

MATERIALS AND METHODS

In the 2021-2022 academic year, a total of six MCQ tests were applied to 346 students studying at Dokuz Eylül University Faculty of Medicine (DEUFM) Term 1 for knowledge evaluation throughout the year. The tests were prepared using the blueprint. The number of questions to be included in the tests varies depending on the block time and total number of targets (min: 100 - max: 125 MCQs). MCQs in the tests have five options and one correct answer. All of the questions were used for the first time. Item analysis was performed routinely after each exam. The results were used as a guide to decide on the reuse of questions stored in the question bank. In the 2021-2022 academic year, MCQ authors recorded their estimation of DIF I as 'very easy, acceptable or very difficult' when preparing the question. Before all MCQs were used in the tests, they were reviewed by an evaluator other than the MCQ authors in terms of grammatical clues, logical clues, having more details in the right option, the arrangement of options (chronological or numerical order), and unnecessary information in the stem. After the necessary arrangements and corrections were made, they were used in the exams.

In our faculty, a question discussion session was held after each exam. Questions and correct answers were shared with students in discussion sessions. After these sessions, students had the right to object to the information contained in the MCQs and the correct answer by citing literature. According to the item analysis results, questions with a known rate of 10% or less, questions with a noticeably high rate of marking a particular distractor, questions with DI ≤0.19 and DIF I value <30, and questions objected to by students citing literature support were consulted with the MCQ author.

A total of 700 MCQs were used in six Term I tests that took place during the period covered by the research, and the authors of 40 MCQs were consulted in line with the criteria listed above. Twenty of the MCQs whose authors were consulted were excluded from the evaluation because they were found to contain informational errors. This process was routinely applied in all MCQ exams in our faculty, and the final calculation of student scores was made after these procedures. The research results were based on the evaluation of data from the item analysis of 688 MCQs used in calculating student scores.

Item Analysis

DIF I and DI are calculated and categorized as follows:

H= Number of students giving correct responses in the high score group (upper 27%).
L= Number of students giving correct responses in the low score group (lower 27%).
N= Total no of responses in both groups.

DIF I = [(H+L) / N] (DIF I of an item range between 0-1)
Criteria for categorization of DIF I is,
DIF I ≥0.7 = too easy
DIF I = 0.3 – 0.7= acceptable
DIF I = 0.5-0.6= ideal
DIF I ≤0.29= too difficult

DI = 2 x [(HL) / N] [DI of an item range between (-1) – (+1)]
Criteria for categorization of DI are,
DI ≤ 0.2 = poor
DI = 0.21-0.24 =acceptable
DI = 0.25-0.34=good
DI ≥0.35 = excellent

For DE, a distractor with a preference rate of <5% was considered non-functional, and the number of non-functional distractors (NFD) was determined for each MCQ.

Statistical Analysis
Statistical analyses of the research were carried out via SPSS v.24.0 (IBM, Armonk, NY, United States of America) using the item analysis results of the education management system used in our faculty. The data were reported as a percentage and mean ± standard deviation (SD), minimum and maximum values of items. By grouping as Estimated and actual DIF I, acceptable DIF I, and other DIF I (easy DIF I + difficult DIF I), one-to-one matching was evaluated with Mc neamer chi-square test. DIF I and DI values among the groups formed according to the distractor activity were compared using the t-test, and the effect size was calculated. A p-value of <0.05 was considered statistically significant.

Ethical Approval: The study was conducted after receiving approval from Non-interventional Research Ethics Committee of Dokuz Eylül University (Decision Date: 11.03.2023, No:2023/02-11).

Data usage permission*:* The data used in the research were obtained retrospectively from the item analysis results of the examinations conducted by the Dean's Office of Dokuz Eylül University Faculty of Medicine. The usage of the data has been granted permission by the Dean's Office of Dokuz Eylül University Faculty of Medicine (29.12.2022 / Document number: E-13511134-044[044]-470153). This permission document, along with other requested documents, was submitted to the Ethics Committee of Dokuz Eylül University for Non-interventional Studies. No personal data belonging to individuals were used, and no interventional procedures were performed.
This research dataset is accessible at https://doi.org/10.5281/zenodo.10461566.The anonymized data can be made accessible on request.

Table 1. Distribution of items according to their DIF I, DI and NFD* (n=688)

		Number of items	%
DIF I	≤ 0.29 (too difficult)	69	10.0
	0.3 - 0.7 (acceptable)	414	60.2
	≥ 0.7 (too easy)	205	29.8
	0.5-0.6 (ideal)	327	47.5
DI	≤ 0.2 (poor)	183	26.6
	0.21-0.24 (acceptable)	57	8.3
	0.25-0.34 (good)	148	21.5
	≥0.35 (excellent)	300	43.6
NFD	0 NFD	207	30.1
	1 NFD	166	24.1
	2 NFD	154	22.4
	3NFD	104	15.1
	4 NFD	57	8.3

*DIF I: Difficulty Index, DI: Discrimination Index, NFD:Non-Functional Distractors

RESULTS
DIF I mean in post-evaluation item analysis was determined as 0.57±0.21 (min:0.06 max: 0.99). 60.2% (205 questions) of all MCQs were at the acceptable difficulty level, and 47.5% (327 questions) were at the ideal difficulty level (Table 1).
According to the difficulty estimates made by the MCQ authors while preparing the questions, 52.0% (358 questions) of the questions were labeled acceptable, 39.0% (268 questions) were labeled too easy, and 9.0% (62 MCQs) were labeled too difficult (Figure 1).

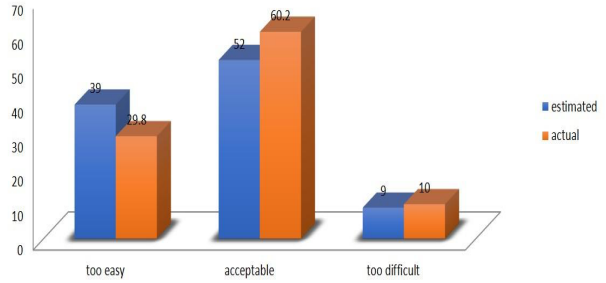


Figure 1. Distribution of items according to their estimated DIF I and actual DIF I (n=688) (%).

It was determined that there was a significant difference between the DIF I predicted by the MCQ authors and the actual DIF I groups ($x2_{mc\ neamer}$ =9.45, p=0.002) (Table 2).

The DI average for all items was 0.31 ± 0.17 (min: -0.19, max:0.84). In the grouping according to the DI level, the discrimination of 43.6% (300 questions) of the items was at a very good level, while the discrimination of 26.6% (183 questions) was very low (Table 1).

There were a total of 2752 distractors in 688 MCQs. 36.8% of the distractors (1014 distractors) were NFD. It was determined that all distractors worked in 30.1% of the MCQs (207 questions), and none of the distractors worked in 8.4% (57 MCQs) (Table 1).

In the comparison between DIF I and DI levels according to the operating status of the distractors, it was determined that there was a significant difference between the averages of the groups (p<0.001for all, η^2 =0.569 and 0.083, respectively) (Table 3).

DISCUSSION

In our study, it was determined that the DIF I value of 60.2% of all items was at an acceptable level, and 47.5% of them were at an ideal level. When we look at the estimated DIF I proportional distribution 52.0% acceptable, 39.0% too easy, 9.0% too difficult. There is a statistically significant difference between estimated and actual DIF ($x2_{mc\ neamer}$ =9.45, p=0.002). MCQs DI values, we found that 43.6% were at an excellent level and 21.5% were at a good level and it was found that all distractors worked in 30.1% of MCQs. When we compared the DIF I values of MCQs according to the number of NFDs, we saw that, as expected, as the number of NFDs increased, the DIF I value approached one, and the effect size was significant (p= 0.000, η^2= 0.569).

It is common to use tests consisting of MCQs for knowledge assessment in medical education. Item analyses are applied after the questions are used and provide valuable information about the test's overall quality and the MCQ's quality.

In the literature, many studies evaluated the results of item analysis of tests consisting of multiple-choice and single-correct answers applied in medicine and the health field. These studies generally aim to evaluate the items of only a single test (13, 14, 17,19). Unlike these studies, our research is based on the item analysis results of 688 of the 700 MCQs used in the Term 1 knowledge evaluation exams in the 2021-2022 academic year, which contained no information errors and were included in the question bank after the exams. These questions were used for the first time in the relevant exams.

Recognition/frequent use of MCQs by students has an impact on item analysis results. Therefore, we think it is important that all MCQs are used for the first time. However, we found no information on this subject in the studies we compared the results of.

In our study, it was determined that the DIF I value of 60.2% of all items was at an acceptable level, and 47.5% of them were at an ideal level. When our results are compared with similar studies in the literature, it is seen that our acceptable DIF I rate is lower than some studies (15, 18, 21, 22). However, approximately half (47.5%) of the 688 MCQs we evaluated in our research have an ideal DIF I value. This finding indicates that most questions within acceptable limits were stacked at an ideal level. The range defined as the acceptable limit is quite wide. MCQs in tests have a certain difficulty, and discrimination limit is a criterion that must be

Table 2. Distribution of MCQs according to Estimated and actual DIF I

		Actual DIF I						Total		
		Acceptable			Other					
		n	Row %	Column %	n	Row %	Column %	n	Row %	Column %
Estimated DIF I	**Acceptable**	226	63.1	54.6	132	36.9	48.2	358	100.0	52.0
	Other	188	57.0	45.4	142	43.0	51.8	330	100.0	48.0
Total		414	60.2	100.0	274	39.8	100.0	688	100.0	100.0

Table 3. Comparison of MCQs' DIF I and DIF Levels

		N	Mean	SD	Min.	Max.	F	p	Eta Squared(η^2)
DIF I	4 NFD	57	.8961	.04242	.81	.99	225.37	0.000	0.569
	3 NFD	104	.7550	.12403	.30	.90			
	2 NFD	154	.6353	.14244	.16	.84			
	1 NFD	166	.4868	.15984	.06	.78			
	0 NFD	207	.4127	.13096	.09	.71			
	Total	**688**	**.5722**	**.20576**	**.06**	**.99**			
DI	4 NFD	57	.1695	.08589	.00	.37	15.36	0.000	0.083
	3 NFD	104	.2905	.14291	-.06	.84			
	2 NFD	154	.3425	.15454	-.03	.77			
	1 NFD	166	.3449	.17484	-.10	.73			
	0 NFD	207	.3217	.16996	-.19	.66			
	Total	**688**	**.3146**	**.16502**	**-.19**	**.84**			

considered for the tests to serve their purpose and obtain valid and reliable measurement tools. Tests consisting of MCQs without appropriate values can also impact student exam success, both in terms of failure and passing (5, 8, 23, 24). Therefore, we think that the ideal level should be tried to be achieved rather than the acceptable level, and these questions should be given priority in the selection for the question bank.

MCQ writers need to consider these criteria while preparing their questions and try to prepare questions suitable for the ideal DIF I and DF level, free from spelling and editing errors. Our faculty has been providing training on MCQ preparation and item analysis for many years. However, as a common behavior, there are problems in complying with existing guidelines or training materials, as described in the literature (8, 24 - 29). Hence, MCQs in our Faculty are reviewed for item writing flaws by a measurement evaluator other than the question authors before they are used in the tests. Detected errors are corrected. In this way, the effect of common errors carried by MCQs is tried to be minimized. In the literature, in similar studies on item analysis, no information was found indicating that MCQs were reviewed/corrected by measurement and evaluator before being used. In the study of Ali and Ruit, based on the item analysis results, the results obtained in the subsequent use of the MCQs reviewed in terms of item writing flaws and NFD were evaluated (30). Research that provides the opportunity to demonstrate the effect of the regulations by comparing them with the item analysis results of equivalent exams consisting of MCQs without final adjustments will allow us to evaluate the real impact of the intense effort given.

When determining the difficulty of a question, the MCQ writer needs to consider the level of the learning goal related to the question and the cognitive level of the question, which is often overlooked. Our study evaluates the consistency of the item difficulty level predicted by the MCQ author with the actual difficulty level. When we look at the estimated DIF I proportional distribution (52.0% acceptable, 39.0% too easy, 9.0% too difficult), it can be thought that question writers generally tend to prepare MCQs at an acceptable difficulty level. However, when we examined the distribution of actual DIF I values, it was determined that there are proportional differences in the DIF I distribution compared to the estimated DIF I, within very easy and acceptable limits. In a one-to-one comparison, it was determined that only half of the MCQs, which were within acceptable limits according to the actual DIF I, were labeled in the same way by the question authors. There is a statistically significant difference between estimated and actual DIF ($x2_{\text{mc neamer}}$ =9.45, p=0.002). This situation is most likely because MCQ authors label DIF I without giving it much thought/care. It may also be effective that students do not have a realistic prediction about their knowledge level or that the MCQs are prepared by an assessment evaluator other than the author before the exams.

In our study, when we grouped the MCQs according to their DI values, we found that 43.6% were at an excellent level and 21.5% were at a good level. In our study, the excellent DI level is lower than that of Uddin et al.'s study; however, the number of evaluated MCQs specifically given in percentage was not clearly

defined in the article (20). Our excellent DI level question rate was at a higher level than similar studies, except for the study by Rao et al. The high rate of questions with ideal DIF I and excellent DI levels can also be considered an important clue about exam reliability (15, 18, 21, 22).

The presence of NFD is one of the factors affecting the quality of MCQ. In our research, it was found that all distractors worked in 30.1% of MCQs. In 8.4% of MCQs, all distractors were non-functional. These MCQs may have irrelevant distractors, the cognitive level may be very low, or they may indicate rare situations in which all students achieve correct learning. However, the rate of these MCQs is quite low. The results of the study are consistent with the study of Kumar et al., where the rate of MCQs with all distractors being functional was found to be 33%, and the rate of MCQs with all distractors being non-functional was found to be 2% (22). However, Bhattacherjee et al., found in their study that the rate of MCQ with all distractors working was 13.33%, and the rate of MCQ with all distractors being non-functional was 16.67% (21).

We use five-choice MCQs with one correct answer in our exams. However, in studies conducted on medical and health education exams related to item analysis, it is observed that MCQs are arranged with one correct answer and four options. Studies are showing that the number of options in the MCQ being less than five does not have a significant effect on the DIF I and DI values or that increasing the number of distractors in the MCQ does not have a positive effect (31-37). Kheyami et al., state that using an MCQ with four options may be better than using an MCQ with five options (38). Rodríguez, reported that removing the least functional distractor did not have a negative effect on DIF I, while the remaining ones may have a positive effect on DI with higher selection frequency (39).

When we compared the DIF I and DI values of MCQs according to the number of NFDs, we saw that, as expected, as the number of NFDs increased, the DIF I value approached one, and the effect size was significant ($p= 0.000$, $\eta^2= 0.569$). In our analysis of the DI values of MCQs according to the number of NFDs, we revealed that although we found a significant difference, the effect size was very low ($p= 0.000$, $\eta^2=0.083$). This finding is consistent with the results of the studies of Rodriguez, Hingorjo and Jaleel (39, 40). The NFD number affects both the DIF I and DI value of the problem. This effect is worth considering, especially on DIF I. It is a difficult task to prepare MCQs with DIF I and DI values that can be considered ideal for assessments in medical education, and as the number of options increases, more editing effort and time is required for the authors. Based on this finding, which is compatible with the literature, we think that it would be appropriate to prepare MCQs with four well-constructed options.

CONCLUSION

In our study, we found that MCQs had mostly ideal DIF I values, but the MCQ authors were not very accurate in their DIF I estimations. In our study, we found that the DI value of approximately half of the questions was excellent. We think that questions with ideal DIF I and DI values will provide a realistic evaluation opportunity. While the number of non-functional distractors has a significant effect on the DIF of a question, we found that it has a significant but small effect on the DI. The effect of the number of NFDs on DIF I and DI suggested that questions with four options could be used instead of having difficulty and making mistakes while trying to create questions with five options. We did not have the opportunity to evaluate the effect of reviewing MCQs in terms of item writing flaws before being used in exams on item analysis values, but we think that studies on this subject will be valuable. It is important for MCQ authors to use the item analysis results in the question bank records as a guide for their development and to avoid repeating the same mistakes in the questions they have just prepared to create reliable tests with high measurement values.

Assessing the item analyses of numerous MCQs, particularly examining the impact of NFDs on DIF I and DI, and comparing question writers' difficulty predictions with the actual difficulty encountered constitute the strong aspects of this study. On the other hand, the failure to evaluate the impact of having questions reviewed by someone other than the question writers before usage constitutes a weakness of this study.

Acknowledgements: None.

Author Contribution: The author SK worked independently in conceptualizing and designing the study, collecting and analyzing data, drafting, and finalizing the manuscript.

Conflict of interest: The author declares that there is no potential conflict of interest to be disclosed.

Ethical Approval: The study was approved by Non-interventional Research Ethics Committee of Dokuz Eylül University (Decision Date: 11.03.2023, No:2023/02-11).

Funding: No funding sources.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Carneson J, Delpierre G, Masters K. Designing, and managing multiple choice questions. 2nd ed. 2016; pp. 3–6. University of Cape Town. Available from: https://www.researchgate.net/publication/309263856_Designing_and_Managing_Multiple_Choice_Questions_2nd_Ed=channel=doi&linkId=58074fef08ae03256b783474&showFulltext=true .
2. Coderre SP, Harasym P, Mandin H, Fick G. The impact of two multiple-choice question formats on the problem-solving strategies used by novices and experts. BMC Med Educ. 2004;4:23.
3. Gierl MJ, Lai H, Turner SR. Using automatic item generation to create multiple-choice test items. Med Educ 2012;46(8):757-765.
4. Palmer EJ, Devitt PG. Assessment of higher order cognitive skills in undergraduate education: modified essay or multiple choice questions? Research paper. BMC Med Educ 2007;7:49.
5. Tarrant M, Ware J. Impact of item-writing flaws in multiple-choice questions on student achievement in high-stakes nursing assessments. Med Educ 2008;42(2):198-206.
6. Tavakol M & Dennick R. Post-examination analysis of objective tests. Medical Teacher 2011;33(6):447–458.
7. Case SM, Swanson DB. Constructing written test questions for the basic and clinical sciences. 3rd ed. Philadelphia: National Board of Medical Examiners; 2000. Availablefrom:https://www.researchgate.net/publication/242759434_Constructing_Written_Test_Questions_For_the_Basic_and_Clinical_Sciences
8. Downing SM. The effects of violating standard item writing principles on tests and students: the consequences of using flawed test items on achievement examinations in medical education. Adv Health Sci Educ Theory Pract. 2005;10(2):133-143.
9. Haladyna TM, Downing SM & Rodriguez MC A Review of Multiple-Choice Item-Writing Guidelines for Classroom Assessment, Applied Measurement in Education 2002;15(3):309-333.
10. Medical Council of Canada (MCC). Guidelines for the Development of Multiple-Choice Questions. Ottawa, ON: MCC 2010. Available from: https://mcc.ca/media/Multiple-choice-question-guidelines.pDI
11. Paniagua MA, Swygert K A editors. Constructing written test questions for the basic and clinical sciences (2016). Available from: https://www.bumc.bu.edu/busm/files/2018/10/NBME-Constructing-Written-Test-Questions.pDI
12. Sutherland K, Schwartz J, Dickison P. Best Practices for Writing Test Items. Journal of Nursing Regulation 2012;3(2):35-39.
13. Christian DS, Prajapati AC, Rana BM, Dave VR. Evaluation of multiple choice questions using item analysis tool: a study from a medical institute of Ahmedabad, Gujarat. Int J Community Med Public Health 2017;4(6):1876-81.
14. Date AP, Borkar AS, Badwaik RT, Siddiqui RA, Shende TR, & Dashputra AV. Item analysis as tool to validate multiple choice question bank in pharmacology. International Journal of Basic & Clinical Pharmacology 2019;8(9):1999–2003.
15. Rehman A, Aslam A & Hassan SH. Item analysis of multiple choice questions. Pakistan Oral & Dental Journal 2018;38(2): 291-293.
16. Gierl MJ, Bulut O, Guo Q & Zhang X. Developing, Analyzing, and Using Distractors for Multiple-Choice Tests in Education: A Comprehensive Review. Review of Educational Research 2017;87(6):1082–1116.
17. Hassan S & Hod R. Use of item analysis to improve the quality of single best answer multiple choice question in summative assessment of undergraduate medical students in Malaysia. Education in Medicine Journal 2017;9(3):33-5-43.
18. Rao C, Kishan Prasad H L, Sajitha K, Permi H, Shetty J. Item analysis of multiple choice questions: Assessing an assessment tool in medical students. Int J Educ Psychol Res 2016;2:201-4.
19. Kolte V. Item analysis of Multiple Choice Questions in Physiology examination. Indian Journal of Basic and Applied Medical Research; 2015;4(4):320-326.
20. Uddin I, Uddin İ, Rehman IU, Siyar M, Mehbob U. Item Analysis of Multiple Choice Questions in Pharmacology. J Saidu Med Coll Swat 2020;10(2):128-13.
21. Bhattacherjee S, Mukherjee A, Bhandari K, Rout AJ. Evaluation of Multiple-Choice Questions by Item Analysis, from an Online Internal Assessment of 6th Semester Medical Students in

a Rural Medical College, West Bengal. Indian J Community Med. 2022;47(1):92-95.
22. Kumar D, Jaipurkar R, Shekhar A, Sikri G, & Srinivas V. Item analysis of multiple choice questions: A quality assurance test for an assessment tool. Medical journal, Armed Forces India, 2021;77(1):85–89.
23. Masters JC, Hulsmeyer BS, Pike ME, Leichty K, Miller MT & Verst AL. Assessment of multiple-choice questions in selected test banks accompanying text books used in nursing education. The Journal of Nursing Education 2001;40(1):25–32.
24. Walsh K. Advice on writing multiple choice questions (MCQs). BMJ 2005;330: 25 - 27.
25. Costello E, Holland JC, Kirwan C. Evaluation of MCQs from MOOCs for common item writing flaws. BMC Res Notes. 2018;11(1):849.
26. Downing SM. Construct-irrelevant variance and flawed test questions: Do multiple-choice item-writing principles make any difference? Academic medicine: journal of the Association of American Medical Colleges 2002;77(10):103–104.
27. Gupta P, Meena P, Khan AM, Malhotra RK & Singh T. Effect of Faculty Training on Quality of Multiple-Choice Questions. International journal of applied & basic medical research 2020; 10(3):210–214.
28. Huang Yi-Min, Trevisan M, Storfer A. The Impact of the "all-of-the-above" Option and Student Ability on Multiple Choice Tests. International Journal for the Scholarship of Teaching and Learning 2007;1(2):11.
29. Scott KR, King AM, Estes MK, Conlon LW, Jones JS & Phillips AW. Evaluation of an Intervention to Improve Quality of Single-best Answer Multiple-choice Questions. The Western Journal of Emergency Medicine 2019;20(1):11–14.
30. Ali SH & Ruit KG. The Impact of item flaws, testing at low cognitive level, and low distractor functioning on multiple-choice question quality. Perspectives on medical education 2015; 4(5): 244–251.
31. Al-Lawama M & Kumwenda B. Decreasing the options' number in multiple choice questions in the assessment of senior medical students and its effect on exam psychometrics and distractors' function. BMC Medical Education 2023;23(1):212.
32. Belay LM, Sendekie TY & Eyowas FA. Quality of multiple-choice questions in medical internship qualification examination determined by item response theory at Debre Tabor University, Ethiopia. BMC Medical Education 2022;22(1):635.
33. Fozzard N, Pearson A, du Toit E, Naug H, Wen W & Peak IR. Analysis of MCQ and distractor use in a large first year Health Faculty Foundation Program: assessing the effects of changing from five to four options. BMC Medical Education 2018;18(1):252.
34. Pawade YR & Diwase DS. Can Item Analysis of MCQs Accomplish the Need of a Proper Assessment Strategy for Curriculum Improvement in Medical Education? i-manager's Journal of Educational Technology 2016;13(1):44-53.
35. Rogausch A, Hofer R & Krebs R. Rarely selected distractors in high stakes medical multiple-choice examinations and their recognition by item authors: a simulation and survey. BMC medical education 2010;10:85.
36. Tarrant M, Ware J & Mohammed AM. An assessment of functioning and non-functioning distractors in multiple-choice questions: a descriptive analysis. BMC Medical Education, 2009; 9: 40.
37. Rahma A, Shamad M, Idris ME, Elfaki O, Elfakey W, Salih KM. Comparison in the quality of distractors in three and four options type of multiple-choice questions. Adv Med Educ Pract. 2017;8:287–91.
38. Kheyami D, Jaradat A, Al-Shibani T & Ali FA. Item Analysis of Multiple Choice Questions at the Department of Paediatrics, Arabian Gulf University, Manama, Bahrain. Sultan Qaboos University medical journal 2018;18(1):68–74.
39. Rodriguez MC. Three Options Are Optimal for Multiple-Choice Items: A Meta-Analysis of 80 Years of Research. Educational Measurement: Issues and Practice 2005; 24(2):3-13.
40. Hingorjo MR & Jaleel F. Analysis of one-best MCQs: the difficulty index, discrimination index and distractor efficiency. JPMA. The Journal of the Pakistan Medical Association 2012;62(2): 142–147.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 498-506
https://doi.org/10.30621/jbachs.1282825
RESEARCH ARTICLE

ADHERENCE TO GLUTEN-FREE DIET AND THE SOCIAL RELATED FACTORS IN ADULTS WITH THE CELIAC DISEASE

Neslihan Öner[1], Arda Borlu[2], Aslı Gizem Çapar[3], Mualla Aykut[3]

[1] Erciyes University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Kayseri Turkey
[2] Erciyes University, Faculty of Medicine, Department of Public Health, Kayseri Turkey
[3] Nuh Naci Yazgan University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Kayseri Turkey

ORCID: N.O. 0000-0001-6773-4963; A.A. 0000- 0002-1424-8037; A.G.Ç. 0000-0001-5459-9424; M.A. 0000-0002-9308-0454

Corresponding author: Neslihan Öner, **E-mail:** neslihancelik@erciyes.edu.tr
Received: 20.04.2023; **Accepted:** 15.09.2023; **Available Online Date:** 31.05.2024

Cite this article as: Öner N, Borlu A, Capar AG, Aykut M. Adherence to Gluten-Free Diet and The Social Related Factors in Adults With The Celiac Disease. J Basic Clin Health Sci 2024; 8: 498-506.

ABSTRACT

Purpose: Lifelong dietary adherence is very important in celiac disease. Several factors may affect adherence to a gluten-free diet (GFD). In this study, it was aimed to determine the adherence to a gluten-free diet (GFD) and the factors affecting social life in adults with celiac disease.
Material and Methods: This cross-sectional study was conducted on 98 adults diagnosed with celiac disease, using the telephone interview method of data collection. The level of adherence to GFD was accepted as the dependent variable. Several factors including age, gender, economic status, educational level, and marital status were considered as independent variables. Quantitative variables were compared using the student's t-test, while the Chi-square test was used for qualitative variables. Multiple logistic regression analysis was performed to determine related factors associated with "excellent" adherence to GFD.
Results: 53.1% of the celiac patients reported their adherence to GFD was "excellent", 46.9% was "poor". The celiac patients' 61.2% reported difficulties about to access GFPs and 49.0% of them never consume commercial GFPs. Before eating out, 67.3% of the celiac patients call the restaurant to ask if they have a gluten-free menu. The celiac patients' 69.4% reported that they use a gluten-scanner application. The rate of "excellent" adherence to GFD of the celiac patients who had ≥4 family members were significantly lower (OR: 0.112 CI: 0.15-0.832, p=0.017). The celiac patients with ≥10 diagnosis years had significantly lower adherence to GFD (OR: 0.053 CI: 0.010-0.292, p=0.001). Gluten-scanner applications non-users had 0.163-fold lower "excellent" adherence to GFD (OR: 0.163 CI: 0.034-0.779, p=0.016).
Conclusion: This study emphasizes that having nuclear family, new diagnosis, and use of mobile applications positively affect adherence to GFD.

Keywords: Celiac disease, chronic disease, diet, mobile applications

INTRODUCTION

Celiac disease (CD) is a gastrointestinal system disease that causes deterioration of the villus structures in the intestines and damages the small intestine in individuals with a genetic predisposition (1-4). It has been reported that CD is a rare disease in previous studies, but more recent studies have shown that the prevalence of CD in different populations has increased to 0.3-1% and is gradually increasing all over the world (4, 5). With celiac disease affecting all age ranges in the population, and with a documented higher frequency, there is a growing awareness in society that can be easily seen

Table 1. The celiac patients' socio-demographic, anthropometric, and disease characteristics.

Items	n	%
Gender		
Male	21	21.4
Female	77	78.6
Age groups (years)		
≤30	36	36.7
31-44	38	38.8
≥45	24	24.5
BMI (kg/m^2)		
<18.5	11	11.2
18.5-24.9	51	52.1
25.0-29.9	24	24.5
≥30.0	12	12.2
Working status		
Working	25	25.5
Not working	73	74.5
Education status		
Primary school	21	21.4
Secondary school	10	10.2
High school	44	44.9
College	23	23.5
Marital status		
Married	71	72.4
Not married	27	27.6
Number of family members		
<4	22	22.4
≥4	76	77.6
Economic status		
Bad	13	13.3
Moderate	27	27.5
Good	58	59.2
Diagnosed years		
<10	38	38.8
≥10	60	61.2
Presence of concomitant disease		
Yes	52	53.1
No	46	46.9
Most common concomitant disease*		
Anemia	23	45.1
Osteoporosis	11	21.6
Thyroid diseases	17	33.3
Family members diagnosed with CD		
Yes	18	19.0
No	80	81.0
Self-reported health status		
Good	57	58.2
Not good	41	41.8
Total	**98**	**100.0**

* (n=51), those only who had concomitant disease.

in grocery stores, restaurants, and food manufacturers (5).

Patients diagnosed with CD are advised to consume "gluten-free diet (GFD)" to reduce the severity of gluten-induced acute gastrointestinal symptoms and reduce the risk of chronic complications (4, 6). Currently, there are no scientific proven drugs that can prevent gluten-induced mucosal damage in celiac patients. There are some studies showing that there is a significant relationship between increased celiac patients' adherence to GFD and reduced risk of malabsorption, osteoporosis, and some autoimmune diseases (4, 7, 8). Therefore, adherence to a lifelong GFD is very important in reducing the inflammatory process and mucosal damage in the intestines. In addition, adherence to GFD may reduce health expenditures due to complications that may develop due to celiac disease.

Celiac patients must cope with major changes in their eating habits and even in their social lives because GFD in CD is the only accepted treatment (9, 10). Further, it is very difficult to maintain GFD, which makes radical changes in eating habits, consistently throughout life (9). Lifelong strict adherence to a GFD is necessary to prevent complications. Nurses and specialist pediatric dietitians have an important role in recognizing and diagnosing CD early, as well as offering ongoing dietary and clinical support (11).

In previous studies, the most frequently reported reasons for the difficulties faced by celiac patients in adherence to GFD are the high costs of GFPs, difficulty to access GFPs (3, 12), not supporting by the other members of family (13), and dislike of the organoleptic properties of GFPs (4). In this study, it was aimed to determine the adherence to GFD and the related factors affecting social life in adults with CD.

MATERIAL AND METHODS

Study Design and sampling

This cross-sectional study was performed with adults diagnosed celiac disease in Kayseri province, a Central Anatolian Region city. The participants were local members of the Turkish Life with Celiac Association which is a member of the Association of European Celiac Societies (AOECS). In addition to the GFD, those who had to follow another diet for a different reason (pregnancy, lactation, or chronic disease) were excluded from the study. The local members of the Turkish Life with Celiac Association included a total of 112 officially registered celiac

Table 2. The celiac patients' adherence to GFD and other nutritional behaviors.

Items	n	%
Self-reported adherence to GFD		
Excellent	52	53.1
Poor	46	46.9
Number of consumed meals in a day		
2	35	35.7
3	63	64.3
Consumption of snacks		
0	32	32.7
1	35	35.7
2	25	25.5
3	6	6.1
Skipping meals		
Yes	60	61.2
No	38	38.8
Most skipped meal*		
Breakfast	14	23.3
Lunch	44	73.3
Dinner	2	3.4
Favorite food preferences for snacks**		
Fruits	44	66.6
Nuts	14	21.2
Dairy products	8	12.2
Regular use of vitamin-mineral supplements		
Yes	24	24.5
No	76	75.5
Total	**98**	**100.0**

* (n=60), those only who skip meals, and ** (n=66), those only who consumption snacks.

patients. In this study, it was aimed to reach the study population without a specific sample selection. However, 12 celiac patients refused to participate. They were therefore excluded. In addition, two celiac patients were excluded from the study due to errors in their data. As a result, this study was conducted using data from a sample size of 98 celiac patients.

To assess dietary adherence in celiac patients, G power analysis with a medium effect size was performed using a one-sample case test with α=0.05 and β=0.80. The sample size was determined as a minimum of 90 participants.

Data Collection

The data were collected between September 2017 and May 2018 by using telephone-interview method. The answers were recorded on the questionnaire forms by the researchers. After giving detailed information about the study, a suitable time was determined with the celiac patients to ensure the reliability of the data, and the telephone-interview was made during this time. The celiac patients who did not want to participate were not included in the study.

Adherence to GFD was the dependent variable, while various variables (age, gender, economic, educational, and marital status, etc.) were independent. A questionnaire consisting of three parts and 41 questions, developed by the researchers in accordance with the literature review was performed. In the first part, there were questions about the socio-demographic and disease characteristics, and anthropometric measurements of the celiac patients. In the second part, under the title of “adherence to gluten-free diet (GFD) and accessibility of gluten-free products (GFPs)”; it was aimed to determine the challenging situations to access GFPs and adapting and maintaining to the GFD. The questions under the title "Adherence to gluten-free diet (GFD) and accessibility to gluten-free products (GFPs)" were determined by analyzing the literature. Celiac patients were asked for their most recent measurements and their self-reports were obtained. The BMI was calculated from these values. Body mass index (BMI) (weight (kg)/height (m)²) was calculated from self-reported weight and height measurement values (14). Celiac patients with BMI < 18.5 kg/m2 were evaluated as “underweight”, 18.5-24.9 kg/m2 as “normal”, 25.0-29.9 kg/m2 as “overweight”, and ≥ 30.0 kg/m2 as “obese” (15).

For the categorization of adherence to the gluten-free diet, which is the most basic variable of the study; those who declared that they strictly adherence to GFD were characterized as "excellent" adherence, while those who declared all other conditions were characterized as "poor" adherence.

Statistical Analysis

Data was analyzed using SPSS 22.0 (SPSS Inc., Chicago, IL) package program. Data was tested with Shapiro-Wilk test for normal distribution. Percentage values were used for qualitative data. Student-t test was used to compare quantitative variables, and Chi-square test was used to compare qualitative variables. The factors that were significant in the Chi-square comparison of qualitative variables were evaluated by multiple logistic regression analysis. Multiple logistic regression analysis was performed to determine which variables affected “excellent”

Table 3. GFD and GFPs related issues experienced by the celiac patients

Items	n	%
Can you easily access GFPs?		
Yes	38	38.8
No	60	61.2
How often do you consume commercial GFPs?		
Everyday	15	15.3
Every other day	35	35.7
Never	48	49.0
How do you get GF bread?		
Purchasing from a market	36	36.7
Cooking by self	46	47.0
Both	16	16.3
What do you do while eating out?		
I only prefer the restaurants that have GF menus to eat out.	66	67.3
I go randomly.	20	20.4
I never eat out.	12	12.3
What do you think about the prices of commercial GFPs?		
Normal	4	4.1
Expensive	94	95.9
Do you easily access to commercial GFPs in every market?		
Yes	17	17.3
No	81	82.7
Do you use gluten-scanner applications?		
Yes	68	69.4
No	30	30.6
Total	**98**	**100.0**

adherence to GFD modelled by multiple logistic regression analysis with independent groups. Odds ratio (OR) at 95% confidence interval (CI) for every model was calculated. Values were considered significant at $p<0.05$.

Ethical Consideration

The study was approved by Nuh Naci Yazgan University Ethical Committee (Decision Date: 13.11.2017, No: 2017-338). Written permission was obtained from the Kayseri Life with Celiac Association to conduct the study and the procedures followed were in accordance with the Helsinki Declaration. The celiac patients who participated in the study were given detailed information about the study and were assured of the confidentiality of their responses. Verbal informed consent were provided.

RESULTS

In this study data of 98 celiac patients were evaluated. The mean age of the celiac patients was 36.22±12.28 years (min: 18, and max: 69 years). The celiac patients' 21.4% were men and 78.6% were women. According to the BMIs of the celiac patients, 11.2% were underweight, 52.1%, were normal, 24.5% were overweight and 12.2% were obese. The celiac patients' 74.5% were not working. Most of the celiac patients (68.4%) had high school and above education level. The celiac patients' 72.4% were married, 77.6% had ≥4 family members. 59.2% of the celiac patients had good economic status. The celiac patients' 61.2% had ≥10 diagnosed years and 53.1% had concomitant disease. The mean diagnosed years of the celiac patients was 29.50±12.69 years (Data not shown in a table). The celiac patients' 19.0% had a family member diagnosed with CD. The celiac patients' 58.2% evaluated their health status as "good". The celiac patients' sociodemographic, anthropometric, and disease characteristics were presented in the Table 1.

The celiac patients' adherence to GFD and other nutritional behaviors were showed in the Table 2. 53.1% of the celiac patients reported their adherence to GFD was "excellent", 46.9% was "poor". The celiac patients' 64.3% consume three main meals, and 35.7% consume one snack in a day. It was found that 61.2% of the celiac patients skipped some meals. The most skipped meal was lunch with the rate of 73.3%. The rate of fruit consumption as a snack was 66.6%. The proportion of using regular vitamin-mineral supplements among celiac patients was 24.5% (Table 2).

Table 3 shows GFD and GFPs related issues experienced by the celiac patients. The celiac patients' 61.2% reported difficulties about to access GFPs and 49.0% of them never consume commercial GFPs. The rate of those who baked the gluten-free bread themselves was 47.0%. Before eating out, 67.3% of the celiac patients call the restaurant to ask if they have a gluten-free menu. While 95.9% of the celiac patients stated that GFPs were expensive, 82.7% reported that they could not find GFPs in every market. The celiac patients' 69.4% reported that they use a gluten-scanner application. In addition, taste, odor, and texture evaluations of GFPs products were similar for age groups and genders (Data not shown in the table).

Table 4. Comparison of celiac patients' adherence to GFD according to some characteristics.

Items	Adherence to GFD						p
	Excellent (n=52)		Poor (n=48)		Total (n=98)		
	n	%	n	%	n	%	
Gender							
Male	10	47.6	11	52.4	21	21.4	0.573
Female	42	54.5	35	45.5	77	78.6	
Age groups (years)							
<35	21	46.7	24	53.3	45	45.9	0.334*
≥35	31	58.5	22	41.5	53	54.1	
BMI (kg/m^2)							
<24.9	29	46.8	33	53.2	62	63.3	0.154*
≥25.0	23	63.9	13	36.1	36	36.7	
Working status							
Working	17	68.0	8	32.0	25	25.5	0.133*
Not working	35	47.9	38	52.1	73	74.5	
Education status							
Less than high school	16	51.6	15	48.4	31	31.6	1.000*
High school and upper than high school	36	53.7	31	46.3	67	68.4	
Marital status							
Not married	13	48.1	14	51.9	27	27.6	0.708*
Married	39	54.9	32	45.1	71	72.4	
Number of family members							
<4	18	81.8	4	18.2	22	22.4	**0.005***
≥4	34	44.7	42	55.3	76	77.6	
Economic status							
Bad	7	53.8[a]	6	46.2[a]	13	13.3	**0.003**
Moderate	7	25.9[a]	20	74.1[b]	27	27.5	
Good	38	65.5[a]	20	34.5[a]	58	59.2	
Diagnosed years							
<10	33	86.8	5	13.2	38	38.8	**<0.001**
≥10	19	31.7	41	68.3	60	61.2	
Presence of concomitant disease							
Yes	27	51.9	25	48.1	52	53.1	0.970*
No	25	54.3	21	45.7	46	46.9	
Family members diagnosed with CD							
Yes	10	55.6	8	44.4	18	18.4	1.000*
No	42	52.5	38	47.5	80	81.6	
Self-reported health status							
Good	39	68.4	18	31.6	57	58.2	**<0.001***
Not good	13	31.7	28	68.3	41	41.8	
Regular use of vitamin-mineral supplements							
Yes	11	45.8	13	54.2	24	24.5	0.561*
No	41	55.4	33	44.6	74	75.5	
Can you easily access GFPs?							
Yes	27	69.2	12	30.8	39	39.7	**0.016***
No	25	42.4	34	57.6	59	60.3	
How often do you consume commercial GFPs?							
Everyday	9	60.0	6	40.0	15	15.3	0.191
Every other day	22	62.9	13	37.1	35	35.7	
Never	21	43.8	27	56.3	48	49.0	
How do you get GF bread?							
Purchasing from a market	17	47.2	19	52.8	36	36.7	0.566
Cooking by self	27	58.7	19	41.3	46	46.9	
Both	8	50.0	8	50.0	16	16.4	

Table 4. Continue

What do you do while eating out?							
I randomly eat out.	6	18.8	26	81.3	32	32.7	**<0.001**
I only prefer the restaurants that have GF menus to eat out.	40	71.4	16	28.6	56	57.1	
I never eat out.	6	60.0	4	40.0	10	10.2	
Do you use gluten-scanner applications?							
Yes	44	64.7	24	35.3	68	69.4	**0.001***
No	8	26.7	22	73.3	30	30.6	

[a, b]: Different letter indicates statistically significant difference.
Yates correction was made for p values with "*".

Comparison of celiac patients' adherence to GFD according to some characteristics is presented in Table 4. The rates of adherence to GFD in males and females were similar ("excellent" adherence to GFD 47.6% in males and 54.5% in females, "poor" adherence to GFD 52.4% in males and 45.5% in females, respectively). There was no significant relationship between age groups, BMI, working, education and marital status and adherence to GFD. Likewise, there was no significant relationship between diagnosed years, presence of concomitant disease, family members diagnosed with CD, regular use of vitamin-mineral supplements, how to get gluten-free bread. The rate of "excellent" adherence to GFD was significantly higher among the celiac patients could easily access GFPs ($p<0.05$). The rate of "excellent" adherence to GFD was significantly higher in celiac patients who have <4 persons in their family ($p<0.05$). "Poor" adherence to GFD was found to be significantly higher in those with moderate economic status ($p=0.003$). Furthermore, the rate of "excellent" adherence to GFD in celiac patients who reported "good health status" was found to be significantly higher than those with in celiac patients who reported "not good health status" ($p<0.001$). The rate of "poor" adherence to GFD was significantly higher in celiac patients with who were eating out randomly ($p<0.001$). Significantly lower "excellent" adherence to GFD was found in those who did not use a gluten-free scanner ($p=0.001$) (Table 4).

Multiple logistic regression analysis of the factors affecting "excellent" adherence to GFD in the celiac patients was showed in Table 5. The celiac patients' 69.4% reported that they used a gluten-scanner application. The rate of "excellent" adherence to GFD of the celiac patients who had ≥4 family members were significantly lower (OR: 0.112 CI: 0.15-0.832, $p=0.017$). The celiac patients with ≥10 diagnosis years had significantly lower adherence to GFD (OR: 0.053 CI: 0.010-0.292, $p=0.001$). Although adherence to the GFD was higher in those who never ate out (OR: 12.430 CI: 0.995-155.294, $p=0.003$), the result was not considered significant because the confidence interval included 1.00. Gluten-scanner applications non-users had 0.163-fold lower "excellent" adherence to GFD (OR: 0.163 CI: 0.034-0.779, $p=0.016$).

DISCUSSION

WHO defines adherence to a treatment as "the extent to which an individual's behavior, such as taking medication, following a diet, and/or making lifestyle changes, corresponds to the agreed-upon recommendations of a healthcare provider" (16). The previous studies on CD have reported there are too many factors affecting adherence to a GFD like socio-demographic characteristics, diagnosis age, practical barriers associated with GFD, and membership in a CD-related association (17, 18). Most of the studies on CD were predominantly focused to determine clinical perspective of the disease (19, 20), prevalence (21, 22), and quality of the life (23, 24) in celiac patients. To best of our knowledge, there are limited studies evaluating the impact of GFD on patients' social lives, some in children and adolescents, and some in adults (25, 26). Therefore, assessing the effects of GFD adherence on social life in a small group of people who were active memberships in a celiac-related association was worth investigating.

In the literature review, the adherence rates to GFD vary between 34%-95% (27). In this study, similar to the literature, 53.1% of celiac patients reported that their adherence to GFD was "excellent". Among the possible reasons for this variability, using different methods and the different characteristics of the study population (such as different diagnosis times, membership in a CD-related association, and several cultural factors, etc.). Therefore, population-specific

data is highly necessary. Also, the comparability between studies is also very limited.

Some recent studies indicated there were several difficulties to adherence a GFD which could affect BMI of celiac patients (18, 28). Some population-based studies showed that celiac patients unable to adapt to a GFD have malnutrition. On the other hand, some studies reported the rates of being obese among celiac patients' changes between 7.0-12.0% (29-31). A large cohort study conducted by Cheng et al. (29) reported 60.0% of the patients with CD had normal BMI, whereas 17.3% were underweight and 15.2% were overweight, and 6.8% obese. However, Drosdak et al. (32) reported the obesity prevalence in celiac patients as 45%, which is quite far from the other results. In this study, the rates of "underweight", "normal", "overweight" and "obese" of celiac patients were 11.2%, 52.1%, 24.5% and 12.2%, respectively, which supported the findings of Cheng et al. (29).

Involving family members in the management of CD is very important. The presence of a celiac patient at home who must follow a GFD will certainly affect whole eating practices at home. For the celiac patients to "excellent" adherence to a GFD, it is important that the prepared food does not contain and contaminated with gluten. Therefore, the support of family members becomes very important in the management of CD (33). We found "excellent" adherence to GFD of the celiac patients who had ≥4 family members were significantly lower (OR: 0.112 (0.15-0.832), $p<0.05$). van Overbeek et al. (13) reported that failure of family members without CD to adopt GFD would affect home-cooked meals, which in turn would affect the celiac patient's adherence to GFD. Our results showed that having fewer family members may be effective in supporting the dietary adherence of the celiac patient.

The prevalence of CD in first-degree relatives of celiac patients has been reported to be approximately 10.0% (33). The prevalence of CD in first-degree relatives of patients with celiac disease who participated in this study was found to be 19.0%. As the reason why this rate was higher than the rate stated in previous study; it was thought that the celiac patients in this study had more awareness because they are registered to an association working on CD.

The data about the relationship between economic status and CD are conflicting. Economic status may affect celiac diagnosis (34) and the celiac patient's adherence to GFD, purchasing power of GFPs, and quality of life (2, 3, 25, 26). In this study there was no significant relationship between the economic status of celiac patients' adherence to GFD. In a study conducted by Villafuerte-Gallez et al. (27) examining both quantitative and qualitative measures adherence to GFD, reported that median household income was not associated adherence to GFD. A multidimensional examination of the effect of economic dimension on adherence to GFD in celiac patients may be a research area for future studies.

The relationship between adherence to GFD and age at diagnosis has been reported in CD (12). In this study, instead of establishing the relationship between the age at diagnosis and adherence to GFD, when the effect of years after diagnosis on adherence to GFD was evaluated. It was shown that celiac patients with ≥10 diagnosis years had significantly lower adherence to GFD. Especially in newly diagnosed celiac patients, it is possible to experience tighter adherence to GFD due to the more frequent appointments with the dietitian or practitioner.

Difficulties accessing GFPs or risk of cross-contamination with gluten makes it challenging for celiac patients to eat out (35). A previous study highlighted the lack of gluten-free menu options when eating out as a cause of "poor" adherence to GFD (27). To social support of celiac patients, who are a disadvantaged group in participating in social activities such as eating out, local governments' efforts to create and increase gluten-free menu options in restaurants will be an approach that will be appreciated for celiac patients of all age groups.

Best of our knowledge, there are limited studies investigating the relationship between mobile GFD application use and dietary adherence to GFD (36, 37). Notably, there is a need for future intervention studies that examine in detail the use of mobile application and wearable technologies in the management of celiac and even other chronic diseases. In fact, intervention studies can be designed with the use of mobile applications and wearable technologies, especially to increase adherence to GFD. It is to demonstrate that active memberships in a celiac-related association who must follow a strict diet constantly increase their adherence to their diet with the use of the application.

Limitations

There are some limitations in this study. The first of these is the adherence to GFD was obtained only through self-assessment of CD patients and the study included local results. Supporting the

adherence to GFD not only with the expressions of celiac patients or any measurement tool, but also with serological tests will reveal more information. Symptom frequency, food consumption record or food consumption frequency were not questioned. Questioning of symptom frequency may be an important factor revealing the dietary adherence of celiac patients. Future studies can be planned by considering these limitations. However, this study also has an important strength. To the best of our knowledge, this is the first study to emphasize the relationship between mobile GFD application use and dietary adherence to GFD in Turkey.

CONCLUSION

This study showed that adherence to GFD in celiac patients increased with family support, new diagnosis of celiac disease, lack of eating out habits and mobile application use. Based on these results, in order to increase adherence to GFD, nutrition education should be given to family members, gluten-free meals should be included in restaurant menus by local municipalities. The widespread use of gluten-free mobile applications may facilitate the management of medical nutrition therapy.

Acknowledgement: None.
Author contributions: Conception: MA, AGÇ. Design: MA, AGÇ. Supervision: NÖ, AB. Data collection: AGÇ. Statistical analysis: NÖ, AB. Literature review: NÖ, AGÇ, AB. Writing: NÖ, AB Critical review: NÖ, AB, MA.
Conflict of interests: The authors declare no conflict of interest.
Ethical approval: Ethics committee approval was obtained from Nuh Naci Yazgan University Ethical Committee (Decision Date: 13.11.2017, No: 2017-338). Verbal informed consent was obtained from the participants.
Funding: None.
Peer-review: Externally peer-reviewed.

REFERENCES

1. Roka V, Potamianos SP, Kapsoritakis AN, et al. Prevalence of celiac disease in the adult population of central Greece. Eur J Gastroenterol Hepatol 2007;19(11):982-987.
2. Lee AR, Ng DL, Zivin J, et al. Economic burden of a gluten-free diet. J Hum Nutr Diet 2007;20(5):423–430.
3. Lee AR, Wolf RL, Lebwohl B, et al. Persistent economic burden of the gluten free diet. Nutrients 2019;11(2), 399.
4. Demir E, and Comba A. The evolution of celiac disease publications: A holistic approach with bibliometric analysis. Ir J Med Sci 2020;189:267–276.
5. Ryan M, and Grossman S. Celiac disease: Implications for patient management. Gastroenterol Nurs 2011;34(3):225–228.
6. Gutowski ED, Weiten D, Green KH, et al. Can individuals with celiac disease identify gluten-free foods correctly? Clin Nutr ESPEN 2020;36:82–90.
7. Catassi C, Fabiani E, Corrao G, et al. Italian Working Group on Celiac Disease and Non-Hodgkin's-Lymphoma. Risk of non-Hodgkin lymphoma in celiac disease. JAMA 2002;287(11):1413–1419.
8. Kemppainen T, Kröger H, Janatuinen E, et al. Osteoporosis in adult patients with celiac disease. Bone 1999;24(3):249–255.
9. Barberis N, Quattropani MC, and Cuzzocrea F. Relationship between motivation, adherence to diet, anxiety symptoms, depression symptoms and quality of life in individuals with celiac disease. J Psychosom Res 2019;124:109787.
10. Arias-Gastelum M, Cabrera-Chávez F, Vergara-Jiménez MDJ, et al. The gluten-free diet: Access and economic aspects and impact on lifestyle. Nutr Diet Suppl 2018;10 (27):34.
11. Paul SP, Ranjan A, Bremner G, et al. () Diagnosis and management of celiac disease in children. Br J Nurs 2021;30(13):6-10.
12. do Nascimento AB, Fiates GMR, dos Anjos A, et al. Gluten-free is not enough perception and suggestions of celiac consumers. Int J food Sci Nutr 2014;65(4):394–398.
13. van Overbeek FM, Uil-Dieterman IG, Mol IW, et al. The daily gluten intake in relatives of patients with celiac disease compared with that of the general Dutch population. Eur J Gastroenterol Hepatol 1997;9(11):1097-1099.
14. World Health Organization, 1998 [Internet]. Obesity: Preventing and Managing the Global Epidemic [Accessed date: 12 September 2018] Available from: https://apps.who.int/iris/handle/10665/42330
15. WHO Expert Consultation, 2004. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet (London, England), 363(9403):157-163.
16. World Health Organization, 2003) [Internet]. Adherence to long-term therapies: Evidence for action. [Accessed date: 14 September 2018] Available from: https://apps.who.int/iris/handle/10665/42682

17. Leffler DA, Edwards-George J, Dennis M, et al. Factors that influence adherence to a gluten-free diet in adults with celiac disease. Dig Dis Sci 2008;53(6):1573–1581.
18. Muhammad H, Reeves S, Jeanes YM. Identifying and improving adherence to the gluten-free diet in people with celiac disease. Proc Nutr Soc 2019;78(3):418-425.
19. Yaşar S, Yaşar B, Abut E, et al. Clinical importance of celiac disease in patients with recurrent aphthous stomatitis. Turk J Gastroenterol 2012;23(1):14-8.
20. Unal E, Demiral M, Baysal B, et al. Frequency of celiac disease and spontaneous normalization rate of celiac serology in children and adolescent patients with type 1 diabetes. J Clin Res Pediatr Endocrinol 2021;13(1):72-79
21. Dogan B, Oner C, Bayramicli OU, et al. Prevalence of celiac disease in adult type 1 patients with diabetes. Pak J Med Sci 2015;31(4):865-868.
22. Bengi G, Cıvak M, Akarsu M. Prevalence of celiac disease in patients with inflammatory bowel disease in Turkish population. Gastroenterol Res Pract 2019;6272098.
23. Sevinç E, Çetin FH, Coşkun BD. Psychopathology, quality of life, and related factors in children with celiac disease. J Pediatr 2017;93(3):267-273.
24. Oflu AT, Bukulmez A, Icigen E, et al. Life quality and empathy in children with celiac disease. North Clin Istanb 2020;7(6):557-562.
25. Zysk W, Głąbska D, Guzek D. Social and emotional fears and worries influencing the quality of life of female celiac disease patients following a gluten-free diet. Nutrients 2018;3;10(10):1414.
26. Serin Y and Akbulut G. The impact of gluten-free diet on the lifes of individuals with celiac disease: A Turkish perspective. Beslenme ve Diyet Dergisi 2021;49(1):48-56.
27. Villafuerte-Galvez J, Vanga RR, Dennis M, et al. Factors governing long-term adherence to a gluten-free diet in adult patients with celiac disease. Aliment Pharmacol Ther 2015;42(6):753-60.
28. Pedoto D, Troncone R, Massitti M, et al. Adherence to gluten-free diet in celiac paediatric patients assessed through a questionnaire positively influences growth and quality of life. Nutrients 2020;12(12):3802.
29. Cheng J, Brar PS, Lee AR, et al. Body mass index in celiac disease: beneficial effect of a gluten-free diet. J Clin Gastroenterol 2010;44(4),267-271.
30. Tortora R, Capone P, De Stefano G, et al. Metabolic syndrome in patients with celiac disease on a gluten-free diet. Aliment Pharmacol Ther 2015;41:352-9.
31. Stein AC, Liao C, Paski S, et al. Obesity and cardiovascular risk in adults with celiac disease. J Clin Gastroenterol 2016;50:545–50.
32. Drosdak A, Satyavada S, Ismail M, et al. Obesity prevalence in celiac disease in the United States from 2014 to 2018. Int J Obes 2021;46:441–443.
33. Ludvigsson JF, Card T, Ciclitira PJ, et al. Support for patients with celiac disease: A literature review. United European Gastroenterol J 2015;3(2):146-159.
34. Olén O, Bihagen E, Rasmussen F, et al. Socioeconomic position and education in patients with coeliac disease. Dig Liver Dis 2012;44(6):471–476.
35. Rodrigues M, Yonamine GH, Fernandes Satiro CA. Rate and determinants of non-adherence to a gluten-free diet and nutritional status assessment in children and adolescents with celiac disease in a tertiary Brazilian referral center: A cross-sectional and retrospective study. BMC Gastroenterol 2018;18(1):15.
36. Dowd AJ, Warbeck CB, Tang KT, et al. MyHealthyGut: Findings from a pilot randomized controlled trial on adherence to a gluten-free diet and quality of life among adults with celiac disease or gluten intolerance. Digit 2020;6:2055207620903627.
37. Meyer S, and Naveh G. Mobile application for promoting gluten-free diet self-management in adolescents with celiac disease: Proof-of-concept study. Nutrients 2021;13(5):1401.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 507-510
https://doi.org/10.30621/jbachs.1217436
CASE REPORT

SCOT DEFICIENCY MIMICKING SEPSIS: AN UNUSUAL CAUSE OF INCREASED ANION GAP METABOLIC ACIDOSIS

Pelin Teke Kisa[1], Semra Gursoy[2] , Pınar Seven[3], Neslihan Pirinc[3], Ozlem Sarac Sandal[3], Gulhan Atakul[3], Filiz Hazan[4], Tijen Tanyalcin[5]

[1] Department *Inherited Metabolic Disorders, Faculty of Medicine, Dokuz Eylul University*, Izmir, Turkey.
[2] Department of Pediatric Genetics, *Faculty of Medicine, Dokuz Eylul University*, Izmir, Turkey.
[3] Department of Pediatric Intensive Care Unit, Dr. Behçet Uz Children's Education and Research Hospital, Izmir, Turkey
[4] Department of Medical Genetics, Dr. Behçet Uz Children's Education and Research Hospital, Izmir, Turkey.
[5] Tanyalcin Medical Laboratory, Selective Screening and Metabolism Unit, Izmir, Turkey

ORCID: P.T.K. 0000-0001-6481-3172; S.G. 0000-0002-6795-3012; P.S. 0000-0001-7305-9984; N.P. 0000-0001-6219-1541; O.S.S. 0000-0003-2684-0625; G.A. 0000-0002-3832-9691; F.H. 0000-0002-0382-3446; T.T. 0000-0003-2191-4007

Corresponding author: Pelin Teke Kisa, **E-mail:** pelin.tekekisa@gmail.com
Received: 20.12.2022; **Accepted:** 08.09.2023; **Available Online Date:** 31.05.2024

Cite this article as: Teke-Kisa P, Gursoy S, Seven P, Pirinc N, Sarac-Sandal O, Atakul G, Hazan F, Tanyalcin T. SCOT Deficiency Mimicking Sepsis: An Unusual Cause of Increased Anion Gap Metabolic Acidosis. J Basic Clin Health Sci 2024; 8: 507-510.

ABSTRACT

Introduction: Succinyl-CoA:3-oxoacid CoA transferase (SCOT, EC 2.8.3.5) deficiency is a rare autosomal recessive inborn error of metabolism (IEM). We report here an infant admitted to intensive care unit with the diagnosis of sepsis.
Case Presentation: A five-month-old female patient was admitted to the intensive care unit with lethargy and respiratory distress. She had severe high anion gap metabolic acidosis. The IEM was screened by plasma amino acid analysis, showing no abnormalities, and by acylcarnitine analysis, showing low-normal levels of free carnitine. Urine organic acid analysis revealed massive ketonuria and elevated levels of dicarboxylic acids. Fatty acid oxidation disorder-targeted gene panel revealed a homozygous splice site variant (c.78+1_78+6 del) in the OXCT1 gene.
Discussion and Conclusion: SCOT deficiency should be considered when massive ketosis is detected in increased anion gap metabolic acidosis with sepsis-like manifestation. Supportive therapy should be initiated quickly to prevent irreversible neurological damage.

Keywords: Metabolic acidosis, *SCOT* deficiency, anion gap

INTRODUCTION

SCOT deficiency (OMIM#245050) is an autosomal recessive inborn error of ketone metabolism, caused by mutations in the OXCT1 gene on chromosome 5p13. There are less than 50 patients reported to date (1). Ketone bodies are produced in the liver by fatty acid oxidation or by catabolism of small amounts of ketogenic amino acids (2). When there is a shortage of glucose as an energy source, tissues, and the brain in particular, utilize ketone bodies(KB) to supply energy. Succinyl-CoA:3-oxoacid CoA transferase (SCOT;EC 2.8.3.5), the deficient enzyme in SCOT deficiency, is involved in the first step of ketone body utilization and catalyzes reversible transfer of CoA from succinyl-CoA to acetoacetate (3). In cases of an increased need for energy such as starvation, infection, and surgery, glucose is insufficient to provide energy and needs ketone support. In the patients with SCOT-deficient; KBs cannot be utilized and accumulates in the body.

Table 1. The acylcarnitines profile and urine organic acid analysis for the patient with SCOT deficiency.

	Unit	Value	Reference range
DBS carnitine			
Free carnitine	(µmol/L)	11.9	8–60
C3-DC/C4-OH	(µmol/L)	0.55	< 3.03
Total carnitine	(µmol/L)	28.33	
C2	(µmol/L)	11.01	5–80
C3+C16	(µmol/L)	**1.62**	> 2.0
PHE/C3+C16	(µmol/L)	**19.75**	< 20
Urine organic acid			
Acetoacetic acid	(mmol/mol Crn)	**63.4**	< 19
Adipic acid	(mmol/mol Crn)	**1796**	< 22
2-methylacetoacetic acid	(mmol/mol Crn)	**-**	< 24
3-Hydroxyisovaleric acid	(mmol/mol Crn)	**778.4**	< 24
3-hydroxybutyrate	(mmol/mol Crn)	**9288**	< 63
3-hydroxy-2-methylbutyric acid	(mmol/mol Crn)	**-**	< 10
Suberic acid	(mmol/mol Crn)	**51.1**	< 10

Inborn errors of metabolism (IEM) can present with non-specific symptoms such as vomiting, poor feeding, and lethargy. Clinicians first consider sepsis due to these findings and initiate the treatment. Presentation with neurological deterioration such as sudden coma, and lethargy following an uneventful history is a characteristic of IEM (4). This paper will present an infant with SCOT deficiency that and was diagnosed upon the clue of increased anion gap metabolic acidosis revealed by laboratory examinations.

CASE REPORT

A five-months-old female patient was admitted to the intensive care unit with lethargy and respiratory distress. The patient was born uneventfully at gestational age of 40 weeks and with birth weight of 2010g. Her parents were consanguineous. Her developmental skills were appropriate to age. She started receiving complementary foods one week before the admission and the mealtime started to get longer. On evaluation, body temperature was 36.7°C, blood pressure was 94/52 mmHg, heart rate was 164/min, respiratory rate was 80/min, and Glasgow coma score was 7 (E2V2M3). She had hypotonia, tachycardia, and decreased response to pain. Laboratory analyses revealed metabolic acidosis (pH: 7.10; pCO2: 15 mmHg; HCO3: 4.6 mmol/L; base excess: 23.1) with normoglycemia (6.3 mmol/L) and anion gap of 25.4 mmol/L (Na: 143 mmol/L; Cl: 113 mmol/L). Blood lactate (0.065 mmol/L) and ammonia (69 µmol/L) were within the normal range. Urine ketones were highly positive (++++). There were no laboratory findings suggestive of infection.

We initiated treatment with intravenous fluids containing high dextrose, sodium bicarbonate and vitamin cocktail due to the suspected IEM. Parental administration of sodium bicarbonate resulted in resolution of acidosis over 12 hours. To screen the IEM, we investigated acylcarnitine, plasma amino acids, and urine organic acids. The plasma amino acid analysis showed no abnormalities, while acylcarnitine showed low- normal levels of free carnitine. Urine organic acid analysis revealed massive ketonuria and elevated levels of dicarboxylic acids, (Table 1), and thus SCOT deficiency was diagnosed.

The infant was discharged at day 10 of admission under carnitine therapy and advised to avoid prolonged fasting. Fatty acid oxidation disorder-targeted gene panel (Illumina, MiniSeq®,USA) revealed a homozygous splice site variant (c.78+1_78+6 del) in the OXCT1 (ENST00000196371) gene. The parents were identified as carriers for the same mutation by Sanger Sequencing (Table-1). The patient is currently one year old, growing well, and no further metabolic decompensation has occurred.

DISCUSSION

SCOT deficiency is a rare disease; patients are completely normal in the non-metabolic crisis period (1). In IEMs presenting with metabolic crises with high morbidity, early diagnosis and rapid intervention can prevent irreversible damage (5). Due to their rarity, these diseases are not considered. Capturing the clues of IEM with a comprehensive assessment enables clinicians to reach a diagnosis. Consanguinity is the first clue in the history for IEM

(6). Disorders with a reduced fasting tolerance including fatty acid oxidation and ketogenesis typically present during periods of reduced food intake and/or increased energy need such as prolonged fasting or metabolic stress (7). The onset of patient's complaints after receiving complementary foods, especially the reduced number of meals, was another clue in the history.

Generally, the amount of unmeasured anion increases in circulation due to reasons such as diabetic ketoacidosis, uremia, and salicylate intoxication. When increased anion gap metabolic acidosis is detected, basic tests such as glucose, electrolytes, liver function tests, lactate, ammonia and ketones are used secondarily to reduce the disorders in the differential diagnosis (5). On clinical picture of anion gap metabolic acidosis with neurological deterioration; organic acidemias such as isovaleric acidemia, methylmalonic acidemia, propionic acidemia, or pyruvate metabolism disorders are considered (4). The findings of hyperammonemia in patients with organic acidemia is helpful in differential diagnosis (8). Anion gap metabolic acidosis can also be detected in pyruvate metabolism disorders, but it can be differentiated from inborn errors of ketone metabolism by the normal lactate level. Another clue in the present patient was that a mild symptom such as loss of appetite could turn into a severe clinical picture such as coma during day, which could improve within hours with only hydration therapy. SCOT-deficient patients usually respond to hydration therapy (9) and rarely need dialysis (10). When metabolic screening is examined, low carnitine may cause false negative results in acylcarnitine analysis due to insufficient saturation of acylcarnitine. The second important issue is that if the patient has high level of excretion (due to kidney function, or overhydration or drug use), the diagnostic value of the ACCRN profile would be low (11,12). The patient was diagnosed with SCOT deficiency by the massive ketonuria and elevated levels of dicarboxylic acids in the sample collected in the non-fasting period, detected in the urine organic acid profile. Since 3-hydroxy-2-methylbutyric acid and 2-methylacetoacetic acid were not detected in urine organic acid analysis, 2-Methylacetoacetyl CoA thiolase deficiency, a member of the ketone body utilization disorders, was not considered in this patient (2).

Mutations in the OXCT1 gene have been reported in 38 patients to date (1). The splice site mutation identified in our patient (c.78+1_78+6 del) was previously reported in a 16-month-old female patient of Turkish origin. Similarly, the SCOT activity in the fibroblasts was measured 15% less in the patient who presented with ketoacidosis attack (13). In the present case, functional enzyme analysis could not be performed in our laboratory due to reasons such as financial burden. However, the clinical, biochemical and molecular findings support SCOT deficiency.

In conclusion, SCOT deficiency should be considered in patients with increased anion gap metabolic acidosis. Supportive therapy should be initiated quickly to prevent irreversible neurological damage.

Acknowledgements: The authors would like to thank the patient's family for granting permission to present this case study.

Author contributions: PTK, SG, PS, NP, OSS, GA, FH; patient clinical evaluation, conception and design. PTK and TT; analysis and interpretation of data. PTK, SG, TT; drafting the article and revising it critically for important intellectual content.PTK critically reviewed the manuscript and approved the final version as submitted. All authors participated fully in drafting and revising the manuscript, approved the final manuscript, and agreed to its submission.

Conflict of Interests: The authors declared that they have no potential conflict of interests with respect to the research, authorship, and/or publication of this article.

Funding: The authors of this manuscript agreed to this publication. They did not receive funding for this work.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Sass JO, Fukao T, Mitchell GA. Inborn Errors of Ketone Body Metabolism and Transport: An Update for the Clinic and for Clinical Laboratories. J Inborn Errors Metab Screen 2018;6:2326409818771101.
2. Sass JO. Inborn errors of ketogenesis and ketone body utilization. J Inherit Metab Dis 2012;35(1):23-28.
3. Grünert SC, Foster W, Schumann A, et al. Succinyl-CoA:3-oxoacid coenzyme A transferase (SCOT) deficiency: A rare and potentially fatal metabolic disease. Biochimie 2021;183:55-62.
4. MacNeill EC, Walker CP. Inborn Errors of Metabolism in the Emergency Department (Undiagnosed and Management of the Known). Emerg Med Clin North Am 2018;36(2):369-385.
5. Schillaci L-AP, DeBrosse SD, McCandless SE. Inborn Errors of Metabolism with Acidosis: Organic Acidemias and Defects of Pyruvate and Ketone Body Metabolism. Pediatr Clin

North Am 2018;65(2):209-230.
6. Afzal RM, Lund AM, Skovby F. The impact of consanguinity on the frequency of inborn errors of metabolism. Mol Genet Metab Reports 2018;(15)6-10.
7. Nyhan WL. When to Suspect Metabolic Disease. In: Hoffmann GFF, Zschocke J, Nyhan WL, (eds.). Inherited Metabolic Diseases A Clinical Approach. 2nd ed. Springer-Verlag Berlin Heidelberg; 2017:19-28.
8. Aldubayan SH, Rodan LH, Berry GT, Levy HL. Acute Illness Protocol for Organic Acidemias: Methylmalonic Acidemia and Propionic Acidemia. Pediatr Emerg Care 2017;33(2):142-146.
9. Kim YA, Kim SH, Cheon CK, Kim YM. A Rare Cause of Life-Threatening Ketoacidosis: Novel Compound Heterozygous OXCT1 Mutations Causing Succinyl-CoA:3-Ketoacid CoA Transferase Deficiency. Yonsei Med J 2019;60(3):308-311.
10. Zheng DJ, Hooper M, Spencer-Manzon M, Pierce RW. A Case of Succinyl-CoA:3-Oxoacid CoA Transferase Deficiency Presenting with Severe Acidosis in a 14-Month-Old Female: Evidence for Pathogenicity of a Point Mutation in the OXCT1 Gene. J Pediatr Intensive Care 2018;7(1):62-66.
11. Marquardt G, Currier R, McHugh DMS, et al. Enhanced interpretation of newborn screening results without analyte cutoff values. Genet Med 2012;14(7):648-655.
12. McHugh DMS, Cameron CA, Abdenur JE, et al. Clinical validation of cutoff target ranges in newborn screening of metabolic disorders by tandem mass spectrometry: A worldwide collaborative project. Genet Med 2011;13(3):230-254.
13. Fukao T, Sakurai S, Rolland M-O, et al. A 6-bp deletion at the splice donor site of the first intron resulted in aberrant splicing using a cryptic splice site within exon 1 in a patient with succinyl-CoA: 3-Ketoacid CoA transferase (SCOT) deficiency. Mol Genet Metab 2006;89(3):280-282.

JBACHS
Journal of Basic and Clinical Health Sciences

J Basic Clin Health Sci 2024; 8: 511-515
https://doi.org/10.30621/jbachs.1277737
CASE REPORT

AEROBIC EXERCISE IN INDIVIDUALS WITH RESTLESS LEGS SYNDROME: A CASE SERIES STUDY

Burcin Aktar[1,2], Birgul Balci[2], Sinan Buran[3], Beyza Nur Aslantas[1], Dilara Mermi Dibek[4], Ibrahim Oztura[5], Baris Baklan[5]

[1] Institute of Health Sciences, Dokuz Eylul University, Izmir, Turkey
[2] Faculty of Physical Therapy and Rehabilitation, Dokuz Eylul University, Izmir, Turkey
[3] Department of Heart and Respiratory Physiotherapy and Rehabilitation, Faculty of Physical Therapy and Rehabilitation, Hacettepe University, Ankara, Turkey
[4] Department of Clinic Neurophysiology, Basaksehir Cam and Sakura City Hospital, Istanbul, Turkey
[5] Department of Neurology, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey

ORCID: B.A 0000-0002-5753-7138; B.B. 0000-0002-0873-0900; S.B. 0000-0003-1378-9584; B.N.A. 0009-0007-0538-4882; D.M.D 0000-0001-9963-9450; I.O 0000-0002-2300-7788; B.B 0000-0003-2908-5223

Corresponding author: Burcin Aktar, **E-mail:** burcin.aktar@deu.edu.tr, burcinaktar@gmail.com
Received: 06.04.2023; **Accepted:** 16.08.2023; **Available Online Date:** 31.05.2024

Cite this article as: Aktar B, Balci B, Buran S. Aslantas BN, Mermi-Dibek D, Oztura I, Baklan B. Aerobic Exercise in Individuals with Restless Legs Syndrome: A Case Series Study. J Basic Clin Health Sci 2024; 8: 511-515.

ABSTRACT

Purpose: Exercise has been demonstrated to alleviate symptoms of restless legs syndrome (RLS) in individuals with RLS, but there are few studies on physical health in primary RLS. This case series aims to describe the outcome of supervised aerobic exercise training in individuals with RLS.
Case Report: Five individuals with RLS were given supervised aerobic exercise training 2 days a week for 12 weeks. The International Restless Legs Syndrome Study Group Rating Scale (IRLS) was used to detect the severity of RLS. The Turkish version of the Pittsburgh Sleep Quality Index (PSQI) was used to measure sleep quality. The functional effect of fatigue was assessed using the Fatigue Impact Scale (FIS). The Six-Minute Walk test (6MWT) was used to determine the functional exercise capacity. All assessments were taken at baseline and post-intervention.
Conclusion: Following aerobic exercise, clinically meaningful changes in RLS severity, PSQI, and 6MWT were reported in all individuals with severe RLS. Four out of 5 patients improved their FIS at post-intervention. These results suggest that 24-session supervised aerobic exercise training might help to improve RLS severity, sleep quality, fatigue, and exercise capacity in an individual with RLS.

Keywords: aerobic exercise, restless legs syndrome, sleep, fatigue, six-minute walk test.

INTRODUCTION

Restless legs syndrome (RLS) is a sensory-motor disorder that consists of an irresistible urge to move the legs in the evening and at night, predominantly at rest (1). Symptoms of RLS are common in the general adult population. The prevalence increases with age and is higher in women. Individuals with RLS experience sleep disturbances, including difficulty in falling asleep, increased awakenings with RLS symptoms, and reduced the total sleep time. These conditions can negatively affect the well-being and quality of life of individuals with RLS (2).

The current management of RLS is primarily pharmacological treatment (3). Recent systematic reviews have synthesised studies that investigated the effectiveness of non-pharmacological interventions, such as yoga, exercise, and massage techniques in coping with RLS symptoms (4,5). It has

Table 1. Participant demographics and baseline characteristics

	Participants				
	1	**2**	**3**	**4**	**5**
Sex	Female	Female	Male	Male	Female
Age (*year*)	65	42	68	64	44
Body weight (*kg*)	76.0	72.0	76.0	72.0	59.0
Height (*m*)	1.57	1.73	1.68	1.69	1.70
BMI (*kg/m²*)	30.8	24.1	27.0	25.2	20.4
Duration of symptoms (year)	8	3	19	10	10

Abbreviations: BMI, body mass index

not yet been established whether exercise could improve in RLS symptoms of individuals with RLS. Therefore, the aim of this case series was to describe the outcome of supervised aerobic exercise training in individuals with RLS.

CASE REPORT

Five individuals (3 females, 2 males) with a diagnosis of idiopathic RLS were referred by their neurologist to the Department of Neurology at the Dokuz Eylul University between October 2019 and December 2022. Baseline demographic characteristics of the participants are shown in Table 1. The body weight of the subjects was measured by weighing (Xiaomi Mi Body Composition Scale), while height was measured using a tape measure. Body mass index was calculated as body weight in kilograms divided by height in meters squared. The mean and standard deviation of age was 56.6 ± 12.5 years. Individuals were excluded if they had any of the following: RLS secondary to any other disease (including Parkinson's disease, multiple sclerosis, etc.), iron deficiency (a ferritin of less than 50 ng/mL), regular participation in an exercise program in the past year. The study was carried out with the approval of Dokuz Eylul University, Non-interventional Research Ethics Committee on 13.02.2019 (Decision No: 2019/03-24) and 03.04.2019 (Decision No: 2019/08-32) (Protocol number: 4548-GOA). All individuals provided written informed consent to participate in the study. All study procedures were conducted in accordance with the Declaration of Helsinki.

Aerobic exercise

Participants received a 24-session intervention program, scheduled twice a week, over a period of 12 weeks. The sessions were supervised by a qualified physiotherapist (B.N.A. or S.B. or B.N.A). Aerobic exercise training was performed cycling on a stationary bike according to the guidelines of the American College of Sports Medicine. Each session consisted of a warm-up (10-min), an aerobic activity and a cool-down period (5-min). The warm-up and cool-down periods were performed at an unloaded pedaling on a stationary bike. Participants were instructed to cycle at 40 to 60% of heart rate reserve during aerobic activity period. The targeted heart rate was calculated using the following formula: "[(220–age–HRrest)×% intensity desired]+HRrest" (6). During the first 3 weeks of the participants were instructed to perform 15 min of stationary bicycle training at an intensity of 40-50% of their targeted heart rate. In the sixth week, the intensity of the exercise was increased to 50-60% of the targeted heart rate. The duration of the exercise was gradually increased by 5 minutes each week for 3 weeks. The intensity of the exercise was monitored during each session with a pulse oximeter probe.

Clinical outcome assessments

The International Restless Legs Syndrome Study Group Rating Scale (IRLS) was used to measure the severity of RLS in individuals with RLS. Consisting of 10 questions, the IRLS is scored between 0 (none/never) and 4 (very severe/often). The total point score ranges from 0-40. Participants have been divided into mild [0-10], moderate [11-20], severe [21-30] and very severe [31-40] (7). It has been validated in individuals with RLS in the Turkish population (8). Sleep quality was measured with the Turkish version of the Pittsburgh Sleep Quality Index (PSQI). It comprises 19 items classified into seven components. Each component is scored from 0 to 3. A total PSQI score was generated by summing up the scores of the seven components ranging from 0-21, with higher scores indicating worse sleep quality. It is a valid and reliable questionnaire in the Turkish population (9). The Fatigue Impact Scale (FIS) was used to assess the functional effect of fatigue. Participants respond to the level of fatigue in 40 items

Table 2. RLS severity, sleep quality, fatigue, and exercise capacity outcomes at baseline and post-intervention.

	RLS severity (*0-40*)		PSQI (*0-21*)		FIS (*0-160*)		6MWT (*meter*)	
	B	**Post**	**B**	**Post**	**B**	**Post**	**B**	**Post**
1	27.0	22.0	6.0	4.0	58.0	5.0	400.0	474.0
2	28.0	21.0	11.0	8.0	94.0	19.0	514.8	606.0
3	21.0	22.0	11.0	9.0	23.0	41.0	460.0	576.0
4	24.0	13.0	16.0	15.0	41.0	13.0	462.0	561.0
5	21.0	11.0	13.0	2.0	16.0	11.0	510.0	555.0
Mean ±SD	23.3±3.6	19.0±5.6	9.7±5.4	6.8±4.9	44.7±25.3	20.7±14.3	481.8±51.6	557.0±44.4
MD*	-4.3		-2.9		-24.0		75.2	

Abbreviations: B, baseline; Post, post-intervention; RLS, restless legs syndrome; PSQI, Pittsburgh Sleep Quality Index; FIS, Fatigue Impact Scale; 6MWT, Six-Minute Walk test; SD, standard deviation; MD, mean difference.
*The change scores from baseline to post-intervention

on a 5-point scale (0=no problem, 4=extreme problem). The Turkish version of the FIS was translated by Armutlu et al. (10).

The Six-Minute Walk test (6MWT) was used to detect functional exercise capacity according to the American Thoracic Society guidelines. Participants were asked to walk as quickly as possible on a 15-meter corridor for 6 minutes.

All clinical outcomes were evaluated prior to baseline and post-intervention. All participants were allowed to continue taking their usual medication.

Data analysis

Data were analysed through descriptive statistics using IBM Statistic (version 24.0). Outcome measures were IRLS, PSQI, FIS, and 6MWT scores. The mean difference between baseline and post-intervention was calculated as follows: “the post-intervention score – baseline score”.

Results

Following aerobic exercise, the severity of RLS decreased, and sleep quality (PSQI) and exercise capacity (6MWT) improved in all participants. Four out of 5 patients improved their functional effect of fatigue (FIS) at post-intervention (Table 2). The adherence rate for exercise sessions was more than 90% of sessions. No side effects or adverse eventswere reported by any of the participants.

DISCUSSION

Our study described the outcome of 5 individuals with severe RLS who attended supervised aerobic exercise training. In the current case series, we found that 24-session aerobic exercise training utilized for the treatment of RLS relieved RLS severity, improved sleep quality, exercise capacity. The improvement in fatigue was achieved in all participants, except for subject 3. Supervised aerobic exercise training did not increase the risk of side effects or adverse events. Metabolic factors (hypoxia and muscle fatigue), which contribute to the possible mechanism of RLS may lead to altered central and peripheral excitability and affect peripheral nerve function in individuals with RLS (11). Impaired oxygen transport plays a role in the pathogenesis of RLS through microvascular abnormalities (12) and autonomic alterations (13). Anemia has been linked to the appearance of RLS symptoms (14). Exercise is known to provide an increase in cardiac output (15). Increased blood flow reduces RLS symptoms by decreasing peripheral hypoxia, which is closely related to RLS severity in individuals with RLS (16). Aerobic exercise has also shown to increase mitochondrial function and endorphin production and reduce inflammatory response (17). The first randomized controlled trial published by Aukerman et al. (18) reported that aerobic and lower body resistance exercises can be used to cope with RLS symptoms. They found that RLS symptoms improved over 6 weeks and were maintained throughout the 12-week intervention period. In a study where trauma release exercise (TRE) was applied for 6 weeks, RLS severity tended to decrease in both TRE and control groups although the difference was not statistically significant (19). They also found an improvement in sleep quality. We found that aerobic exercise training decreased the severity of RLS and improved sleep quality after the intervention. Healthcare professionals should emphasize the importance of exercise in the management of RLS and its potential adverse effects.

To the best of our knowledge, our case series is the first to report the effect of aerobic exercise training on exercise capacity and fatigue in individuals with RLS. It is well known that individuals with RLS most commonly complain of sleep disturbances (2). In addition, the importance of sleep for physical performance has been recognised (20). Zhan et al.,2022 reported a relationship between abnormal sleep duration and poor physical performance in hemodialysis patients (21). A randomized controlled systematic review by Song et al. found that exercise can reduce fatigue (22). Our case series supported that the physical performance and fatigue findings of the participants could be improved by supervised aerobic exercise training. Additionally, only one in five patients (subject 3) experienced an increase in the functional effect of fatigue after the intervention. Based on the subject 3 and 4, these participants were male and similar in their body weight and duration of RLS symptoms. This may be due to the severity of RLS (21 vs. 22) after the intervention in subject 3, as well as psychological factors. Further research may be needed to investigate the long-term effectiveness of exercise training and the psychological factors involved.

This case series has strengths and limitations. The most important strength is that the participants in our sample had severe RLS and all participants had a ferritin of more than 50 ng/mL. The lack of a control group and follow-up are the other limitations. We were also unable to describe the outcome of individuals with mild, moderate, or very severe RLS.

CONCLUSION

Twelve weeks of supervised aerobic exercise training reduces the severity of RLS, and improves sleep quality, fatigue and exercise capacity in individuals with RLS. We suggest that further randomized controlled trials be conducted to further validate our clinical findings.

Acknowledgements: This study was funded by the Department of Scientific Research Projects of Dokuz Eylul University (Grant ID: 2020.KB.SAG.015).

Author contributions: Conception: Burcin Aktar, Birgul Balci, Ibrahim Oztura, Baris Baklan; Design: Burcin Aktar, Birgul Balci, Ibrahim Oztura, Baris Baklan; Supervision: Birgul Balci, Ibrahim Oztura, Baris Baklan; Fundings: Sinan Buran (financial bursary for researcher); Materials: Burcin Aktar, Sinan Buran, Beyza Nur Aslantas, Dilara Mermi Dibek; Data collection and/or processing: Burcin Aktar, Sinan Buran, Beyza Nur Aslantas, Dilara Mermi Dibek; Analysis-Interpretation: Burcin Aktar, Birgul Balci, Beyza Nur Aslantas; Literature review: Burcin Aktar, Birgul Balci, Sinan Buran, Beyza Nur Aslantas; Writing: Burcin Aktar, Birgul Balci, Ibrahim Oztura, Baris Baklan; Critical review: Burcin Aktar, Birgul Balci, Sinan Buran, Beyza Nur Aslantas, Dilara Mermi Dibek, Ibrahim Oztura, Baris Baklan.

Conflict of Interest: The authors report there are no competing interests to declare.

Ethical Approval: The study was carried out with the approval of Dokuz Eylul University, Non-interventional Research Ethics Committee on 13.02.2019 (Decision No: 2019/03-24) and 03.04.2019 (Decision No: 2019/08-32) (Protocol number: 4548-GOA).

Funding: This study was funded by the Department of Scientific Research Projects of Dokuz Eylul University (Grant ID: 2020.KB.SAG.015). The funding body had no involvement in the data collection, analysis or interpretation, the writing of the manuscript or the decision to submit the manuscript for publication.

Peer-review: Externally peer reviewed.

REFERENCES

1. Allen RP, Picchietti DL, Garcia-Borreguero D, et al. Restless legs syndrome/Willis–Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria–history, rationale, description, and significance. Sleep Med 2014; 15:860-873.
2. Manconi M, Garcia-Borreguero D, Schormair B, et al. Restless legs syndrome. Nat Rev Dis Primers 2021;7:80.
3. Trenkwalder C, Winkelmann J, Inoue Y, Paulus W. Restless legs syndrome—current therapies and management of augmentation. Nat Rev Neurol 2015;11:434-445.
4. Akbaş P, Yaman Sözbir Ş. Non-pharmacological methods used in coping with restless leg syndrome (RLS): a systematic review. Sleep Biol Rhythms 2021; 19:215-225.
5. Harrison EG, Keating JL, Morgan PE. Non-pharmacological interventions for restless legs syndrome: a systematic review of randomised controlled trials. Disabil Rehabil 2019;41:2006-2014.
6. Pescatello LS, Arena R, Riebe D, Thompson PD. ACSM's guidelines for exercise testing and prescription. Lippincott Williams & Wilkins; 2014.
7. Walters AS, LeBrocq C, Dhar A, et al. Validation of the International Restless Legs Syndrome Study Group rating scale for restless legs syndrome. Sleep Med 2003;4:121-132.
8. Ay E, Helvacı Yılmaz N, Arıcı Düz Ö, Özer FF. Validity and reliability of the Turkish version of the International Restless Legs Syndrome Study Group Rating Scale. Acta Medica Alanya 2019; 3:105-110.

9. Agargun MY, Kara H, Anlar O. The validity and reliability of Pittsburgh Sleep Quality Index. Turkish Journal of Psychiatry 1996;7:107-115.
10. Armutlu K, Keser I, Korkmaz N, et al. Psychometric study of Turkish version of Fatigue Impact Scale in multiple sclerosis patients. J Neurol Sci 2007;255:64-68.
11. Lanza G, Bachmann CG, Ghorayeb I, Wang Y, Ferri R, Paulus W. Central and peripheral nervous system excitability in restless legs syndrome. Sleep Med 2017;31:49-60.
12. Koh SY, Kim MS, Lee SM, Hong JM, Yoon JH. Impaired vascular endothelial function in patients with restless legs syndrome: a new aspect of the vascular pathophysiology. J. Neurol Sci. 2015; 359:207-210.
13. Bertisch SM, Muresan C, Schoerning L, Winkelman JW, Taylor JA. Impact of restless legs syndrome on cardiovascular autonomic control. Sleep 2016;36:565-571.
14. Jiménez-Jiménez FJ, Alonso-Navarro H, García-Martín E, Agúndez JAG. Neurochemical features of idiopathic restless legs syndrome. Sleep Med. Rev. 2019;45:70–87.
15. Ehrman, J.K., D. Kerrigan, and S. Keteyian, Advanced Exercise Physiology: Essential Concepts and Applications. Human Kinetics; 2018.
16. Salminen AV, Rimpilä V, Polo O. Peripheral hypoxia in restless legs syndrome (Willis-Ekbom disease). Neurology 2014;82:1856-1861.
17. Mitchell UH. Nondrug-related aspect of treating Ekbom disease, formerly known as restless legs syndrome. Neuropsychiatric Disease and Treatment 2011; 7:251-257.
18. Aukerman MM, Aukerman D, Bayard M, Tudiver F, Thorp L, Bailey B. Exercise and restless legs syndrome: a randomized controlled trial. J Am Board Fam Med 2006; 19:487-493.
19. Harrison EG, Keating JL, Morgan P. Novel exercises for restless legs syndrome: a randomized, controlled trial. J Am Board Fam Med 2018; 31:783-794.
20. Grandner MA. Sleep, health, and society. Sleep Med Clin 2017; 12:1-22.
21. Zhan Q, Zhao J, Guo Q, et al. Association of Sleep Duration with Physical Performance in Hemodialysis Patients: A Multicenter Cross-Sectional Study. Nephron 2023;147(5):260-265.
22. Song YY, Hu RJ, Diao YS, Chen L, Jiang XL. Effects of exercise training on restless legs syndrome, depression, sleep quality, and fatigue among hemodialysis patients: a systematic review and meta-analysis. J Pain Symptom Manage 2018; 55:1184-95.