

EISSN 2459-1459



Formerly Marmara University Institute of Health Sciences (MUSBED)

CLINICAL AND EXPERIMENTAL HEALTH SCIENCES

Volume 15 | Issue 2 | June 2025

www.dergipark.gov.tr/marusbed



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ABOUT

Clinical and Experimental Health Sciences (Clin Exp Health Sci) is an international, scientific, open-access periodical published in accordance with independent, unbiased, and double-blinded peer-review principles.

The journal was published under the name MUSBED until April 22, 2016.

The target audience of the journal includes specialists and medical professionals working in all disciplines of health sciences. The journal is the official publication of Marmara University, Institute of Health Sciences and it is published four times a year in March, June, September, and December. The journal publishes content in English. The journal publishes clinical and experimental research articles, review articles, case reports, letters to the editor, and editorial comments prepared in accordance with ethical guidelines in all disciplines of health sciences.

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Indexing

TR Dizin

Emerging Sources Citation Index (E-SCI)

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Risk of Problematic Internet Use According to Dominant Handedness in Adolescents

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Received: June 17, 2023

Accepted: June 2, 2025

ABSTRACT

Objective: To investigate whether left or right-handedness influences adolescents' risk of problematic internet use (PIU).

Methods: The study conducted with Çanakkale Onsekiz Mart University students utilized a cross-sectional method. A self-reported questionnaire was completed by the participants regarding demographics. To ascertain the dominant hand and evaluate the extent of problematic internet usage (PIU), the short version of the Edinburgh Handedness Inventory (EHI) and Young's internet addiction test (IAT) were used. Young's IAT scores were analyzed according to handedness and in between left-handers.

Results: The questionnaires were filled out by 1186 university students aged 18-21. The rate of left-handedness was 10.5%, which was more common in males than females (12.6% vs. 9.5%, $p < .01$). The IAT score of the left-handed males was 37.02 ± 24.02 , while the score of the left-handed female was 32.74 ± 16.74 ($p < .05$). The overall prevalence of PIU was 18.8%. Males also had higher IAT scores ($p < .05$). There was no difference in test scores based on the dominant hand ($p > .05$). The risk of problematic internet use increased by 1.42 times more for males ($p > .05$ and $p < .05$, 95% CI: 1.04–1.94, respectively).

Conclusion: Adolescents' PIU cannot be predicted by their dominant hand. However, male left-handers are more prone to PIU behavior.

Keywords: Left-handedness, problematic internet use, internet addiction, adolescents

1. INTRODUCTION

In contemporary society, the internet has become an integral part of our everyday routines. Despite its undeniable convenience, however, the internet also presents a potential hazard in the form of addiction. Most studies on problematic internet use (PIU) prevalence show that the rate is increasing significantly yearly (1-3). Research on PIU has shown different prevalence levels in several countries, and the worldwide rate is estimated to be 10%. The prevalence of PIU among adolescents in Turkey exhibits a significant degree of regional variability, ranging from 1.6% to 19% (3-7). Problematic internet use is defined as "(a) internet maladaptive preoccupation experienced as irresistible use for periods longer than planned, (b) significant distress resulting from behavior, and (c) absence of other axes I pathology that might explain the behavior, i.e., mania or hypomania" (8). During adolescence, the distinct neuro-developmental plasticity of the brain may lead to an elevated susceptibility to PIU which can potentially result in detrimental impacts on

the mental health and overall well-being of young individuals in their daily lives (9). PIU may adversely affect the self-regulation and control abilities of individuals who are not yet fully mature physically and psychologically, which may significantly negatively impact an individual's overall well-being and life outcomes (10,11). There are other additional factors involved with PIU. Research has indicated that Internet addiction is closely associated with various factors, including personality traits, familial characteristics, parenting style, peer relationships, perceived social support, and the ability to regulate emotions (12-15). These findings suggest a comprehensive approach is necessary to address this complex issue (16) effectively. Dominant hand preference has been associated with substance use and addictive behavior in some publications (17,18). Some studies consistently show that alcohol-dependent patients are left-handed more often than healthy individuals (19). The connection between

How to cite this article: Ekin İE, Kaymaz N. Risk of Problematic Internet Use According to Dominant Handedness in Adolescents. Clin Exp Health Sci 2025; 15: 240-248. <https://doi.org/10.33808/clinexphealthsci.1315112>

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handedness and other addictions led us to hypothesize the possible association with PIU.

The brain's left hemisphere is more dominant than the right hemisphere in approximately 95% of individuals (20). It is well-known that handedness originates in the brain (21). Hand preference is established instinctively through hand activities (22). The preferred hand is the dominant one and is regulated by the opposite hemisphere (23). It is a natural variation for either the right or left hemisphere to be dominant in individuals. However, the reason for the prevalence of right-handedness over left-handedness remains to be determined. It has been observed that left-handedness is present in 5% to 25.9% of people across different cultures, with a higher prevalence in men than women (24). In the past, being left-handed was deemed unfavorable and an indication of inferiority in certain nations (25).

Additionally, up until the 1960s, it was typical to attempt to change left-handed individuals to right-handedness, with children being particularly compelled to write with their right hand (26). There is a potential connection between being left-handed and certain developmental issues, such as dyslexia and autism, as well as psychoneurological disorders such as epilepsy, depression, and schizophrenia, as indicated by research (29). It is worth noting that neuroscience and neurogenetics studies sometimes exclude left-handed individuals to minimize data variance (27-29).

The connection between left-handedness and addiction, particularly alcohol addiction, has been studied for many years. Left-handed individuals tend to drink more alcohol and are more likely to struggle with addiction than right-handed individuals (30-32). Reports indicate that left-handed individuals may have a greater propensity towards substance use, explicitly concerning heroin, ecstasy, and hallucinogens, compared to non-lefthanders (33). Considering the prior research on handedness and addiction, this paper investigated whether there is a link between PIU and handedness in university students.

2. METHODS

2.1. Ethics

In the central faculties of Çanakkale Onsekiz Mart University It was conducted with healthy university students between the ages of 17-21. All participants were provided with complete information about the purpose of the study and were invited to participate voluntarily. The students provided written consent letters. The Research Ethics Committee of the Çanakkale Onsekiz Mart University approved the study (Dated 22 March 2022 and numbered 2011-KAEK-27/2022.220.0065766).

2.2. Study Population

A cross-sectional study was conducted on Çanakkale University students between March and July 2022. We

recruited 1186 students who met the inclusion criteria. Inclusion criteria included (i) being between the ages of 17 and 21; (ii) circumstances that may prevent students from participating without assistance; (iii) does not have any known chronic disease; (iii) regularly enrolled college students; (iv) have access to at least one social networking site; (v) actively using the internet.

2.3. Procedure of the Study

Participants were contacted at the schools they attended. After the participants were informed before the study and their informed consent was obtained, the participants who agreed to participate in the study were asked to submit a socio-demographic data form (age, gender, height, weight, birth week and weight, type of birth, dominant hand use, parents' age, parents' education level, smoking/alcohol use, department of education) and the Young internet addiction scale (form with 20 questions). To determine the participants' dominant hand preferences, the 4-item form of the Edinburgh hand preference inventory (writing, throwing, toothbrush, spoon) was questioned.

2.4. Sociodemographic Information and Anthropometric Measurement Form

The authors created this form to gather information about the participants' age, gender, current anthropometric measurements (height and weight, self-reported), birth week, mode of delivery, alcohol consumption habits, smoking status, and parents' age and education level. Those who used alcohol regularly weekly were marked as "yes," and less frequent users were labeled "no." Smoking was marked as "yes" if at least one use per day and as "no" for less frequent users. Parental education level was categorized as less and more than eight years.

2.5. Defining the Handedness

The 4-item (writing, throwing, toothbrush, spoon) form of the Edinburgh Handed Preference Inventory (EHI) was used to objectively determine the subjects' hand preference in daily living activities (34). For each item, the participant is asked to verbally indicate which hand they used to perform the given activity.

2.6. Internet Addiction Survey (Internet Addiction Test, IAT)

Young's Internet addiction scale was used to assess the extent and intensity of self-reported compulsive Internet use (35). It has been validated and adapted into Turkish by Bayraktar. The internal consistency of the standardized Cronbach alpha coefficient and the Spearman-Brown coefficient's reliability is quite high, with values of 0.91 and 0.87, respectively (36). The results obtained from validity and reliability studies show that the validity and reliability of the Young Internet Addiction Test Form are ensured. The scale includes 20 items that use a 6-point Likert-type scale, ranging from 0

(never) to 5 (always). To determine the severity of internet disorder, the total score is computed by adding up the item responses, which range from 0 to 100. A higher score, closer to the theoretical maximum, denotes a more severe disorder. Individuals who score below 50 are identified as having control over their screen usage. A score ranging from 50 to 80 points is categorized as PIU, while a score between 80 and 100 is classified as a “pathological internet user” (37,38).

2.7. Statistical Analysis

We employed the SPSS (Statistical Package for the Social Sciences) software version 23.0 for Windows, developed by SPSS Inc. in Chicago, IL, USA, to conduct our statistical analysis. The criterion for statistical significance was set at $p < 0.05$. The Shapiro-Wilk method was utilized to verify if the data followed a normal distribution. To analyze total scale scores, the student's t-test was utilized for those with normal distribution, while the Mann-Whitney U test was employed for those without normal distribution. To compare normally distributed characteristics among multiple groups, we utilized ANOVA (with post hoc analysis using LSD). For non-normally distributed scale scores, we employed the Kruskal Wallis test (with post hoc analysis using Dunn). The correlation between quantitative variables was determined using the Pearson correlation coefficient. Binary logistic regression analysis was conducted to explore the potential correlation between the independent variables and Young's IAT scores. The report displayed descriptive statistics such as mean, standard deviation, and median values for numerical

variables. For categorical variables, the report provided the number and percentage values.

3. RESULTS

After excluding 510 people who did not agree to participate in the study and 184 people with more than 10% of the data missing, a total of 1186 participants were reached, aged between 18-21 (20.26 ± 0.80). When the quantitative demographic data and scale score values obtained from the participants were evaluated, it was observed that the proportion of female participants was higher (68.1%). Body mass index (BMI) values were determined as 22.58 ± 3.44 kg/m², it was found that 36.2% of the participants were born by cesarean section, while 63.8% were born by normal spontaneous vaginal delivery. Depending on the week of birth, 7.1% were born preterm and 92.9% were born term. It was determined that 48.3% of the participants consumed alcohol and 38% smoked. 125 (10.5%) of the participants were predominantly left-handed. According to the overall chi-square test of independence, left-handedness was more prevalent in males (12.5% vs. 9.5%, $p < .01$). We performed a post-hoc analysis with Bonferroni correction to determine which pairwise group differences were significant. The difference in the proportion of males between right-handed and ambidextrous individuals was statistically significant ($p < .01$), indicating that this subgroup contributed significantly to the overall effect. None of the other sociodemographic variables examined were significantly associated with dominant hand use (Table 1).

Table 1. Comparison of the demographics of the participants according to the dominant hand status

		Dominant hand						p
		Left-handers (n=125)		Right-handers (n=1008)		Ambidextrous (n=53)		
		n	%	n	%	n	%	
Gender	Male	48	38.4	303	30.1	27	50.9	.002*
	Female	77	61.8	705	69.9	26	49.1	
Delivery type	C/S	45	36.0	359	35.6	25	47.2	.233*
	NVD	80	64.0	649	64.4	28	52.8	
Birth week	Term	114	91.2	939	93,2	49	92.5	.718*
	Preterm	11	8.8	69	6.8	4	7.5	
Mother's education	≤8 years	52	41.6	510	50.6	23	43.4	.112*
	>8 years	73	58.4	498	49.4	30	56.6	
Father's education	≤8 years	32	25.6	349	34.6	19	35.8	.125*
	>8 years	93	74.4	659	65.4	34	64.2	
Alcohol usage	Yes	61	48.8	479	47.5	33	62.3	.111*
	No	64	51.2	529	52.5	20	37.7	
Active smoking	Yes	50	40.0	373	37.0	28	52.8	.061*
	No	75	60.0	635	63.0	25	47.2	
Mean±SD								
BMI		22.60±3.55		22.58±3.44		22.60±3.35		.996*
Mother's age		46.4±4.63		46.68±5.12		47.66±6.04		.317*
Father's age		49.44±4.7		50.26±5.48		51.44±7.11		.076*
NVD: normal vaginal deliverv. C/S: cesarean section. BMI: body mass index. SD: standard deviation. * Pearson Chi-Square test. * One-Way ANOVA test								

NVD; normal vaginal delivery, C/S; cesarean section, BMI; body mass index, SD; standard deviation, * Pearson Chi-Square test, * One-Way ANOVA test

The mean Young's IAT score of subjects was 32.68 ± 17.82 (Mean $\pm$ SD). Young's IAT scores were higher in males than females ($p < .05$). No significant difference was observed in IAT scores based on hand preference ($p > .05$).

According to Young's IAT threshold of 50 or higher, the estimated point prevalence of PIU is 18.8%, as shown in Table 2. Comparison of the characteristics of patients with and without PIU in terms of gender, mode of delivery, week of birth, maternal and paternal education levels, and alcohol and cigarette use according to Young's IAT score (Table 3). There was no significant difference in terms of delivery method between participants with and without problematic internet use ($p > .05$). In terms of birth week, 10.8% of participants with problematic internet use were born preterm, while this rate was 6.2% in participants without problematic internet use. This difference is statistically significant ($p < .05$). While 57.0% of the participants with PIU were using alcohol, only 46.3% of the participants without PIU were using alcohol. This difference is statistically significant ($p < .01$). While 45.7% of the participants with PIU smoked, only 36.2% of the participants without PIU smoked. This difference is also statistically significant ($p < .01$). According to the IAT score, it was determined that the BMI and the average age of the mother and father of the participants with and without problematic internet use were at similar values ($p > .05$).

Young's IAT score of the left-handed males was 37.02 ± 24.02 , while the score of the left-handed female was 32.74 ± 16.74 ($p > .05$). Young's IAT score was slightly higher in left-handed males than in right-handed males. However, it was insignificant (37.02 ± 24.02 vs. 34.74 ± 18.52 ; $p > .05$).

Nearly half of the participants (48.3%) reported regular alcohol use, with a significantly higher prevalence among males (60.3%, $p < .001$) compared to females. While 51.9% of males were smokers, the rate was 31.6% for females ($p < .001$). The rates of alcohol consumption and smoking did not exhibit a significant difference among the groups of individuals with varying handedness ($p > .05$ and $p > .05$, respectively). The left-handed males exhibit a statistically significant higher rate of regular alcohol consumption when compared to females (60.4% vs. 41.6%; $p < .05$).

According to logistic regression analysis results (Table 4), males had a 1.4 times higher rate of PIU than females ($p < .05$). It shows that the risk of addiction may increase as the birth week decreases. However, it is not statistically significant ($p > .05$). Although it is observed that the risk of PIU may increase with alcohol and cigarette use, it is not statistically significant ($p > .05$, $p > .05$).

Table 2. Young's IAT scores with three-dimensional cut-offs

			*p	Young's IAT scores						*p
				≥80		50-79		≤49		
		Mean±SD		n (10)	% (0.8)	n (213)	% (18)	n (963)	% (81.2)	
Dominant hand	Right-handers	32.46±17.39	.588 KW-H =1.06	7	0.7	175	17.4	826	81.9	.187
	Left-handers	34.38±19.87		3	2.4	27	21.6	95	76	
	Ambidextrous	32.85±20.64		-	0	11	20.8	42	79.2	
Gender	Male	34.85±19.47	.011 U=138769	4	1.1	87	23	287	75.9	.006
	Female	31.66±16.91		6	0.7	126	15.6	676	83.7	
IAT; Internet addiction test, SD; standard deviation, * Pearson Chi-Square test, U value was obtained from Mann Whitney U test, KW-H Kruskal Wallis analysis.										

IAT; Internet addiction test, SD; standard deviation, * Pearson Chi-Square test, U value was obtained from Mann Whitney U test, KW-H Kruskal Wallis analysis.

Table 3. Comparison of demographics of those with and without PIU according to Young's IAT score

		Young's IAT scores				P
		<50		≥50		
		n	%	n	%	
Gender	Male	287	29.8	91	40.8	<.001*
	Female	676	70.2	132	59.2	
Delivery type	C/S	343	35.6	86	38.6	.409*
	NVD	620	64.4	137	61.4	
Birth week	Preterm	60	6.2	24	10.8	.017*
	Term (≥37)	903	93.8	199	89.2	
Mother's education	≤8 years	491	51.0	94	42.2	.018*
	>8 years	472	49.0	129	57.8	
Father's education	≤8 years	334	34.7	66	29.6	.148*
	>8 years	629	65.3	157	70.4	
Alcohol usage	Yes	446	46.3	127	57.0	.004*
	No	517	53.7	96	43.0	
Active smoking	Yes	349	36.2	102	45.7	.008*
	No	614	63.8	121	54.3	
Mean±SD						
BMI		22.49±3.34		22.98±3.84		.051*
Mother's age		46.61±5.13		47.04±5.05		.204*
Father's age		50.09±5.53		50.81±5.31		.069*
IAT; Internet addiction test, NVD; normal vaginal delivery, C/S; cesarean section, BMI; body mass index, SD; standard deviation, * Student's t-test, * Pearson Chi-Square test						

Table 4. Binary logistic regression results according to Young's IAT scores ≥50 vs. <50

	B	S.E.	Wald	p	OR	95% C.I. for OR	
						Lower	Upper
Gender	.353	.159	4.962	.026	1.424	1.043	1.943
Birth week	-.491	.258	3.625	.057	0.612	0.369	1.015
Mother's education	.226	.176	1.645	.200	1.254	0.887	1.772
Father's education	.049	.187	0.070	.792	1.051	0.728	1.517
Alcohol use	.236	.169	1.962	.161	1.266	0.910	1.762
Smoking	.197	.168	1.379	.240	1.218	0.876	1.693

B; regresyon katsayısı, S:E.; standart hata

Table 5. Post-hoc Analysis of Gender Differences by Dominant Hand Preference

Comparison	p-value	Bonferroni corrected p-value
Left-handers vs Right-handers	.072	.216
Left-handers vs Ambidextrous	.166	.499
Right-handers vs Ambidextrous	.0023	.0069

Bonferroni correction was applied. The significance level was accepted as $p < 0.05$.

4. DISCUSSION

The current research has established that PIU is unaffected by one's preference for the dominant hand. The fact that alcohol addiction has been found more frequently in left-handed individuals in previous studies led us to conclude that there may also be a possible link between left-handedness and other addictions (17). Therefore, in our study, it is thought that the risk of PIU behavior, which has become a

serious problem today, may be affected by hand dominance and may be a determinant before the development of PIU. The prevalence of PIU among university students has been reported to be between 6% and 40% (39). Our data reveal a PIU rate of 18.8% in the previously reported range. The current study observed that the most associated factor with PIU risk was the male sex, which was in line with the literature. However, some recent research state that the female sex has an increasing rate of PIU, while others indicate that gender is

not determinative in this regard. Since these studies mainly focus on the difference in the purpose of using the internet, as stated in the majority of literature, it seems stable that the male sex is more prone to PIU (40-42).

On the other hand, dominant hand use and gender distribution were examined in the study, and it was determined that left-handedness was more common in the male gender. It was determined that 12.7% of men and 9.53% of women were left-handed. In interpreting the significant association between gender and handedness ($p < .01$), a post-hoc analysis was performed to assess pairwise differences. The results indicated that the only statistically significant difference occurred between right-handed and ambidextrous participants (Bonferroni-corrected $p < .01$), with a notably higher proportion of males in the ambidextrous group. This finding suggests that the overall association was driven specifically by the gender composition difference between these two subgroups, rather than a generalized difference across all handedness categories. The testosterone hypothesis can explain this relationship, which indicates that genetic basis is more influential than environmental factors. Studies indicate that the presence of testosterone during pregnancy may hinder the growth of the brain's left hemisphere, leading to a proclivity for the right hemisphere and the ability to manipulate the movements of the right hand. As a result, heightened testosterone levels correlate with an increased probability of left-handedness (43).

In our study, it was observed that the IAT scores of obese individuals were significantly higher than the scores of normal weight participants. Studies have found that adolescents with internet addiction have a higher risk of obesity (44-46). Internet addiction and excessive internet use are conditions associated with obesity, likely due to their negative impact on physical activity, such as reduced regular exercise and unhealthy eating habits. In addition, excessive internet use may also increase the risk of eating disorders, which may be associated with obesity. However, more research is needed to fully explain this relationship (44-47). It means that obese individuals may experience social and psychological stress and can use the internet to reduce this stress. Obese individuals limited physical activity may increase their internet use. Obese individuals may spend more time on the internet instead of exercising (48,49). In the study, no significant difference was found in the mean YIAT scores based on birth week or delivery method. However, a high rate of premature births was observed in the group with problematic internet use. Research on internet addiction based on birth week or delivery method is quite limited. Some studies in the literature have found that premature children have a higher risk of internet addiction (50,51). Overall, there is insufficient information about the effect of birth week or delivery method on internet addiction. Therefore, further research is needed in this area. In our study, no significant difference was found in the IAT scores of the participants according to their smoking and alcohol use. However, smoking and alcohol use rates were found to be higher in participants with PIU. A meta-analysis that

included 13 studies to examine the relationship between alcohol consumption and internet addiction showed that alcohol consumption increases the risk of internet addiction (52). Although the results of these studies are contradictory, it is generally thought that there is a relationship between smoking or alcohol use and internet addiction. However, more research is needed on the direction of this relationship and how strong it is.

In our study, when the education levels of mothers and fathers were compared separately with the YIBÖ scores, no statistically significant difference was found between them. However, it was found that the participants with problematic internet use behavior had a higher rate of mothers with higher education levels ($p > .05$). In a study conducted in Turkey, they examined the effect of the education level of the mother and father on internet addiction and it was revealed that students with highly educated mothers and fathers had lower levels of internet addiction and also showed better academic success (53). Similar studies in the literature have observed that children of low-educated parents have a higher risk of internet addiction (54-56). These studies are based on the idea that the education level of the mother and father has a significant impact on internet addiction, that the children of highly educated parents can be more rational, develop healthy habits and manage digital technologies more effectively, while low-educated parents have a negative impact on their children's use of technology. It was interpreted that they did not have sufficient information, had difficulties in providing supervision, and were inadequate in controlling their children's internet use.

Alcohol and cigarette use were evaluated according to dominant hand use, and no significant differences were found. When the literature was scanned, the relationship between alcohol use and dominant hand use was examined and it was found that the alcohol consumption rate of left-handers was higher than that of right-handers (17,57). On the other hand, considering gender in our study, alcohol and cigarette use were found to be more common in left-handed males than in females.

No significant differences were found when comparing birth method and birth week with dominant hand status. Research on the relationship between birth method, birth week, and dominant hand use is limited. In a study conducted in the literature, dominant hand use of children born through normal vaginal delivery (NSVD) and cesarean section (C/S) was examined, revealing that children born through NSVD more frequently used their left hand. This is attributed to the positioning of the baby's head on the left side during birth, leading to more frequent use of the left arm (58). Further research is needed to identify differences in dominant hand use among children born via C/S. Studies on the relationship between birth week and dominant hand use have yielded conflicting results, indicating the need for additional research.

5. CONCLUSION

Addressing a robust relation between the dominant hand and PIU appears premature once we clarify and understand the possible determinants better. This research offers further understanding regarding how gender impacts the development of problematic internet use (PIU).

Some limitations need to be mentioned. The measurement of PIU was solely based on self-reporting, without the inclusion of any clinical evaluation or other pertinent data sources. This approach might have impacted the accuracy and consistency of the data collected. The fact that the rates of PIU and left-handedness preference vary according to the societies enabled us to represent the general population. Therefore, it is recommended not to overgeneralize. A high educational level also characterizes the investigated cohort.

Internet addiction or inappropriate use of the Internet is not a problem that can be solved through technology or policies alone. This situation is a new social struggle that must be determined through education. Within the scope of this struggle, field studies are urgently needed. Such research can contribute to developing policies to recognize and prevent the problem and to provide effective guidance and psychological counseling services.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Çanakkale Onsekiz Mart University, (Approval date: 22.03.2022; Number: 2011-KAEK-27/2022.220.0065766)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: NK

Design of the study: NK

Acquisition of data for the study: İEE

Analysis of data for the study: İEE

Interpretation of data for the study: NK, İEE

Drafting the manuscript: NK, İEE

Revising it critically for important intellectual content: NK

Final approval of the version to be published: NK, İEE

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Comparison of Single vs. Staged Extractions: Clinical Outcomes of Mandibular Wisdom Tooth Extractions – A Prospective Cohort Study

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Received: July 31, 2023

Accepted: March 06, 2025

ABSTRACT

Objective: To compare the effects of bilateral extraction of wisdom teeth at 1 versus 2 separate appointments on patients' oral health-related quality of life.

Methods: This single-center prospective cohort study included 59 patients aged 18–30 years. Patients who wanted surgical removal of both mandibular third molars at a single appointment were included in group A, while those who wanted to have them removed at 2 separate appointments were included in group B. The primary predictor variable was the Oral Health Impact Profile 14 (OHIP-14) score compared to the control group, while secondary outcome variables included postoperative pain and maximum interincisal opening. The study design was a prospective cohort study, and data analysis was performed using appropriate statistical tests.

Results: No significant differences were found between groups A and B in terms of maximum interincisal opening, Visual Analog Scale score, and oral health-related quality of life ($p < .05$).

Conclusions: This study found that there were no significant differences between 1 and 2 separate appointments for lower third molar extraction. Based on these results, the authors recommend bilateral extraction of wisdom teeth (for mild and moderate cases) at a single appointment to minimize inconvenience to patients without sacrificing treatment outcomes.

Keywords: Oral health, Prospective Studies, Quality of Life, Third Molar

1. INTRODUCTION

Surgical extraction of third molars is one of the most common procedures in oral and maxillofacial surgery (1, 2). Appointments for impacted wisdom teeth are mostly divided into different sessions because of the concerns of patients and the preventive approaches of physicians (3). However, the COVID-19 pandemic has incited changes in dental clinics' routine practices, with a potential increase in demand for fewer, more comprehensive sessions. This change has led to debates about the feasibility and safety of extracting impacted wisdom teeth in a single appointment (3, 4).

There is a controversy surrounding the management of impacted wisdom tooth extraction at the same appointment (5). Some authors have suggested that bilateral extraction of wisdom teeth under local anesthesia with intravenous sedation is safe (6, 7). Others have advocated the possibility of complications; patient discomfort during or after the

procedure may be higher when bilateral lower third molars are removed (8, 9). Bilateral extraction of impacted third molars at the same appointment may not be preferred for reasons such as the possibility of the procedure getting prolonged, an increase in patient fatigue, and a decrease in patient tolerance (6). Additionally, it has been mentioned that there have been several complications because of bilateral mandibular block anesthesia, such as respiratory distress, which may occur as a result of losing control of the tongue movement and may cause fluid collection in the oral cavity so that aspiration may occur (8). This procedure could be performed under general anesthesia or sedation to overcome these problems (10).

On the contrary, most patients do not prefer to undergo general anesthesia or sedation to get their third molars extracted and are unable to afford the related increase in treatment cost (8, 11). The scientific background to these thoughts is lacking and needs to be investigated to obtain more evidence-based information.

How to cite this article: Bayram F, Gedikli G, Göçmen G. Comparison of Single vs. Staged Extractions: Clinical Outcomes of Mandibular Wisdom Tooth Extractions – A Prospective Cohort Study. Clin Exp Health Sci 2025; 15: 249-255. <https://doi.org/10.33808/clinexphealthsci.1335372>

Moreover, there is a scarcity of information reported in the literature on whether patients want to have their wisdom teeth extracted during the same procedure or not.

This study aimed to compare the effects of bilateral extraction of wisdom teeth at 1 appointment to that at 2 separate appointments on patients' oral health-related quality of life (OHRQoL). We hypothesized that bilateral extraction of impacted wisdom teeth would be acceptable to patients. The primary objective was to compare the Oral Health Impact Profile-14 (OHIP-14) questionnaire results of the test group with the control group. The secondary objectives were to assess the Visual Analog Scale (VAS) for pain scores and maximum interincisal opening (MIO) measurements between the groups.

2. METHODS

Ethical approval for this study was obtained from the Institutional Review Board of Marmara University Faculty of Dentistry Clinical Research Ethical Committee, with approval number 2017/78 and registered at ClinicalTrials.gov (NCT05820867). All procedures performed in this study adhere to the ethical guidelines laid down by the Declaration of Helsinki (1964, and its later amendments). This was a quasi-experimental, single-center prospective cohort study conducted at the Marmara University Faculty of Dentistry, Oral and Maxillofacial Surgery Department, between March 2018 – March 2020, in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. After receiving full written and verbal information about the study, all the patients signed a written informed consent form before their participation. They also signed a surgical consent form, which is generally required as a routine before every third molar extraction. In this study, wisdom tooth extraction was decided according to the recommendations of the NICE Guidance on wisdom tooth extraction introduced in 2000 (12).

2.1. Inclusion Criteria

The inclusion criteria were asymptomatic, impacted mandibular third molars with class I, position A impaction according to Pell and Gregory classification (13), and ASA 1 patients (14).

2.2. Exclusion Criteria

The exclusion criteria were as follows:

- Local pathology associated with third molars (e.g., cysts or tumors)
- Diagnosis of acute pericoronitis
- Usage of anti-inflammatory drugs or antibiotics within the last week
- Operations that require osteotomy
- Patients with psychiatric disorders or taking drugs that may impair their mental health
- Patients unwilling to undergo data collection procedures
- Pregnant or lactating women

- Heavy smokers
- Operations lasting longer than 45 minutes for 1 side (from the time the first incision is made to the last suture placed)

2.3. Sample Size Calculation

The sample size was determined based on the primary outcome measure, which was the OHIP-14 score. We considered a power of 80%, a significance level of 0.05, and an estimated effect size (difference in mean OHIP-14 scores between the two groups) of 5 points. Using these parameters, we calculated that a total of 50 patients were required for this study to detect a clinically significant difference with sufficient power.

2.4. Study Design

Patients who met the inclusion criteria and required the removal of both mandibular third molars were identified from the patient registry. Two distinct groups were formed based on patient preference: those opting for extraction of both teeth in a single session were assigned to Group A, while those choosing two separate sessions were assigned to Group B. Patients who decided against contralateral third molar extraction during the study were excluded. The patients in group B waited for at least two weeks after their wisdom tooth extraction on one side, followed by removal of the teeth on the contralateral side. Fifty patients with appropriate data were divided into groups A (n = 26) and B (n = 24), and the results were analyzed [Figure 1].

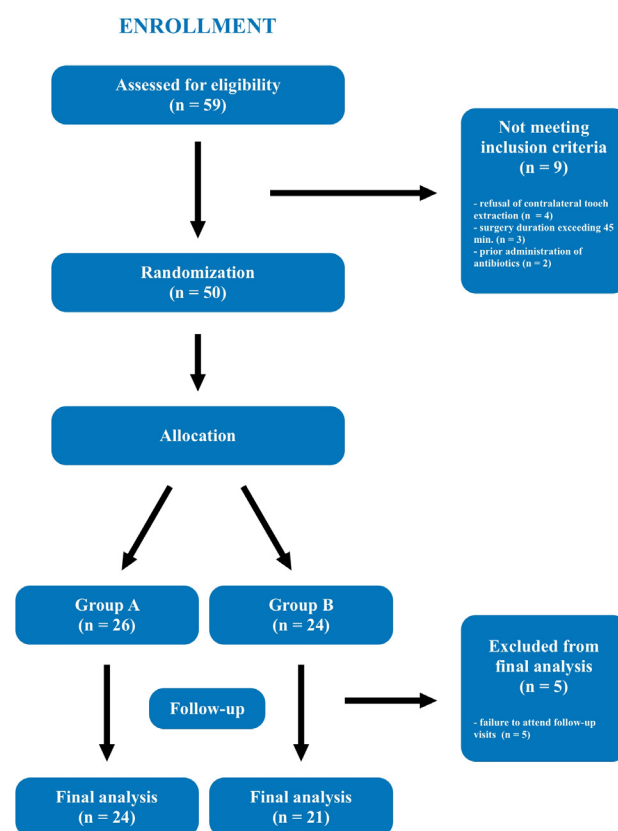


Figure 1. Study flowchart

2.5. Surgical and Postsurgical Design

All surgical removals were performed by one surgeon to standardize the technique. Ipsilateral inferior alveolar nerve block and buccal infiltration anesthesia were performed using 4% articaine (40 mg/ml) with epinephrine (1:100,000) (Ultracain DS forte-Aventis Pharmaceutical Tic. Inc., Istanbul, Turkey). After a 5-minute lag time and total anesthesia of the intended surgical field, a triangular full-thickness mucoperiosteal flap with releasing incision on the mesiobuccal aspect of the second molar was used. After tooth elevation and removal, the surgical field was carefully inspected and debrided. The flap was closed with single interrupted sutures using a 3.0 silk suture (Doğsan, Trabzon, Türkiye).

All patients received 875 mg amoxicillin/125 mg clavulanic acid twice a day for 7 days after surgery, along with 400 mg ibuprofen administered three times daily for 3 days post-surgery. For oral hygiene, 15 ml of 0.12% chlorhexidine mouth rinses 3 times daily for 1 minute for 7 days were advised. Cold compresses were routinely recommended at 5-minute intervals for the first 24 hours post-surgery.

2.6. Data Collection

The patients' demographic information (e.g., age, sex, and nationality), health-related activities (e.g., smoking, consumption of alcohol, and other habits), and indication for third molar extraction were recorded. For data collection, an online form (JotForm, San Francisco, CA, USA) was prepared to monitor the patients.

2.7. OHIP-14

The OHIP-14 is a specific questionnaire used to evaluate quality of life by establishing a relationship with oral health (15). It consists of 7 conceptual domains: functional limitation, pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. Answers to these questions are rated according to a Likert scale: 0 – “never,” 1–“hardly ever,” 2–“occasionally,” 3–“fairly often,” and 4–“very often.” The negative impact of oral health on the participants' lives was rated as 3 and 4, and the positive impact was rated as 0, 1, or 2. The scale ranged from 0 to 56; a lower OHIP-14 score suggested a more significant adverse effect on the patients' physical, psychological, and social well-being because of possessing third molars. This questionnaire has been translated into Turkish and various other languages, with validation studies confirming its reliability and ease of use across different populations (15, 16). All the recorded data were collected from baseline and postoperative 2nd, 3rd, 7th, 9th, and 14th days. The participants were requested to fill out the OHIP-14 questionnaire online.

2.8. VAS

The patients were asked to detail and record their pain experience; the symptoms score was obtained using the VAS. The VAS consisted of a 10-number horizontal line marked 0

(=“no pain”) to 10 (=“most severe pain ever experienced”). The patients were requested to fill out the online questionnaire at postoperative 6th and 12th hours and on postoperative 1st, 2nd, 3rd, and 7th days. The number of analgesics consumed by the patients after surgery was also monitored and recorded.

2.9. MIO

The same examiner performed postoperative assessments before surgery 3rd day and on the 7th day after surgery. MIO measurements were recorded to evaluate the trismus. This was achieved using a ruler to measure the distance between the lower and upper incisors.

Wound healing was assessed (as pain-free, self-cleansing, or a sign of infection-free socket) on the 7th day after surgery.

2.10. Operating Time

The operating times for all patients were recorded using a chronometer, measuring the duration from the initial incision to the placement of the final suture.

2.11. Measurement of Observations and Risk of Bias

All measurements were performed by an independent examiner blinded to the group assignments, minimizing the risk of detection bias.

2.12. Statistical Analysis

The SPSS Statistics program (v22; IBM Corp., Istanbul, Turkey) was used to perform statistical analysis. To compare the two groups, an independent-samples test was used. The Shapiro-Wilk test was used to assess the normality of the data distribution, with p-values less than .05 considered statistically significant.

3. RESULTS

A total of 59 patients were initially enrolled in this study. The study was completed with 45 (85%) of the 59 patients. The reasons for patient exclusion included refusal of contralateral tooth extraction (4 patients), surgery duration exceeding 45 minutes (3 patients), prior administration of antibiotics (2 patients), and failure to attend follow-up visits (5 patients). The mean age of the patients was 23.4 (range: 18–30) years; with 28 (62%) being female and 17 (38%) males.

3.1. OHIP-14

The OHRQoL and satisfaction surveys showed no clinical differences between the groups. Very high satisfaction levels were observed in the participants. Participants reported very high satisfaction levels overall, and comparisons of satisfaction levels between the groups showed no statistically significant differences [Table 1].

Table 1. Comparison of the satisfaction surveys between all the groups

	Satisfaction Surveys					
	Group A & Group B (Right)			Group A & Group B (Left)		
	Mean ± (SD)			Mean ± (SD)		
	Group A	Group B	p	Group A	Group B	p
Peri-op	0,4 ± (0,7)	0,5 ± (0,6)	p > .05	0,4 ± (0,7)	0,5 ± (0,6)	p > .05
Post-op	0,6 ± (0,6)	0,2 ± (0,6)	p > .05	0,6 ± (0,6)	0,3 ± (0,6)	p > .05
Total	2,6 ± (0,7)	2,7 ± (0,7)	p > .05	2,6 ± (0,7)	2,7 ± (0,4)	p > .05

All statistical comparisons were performed using the independent-samples t-test.

3.2. VAS

A comparison of VAS scores at the 6th and 12th hours and on the 2nd, 3rd, and 7th days between the groups was not statistically significant [Table 2].

Table 2. Comparison of the Visual Analogue Scale at the 6th and 12th hours and on the 1st, 2nd, 3rd, and 7th days between all the groups

	VAS (Visual Analogue Scale)					
	Group A & Group B (Right)			Group A & Group B (Left)		
	Mean ± (SD)			Mean ± (SD)		
	Group A	Group B	p	Group A	Group B	p
6 th hour	3,3 ± (2,2)	4,3 ± (1,8)	p > .05	3,3 ± (2,2)	4,1 ± (1,2)	p > .05
12 th hour	3,1 ± (1,8)	3 ± (1,1)	p > .05	3,1 ± (1,8)	2,9 ± (1,0)	p > .05
1 st day	2,9 ± (1,9)	2,3 ± (1,3)	p > .05	2,9 ± (1,9)	2,0 ± (1,1)	p > .05
2 nd day	2,2 ± (2,1)	1,9 ± (1,5)	p > .05	2,2 ± (2,2)	1,5 ± (1,3)	p > .05
3 rd day	1,6 ± (1,9)	1,5 ± (1,5)	p > .05	1,6 ± (1,9)	0,9 ± (1,5)	p > .05
7 th day	0,3 ± (0,6)	0,5 ± (1,5)	p > .05	0,3 ± (0,6)	0,4 ± (1,5)	p > .05

All statistical comparisons were performed using the independent-samples t-test.

3.3. MIO

There was no statistically significant difference in MIO levels between the groups across the three time points [Table 3]. MIO levels increased or returned to average by the end of the first week.

Table 3. Comparison of the maximum interincisal opening between all the groups

	MIO (Maximum Interincisal Opening)					
	Group A & Group B (Right)			Group A & Group B (Left)		
	Mean ± (SD)			Mean ± (SD)		
	Group A	Group B	p	Group A	Group B	p
Pre-op	49,0 ± (5,1)	47,4 ± (4,9)	p > .05	49,0 ± (5,1)	47,0 ± (4,9)	p > .05
3 rd day	42,3 ± (8,6)	43,2 ± (3,0)	p > .05	42,3 ± (8,6)	43,4 ± (5,0)	p > .05
7 th day	46,9 ± (7,2)	46,1 ± (5,2)	p > .05	46,9 ± (7,2)	46,5 ± (4,4)	p > .05

All statistical comparisons were performed using the independent-samples t-test.

3.4. Operating Time

The total operating time was 12,7 (± 0,6) minutes for group B (right), 12,6 (± 0,5) minutes for group B (left), and 27,9 (± 0,8)

minutes for group A. No statistically significant difference (p>.05) was found between the operating times for group B (right vs. left). Similarly, there was no statistical difference between the operating time for Group A and the combined operating time of group B (right and left) The total duration of bilateral extraction was 2.6 minutes longer than the total duration of unilateral extraction [Table 4].

Table 4. Operating times and comparison of the operating times between all the groups

	Operation Time		
	Group A	Group B (Right)	Group B (Left)
Mean Time	27,9	12,7	12,6
SD (±)	0,8	0,6	0,5

4. DISCUSSION

This study aimed to assess how bilateral extraction of mandibular third molars influenced postoperative morbidity following third mandibular molar extraction. According to our results staged wisdom tooth extraction is not superior to single-stage extraction in terms of OHIP-14 surveys, VAS scores, and MIO measurements. To our knowledge, this is the first study to compare the clinical outcomes of bilateral extraction of wisdom teeth at 1 versus 2 separate appointments.

Although no direct correlation between age and surgical pain has been established, some studies have identified age as a significant individual factor influencing surgical difficulty (17, 18). In our study, we did not analyze age as variable but focused on young adults as the age group. Previous studies have reported that women experience more pain and have a higher risk of developing chronic pain (19, 20). Women of reproductive age tend to be more vulnerable to chronic pain (21). Despite these differences, mixed-sex chronic pain risk trials generating bias or lacking essential details and single-sex studies have reduced generalizability (19). In our study, no significant difference was found between gender groups. However, an uneven distribution of males and females in the groups can be a confounding factor and prevent generalized results. The patients in our study either did not have upper wisdom teeth or lacked extraction indication of the existing teeth (12). Since the variables decreased, we were able to focus on the results of bilateral extraction of lower wisdom teeth.

There is no reported contraindication to bilateral extraction of wisdom teeth at the same appointment in the current literature. However, it is not recommended according to many published studies (8, 9). The possibility of prolonged surgery, increased patient fatigue, decreased patient tolerance, and the presence of undesired effects of bilateral mandibular block anesthesia are some reported reasons for not removing third molars simultaneously (6).

There is anecdotal information about performing bilateral mandibular block anesthesia. The idea of losing control of the tongue movement after bilateral anesthesia, fluid collection

in the oral cavity, and respiratory distress are undesirable scenarios. However, there is no reported contraindication for bilateral anesthesia (10). Additionally, College et al (22) found no significant difference in the incidence of trauma between bilateral and unilateral mandibular block anesthesia. They noticed that less soft-tissue trauma was observed in patients with bilateral mandibular block anesthesia than in those with unilateral anesthesia (8).

In some studies, bilateral extraction of mandibular wisdom teeth has been performed under general anesthesia (23). Costantinides et al. demonstrated that the risk of inferior alveolar and lingual nerve damage is higher during mandibular third molar extractions performed under general anesthesia (24). The patient being in the supine position under general anesthesia, increased extension of the mucoperiosteal flap and bone removal, and increased surgical force were explained as possible reasons. However, in the literature, it is not clear in which cases general anesthesia should be chosen, and further studies need to be conducted to arrive at a more comfortable decision.

On average, the mean operating time for third molar extraction is approximately 30 minutes, including the time from the patient entering the operating room to leaving it. About half of this time is spent setting up the surgical field, while the surgical procedure itself takes approximately 15 minutes. Extracting both mandibular wisdom teeth in a single appointment can save about 15 minutes, as the setup time for the second molar is eliminated. In a study by Holland and Stassen, performing bilateral extractions at the same appointment increases the operating time by roughly 15 minutes, resulting in a total duration of 45 minutes (6). Therefore, bilateral extraction of the lower third molar on a single visit saves a considerable amount of time (6).

Increased operating time could be considered as a potential disadvantage from a different perspective, as it may not be well-tolerated or preferred by some patients (6). In our study, no statistically significant difference was found between the bilateral extractions of teeth at the same appointment and two separate appointments in terms of patient satisfaction. Additionally, the impact of prolonged operating time on patient satisfaction could not be evaluated, as patients whose procedures exceeded 45 minutes were excluded from the study.

Maintaining proper access to and clear visualization of the surgical field are critical factors in performing safe surgical procedures. Prolonged operating time can lead to fatigue for both surgeons and patients; during the removal of both third molars, patients may become less tolerant and close their mouth, complicating the procedure. In general, appointments for minor operations take about 30–45 minutes, which is the best duration to maintain adequate access. To avoid the potential impact of extended surgery on postoperative outcomes, the duration of surgery in our study was restricted to 45 minutes, with cases exceeding this time excluded from the analysis (25).

The OHIP-14 was selected for this study because it is one of the most widely used OHRQoL instruments, with over 900 citations in Scopus (16). This allowed for meaningful comparisons between our findings and those from other communities. As noted by Allison et al, quality of life is a “dynamic model” and, therefore, likely to change over time (26). To ensure accurate and consistent data collection, online forms were designed to be user-friendly and to minimize patient discomfort, rushed responses, or undue stress. These forms were completed daily by the patients and closely monitored. In cases of emergencies, such as reports of severe pain or bleeding noted in the forms, patients were promptly contacted by phone for appropriate follow-up.

Studies have suggested that nonsteroidal anti-inflammatory drugs (NSAIDs) may be the first choice for pain control after wisdom tooth extraction, and when taken together with acetaminophen, they may be more effective in pain control (27). In some studies, it has been reported that the increase in the consumption of analgesics is correlated with the increase in VAS scores (25). In our study, all the participants used NSAIDs (400 mg. ibuprofen twice a day) after surgery as a painkiller. Thus, our VAS scores are based on a basis similar to previous studies.

Some authors have found a positive relationship between restricted mouth opening and VAS scores (25, 28). This condition may occur in response to pain and may develop because of stiffness in the muscles. Similarly, Lim and Ngeow reported a positive moderate relationship between edema and pain (25). In our study, a clear correlation observed between VAS scores and trismus, indicating that pain is a significant contributing factor to reduced mouth opening following third molar surgery.

Major complications associated with impacted wisdom tooth extraction include pain, swelling, bleeding, trismus, nerve damage, and alveolitis. Factors such as age, gender, anatomical differences, surgeon’s experience, and wound closure technique could affect these complications (29, 30). There is debate on cryotherapy after tooth extraction (31). In the literature, it was reported that although there was an improvement in VAS scores and mouth opening between the 2nd and 7th postoperative days, it was not completely resolved on the 7th day (28). In our study, the ongoing complaints on the 7th day decreased after the removal of sutures and completely disappeared on the 10th day in most cases. According to this result, the complaints that increased on the first 2 days started to decrease after the 3rd day, and it was seen that the removal of sutures was an important factor in the reduction of the complaints.

In 1996, Holland et al calculated the supply costs for surgical removal of third molars—including all the drugs, armamentarium, and disposable materials such as gloves and drapes—worth 20€ (6). Consequently, extracting both third molars in a single appointment would significantly reduce overall costs (6, 32). This approach also minimizes the occupancy of operating rooms, as well as the time required from staff, assistants, and surgeons.

This study has certain limitations that should be acknowledged. It focused on patients with class I, position A mandibular third molars without the need for osteotomy, minimizing variability and enhancing internal validity. However, this limits generalizability to broader populations with different levels of impaction or surgical complexity. Additionally, all surgeries were performed by a single surgeon at one center, which may affect external validity. Future research should include more diverse patient populations to confirm these findings. Despite these limitations, this study provides valuable insights into the impact of single versus staged extractions on oral health-related quality of life and postoperative outcomes in this specific patient group.

5. CONCLUSION

Our study results support that single-session bilateral wisdom tooth extraction is not inferior to staged extraction regarding VAS scores, MIO measurements, and OHIP-14 surveys. Removing both mandibular third molars in a single session reduces patient anxiety related to a second procedure, saves clinical time, and minimizes recovery periods. The single-session approach also optimizes resource use by requiring fewer drugs and supplies. Although this study focused on lower third molars, its findings suggest potential benefits for the simultaneous extraction of all wisdom teeth. Future studies are needed to validate these results across broader patient groups and different clinical settings.

Funding: The project (No:SAG-A-170.419.0139 and SAG-A-070.317.0084) was funded by The Commission of Scientific Research Projects of Marmara University

Conflict of interests: The authors declare that they have no conflict of interest.

Ethics: This study was approved by Ethics Committee of Marmara University Faculty of Dentistry Clinical Research Ethics Committee (Approval date: 10.02.2017; Number: 2017-78)

Peer-review: Externally peer-reviewed.

Author Contribution

Research idea: FB, GG, GG

Design of the study: FB, GG, GG

Acquisition of data for the study: FB, GG, GG

Analysis of data for the study: FB, GG, GG

Interpretation of data for the study: FB, GG, GG

Drafting the manuscript: FB, GG, GG

Revising it critically for important intellectual content: FB, GG, GG

Final approval of the version to be published: FB, GG, GG

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Clinical Performance Self-Efficacy and Professional Readiness of Senior Nursing Students who Received Online Practice Education in the Pandemic Period

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Received: September 21, 2023 **Accepted:** June 17, 2025

ABSTRACT

Objective: This study was applied to examine the clinical performance self-efficacy and professional readiness of senior nursing students who received online education in the pandemic period.

Methods: The study, applied in a descriptive and correlational design, was carried out at the faculty of health sciences of a state university in Istanbul between January and May 2022. The population of the study consisted of 4th year nursing students (n=246). The research participant were 173 students. An introductory information form, Self-Efficacy in Clinical Performance Scale (SECP) and a questionnaire form for professional readiness of nursing students were used to collect data. In addition to descriptive statistics, t-test, analysis of variance and correlation were used to evaluate the data.

Results: It was determined that the SECP scores of the students (69.31; SD=47.34) did not show a significant difference according to gender, graduated high school and cumulative grade point average. It was determined that there was no significant relationship between the SECP score and the feeling ready for professional psychological difficulties ($r=0.144$; $p=.05$). It was determined that there was an intermediate, positive and significant relationship between the SECP score average and the views on other professional readiness.

Conclusion: It was seen that the students participating in the study had high level of Self-Efficacy in Clinical Performance and a moderate level of professional readiness. It was determined that as the self-efficacy in clinical performance of the students increased so did their perception of professional readiness.

Keywords: COVID-19, distance education, nursing student, self-efficacy.

1. INTRODUCTION

COVID-19 is a virus that emerged in Wuhan city of China and spread all over the world (1). COVID-19 that emerged in the late 2019 was declared to be a pandemic by the World Health Organization (WHO) (2). One of the sectors that suffered the most harm is education sector. In many countries, face-to-face education was interrupted, and soon, transition to distance education was implemented (3). In our country, with the decision of Council of Higher Education (CoHE), firstly, face-to-face education was stopped, and then, distance education was started (4).

Departments that offer applied education such as nursing were affected more by the transition to distance education. Under normal conditions, nursing education is intense and stressful. The aim of this education is to get the students to gain critical thinking and psychomotor skills in order for them to provide nursing care for sick/healthy individuals

and their relatives (5). Nursing education is a type of education depending on application as well as theory. Clinical teaching in nursing is indispensable in terms of the development of professional awareness and competence (6). The most important objective of clinical teaching in nursing is to improve students' professional skills by applying the knowledge obtained in theoretical lessons and get them to become competent in nursing care (7). Clinical teaching contributes to gaining and improving basic professional skills as well as improving students' skills of problem solving, decision-making, and communication (8, 9, 10). Henderson et al (11) have stated that clinical education process contributes to students in terms of actively managing clinical applications and developing their self-efficacy. In this context, it has been emphasized that it is necessary to measure students' clinical performance self-efficacy in order to determine to

How to cite this article: Çın D, Yetimler Çanakçı SŞ, Keskin E, Sadan FN, Balkay Z, Karahan Okuroğlu G. Clinical Performance Self-Efficacy and Professional Readiness of Senior Nursing Students who Received Online Practice Education in the Pandemic Period. Clin Exp Health Sci 2025; 15: 256-263. <https://doi.org/10.33808/clinexphealthsci.1363437>

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what degree the objectives of nursing education have been achieved (12).

Self-efficacy is defined as the individual's belief in their skills of organizing and implementing their actions (13). This belief is the basis of the achievements, motivation, and emotional power that the individual displays (14). Increase in self-efficacy positively affects nurses' performances (15). It has been demonstrated that nursing students who have played an active role in their education process have high self-efficacy and learn more easily (16).

As professional competence develops, adaptation of knowledge and skills becomes easier (17). If the gap between skills and knowledge is filled and developed, the graduating students become prepared for professional practice (18). Professional readiness is defined as becoming fully prepared for the actions that should be performed and getting adapted and being successful in a short time when starting professional life. Smooth transition of nurses to practice is described as readiness for applying the profession (19, 20). It has been observed that students who provide evidence-based and safe care, analyze, and are competent in terms of being solution-oriented are ready to practice the profession (21). Educational factors that encompass personal factors which are made up of experience and emotions, and professional competence and clinical practices affect nursing students' perceptions in the transition period to the profession, and clinical practices support the process of transition to the profession (22).

However, during the pandemic period, nursing students have faced various concerns. These concerns include lack of clinical practices, how to integrate theoretical knowledge into clinical practices, technical problems, loss of motivation and social isolation (20, 23). In light of this information, it was deemed necessary to investigate how 4th year nursing students, who had to receive theoretical knowledge and clinical education through online method in the pandemic period, perceived their clinical performance self-efficacy and what they thought about their professional readiness. Studies have shown that nursing students who received online education in the pandemic period had insufficient professional readiness (24, 25). Akkuş and Bostancı Daştan (26) found the clinical performance self-efficacy of these students to be at a moderate level. However, no study has been found for examining the relationship between these two variables. Conducting the study with 4th year nursing students will help us better understand the process of transitioning to the profession after graduation. Hence, the present study was planned in order to examine clinical performance self-efficacy and professional readiness of 4th year nursing students who received online education in the pandemic period. The results of this research will be important in providing guidance for improving online education processes in nursing education and preparing future health professionals more effectively.

2. METHODS

2.1. Ethical Considerations

Ethical approval for the study was received from Marmara University Faculty of Medicine with the decision dated 07.01.2022 and numbered 09.2022.55. Institutional permission was obtained from Marmara University Faculty of the Health Sciences where the study was conducted. Throughout the study, all principles of the Declaration of Helsinki were observed (General Assembly of the World Medical Association, 2014).

2.2. Study Design

The study was conducted with a descriptive and correlational design.

2.3. Research Questions

- What are the clinical performance self-efficacy levels of senior nursing students?
- What are the opinions of senior nursing students about their professional readiness?
- Is there a relationship between senior nursing students' clinical performance self-efficacy and professional readiness?

2.4. Time and Location of the Study

The study was conducted at the Health Sciences Faculty of a state university in Istanbul between January-May 2022.

2.5. Study Population and Sample

The population of the study consisted of 4th year students (n=246). No sampling was made, and the population was studied. The research participant were 173 nursing students, and thus, 70.3% of the population were accessed.

2.6. Data Collection Tools

In collecting the study data, Identifying Information Form, Self-Efficacy in Clinical Performance Scale, and Questionnaire Form for Professional Readiness of Nursing Students were used.

2.6.1. Identifying Information Form

The form prepared by the researchers consists of 9 questions inquiring about sociodemographic characteristics of nursing students.

2.6.2. Self-Efficacy in Clinical Performance Scale (SECP)

The scale was developed by Cheraghi et al (27). It aims to determine nursing students' perception of their self-efficacy regarding their clinical performance. The Likert type scale consists of 37 items. The scale has 11 responses, which are 0%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, and 100%. 0% response indicates "I am not sure", while 100% response represents "I am totally sure". The scale has four subscales,

which are “data collection” (the first 12 items), “diagnosis and planning” (items 13-21), “implementation” (items 22-31), and “evaluation” (items 32-37). The scale was adapted to Turkish by Pozam and Zaybak (28), and it was reported that the Cronbach’s alpha coefficient of the Turkish form of the scale was 0.98 for the total scale, and it varied between 0.95-0.97 for the subscales. In the present study, the Cronbach’s alpha coefficient of the scale was found to be 0.95.

2.6.3. Questionnaire Form for Professional Readiness of Nursing Students

The questionnaire form prepared in light of the relevant literature consists of 13 questions on students’ professional readiness (29). Students respond to each questionnaire items from 1 to 10. As the scores obtained from the form increase, the students’ professional readiness also increases. The form is evaluated through the mean scores of responses given to each item.

2.7. Data Collection Method

The data were collected online. The data collection tools were converted into online format by using Google Forms. Google Forms was sent to the class representative via WhatsApp. The class representative was asked to share the Google Forms in the class WhatsApp group. Volunteer students filled out data collection forms.

2.8. Data Analysis

In the statistical analysis of the data, SPSS (Statistical Package for the Social Sciences) software was used. Kolmogorov-Smirnov test was used to test whether the data set exhibits a normal distribution and it was seen that the data set exhibited a normal distribution. In the analysis of the data, in addition to descriptive statistics such as percentage, frequency, mean, and standard deviation, t test was used in intergroup comparisons of quantitative data, and variance analysis was employed in multigroup comparisons. The correlation between the two scales was evaluated with Pearson correlation analysis. All results were evaluated at 95% confidence interval and $p < .05$ significance level.

3. RESULTS

It was found that the mean age of the participating nursing students was 22.13 years ($SD=1.25$), and that 75.7% were female. The majority of the participants (93.6%) were graduates of high schools other than health vocational high school. Almost half of the students (44.5) had a CGPA of “3 and above”. The rate of those who willingly chose the nursing department was 32.4%. The rate of those who were satisfied with studying nursing was 31.8%. The rate of those who found the online education given in applied courses “partially effective” was 31.8%. It was also determined that 34.1% of the students felt themselves belonging to nursing, and that

more than half of the students (52.6%) were worried about the clinical practice they would start (Table 1).

Table 1. Socio-demographic data of the participants (N=173)

Results	Mean	SD
Age	22.13	1.25
	n	%
Gender		
Female	131	75.7
Male	42	24.3
High school you graduated from		
Health vocational high school	11	6.4
Other	162	93.6
*CGPA		
1.99 and below	2	1.2
2.00-2.99	94	54.3
3 and above	77	44.5
Did you choose willingly to the nursing department?		
Yes	56	32.4
Partially	79	45.7
No	38	22
Are you satisfied with studying nursing?		
Yes	55	31.8
Partially	82	47.4
No	36	20.8
Do you think the online education provided in applied courses is efficient?		
Yes	24	13.9
Partially	55	31.8
No	94	54.3
Do you feel that you belong to nursing?		
Yes	59	34.1
Partially	67	38.7
No	47	27.2
**What emotions do you feel when you think that you will go into clinical practice?		
Excited	69	39.9
Delighted	57	32.9
Frightened	17	9.8
Worried	91	52.6

SD: Standard Deviation; * Cumulative Grade Point Average; ** More than one answer has been given.

It was determined that SECP mean score of the participating nursing students was 69.31 ($SD=47.34$). The mean scores obtained from the subscales were as follows: 87.08 ($SD=24.18$) for “data collection”, 63.87 ($SD=13.43$) for “diagnosis and planning”, 78.66 ($SD=16.60$) for “implementation”, and 47.66 ($SD=9.81$) for “evaluation”. Regarding the students’ professional readiness (min=0; max=10), the mean score of those who felt ready to start the profession was 5.31 ($SD=2.67$), and while the lowest mean score was obtained from the statement “I feel ready for advanced clinical practices” with 4.21 ($SD=2.82$), the highest mean score was obtained from the statement “I feel ready to perform basic nursing skills” with 7.10 ($SD=2.41$) (Table 2).

Table 2. Findings related to the participants SECP mean score and professional readiness (N=173)

	Min	Max	Mean	SD
SECP	69	359	69.31	47.34
Data collection subscale	0	120	87.08	24.18
Diagnosis and planning subscale	0	90	63.87	13.43
Implementation subscale	0	100	78.66	16.60
Evaluation subscale	0	60	47.66	9.81
Statements about professional readiness				
Feeling ready to start the profession	0	10	5.31	2.67
Feeling ready to work with the best performance	0	10	5.77	2.78
Feeling ready for professional psychological difficulties (death, loss, anger, mourning, etc.)	0	10	5.29	2.88
Feeling ready to work in the profession with ethical sensitivity	0	10	7.66	2.19
Feeling ready to adapt to the team in the clinic	0	10	7.27	2.37
Feeling ready for patient care applications	0	10	6.03	2.59
Feeling ready to provide education to patients/patient relatives	0	10	6.33	2.57
Feeling ready to perform emergency intervention for the patient	0	10	4.61	2.85
Feeling ready to apply invasive procedures	0	10	6.14	2.65
Feeling ready to perform physical examination of the patient	0	10	6.21	2.72
Feeling ready to apply basic nursing skills (hand washing, drug application, IV catheter application, etc.)	0	10	7.10	2.41
Feeling ready for advanced clinical practices (tracheostomy, stoma, wound, burn, chest tube, decubitus care, etc.)	0	10	4.21	2.82
Feeling ready to provide the patient with psychological support	0	10	6.56	2.57

SECP: Self-Efficacy in Clinical Performance Scale; Min: Minimum; Max: Maximum; SD: Standard Deviation

It was determined that there was not a significant difference between the students' SECP mean scores according to their gender ($t=0.47$; $p=.63$), the high school they finished ($t=1.41$; $p=.18$), and their CGPA values ($F=1.42$; $p=.24$) (Table 3).

It was found that the students' SECP mean scores significantly differed according to choosing nursing department willingly ($F=3.51$; $p=.03$), being satisfied with studying nursing ($F=3.98$; $p=.02$), and feeling themselves belonging to nursing profession ($F=5.71$; $p=.00$), and that their mean scores did not differ significantly according to their opinions that online education provided in applied courses was efficient ($F=1.31$; $p=.27$) (Table 3).

It was determined that there was no significant relationship between the SECP score and the feeling ready for professional psychological difficulties ($r=0.144$; $p=.05$).

It was determined the relationship between students' SECP score average and their professional readiness. There was no significant relationship between the SECP score and the feeling ready for professional psychological difficulties ($r=0.14$; $p=.05$). The least significant relationship was found between the SECP score and the feeling ready to start the profession ($r=0.31$; $p=.00$). The highest significant relationship was found between the SECP score and the feeling ready to provide the patient with psychological support ($r=0.53$; $p=.00$) (Table 4).

Table 3. Comparison of students' SECP score averages according to some variables (N=173)

		Mean (SD)	Statistical test	p	Post-Hoc
Gender	Female	277.42 (49.53)	0.47*	.63	
	Male	273.86 (40.16)			
High school you graduated from	Health vocational high school	291.55 (35.48)	1.41*	.18	
	Other	275.54 (47.95)			
CGPA	1.99 and below	271.00 (2.82)	1.42**	.24	
	2.00-2.99	271.13 (53.31)			
	3 and above	283.32 (38.87)			
Did you choose willingly to the nursing department?	Yes (a)	284.38 (44.84)	3.51**	.03	a>c
	Partially (b)	279.30 (47.14)			
	No (c)	259.32 (48.26)			
Are you satisfied with studying nursing?	Yes (a)	290.07 (46.87)	3.98**	.02	a>c
	Partially (b)	273.33 (43.97)			
	No (c)	263.25 (51.53)			
Do you think the online education provided in applied courses is efficient?	Yes (a)	282.00 (40.11)	1.31**	.27	
	Partially	283.27 (43.26)			
	No (c)	271.23 (50.96)			
Do you feel that you belong to nursing?	Yes (a)	290.93 (46.05)	5.71**	.00	a>c
	Partially (b)	275.07 (38.59)			
	No (c)	260.62 (55.14)			

SECP: Self-Efficacy in Clinical Performance Scale; SD: Standard Deviation; CGPA: Cumulative Grade Point Average; *Independent Samples t Test; ** One-Way ANOVA; $p<.05$

Table 4. The relationship between students' SECP score average and their professional readiness

	r	p
SECP score average: 69.31±47.34		
Feeling ready to start the profession	0.31	.00
Feeling ready to work with the best performance	0.36	.00
Feeling ready for professional psychological difficulties (death, loss, anger, mourning, etc.)	0.14	.05
Feeling ready to work in the profession with ethical sensitivity	0.47	.00
Feeling ready to adapt to the team in the clinic	0.40	.00
Feeling ready for patient care applications	0.42	.00
Feeling ready to provide education to patients/patient relatives	0.42	.00
Feeling ready to perform emergency intervention for the patient	0.34	.00
Feeling ready to apply invasive procedures	0.43	.00
Feeling ready to perform physical examination of the patient	0.41	.00
Feeling ready to apply basic nursing skills (hand washing, drug application, IV catheter application, etc.)	0.37	.00
Feeling ready for advanced clinical practices (tracheostomy, stoma, wound, burn, chest tube, decubitus care, etc.)	0.33	.00
Feeling ready to provide the patient with psychological support	0.53	.00

SECP: Self-Efficacy in Clinical Performance Scale; $p < .01$

4. DISCUSSION

The present study was conducted in order to determine 4th year nursing students' self-efficacy levels regarding their clinical performances and their professional readiness. In addition, statistical analyses were performed on the variables which were predicted to affect their clinical performance self-efficacy and professional readiness.

The participating students' SECP total scale and subscale mean scores were found to be high. This finding shows that the students perceived their self-efficacy regarding data collection, diagnosing and planning, implementation, and evaluation steps of nursing care at a high level. The students received the lowest score on SECP from the subscale of evaluation and the highest score from the subscale of data collection. When the literature was reviewed in this regard, it was determined that Pozam and Zaybak (30) stated that the part that nursing students experienced the highest difficulty in was the diagnosing-planning step while planning patient care, while the part they had the least difficulty was the implementation step. Yilmaz et al (31) found that the steps in which the students experienced the most problems were data collection and diagnosing steps, and the step in which they had the least problems was planning step. In the study conducted by Uysal et al (32), it was reported that determining nursing diagnosis was the part in which nursing students had the most difficulty, and that the students could not perform the data collection, diagnosing, planning, and evaluation steps at the desired level. Compared to the literature findings, according to the finding obtained in the present study, it is thought that conducting the present study with 4th year students led to the finding that they had higher self-efficacy regarding nursing process.

The findings obtained in the study show that gender did not have significant relationship with self-efficacy in clinical performance. In a similar study conducted on self-efficacy levels of intern nurses in the pandemic period, the same result was obtained (23). Similarly, in the study of Pozam and

Zaybak (30), it was found that SECP scores of the students did not differ significantly according to gender. In the present study, no significant difference was determined between the high school type the students graduated from and their self-efficacy in clinical performance. However, in the study conducted by Arslan (33), it was reported that the students who had graduated from health vocational high schools had the highest self-efficacy levels. It is thought that the reason for obtaining a result different from the literature in this regard can be that the study was conducted with 4th year students, and that the education provided at the institution of the study for four years may have closed the gap resulting from the students' graduating from different high school types.

In the present study, no significant difference was observed between 4th year nursing students' CGPA values and their SECP mean scores when they were compared. On the other hand, in their study, Pozam and Zaybak (30) found a positive and significant relationship at a low level between CGPA values and SECP mean score of nursing students. Similarly, Göger and Çevirme (34) reported that there was a relationship between self-efficacy and academic achievement scores of nursing students, and that a high level of self-efficacy would positively affect the students' academic achievement. According to the literature, a positive relationship is expected between students' academic score averages and clinical performance self-efficacy.

In the present study, it was determined that SECP mean score of the students showed a significant difference according to choosing nursing department willingly, being satisfied with studying nursing, and feeling themselves belonging to nursing profession. When the literature is reviewed, it is seen that students who choose nursing department willingly and love the profession and who perceive their self-efficacy and academic achievement as high have lower levels of stress/

anxiety related to clinical practice, and thus their clinical experiences are positively affected (35, 36, 37).

It was seen in the present study that professional readiness of the participating students was at a moderate level. In a study conducted in the COVID-19 pandemic period on professional readiness status of intern nurses, their perceived professional readiness was found to be at a moderate level (35). When the nursing students' opinions on their professional readiness were examined, it was seen that those who felt ready to work in the profession with ethical sensitivity had the highest mean score. Although Borhani et al (38) stated that clinical work experience and being directly by the side of patients resulted in a higher level of ethical sensitivity, it is seen that applied courses run with case studies in the pandemic period supported increasing the students' ethical sensitivity. In addition, the students gave the lowest score to the statement "I feel ready for advanced clinical practices". It is an expected result that the students, who could not find enough opportunities to do applications, did not feel themselves ready for advanced clinical practices.

When the participating students' opinions on SECP mean score and professional readiness were examined, it was seen that as the students' SECP mean score increased, they felt more ready to start the profession. Similarly, a significant relation was found between SECP mean score and feeling ready for starting the profession, professional psychological difficulties, working with their best performance, working in the profession with ethical sensitivity, adaptation to the team in the clinic, patient care applications, providing education to patients/patient relatives, performing emergency intervention for the patient, applying invasive procedures, performing physical examination of the patient, applying basic nursing skills, advanced clinical practices, and providing the patient with psychological support. In the study conducted by Özkan (24), a positive, weak, and significant relationship was seen between students' general self-efficacy scale scores and their perceived professional readiness. In the study he conducted, Eraydin (29) found that self-efficacy scores of the students who stated that they were not ready for professional psychological difficulties were low. According to İzci et al (39), health professionals are among individuals who work under the most challenging conditions in the pandemics that affect the whole world and lead to deaths. Especially when it is considered that the students who continued their education in the COVID-19 pandemic period can also assume responsibilities and duties in various pandemic processes after they graduate, it can be stated that their professional readiness becomes more prominent (35). Considering all these findings, it is believed that strategies that will increase nursing students' clinical performance self-efficacy levels should be developed in order to increase their professional readiness.

4.1. Study Limitations

The study results are limited to the 4th year nursing students of the university where the study was conducted.

5. CONCLUSION

As a result of the study, it was determined that clinical performance self-efficacy levels of the students participating in the study were high, and their professional readiness levels were moderate. It was also determined that as the students' clinical performance self-efficacy levels increased, their professional readiness levels increased as well.

In line with these results, it can be stated that it is important for 4th year nursing students to graduate with high levels of clinical performance self-efficacy and professional readiness, and that increasing the students' clinical performance self-efficacy levels is effective in terms of increasing their professional readiness. Hence, students' professional readiness levels can be increased by increasing simulations, laboratory studies. More internship opportunities can be provided to students in clinical environments. Students' clinical skills and professional knowledge can be improved through mentoring programs. With stress management education, students' ability to cope with the difficulties they may encounter during their professional readiness can be improved. By giving students regular and constructive feedback about their performance, their self-efficacy and professional readiness can be increased. In addition, it can also be recommended that institutions should appropriately structure the orientation process for the nurses starting the profession, and that in-service training activities in the post-graduation period should be repeated at regular intervals.

Acknowledgement: This study was presented as a oral presentation in the 2nd International and 8th National Nursing Education Congress (24-26 November 2022, Turkey).

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: Ethical approval for the study was obtained from Marmara University Medical Faculty with the decision dated 07.01.2022 and numbered 09.2022.55.

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: DÇ, SŞYÇ, EK, FNS, ZB, GKO

Design of the study: DÇ, SŞYÇ, EK, FNS, ZB, GKO

Acquisition of data for the study: DÇ, SŞYÇ, EK, FNS, ZB

Analysis of data for the study: DÇ, SŞYÇ, GKO

Interpretation of data for the study: DÇ, SŞYÇ, EK, FNS, ZB, GKO

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Effect of Non-surgical Periodontal Therapy on Interleukin 17 in Gingival Crevicular Fluid and Serum of Coronary Artery Disease Patients with Periodontitis

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Received: November 11, 2023 **Accepted:** May 26, 2025

ABSTRACT

Objective: The role of proinflammatory cytokines in chronic periodontitis (P) and coronary artery diseases (CAD) is currently under investigation. Interleukin 17 (IL 17) may play a role in the bidirectional pathogenesis of both conditions. The aim of the study is to explore the effect of non-surgical periodontal therapy on the gingival crevicular fluid (GCF) and serum levels of IL 17 in stable CAD patients with P.

Methods: Sixty-one individuals were enrolled in the study including 32 chronic periodontitis [16 periodontitis (CAD-P+), 16 coronary artery disease with periodontitis (CAD+P+)] and 29 periodontally healthy subjects [15 (CAD-P-) and 14 patients with coronary artery disease (CAD+P-)]. GCF and serum samples were obtained and probing pocket depth (PPD), clinical attachment level (CAL), plaque index (PI) and gingival index (GI) were recorded at baseline and three months post-treatment. GCF and serum IL 17 levels were analyzed by enzyme-linked immunosorbent assay (ELISA).

Results: We observed significant improvements in the whole mouth and sample tooth periodontal parameters (both with $p < .001$) and as well as a reduction in GCF volume ($p < .05$) following periodontal treatment in periodontitis groups (CAD-P+ and CAD+P+). Serum IL 17 levels significantly decreased in CAD+P+ group following the periodontal therapy (baseline: 24.39 (13.04) pg/ml; 3rd month 19.16 (15.07) pg/ml, $p < .05$) while no significant alterations were observed in GCF samples.

Conclusion: IL 17 is linked to proinflammatory response in atherosclerosis. Its post-treatment decrease in CAD+P+ group suggests IL 17 might be a useful biomarker for CAD-periodontitis relationship.

Keywords: Interleukin 17, Periodontal disease, Coronary artery disease, Inflammation.

1. INTRODUCTION

Periodontitis and cardiovascular disease (CVD) are both highly prevalent worldwide, and an altered immune response plays a crucial role in the pathogenesis of both conditions (1, 2). A substantial amount of data, including meta-analyses, has demonstrated a relationship between CVD and periodontitis. According to these studies, periodontal disease severity is associated with CVD risk and periodontitis is recognized as a risk factor for future cardiovascular issues (3, 4, 5). These epidemiological findings support the biological plausibility of a connection between periodontal disease and CVD, yet a definitive mechanism linking the two diseases has not been fully elucidated. The widely accepted opinion is that bacteremia from the ulcerated gingiva induces endothelial injury and activates the host immune response. As a result of immune activation, inflammatory cytokines may induce adaptive immunity, thereby promoting

atherothrombogenesis (6). Recently, Corredor et al. (7) reinforces this paradigm by demonstrating the presence of subgingival plaque bacterial complexes in the blood of patients with CAD.

The Th1/Th2 paradigm provided the foundation for understanding the pathogenesis of several inflammatory conditions, including periodontitis. However, the discovery of Th17 cells has greatly broaden the understanding of autoimmunity and inflammation, addressing gaps that the Th1/Th2 paradigm could not explain in host immunity (8, 9). This paradigm shift has directed focus toward the role of Th17 cells in the pathogenesis of periodontitis. Different research groups have reported elevated IL 17 in periodontally inflamed tissues (10) and in GCF samples (11, 12). Additionally, a study on gingival biopsies found a positive correlation between IL 17 expression and clinical attachment loss (13).

How to cite this article: Sume SS, Olgun E, Kısa U, Berker E. Effect of Non-surgical Periodontal Therapy on Interleukin 17 in Gingival Crevicular Fluid and Serum of Coronary Artery Disease Patients with Periodontitis. Clin Exp Health Sci 2025; 15: 264-271. <https://doi.org/10.33808/clinexphealthsci.1381366>

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The impact of IL 17 on distinct parts of the cardiovascular system has been extensively studied. In an in vitro study, IL 17 was found to induce the synthesis of IL 6 and IL 8 in endothelial cells (14). When combined with TNF α , IL 17 significantly increased the levels of adhesion molecules, leading to enhanced leukocyte aggregation and endothelial activation (15, 16). Additionally, under in vitro conditions, IL 17A alone or in combination with IFN γ elevated IL 8 and IL 6 levels in vascular smooth muscle cells compared to unstimulated cells (17). Beyond these in vitro findings, a clinical study revealed that serum IL 17A levels are positively correlated with the formation of complex plaque structures in asymptomatic individuals with ischemic symptoms (18). These results suggest that IL 17 may be a critical factor in the pathogenesis of CAD.

A meta-analysis consists of six randomized clinical trial showed that non-surgical periodontal therapy caused significant reduction in C reactive protein (CRP) in CAD patients and concluded that periodontal treatment could be an important preventive strategy for major cardiovascular events (19).

Based on these information, we hypothesized that non-surgical periodontal therapy may play an important role in improving IL 17 levels which is believed to be playing a crucial role in the relationship between periodontitis and CAD. The aim of this study is to determine the effect of non-surgical periodontal therapy on GCF and serum levels of IL 17 in chronic periodontitis patients with and without CAD.

2. METHODS

2.1. Subjects and Study Groups

This clinical trial was approved by Kırıkkale University Clinical Research Ethics Committee (project number: 2018/02/02) in accordance with the Declaration of Helsinki. Sixty-one individuals aged between 40-70 years were included and written informed consent was obtained. Patients were screened between February 2018 and March 2019. Baseline examinations of the participants who admitted to the Department of Periodontology were conducted and they were divided into 4 groups: Group 1 (CAD-P-): periodontally healthy individuals without stable coronary artery disease (n = 15); Group 2 (CAD-P+): chronic periodontitis patients without stable coronary artery disease (n = 16); Group 3 (CAD+P-): stable coronary artery disease patients with a healthy periodontium (n = 14); Group 4 (CAD+P+): stable coronary artery disease patients with chronic periodontitis (n = 16).

The exclusion criteria were determined as follows: individuals who smoke, who have had a myocardial infarction or bypass surgery within the last 6 months, who have unstable coronary artery disease symptoms, who have undergone periodontal therapy within the last 6 months, who have used antibiotics or anti-inflammatory drugs within the last 6 months, who have a systemic disorder other than coronary artery disease,

who have fewer than 15 teeth, and pregnant or lactating women were all excluded.

Periodontal status was determined at the Kırıkkale University Department of Periodontology by assessing clinical and radiographic manifestations according to the criteria proposed by the Consensus Report of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions (20). Subjects with a PPD <3 mm, no attachment loss, no history of periodontal disease, and whole-mouth bleeding scores below 10% were classified as periodontally healthy individuals. Patients with a PPD $\geq$ 5 mm in at least two non-adjacent teeth per quadrant, bleeding on probing, other signs of inflammation, and periodontal bone loss affecting more than 30% of the root length were classified as having chronic periodontitis. Alveolar bone loss extending to the mid-third of the root and beyond was considered to be more than 30%. These criteria correspond to stage II/III periodontitis in the new classification system (20). To determine the coronary artery disease status of each participant, we evaluated cardiac reports approved by a cardiologist. Inclusion criteria for stable CAD patients were defined as having an obstruction in at least one major coronary artery, confirmed by angiography, and no current disease symptoms. Information about the medications used by patients during the study, including statins, was also collected. All periodontitis and CAD statuses were assessed by authors EO and SSS.

2.2. Clinical Parameters and Non-surgical Periodontal Therapy

Periodontal status was determined by measuring the whole mouth (WM), (PI) (21), (GI) (22), (PPD), and (CAL). Similarly, all clinical parameters were recorded for sampling teeth (ST). Panoramic radiographs were taken to assess the alveolar bone level. PPD and CAL were measured at six sites per tooth with a periodontal probe (Hu – Friedy, Chicago, IL, USA), while PI and GI were recorded at four sites.

All participants received oral hygiene instructions following diagnosis. In the periodontitis groups (CAD-P+ and CAD+P+), supragingival scaling and root debridement were performed using hand instruments (Hu-Friedy, Chicago, IL, USA). No antibiotics or anti-inflammatory drugs were prescribed. Patients in the CAD-P+ and CAD+P+ groups were recalled 12 weeks after non-surgical periodontal therapy.

Periodontal clinical measurements, along with GCF and serum sample collection, were recorded at two intervals (baseline and 3rd month following the periodontal treatment) in the periodontitis groups (CAD-P+ and CAD+P+). In the periodontally healthy groups (CAD-P- and CAD+P-), these measurements were taken only at baseline. All clinical measurements were conducted by a single investigator (SSS).

2.3. GCF and Serum Sampling

In the periodontitis groups (CAD-P+ and CAD+P+), GCF samples were collected from single-rooted teeth with a PPD of ≥ 5 mm and < 7 mm, and $\geq 30\%$ bone loss. For periodontally healthy individuals (CAD-P- and CAD+P-), maxillary anterior teeth were chosen for sampling. GCF samples were obtained by the method described by Rüdin et al. (23). Briefly, the crevicular site was isolated with cotton rolls and gently dried. Standardized strips were inserted into the gingival sulcus for 30 seconds to collect GCF from each tooth, and the GCF volume was determined by Periotron 800 (Oraflow Inc., Plainview, NY, USA). Two paper strips were collected from each participant and transferred into the Eppendorf tubes. Then, 250 μ l of phosphate-buffered saline (PBS, pH 7.2) was added to the tubes, which were vortexed (Vortex, Velp Scientifica, Usmate Velate, Italy) for 1 minute, mixed on Orbital Shaker OS-10 (Biosan Inc., Riga, Latvia) for 20 minutes, and centrifuged in Hettich EBA 20 Centrifugal Machine (Hettich Inc., Tuttlingen, Germany) at 5800 rpm for 5 minutes.

Venous blood samples were obtained from the antecubital vein and collected in a BD Vacutainer® SST™ II Advance Tube (Becton Dickinson Inc., NJ, USA). Each sample was centrifuged at 1500 rpm for 10 minutes and then isolated serum samples were transferred into the Eppendorf tubes. All samples were stored at -80°C until analysis.

2.4. Biochemical Analysis

To prevent bias and ensure a blind lab analysis, each Eppendorf tube was assigned a number by author SSS during the collection of GCF and serum samples. The ELISA analysis was then carried out by author UK, who was unaware of the group assignments corresponding to each number.

GCF and serum IL 17 levels were measured by ELISA using a commercial kit (SEA063Hu, Cloud Clone Corp., Katy, TX, USA), following the manufacturer's instructions. Briefly, microplate wells were filled with 100 μ l of the standard, serum, and GCF samples. Then, 100 μ l of Detection Reagent A was added to each well. The plate was covered and incubated at 37°C for 60 minutes with gentle mixing. After incubation, the plate was washed with 350 μ l of washing solution. Next, 100 μ l of Detection Reagent B was added to each well, and the plate was incubated again at 37°C for 30 minutes. Following this, the wells were washed once more with the washing solution and 90 μ l of substrate solution was added to each well. The plate was kept in the dark at 37°C for 20 minutes. The reaction was stopped by adding 50 μ l of stop solution to each well. Optical densities were read at a wavelength of 450 nm. Standard concentrations and their corresponding optical density values, along with the optical density values of the samples, were recorded. A standard curve was plotted based on the optical densities and concentrations of the standards, and the concentrations of all samples were calculated using the linear regression equation derived from the standard curve. The sensitivity of the ELISA for IL 17 was less than 5.5

pg/ml, and the assay detection range for IL 17 was 15.6 pg/ml – 1000 pg/ml.

2.5. Statistical Analysis

The required sample size and power for the study were determined using the G Power Ver. 3.0.10 (Franz Faul, Universität Keil, Germany). To achieve 85% power with an effect size of $f=0.25$ and detect differences among groups, 14 participants were required in each group. Number and percentage (n, %) were used in the representation of demographic variables. Shapiro-Wilk test was conducted to detect the normal distribution of the data. Non-normally distributed data were presented as median (Interquartile Range – IQR). Kruskal-Wallis test was used to identify the differences among groups. In periodontitis groups (CAD-P+; CAD+P+), comparisons of variables at baseline and 3rd months post-treatment were evaluated using the Wilcoxon Signed Rank test. Mann-Whitney U test was applied to determine the groups leading to differences. SPSS for Windows Version 20.0 (SPSS Inc., Chicago, IL, USA) was used to conduct statistical analyses. Significance level set at $p < .05$.

3. RESULTS

3.1. Demographic Characteristics

A total of 61 individuals, aged between 40 and 70, 23 women (37.7%) and 38 men (62.2%), were included in this clinical study (Table 1). Regarding age comparison among groups, individuals in the CAD+P+ group were significantly older than the systemically healthy participants ($p < .05$). Similarly, gender distribution differed between groups ($p < .05$), with the CAD+P+ having significantly more males than the systemically healthy groups (CAD-P- and CAD+P-).

Table 1. Demographic characteristics.

Demographic Characteristics	CAD-P- (n=15)	CAD-P+ (n=16)	CAD+P- (n=14)	CAD+P+ (n=16)	p value
Age (mean $\pm$ SD)	50.93 $\pm$ 4.66*	53.59 $\pm$ 7.97*	56.14 $\pm$ 9.29	60.23 $\pm$ 6.93	.002
Gender (n %)					
Female	7(46.6)*	10(62.5)*	4(28.5)	2(12.5)	.02
Male	8(53.3)	6(37.5)	10(71.4)	14(87.5)	

CAD-P+, chronic periodontitis group; CAD+P-, coronary artery disease group without periodontitis; CAD+P+, coronary artery disease group with chronic periodontitis. SD, standard deviation. *Significant difference compared to CAD+P+.

3.2. Clinical Parameters and GCF Volume at Baseline

Table 2 shows the WM and ST clinical parameters. At baseline, all recorded values, including WM and ST, in the periodontitis groups were significantly higher than those in periodontally healthy individuals ($p < .001$). Among periodontally healthy subjects, the CAD+P- group had significantly higher full-mouth CAL compared to the CAD-P- ($p < .05$). Additionally, within the periodontitis groups, the CAD+P+ group had

significantly higher full-mouth CAL compared to the CAD-P+ group ($p < .001$).

Table 2. Comparison of initial clinical parameters of whole mouth (WM) and sampling teeth (ST) among groups.

Clinical Parameters	CAD-P- Median (IQR)	CAD-P+ Median (IQR)	CAD+P- Median (IQR)	CAD+P+ Median (IQR)	p value
WMPI	0.00 (1.00)	2.00 (0.00)*	0.12 (1.00)	2.00 (0.00)*	.001
WMGI	0.00 (0.50)	2.00 (0.013)*	0.00 (0.50)	2.00 (0.50)*	.001
WMPPD (mm)	1.90 (0.53)	2.57 (0.41)*	2.04 (0.40)	3.10 (0.65)*	.001
WMCAL (mm)	1.90 (0.53)	2.77 (0.70)*#	2.13 (0.60)†	3.69 (1.28)*	.001
STPI	0.00 (1.00)	2.00 (0.00)*	0.00 (1.00)	2.00 (0.00)*	.001
STGI	0.00 (0.00)	2.00 (0.00)*	0.00 (0.63)	2.00 (0.50)*	.001
STPPD (mm)	2.00 (1.00)	5.00 (0.63)*	2.00 (0.50)	5.50 (1.00)*	.001
STCAL (mm)	2.00 (1.00)	5.00 (1.13)*	2.00 (0.50)	5.50 (1.00)*	.001

CAD-P+, chronic periodontitis group; CAD+P-, coronary artery disease group without periodontitis; CAD+P+, coronary artery disease group with chronic periodontitis. WMPI, whole mouth plaque index; WMGI, whole mouth gingival index; WMPPD, whole mouth probing pocket depth; WMCAL, whole mouth clinical attachment level; STPI, sampling teeth plaque index; STGI, sampling teeth plaque index; STPPD, sampling teeth probing pocket depth; STCAL, sampling teeth clinical attachment level. *Significant difference compared with CAD+P- and CAD-P-, $p < .001$. #Significant difference compared with CAD+P+, $p < .001$. †Significant difference compared with CAD-P-, $p < .05$.

At the initial measurements, we observed a significant difference in GCF volume between groups ($p < .05$, Table 3). GCF volume in the CAD-P+, CAD+P-, and CAD+P+ groups was significantly higher than the CAD-P- group ($p < .05$). Moreover, the CAD-P+ group had significantly higher GCF volume than the CAD+P- and CAD+P+ groups. Compared to the CAD+P+ group, the CAD+P- group exhibited a markedly lower GCF volume ($p < .05$).

Table 3. Comparison of initial GCF volume, IL 17 GCF and Serum levels among groups.

	CAD-P- Median (IQR)	CAD-P+ Median (IQR)	CAD+P- Median (IQR)	CAD+P+ Median (IQR)	p value
GCF volume	32.00 (12.00)	96.50 (53.00)*#	52.50 (41.63)*	81.00 (30.00)*†	.001
IL 17 /GCF (total amount) pg	8.873 (8.2)#	5.508 (8.3)†	5.388 (2.5)	4.180 (3.3)	.003
IL 17/ GCF (concentration) pg/μl	35.49 (32.30)#	22.03 (33.33)†	21.55 (9.84)	16.73 (13.34)	.001
IL 17/ Serum pg/ml	16.83 (8.96)	17.02 (9.42)	19.86 (8.86)	24.39 (13.04)‡	.044

CAD-P+, chronic periodontitis group; CAD+P-, coronary artery disease group without chronic periodontitis; CAD+P+, coronary artery disease group with chronic periodontitis. GCF, gingival crevicular fluid; IQR, interquartile range. *Significant difference compared with CAD-P-, $p < .05$. #Significant difference compared with CAD+P- and CAD+P+, $p < .001$. †Significant difference compared with CAD+P-, $p < .05$. ‡Significant difference compared with CAD+P+, $p < .05$. §Significant difference compared with CAD-P+, $p < .05$.

3.3. IL 17 Levels in GCF and Serum at Baseline

At baseline, we observed a significant difference in IL 17 levels in GCF between the study groups (Table 3). The CAD-P- group had significantly higher levels of both the total amount (pg) and concentration (pg/ml) of IL 17 in GCF compared to the CAD+P- and CAD+P+ groups ($p < .001$). When evaluating the periodontitis groups, we found a significantly higher total amount and concentration of IL 17 in the CAD-P+ group compared to the CAD+P+ group ($p < .05$).

In addition to GCF, we measured serum IL 17 (pg/ml) levels at baseline. Levels in the CAD+P+ group were significantly higher compared to the CAD-P+ group ($p < .05$).

3.4. Clinical Parameters and GCF Volume in Chronic Periodontitis Patients after Initial Periodontal Therapy

In the chronic periodontitis groups (CAD-P+ and CAD+P+), a significant reduction was observed in all clinical parameters (including WM and ST) following non-surgical periodontal therapy compared to baseline ($p < .001$, Table 4). When comparing the two periodontitis groups, WMPPD and CAL in the CAD+P+ group were significantly higher than in the CAD-P+ group following treatment ($p < .05$, Table 4).

Table 4. Comparison of clinical parameters of whole mouth (WM) and sampling teeth (ST) among groups at baseline and 3rd month in chronic periodontitis patients.

Groups	Clinical Parameters	Baseline Median (IQR)	3 rd month Median (IQR)	p value
CAD-P+	WMPI	2.00 (0.00)	1.00 (0.75)*	.001
	WMGI	2.00 (0.013)	1.00 (1.00)*	.001
	WMPPD (mm)	2.57 (0.41)	2.26 (0.67)*	.001
	WMCAL (mm)	2.77 (0.70)	2.33 (0.46)*	.001
	STPI	2.00 (0.00)	1.00 (0.75)*	.001
	STGI	2.00 (0.00)	1.00 (1.00)*	.001
	STPPD (mm)	5.00 (0.63)	3.00 (1.50)*	.001
	STCAL (mm)	5.00 (1.13)	3.00 (1.50)*	.001
CAD+P+	WMPI	2.00 (0.00)	1.00 (0.94)*	.001
	WMGI	2.00 (0.50)	1.00 (1.00)*	.001
	WMPPD (mm)	3.10 (0.65)	2.50 (0.62)*#	.001
	WMCAL (mm)	3.69 (1.28)	3.03 (1.35)*†	.001
	STPI	2.00 (0.00)	1.00 (0.94)*	.001
	STGI	2.00 (0.50)	1.00 (1.00)*	.001
	STPPD (mm)	5.50 (1.00)	3.00 (1.50)*	.001
	STCAL (mm)	5.50 (1.00)	3.25 (1.38)*	.001

CAD-P+, chronic periodontitis group; CAD+P+, coronary artery disease with chronic periodontitis group. WMPI, whole mouth plaque index; WMGI, whole mouth gingival index; WMPPD, whole mouth probing pocket depth; WMCAL, whole mouth clinical attachment level; STPI, sampling teeth plaque index; STGI, sampling teeth gingival index; STPPD, sampling teeth probing pocket depth; STCAL, sampling teeth clinical attachment level. IQR, interquartile range. *Significant difference compared to Baseline, $p < .001$. #Significant difference compared to WMPI in CAD-P+ group at 3rd month, $p < .05$. †Significant difference compared to WMCAL in CAD-P+ group at 3rd month, $p < .05$.

Consistent with the clinical parameters, we observed a significant reduction in GCF volume in both periodontitis groups compared to baseline after periodontal therapy ($p < .05$, Table 5). At the 3rd month, the GCF volume in the CAD-P+ group was significantly higher than in the CAD+P+ group ($p < .05$, Table 5).

3.5. GCF and Serum IL 17 Data in Chronic Periodontitis Patients after Initial Periodontal Therapy

Following periodontal therapy, we evaluated IL 17 levels in GCF compared to baseline. There was no significant change in either group for the total amount and concentration after treatment ($p > .05$, Table 5).

Regarding serum IL 17 levels, we observed a significant reduction in the CAD+P+ group compared to baseline following therapy ($p < .05$, Table 5).

Table 5. Comparison of GCF volume, GCF and Serum IL 17 levels at baseline and 3rd month in chronic periodontitis groups.

Groups		Baseline Median (IQR)	3 rd month Median (IQR)	p value
CAD-P+	GCF volume	96.50 (53.00)	80.00 (35.00)*#	.002
	IL 17 /GCF (total amount) (pg)	5.508 (8.3)	3.19 (9.9)	.617
	IL 17/ GCF (concentration) (pg/μl)	22.03 (33.33)	12.77 (39.9)	.617
	IL 17/ SERUM (pg/ml)	17.02 (9.42)	11.16 (14.77)	.197
CAD+P+	GCF volume	81.00 (30.00)	67.50 (45.00)*	.020
	IL 17 /GCF (total amount) (pg)	4.180 (3.3)	3.59 (3.71)	.317
	IL 17/ GCF (concentration) (pg/μl)	16.73 (13.34)	14.37 (14.84)	.617
	IL 17/ Serum (pg/ml)	24.39 (13.04)	19.16 (15.07)*	.046

CAD-P+, chronic periodontitis group; CAD+P+, coronary artery disease with chronic periodontitis group. GCF, gingival crevicular fluid; IQR, interquartile range. *Significant difference compared to Baseline, $p = .002$; $p = .02$, $p = .046$. #Significant difference in GCF volume in compared to CAD+P+ at 3rd month, $p = .04$.

4. DISCUSSION

Immune system plays a crucial role in maintaining periodontal health; however, an excessive immune response can lead to periodontal tissue damage through the release of inflammatory mediators and destructive enzymes (24). Atherosclerosis develops as a result of an immune-inflammatory response, which is the underlying cause of the majority of cardiovascular events (25). Periodontitis can contribute to the body's overall inflammatory load and exacerbate pre-existing conditions such as diabetes and atherosclerosis (26). Therefore, reducing the inflammatory burden in the body can also decrease the risk of atherosclerosis and subsequent cardiovascular events. Current findings suggest that periodontal therapy may lower CVD risk by controlling biomarkers associated with it. For example, Vidal et al. (27) reported a significant decrease in IL-6, CRP, and fibrinogen plasma levels three months after

treatment. IL 17, which plays a key role in the pathogenesis of both periodontal disease and CVD, was found significantly higher in the serum of individuals with chronic periodontitis and CAD compared to healthy individuals (28). In this clinical trial, we demonstrated that non-surgical periodontal therapy significantly reduced serum IL 17 levels in stable CAD patients with chronic periodontitis, in line with a marked improvement in periodontal health.

Increased plaque accumulation and age-related degenerative changes contribute to severe gingival inflammation in the elderly population (29). In addition to traditional risk factors such as gender, smoking, total cholesterol levels, and systolic blood pressure, age is also recognized as a risk factor for CVD (30). The prevalence of CAD increases significantly with age in both men and women (31). These findings highlight the impact of aging on both periodontal disease and CAD. In our study, we observed a significantly higher mean age in the CAD+P+ group, consistent with the literature, indicating the cumulative effect of both diseases. Periodontal disease is more common and severe in men compared to women of similar age (32). Similarly, the prevalence of CAD is higher in men across different age groups (33). In this study, significantly more males were enrolled in the CAD+P+ group compared to the CAD-P- and CAD-P+ groups, which aligns with previous findings.

To assess the periodontal status of each individual, we recorded PI, GI, PPD, and CAL across all groups. At baseline, the WM and ST periodontal parameters were significantly lower in the CAD-P- and CAD+P- groups compared to the periodontitis groups, which is consistent with the clinical manifestations of periodontitis. Within the periodontitis groups, PPD and CAL were significantly higher in the CAD+P+ group. Similarly, previous studies have reported a significant increase in periodontal parameters in individuals with coronary heart disease compared to healthy individuals (34). Systemic conditions can alter the immune response of the periodontium to dental plaque, leading to an enhanced acquired immune response that results in deeper periodontal pockets and greater attachment loss compared to healthy individuals. In this study, the improvement in WMPPD and WMCAL in the CAD+P+ group was markedly greater than in the CAD-P+ group at the third month following periodontal therapy. The further improvement in WMPPD and WMCAL in the CAD+P+ group, compared to the CAD-P+ group, may be associated with the use of statins in individuals with CAD.

Statins are inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMG-CoA) in cholesterol synthesis. They are widely used to lower blood cholesterol levels and treat atherosclerosis (35). Additionally, statins possess antioxidant, anti-inflammatory, and angiogenetic properties (36). Several studies have explored the effects of statins on the periodontium. For instance, a retrospective study reported a lesser extent of deep periodontal pockets in individuals taking statins compared to a control group, attributing this difference to the anti-inflammatory effects of statins (37). Moreover, a meta-analysis examining the effects of local statin administration alongside mechanical

periodontal therapy found reduced probing pocket depths in the statin groups compared to the control (38). Similarly, a study evaluating systemic statin use among hyperlipidemic individuals following non-surgical periodontal therapy observed significant clinical improvements in subjects on statins (39). In our study, following periodontal therapy, we observed a greater decrease in WMPD and WMCAL in the CAD+P+ group compared to the CAD-P+ group. This difference may be attributed to the anti-inflammatory activity of statins in addition to the mechanical treatment.

GCF is used for biomarker analysis in periodontitis (40). The volume of GCF increases in the presence of inflammation (41), and medications can influence both its volume and content (42, 43). At baseline, we observed significant differences in GCF volume between the groups. The higher GCF volume in the periodontitis groups corroborates the association between increased GCF volume and inflammation. The lower GCF volume at baseline and following periodontal therapy in the CAD+P+ group, compared to the CAD-P+ group, aligns with the understanding that anti-inflammatory drugs can affect both the amount and content of GCF (42, 43). Additionally, we found a significant negative correlation between baseline GCF volume and statin use ($p < .05$), supporting the observation of lower GCF volumes in the CAD+P- and CAD+P+ groups. The inflammatory burden in the body can impact an individual's immune response; therefore, the elevated GCF volume in the CAD+P- group compared to the control group may be due to altered immunity.

Sadeghi et al. (44) detected markedly higher IL 17 levels in the GCF of healthy individuals compared to those with chronic and aggressive periodontitis. The authors attributed this difference to the consumption of IL 17, which plays a prominent role in bone resorption in periodontitis. Similar studies have reported higher amounts of IL 17 in control groups compared to those with chronic periodontitis (45). For instance, Yetkin Ay et al. (46) observed lower IL 17 concentrations in the GCF of patients with aggressive periodontitis. Additionally, they did not find any significant difference in the total amount of IL 17 between groups, attributing this to the degradation of IL 17 in GCF and potential racial variations. Another study reported decreased IL 17 concentrations in regions adjacent to deep periodontal pockets (47), which they attributed to changes in the microenvironment during the early stages of periodontitis. Contrary to these findings, Majeed et al. (12) found higher total IL 17 levels in GCF samples from patients with chronic periodontitis compared to healthy controls. In line with the aforementioned studies, we detected low levels of IL 17 in the GCF samples of periodontitis groups. This finding may reflect either the degradation of IL 17 in GCF or alterations in the periodontal pocket environment. Additionally, we observed the lowest IL 17 levels in the CAD+P- group, which may be associated with the anti-inflammatory effects of statins.

According to Bartold et al. (26), the effect of periodontal treatment on a systemic condition needs to be evaluated to establish a plausible relationship. In this context, we assessed IL

17 levels following periodontal therapy in both GCF and serum samples. At baseline, serum samples showed significantly higher IL 17 levels in the CAD+P+ group compared to the CAD-P+ group, which may be attributed to the cumulative effect of coronary artery disease and periodontitis. Similarly, Qi et al. (28) reported elevated IL 23/IL 17 serum levels in individuals with both coronary heart disease and periodontitis. Following periodontal therapy, serum IL 17 levels were significantly reduced only in the CAD+P+ group, aligning with the notion that periodontal therapy decreases systemic biomarkers (48). Although a similar trend was observed in the CAD-P+ group, it was not statistically significant. Conversely, when comparing baseline and post-treatment samples, no significant changes in IL 17 levels were observed in the GCF samples of the CAD-P+ and CAD+P+ groups.

As previously mentioned, statins possess strong anti-inflammatory properties. To address why a significant change was observed only in serum samples, but not in GCF samples, following periodontal therapy in the CAD+P+ group, we examined the effect of statins. We divided the CAD+P+ group into statin (+) and statin (-) subgroups. When comparing IL 17 levels in GCF samples between statin (+) and statin (-) participants, no significant difference was observed ($p > .01$). Similarly, in serum samples, there was no marked difference between statin (+) and statin (-) individuals ($p > .01$). As noted earlier, statins have notable effects on both local and systemic cytokine levels in addition to clinical parameters. To fully elucidate the impact of statins on IL 17 expression levels, larger study groups are needed. Another potential factor contributing to the higher IL 17 levels in GCF following therapy could be the presence of dental plaque. The presence of dental plaque may have induced low-level inflammation, thereby masking the effect of therapy on IL 17 levels in GCF samples after periodontal treatment in the periodontitis groups.

Hashmi and Zeng (49) reported lower plasma IL 17 levels in stable angina patients compared to the unstable angina patients. We observed similar serum IL 17 levels both in CAD+P- and CAD-P- groups. This might be the reflection of a stable period in the CAD group.

In this study, some limitations should be acknowledged. In the study design, an additional time point before the third month of post treatment, such as the fourth week after periodontal therapy, could have been included to improve the oral hygiene habits of the study population, which would have ultimately improved the results. Additionally, implementing antimicrobial plaque control in the first week following periodontal treatment would have increased each patient's awareness of oral hygiene. Future studies with a better dental plaque control would yield significant findings in particular on GCF samples.

5. CONCLUSION

The increased expression of pro-inflammatory cytokine IL 17 in serum found in the present study suggests a possible association between chronic periodontitis and CAD. It can be thought that IL 17 plays a key role in connecting both

conditions. However, the current evidence is not strong enough to draw definitive conclusions. Future longitudinal studies with larger patient populations and controlling for confounding factors and comorbidities are needed to expand our knowledge and elucidate the role of periodontal inflammation in the pathogenesis of atherosclerotic disease.

Acknowledgments: Kirikkale University Scientific Research Project Coordination Unit supported the study.

Funding: Kirikkale University Scientific Research Project Coordination Unit supported the study.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Kirikkale University, Clinical Research Ethics Committee (Approval date: 16.01.2018; Number: 02/02)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: SSS, EO, EB

Design of the study: SSS, EO

Acquisition of data for the study: SSS

Analysis of data for the study: UK, SSS

Interpretation of data for the study: SSS, EO

Drafting the manuscript: SSS, EO

Revising it critically for important intellectual content: EO, EB

Final approval of the version to be published: SSS, UK, EO, EB

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Psychometric Properties of the Turkish Version of the Exclusive Breastfeeding Social Support Scale

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Received: February 20, 2024

Accepted: May 12, 2025

ABSTRACT

Objective: This study aimed to evaluate the psychometric properties of the Turkish version of the Exclusive Breastfeeding Social Support Scale, which was designed to determine the social support perceived by mothers of infants aged 0–6 months who use any method of exclusive breastfeeding.

Methods: This methodological research involved 290 mothers and their infants aged 0–6 months. Data were collected using a sociodemographic and breastfeeding-related information form and the Exclusive Breastfeeding Social Support Scale. Thereafter, content and construct validities were assessed; item and confirmatory factor analyses were conducted; and internal consistency was evaluated. The study adhered to the Guidelines for Reporting Reliability and Agreement Studies.

Results: The Turkish version of the Exclusive Breastfeeding Social Support Scale achieved a content validity index of 0.94. The correlations between the item scores and total scale scores ranged from 0.56 to 0.87. The confirmatory factor analysis confirmed the scale's 16-item, three-factor structure, with factor loadings exceeding 0.30 and fit indices above 0.80. The scale demonstrated a Cronbach's alpha coefficient of 0.95.

Conclusions: The Turkish version of the Exclusive Breastfeeding Social Support Scale is proven to be a valid and reliable measurement tool. This scale facilitates the assessment of perceived social support levels among mothers who exclusively breastfeed their infants for the first 6 months after birth.

Keywords: Exclusive breastfeeding, scale, social support, validity, reliability.

1. INTRODUCTION

Globally, breastfeeding is considered one of the top priorities and a fundamental concept of public health (1). It reduces the risk of noncommunicable diseases such as diabetes, childhood asthma, heart disease, and obesity in later life. Additionally, breastfeeding improves birth intervals and reduces the risk of conditions such as postpartum hemorrhage, breast cancer, and cardiovascular disease, thereby enhancing maternal well-being (2). According to the American Academy of Pediatrics, UNICEF, and the World Health Organization, all infants should receive exclusive breastfeeding (EBF) for at least 6 months after birth and continue receiving breast milk and complementary foods for at least 2 years thereafter (3,4). Despite all these benefits, the EBF rate for the first 6 months has yet to reach the desired level. Approximately 48% of infants worldwide are breastfed exclusively for their first 6 months, and 45% continue to breastfeed until 2 years of age (5). In Turkey, the EBF rate is 41% during the first 6 months of life but drops to 34% by the age of 2 years (6).

Research has revealed that several factors must be considered to achieve breastfeeding goals. These factors include cultural, economic, social, and health policies, as well as maternal demographics and psychological characteristics that impact breastfeeding and its sustainability. One of the key factors affecting breastfeeding in this context is social support (7,8). Perceived social support is defined as individuals' belief that other members of their social network will provide them with emotional, informational, and appraisal support when necessary (9). Social support as a social network helps individuals overcome stressful life conditions and problems by providing important psychological resources (10). Individuals can access this support from a variety of sources, including their spouses, families, friends, and healthcare providers (9). These sources play a critical role in the maintenance and establishment of breastfeeding (11). Social support is divided into four supportive behavior groups including emotional, instrumental, informational, and appraisal (7). Emotional support includes providing empathy and other

How to cite this article: Ayran G, Köse S. Psychometric Properties of the Turkish Version of the Exclusive Breastfeeding Social Support Scale. Clin Exp Health Sci 2025; 15: 272-279. <https://doi.org/10.33808/clinexphealthsci.XX>

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emotional support for breastfeeding. Instrumental support involves providing physical support and helping breastfeeding mothers find places to express or feed. Informational support encompasses advice, lessons, and information about breastfeeding. Evaluative support includes offering support and feedback on breastfeeding assessments. A lack of social support is a major barrier to EBF (12).

Social support is complex and multidimensional because it requires the measurement of both the quantity of support given (i.e., the frequency of supportive actions and the number of individuals providing support) and the quality of support received (1). Although there are studies in the current literature demonstrating a positive correlation between breastfeeding and social support (11,13,14), some studies indicate no relationship between them (15,16). The current measurement tools focus on the perceptions of general social support, are poorly adapted to specific contexts, and fail to assess the level of EBF and nutrition-specific support.

It is crucial to use a valid and reliable measurement tool for analyzing each concept. This highlights the need for a valid, reliable, objective, and standardized measurement tool to conduct quality research on social support for EBF in the first 6 months after birth. While valid and reliable data collection tools are limited in the international literature (17), there is no known measurement tool available in Turkey. Consequently, this study aimed to assess the psychometric properties of the Turkish version of the Exclusive Breastfeeding Social Support (EBFSS) Scale.

2. METHODS

2.1. Study Design and Participants

The study was conducted using a methodological approach and adhered to the Guidelines for Reporting Reliability and Agreement Studies (18). Data were collected from mothers utilizing any feeding method who visited the pediatrics polyclinic of a research hospital in a province in eastern Turkey from February to March 2023.

In validity and reliability studies, the sample size should be 5–20 times the number of items in the measurement tool. For an 18-item tool, the target was to reach 10 times as many participants as there are items (19,20). Therefore, data were collected from a total of 290 mothers who volunteered to participate in this study. The study was completed with a sample size of 290 mothers.

2.2. Data Collection Tools

2.2.1. Sociodemographic and Breastfeeding-Related Information Form

A sociodemographic and breastfeeding-related information form with a total of 14 questions regarding the sociodemographic and

breastfeeding-related characteristics of mothers was utilized. The sociodemographic characteristics included age, educational level, employment status, family type, income level, and number of children. Conversely, the breastfeeding-related characteristics were the baby's age and sex, breastfeeding experience, previous breastfeeding training, and feeding habits.

2.2.2. EBFSS Scale

The EBFSS Scale was developed by Boateng et al. (17) to measure the perceived social support for EBF among mothers who use any feeding method for their infants aged 0–6 months. The scale consists of a total of 16 items divided into three subscales: Instrumental Support, Emotional Support, and Informational Support. The Instrumental Support Subscale involves the concrete support received (e.g., “He prepared the meals”) and consists of three items (items 3, 6, and 7). The Emotional Support Subscale encompasses emotional support (e.g., “He believed that I was a good mother”) and consists of eight items (items 1, 2, 5, 8, 9, 10, 15, and 16). The Informative Support Subscale covers useful informational support (e.g., “She showed me how to breastfeed my baby”) and consists of five items (items 4, 11, 12, 13, and 14). All items are scored on a 3-point Likert scale with the following response options: “no help at all” (1 point), “less help than I want” (2 points), and “as much as I want” (3 points). A minimum of 16 points and a maximum of 48 points can be obtained from the scale. A high score indicates a high level of social support. In the original version of the scale, the Cronbach's alpha coefficient was 0.78, 0.85, and 0.78 for the Instrumental, Emotional, and Informational Support Subscales, respectively. In the Turkish version of the scale, the Cronbach's alpha coefficient was 0.85, 0.94, and 0.92 for the Instrumental, Emotional, and Informational Support Subscales, respectively.

2.3. Study Process

2.3.1. Language Validity

During language validation, the EBFSS Scale, originally in English, underwent a two-stage translation process: It was first translated from English to Turkish and then translated from Turkish back to English. In the first stage, three linguists proficient in both Turkish and English translated the scale. In the second stage, the translated Turkish version was consolidated into a single tool by three experts fluent in both languages (three academic nurses holding doctoral titles). Finally, a native English translator proficient in both languages translated the document back into English. A comparison between the translated English scale and the original English scale showed no significant changes in meaning, confirming the language validity of the scale.

2.3.2. Content Validity

The Davis technique was used to assess the content validity of the EBFSS Scale. In this technique, experts rate each item on a scale from 1 to 4, where 1 indicates “not suitable”; 2, “requires major revision”; 3, “requires minor revision”; and 4, “very suitable” (21). In this study, the number of experts who rated the items as 3 and 4 was divided by the total number of experts to calculate the item-level content validity index (I-CVI). At least three expert opinions were required to establish the scale’s content validity (22). No statistical comparison was made for the content validity index; instead, a value of 0.80 was accepted as the criterion (23). After the scale was re-translated, it was compared to the original English version. Subsequently, the Turkish version was reviewed by 11 Turkish field experts specializing in child health and diseases nursing. The final version of the Turkish scale was developed by making necessary adjustments to each item following the Davis technique.

2.3.3. Pilot Study

Following expert consultation, a pilot study was recommended to be administered to a group of approximately 20–30 individuals with similar characteristics to the sample (24). In this study, the scale was initially administered to 30 mothers who volunteered to participate, but these 30 mothers were not included in the final sample. These mothers did not provide any negative feedback regarding the readability, intelligibility, and response process of the scale.

2.3.4. Test–Retest Method

The test–retest method involves applying the same measurement tool to the same group at different periods to determine its consistency and invariance over time (20). Correlation coefficients are calculated between the scores obtained from the tool applied in both periods, and those approaching +1 indicate a high degree of reliability (25). In this study, nicknames and telephone numbers were obtained from mothers who volunteered to participate during the first scale administration. Four weeks later, the scale was readministered to a total of 30 mothers in the target hospital. In the Pearson correlation analysis, a positive and strong relationship ($r=0.794$; $p<.05$) was found between the measurements, with the correlation coefficient falling within the range of 0.60–0.79.

2.4. Data Analysis

The data obtained in this study were analyzed using the Statistical Package for the Social Sciences for Windows version 25.0 and AMOS software version 21. Descriptive

statistics including numbers, means, percentages, and standard deviations were utilized for the data analysis. The reliability of the scale was tested using Cronbach’s alpha and split-half methods. Additionally, both exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) were conducted to determine the construct validity of the scale. Item discrimination was assessed using a 27% top–bottom item analysis. Composite reliability (CR) and average variance extracted (AVE) values were also calculated to assess convergent and divergent validities.

2.5. Ethical Considerations

For the validity and reliability testing of the Turkish version of the EBFSS Scale, permission was obtained from the authors of the original scale via e-mail. In addition, legal and ethical approvals were obtained from the Erzincan Binali Yıldırım University Human Research Ethics Committee (31/08/2022/07-08/10) and the target hospital. Participating mothers were informed about the study, and their written and verbal consents were obtained.

3. RESULTS

3.1. Validity Analyses

3.1.1. Content Validity

Among the experts, the majority of the scale items were rated as either “requires minor revision” or “very suitable.” The I-CVI ranged from 0.80 to 1.0 for each item. After expert opinions were analyzed, a content validity index of 0.94 was obtained.

3.1.2. EFA

Promax rotation was utilized in the EFA. Before the analysis, the Kaiser–Meyer–Olkin (KMO) test was performed to assess the adequacy of the sample size for factorization. The KMO value obtained was 0.951, indicating excellent suitability. Additionally, Bartlett’s test of sphericity yielded a significant χ^2 value [$\chi^2(120)=4129.265$, $p<.01$], further supporting the factorability of the correlation matrix. Ultimately, the resulting measurement tool comprised three factors and 16 items, with no items excluded from the analysis. Based on the findings of the EFA, the adapted scale explained 75.080% of the total variance. Initially, two factors had eigenvalues exceeding 1. However, when the scale was forced into three dimensions, the eigenvalues returned to their original levels, which better aligned with the original distribution (Table 1).

Table 1. Demographic characteristics of the participants

		n	%
Age (Year)	18-24	54	18.6
	25-34	186	64.1
	35-44	50	17.2
Education Status	Primary school	46	15.9
	Middle school	49	16.9
	High school	87	30.0
	University and above	108	37.2
Working status	Working	52	17.9
	Not working	238	82.1
Income status	Income more than outgoing	86	29.7
	Income equals expense	181	62.4
	Income less than expenses	23	7.9
Family Type	Nuclear family	267	92.1
	Extended family	23	7.9
Children Number	1	109	37.6
	2	108	37.2
	3	50	17.2
	4 and above	23	7.9
Type of birth	Normal delivery	142	49.0
	Cesarean delivery	148	51.0
Infant's gender	Female	117	40.3
	Male	173	59.7
Infant's Age	1	80	27.6
	2	76	26.2
	3	48	16.6
	4	37	12.8
	5	25	8.6
	6	24	8.3
Breastfeeding status of another infant	Yes	167	57.6
	No	123	42.4
Breastfeeding education	Yes	100	34.5
	No	190	65.5
Nutrition Type	Exclusive Breastfeeding	167	57.6
	Breastfeeding and formula	102	35.2
	Formula	21	7.2
		X±SD	
Week of birth		38.53±1.07	
Birth weight		3157.51±423.88	
Exclusive Breastfeeding Duration		6.00±1.69	

3.1.3. CFA

In the CFA, the scale exhibited significance at a p-value of 0.000, demonstrating a relationship among the 16 items and the three-factor structure of the scale. Covariance between errors of the same factor was observed in the model. In the analysis of the goodness-of-fit indices of the scale, the χ^2/df was 2.286, and the root mean square error of approximation (RMSEA) was 0.067. Additionally, in the three-factor CFA, the factor loadings of all subscales were >0.30, indicating satisfactory goodness-of-fit indices. These

indices included the goodness-of-fit index (GFI), normed fit index (NFI), relative fit index (RFI), comparative fit index (CFI), and incremental fit index (IFI), all of which were >0.90. The RMSEA was <0.080 (Table 2).

3.2. Reliability Analyses

Based on the CFA results of the three-factor model, Factor 1 exhibited factor loadings ranging from 0.78 to 0.90; Factor 2, from 0.56 to 0.98; and Factor 3, from 0.72 to 0.89 (Figure 1 and Table 3).

Table 2. Exploratory Factor Analysis Results of Exclusive Breastfeeding Social Support Scale

Items	Factor 1	Factor 2	Factor 3
Q16		0.915	
Q2		0.889	
Q10		0.854	
Q9		0.815	
Q5		0.795	
Q8		0.783	
Q1		0.743	
Q15		0.649	
Q13			0.996
Q12			0.921
Q14			0.768
Q4			0.732
Q11			0.610
Q3	0.952		
Q7	0.828		
Q6	0.755		
Eigenvalue	0.880	9.852	1.280
Rate of Explained Variance	5.503	61.578	7.999
<i>KMO =0.951 X²(120) = 4129.265; Bartlett Sphericity Test (p) = 0.000 Rate of Total Explained Variance=75.080</i>			

3.2.1. Item–Total Test Correlation

The item–total test correlation coefficients for the responses to all scale questions varied from 0.561 to 0.876 (Table 3).

Table 3. Findings on Confirmatory Factor Analysis (GU)

Index	Perfect Fit Criteria	Acceptable Fit Criteria	After Modification
χ^2/SD	$0 \leq \chi^2/df \leq 3$	$3 \leq \chi^2/df \leq 5$	2.286
RMSEA	$0.00 \leq RMSEA \leq 0.05$	$0.05 \leq RMSEA \leq 0.08$	0.067
SRMR	$0.00 \leq SRMR \leq 0.05$	$0.05 \leq SRMR \leq 0.08$	0.031
CFI	$0.95 \leq CFI$	$0.85 \leq CFI$	0.969
GFI	$0.90 \leq GFI$	$0.85 \leq GFI$	0.912
AGFI	$0.90 \leq AGFI$	$0.85 \leq AGFI$	0.879
IFI	$0.90 \leq IFI \leq 1.00$	$0.80 \leq IFI$	0.969
TLI	$0.90 \leq TLI$	$0.80 \leq TLI$	0.962
NFI	$0.90 \leq NFI$	$0.80 \leq NFI$	0.946

Chi-square/ Degrees of Freedom (χ^2/SD) ; Root Mean Square Error of Approximation (RMSEA); Comparative Fit Index (CFI); NNFI (TLI): Normed Fit Index; Goodness of Fit Index (GFI); Adjusted Goodness of Fit Index (AGFI)

Table 4. Reliability Analysis of the Exclusive Breastfeeding Social Support Scale

Factor	Item	Factor Load	Item-total test correlation	AVE	CR	Cronbach's Alpha if Item Deleted	Cronbach's Alpha
Factor 1	Q3	0.563	0.561	0.70	0.87	0.944	0.856
	Q6	0.982	0.827			0.704	
	Q7	0.910	0.820			0.707	
Factor 2	Q1	0.725	0.694	0.67	0.94	0.939	0.940
	Q2	0.893	0.876			0.927	
	Q5	0.839	0.808			0.931	
	Q8	0.790	0.761			0.934	
	Q9	0.842	0.817			0.931	
	Q10	0.848	0.828			0.929	
	Q15	0.851	0.812			0.931	
	Q16	0.719	0.715			0.938	
Factor 3	Q4	0.869	0.821	0.71	0.92	0.901	0.923
	Q11	0.896	0.828			0.901	
	Q12	0.779	0.753			0.916	
	Q13	0.814	0.798			0.906	
	Q14	0.842	0.808			0.903	

The AVE value for Factor 1 was 0.70; Factor 2, 0.67; and Factor 3, 0.71. Conversely, the CR value for Factor 1 was 0.87; Factor 2, 0.94; and Factor 3, 0.92. In the 16-item analysis of the scale, the item–total test correlation coefficients were found to vary from 0.56 to 0.87 (Table 3).

The reliability of the Turkish version of the scale was 0.955. The alpha coefficient for Factor 1 was 0.85; Factor 2, 0.94; and Factor 3, 0.92.

For the split-half reliability analysis of the scale, the items were divided into two halves based on their odd and even row numbers. The correlation coefficient between the two halves was calculated to be over 0.70 for each measurement tool. Specifically, the correlation coefficient between the two halves was 0.931; the Spearman correlation coefficient was 0.965; and the Guttman split-half coefficient was 0.964 (Table 5).

Table 5. Split-half reliability of the scale

Cronbach's Alpha	Half 1= Q1, Q3, Q5, Q7, Q9, Q11, Q13, Q15,	0.899
	Half 2= Q6, Q2, Q8, Q10, Q16, Q4, Q12, Q14,	0.924
Correlation between the two halves		0.931
Spearman-Brown coefficient		0.965
Guttman Split-Half coefficient		0.964

4. DISCUSSION

In countries where traditional practices are prevalent, the breastfeeding behaviors of mothers are often influenced by their families, close social circles, and religious communities. While breastfeeding is a common practice in these countries, it is also typical to introduce other foods and liquids before the recommended age of 6 months. Despite receiving substantial support from their social networks, mothers may encounter pressure from the same individuals to introduce complementary foods early, thereby disrupting EBF. In Turkey, where traditional practices are prominent, breastfeeding is widely practiced, but EBF during the first 6 months of life is not as commonly observed (17,26). Given that perceived social support in the first 6 months is a crucial factor influencing breastfeeding behavior, there is a need for a scale to assess support during breastfeeding specifically within this timeframe (11,13,14). Hence, this research was undertaken to establish the validity and reliability of the Turkish version of the EBFSS Scale, developed to address this existing gap. The findings of the study indicate that the Turkish version of the scale exhibits acceptable validity and reliability.

A newly developed or adapted measurement tool should meet validity and reliability criteria (27,28). A crucial initial step in scale adaptation studies is translating the original scale into the language of the target society. The I-CVI should typically exceed 0.80 to ensure agreement between expert opinions (29). In this study, the I-CVI of the scale was 0.94. Similarly, an adaptation study conducted in Iran reported an I-CVI of 0.98 (30). Based on the I-CVI, expert consensus confirmed that the scale accurately measured the intended subject, thereby establishing the content validity of the scale.

The KMO test was utilized to assess the adequacy of the sample size for factorization. According to the literature, conducting a factor analysis necessitates a significant Bartlett's test of sphericity value and a KMO value of at least 0.60 (10, 31). In this study, the KMO value was determined to be 0.951, while in the adaptation study conducted in Iran, the value was 0.88 (30). Bartlett's test of sphericity revealed a significant χ^2 value [$\chi^2(120)=4129.265$, $p<0.01$], indicating that the items had a multivariate normal distribution. Therefore, the sample size and dataset were deemed suitable for the factor analysis.

For the number of factors to be determined, the eigenvalue must be at least 1 (31,32). In the present study, the scale was constrained into three dimensions to better fit the original distribution. Consequently, no items were excluded, and

the scale consisted of 16 items across three factors. The three-factor scale explained 75.080% of the total variance. Conversely, it explains 66% of the total variance in the original version of the scale and 59.26% in an adapted Iranian version of the scale (17,30). Multidimensional scales should have an explanation variance of at least 40%, and the higher the explanation variance, the stronger the construct validity (31,32). In this study, the total variance explained by the scale exceeded 50%, consistent with previous reports. This high level of total variance confirmed the construct validity of the scale.

The EFA of the three-factor model in the present study revealed factor loadings ranging from 0.61 to 0.99. Items with factor loadings exceeding 0.30 were considered suitable for the structure, confirming the validity of the structure. Items with factor loadings below this threshold were considered for exclusion from the scale (33). In the original scale, factor loadings ranged from 0.22 to 0.90, and items with factor loadings below 0.30 were removed from the scale (17). In the adaptation study conducted in Iran, factor loadings ranged from 0.45 to 0.88 (10). In this study, the EFA revealed a 16-item, three-factor structure: informative, emotional, and instrumental support. The factor loadings obtained from each subscale were >0.30 , indicating that the scale had a robust factor structure. This finding is consistent with previous reports that support a three-factor structure similar to that of the Hughes Breastfeeding Social Support Scale (34). In addition, the 16-item EBFSS Scale offers the advantage of a shorter administration time compared to the 30-item Hughes Breastfeeding Social Support Scale.

The CFA was conducted on the model based on the dimensions identified in the EFA. The adequacy of the theoretical structure proposed by the CFA for explaining the observed data was evaluated (35). The CFA revealed that the structural equation modeling results of the scale were significant ($p=.000$), indicating a strong relationship between the 16 items and the three-factor structure of the scale. Covariance was established between errors of the same factor in the model. In the three-factor CFA, the factor loadings of all subscales were found to be >0.30 . The goodness-of-fit indices including the GFI, NFI, RFI, CFI, and IFI were all >0.90 , while the RMSEA was <0.080 . Additionally, the model demonstrated a perfect fit with a χ^2/df of 2.286. In their study, Boateng et al. (17) reported overall goodness-of-fit indices of >0.90 and an RMSEA of <0.08 . Mashayekh-Amiri et al. (30) examined the three-factor structure found in their EFA using a CFA and found that the model fit the data well. In this study and other studies, the CFA results are compatible with the criteria stated in the literature. The CFA indicated that the data aligned with the model, confirming the three-factor structure and the association of the subscales with the scale. Moreover, the items within each subscale adequately represented their respective factors. Both EFA and CFA results in this study support the construct validity of the scale, suggesting that it is a valid measurement tool.

Reliability analyses are conducted to assess whether the items on a scale are internally consistent and measure the same construct. Cronbach's alpha coefficients are used for this purpose, with values ranging from 0 to 1. A coefficient of 0.00–0.40 indicates low reliability; 0.40–0.60, fair reliability; 0.60–0.80, good reliability; and 0.80–1.00, excellent reliability (36). In the current study, the Cronbach's alpha coefficient for the EBFSS Scale was 0.955, while that for its subscales ranged from 0.856 to 0.940. In their study, Boateng et al. (17) calculated a total Cronbach's alpha coefficient of >0.70 for their scale. In the study by Mashayekh-Amiri et al. (30), the total Cronbach's alpha coefficient for their scale was 0.92, while that for the subscales varied from 0.79 to 0.82. The scale in the present study is similar to the original version and the adapted Iranian version and has strong internal consistency.

The study has several limitations. First, the validity and reliability of the scale were tested solely on mothers who sought care at a hospital in a specific province in Turkey, limiting the generalizability of the results. Second, the study was conducted in a single location with a relatively small sample size. Third, the scale used relied on self-report measures.

5. CONCLUSIONS

In conclusion, the EBFSS Scale, comprising 16 items and three subscales, is a valid and reliable measurement tool for evaluating the level of social support for EBF perceived by mothers of infants aged 0–6 months in Turkey. This tool can be utilized by professionals to assess the perceptions of social support among mothers with infants aged 0–6 months and by researchers to facilitate cross-cultural comparative studies. Mothers often encounter various challenges during breastfeeding. Given the established relationship between perceived social support and breastfeeding, nurses are poised to play a pivotal role in identifying mothers lacking adequate social support and in enhancing breastfeeding attitudes and behaviors. The initial step in assisting mothers involves assessing their situation. This study provides Turkish pediatric and public health nurses, pediatricians, and other healthcare professionals with a valid and reliable tool for evaluating the perceived level of social support for EBF. By using this scale, nurses can assess the level of informative social support and develop community-based interventions. Moreover, the scale can be instrumental in formulating policies aimed at enhancing support for EBF.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Erzincan Binali Yıldırım University, Noninvasive Clinic Ethics Committee (Approval date: 31.08.2022; Number:07-08/10)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: GA

Design of the study: GA, SK

Acquisition of data for the study: GA, SK

Analysis of data for the study: GA, SK

Interpretation of data for the study: GA, SK

Drafting the manuscript: GA, SK

Revising it critically for important intellectual content: GA, SK

Final approval of the version to be published: GA, SK

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Examination of Factors Affecting Mental Distress Among Dental Students: A Cross-Sectional Study

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Received: March 25, 2024

Accepted: March 03, 2025

ABSTRACT

Objective: Depression, anxiety, and stress (DAS) are quite common among dental students. It should be the duty of the educational institution to deal with these mental disorders that are observed during a challenging education. The aim of this study was to determine the levels of DAS among dental students and explore possible factors that may cause these disorders.

Methods: This cross-sectional study was conducted among dental students at Çanakkale Onsekiz Mart University, which offers dental education in Turkey. The form created with Google Forms was distributed to the students with a URL link to collect socio-demographic information and data related to DAS levels.

Results: The majority of dental students exhibited levels of DAS severity ranging from 'severe' to 'extremely severe'. Females exhibited higher levels of anxiety and stress than males, while their resilience was lower. Those with financial support responsibilities towards their families similarly showed significantly higher anxiety and stress levels ($p < .05$, for both). It was also found that DAS levels increased up to the fourth-grade, peaking at the fourth-grade, and then significantly decreased in the fifth-grade. Dissatisfaction regarding examination and teaching methods was associated with the DAS level of dental students.

Conclusion: It is believed that methodological improvements in education will have a positive contribution to the mental health of dental students. Dealing with related mental disorders is also of critical importance for enhancing the quality of treatments provided to patients and consequently, making progress in the healthcare system.

Keywords: Anxiety, dental students, depression, mental health, stress

1. INTRODUCTION

Mental disorders such as depression and anxiety, which are attracting increasing attention globally, negatively affect individuals' lives, performance, working life, etc (1). In addition, stress occurs when environmental pressure and demands exceed the abilities of individuals (2). Therefore, depression, anxiety, and stress (DAS) levels are critical and significant indicators of mental health (3).

Deterioration in mental health, which is an important determinant of quality of life and satisfaction, has become a common problem for university students in developed and developing countries (4). Students need to adapt to the university period to cope with academic demands along with new challenges and responsibilities (5). It has been shown

that students who choose departments that provide health education are more prone to stress (6). However, stress is higher among dental students compared to other healthcare branches (7). High demand due to the need for manual skills for clinical practice, sensitive and greater laboratory workload, increased competition, and most importantly, a small working area such as the oral cavity in patients who mostly have phobias, are among the reasons. Moreover, due to its versatility, dental education involves the challenging task of both conveying up-to-date content and preparing students to overcome the challenges that may arise after graduation. Therefore, students are faced with an overloaded curriculum (8).

How to cite this article: Alan R, Terlemez A, Bakay H, Gıca Ş, Ercan E. Examination of Factors Affecting Mental Distress Among Dental Students: A Cross-Sectional Study. Clin Exp Health Sci 2025; 15: 280-289. <https://doi.org/10.33808/clinexphealthsci.1458804>

Eremsoy et al. (9) stated that the relationship between anxiety and depression is very important. In addition, increased stress might be related to moderate anxiety and depression symptoms (10). Previous research showed that students who frequently exhibit stressful lives experience high levels of burnout (11). Similarly, Koh et al. (12) detected high levels of IL-2 in highly stressed students and demonstrated the effect of stress on the immune system.

Considering the relationships between stress, depression, and anxiety, identifying and resolving the causative factors is extremely critical. This type of information has extremely important contributions to institutions that determine health policies in improving the mental health of students (13). Although there are studies conducted for this purpose, there is a lack of research on which factors are effective among dental students. In addition to all these reasons, the university should be taken into consideration in dental education policy as an institution that supports students' mental health and quality of life in addition to dental education (14). Therefore, this study aims to shed light on health policymakers by determining the levels of DAS among dental students and exploring possible factors that may cause these disorders.

2. METHODS

2.1. Ethics Statement

This cross-sectional study was approved by the Ethics Committee of Çanakkale Onsekiz Mart University Graduate Education Institute (*project no*: 2023-YÖNP-0400; *app. no*: 07/44) and was conducted in accordance with the Helsinki Declaration. All students participating in the study were informed about the purpose of the study. They participated in the study voluntarily and had the right to withdraw their participation.

2.2. Study Population and Design

The data of the study were gathered from dental students of the Faculty of Dentistry at Çanakkale Onsekiz Mart University. The power of the study was calculated as 0.95 using G*Power software (V3.1.9.2) (α -error 0.05, and effect size 0.25). Due to the intense curriculum, lack of common free time, and most importantly, to fill out the questionnaires without feeling pressured, a data collection form was created using Google Forms, and a URL link was distributed to the students. There was an information note at the beginning of the questionnaire, accompanied by detailed information about the study, explaining that completion was voluntary, anonymous, and not part of the course notes. Participants who were younger than 18 years of age, did not complete the psychometric tests or refused to confirm the informed consent form were not included in the study. At the end of the study, data from 198 participants who completed the questionnaire completely were included in the final analysis. To ensure data security, the form was not set to public. The form consisted of questions to gather data on the following

main two headings: socio-demographic information and questionnaires.

2.3. Data Collection Tools

2.3.1. Socio-demographic information form

The following information about the participants was recorded: gender, age, body mass index, number of siblings, place of birth, and family status. In addition, information about their university life, such as grade, grade repetition, and last term's average, as well as information about their social life, such as smoking, alcohol consumption, substance addiction, and place of residence, were recorded. Additionally, educational, social, and family information regarding possible stressors were also recorded.

2.3.2. Depression Anxiety Stress Scale-21 (DASS-21)

DASS-21, which is the short form of the Depression Anxiety Stress (DAS) Scale, measures DAS simultaneously, was designed to provide the highest level of discrimination between the three components and also exhibits high validity and reliability. The validity of DASS-21 for the Turkish population was confirmed by Saricam (15). This scale, which has 21 items, is scored on a 4-point Likert scale from zero (never) to 3 (always).

2.3.3. The Patient Health Questionnaire-9 (PHQ.9)

PHQ.9 is a nine-item survey intended to identify depression in primary care and other medical settings. The standard cut-off score determined in the first study on PHQ.9 in determining possible major depression is 10 or above (16).

Due to the widespread usage of the PHQ.9 for evaluating and tracking the severity of depression, a seven-item anxiety scale, designed with a response format similar to the PHQ-9, was created to diagnose generalized anxiety disorder (GAD.7) (17). While its primary objective was originally to diagnose generalized anxiety disorder, it was soon discovered that the GAD.7 also demonstrated a high degree of accuracy in screening for panic disorders, social anxiety, and post-traumatic stress disorder (18). Additionally, the PHQ-15, which evolved from the original PHQ research, is now increasingly employed to gauge the severity of somatic symptoms and potentially identify the presence of somatization and somatoform disorders (19).

2.3.4. Connor-Davidson Resilience Scale (CD-RISC)

Among various tools for measuring resilience, the original CD-RISC received high marks in psychometric assessments, demonstrating sufficient internal consistency, test-retest reliability, and construct validity. A factor analysis of the 25-item scale identified five dimensions related to personal characteristics that facilitate successful adaptation to adversity: personal competence, high standards, and tenacity; trust in one's instincts, tolerance of negative emotions, and

the fortifying effects of stress; positive acceptance of change and secure relationships; control; and spirituality (20).

Spearman correlation was applied. The significance level was set at $p < .05$.

2.4. Statistical Analysis

Statistical analyses were performed using SPSS (version 20.0.; IBM SPSS Statistics for Windows, Armonk, NY) and MedCalc® statistical software (version 22.002; MedCalc Software Ltd, Ostend, Belgium). The Kolmogorov-Smirnov test was applied to test the normality of data. Descriptive analysis involved the utilization of means, standard deviations, and percentages. To conduct a comparative analysis, we employed Independent Samples t-tests and One-way ANOVA. In the case of correlational analysis, the

3. RESULTS

Of the 198 dental students included in this study, 138 were female participants (69.7%) and 60 were male participants (30.3%), and their average ages were 21.43 ± 1.43 and 22.10 ± 1.75 , respectively. Of the included participants, 28 (14.1%) were first-grade, 35 (17.7%) were second-grade, 61 (30.8%) were third-grade, 38 (19.2%) were fourth-grade and 36 (18.2%) were fifth-grade students. Other sociodemographic characteristics of the dental students participating in the study are presented in Table 1.

Table 1. Comparison of DAS scores among dental students with different sociodemographic characteristics.

Variable	DASS-21			PHQ.9 mean±SD	GAD.7 mean±SD	PHQ.15 mean±SD	CD-RISC mean±SD
	Depression mean±SD	Anxiety mean±SD	Stress mean±SD				
Gender							
Male (n=60)	11.18±5.03	7.97±5.56	11.08±4.96	14.15±7.19	11.87±6.05	12.32±6.18	63.85±16.35
Female (n=138)	12.33±5.35	10.33±5.46	12.79±4.91	16.53±6.34	13.80±5.37	17.02±5.92	54.83±16.07
p-value (t)	.159 (1.415)	< .05* (2.780)	< .05* (2.241)	< .05* (2.328)	< .05* (2.237)	< .001** (5.070)	< .001** (-3.609)
BMI							
Below 18.5 (n=27)	12.56±5.24	10.15±4.63	13.26±4.58	16.11±6.35	14.07±5.41	17.85±5.19	58.89±15.96
18.5 – 24.9 (n=137)	11.76±5.26	9.51±5.76	12.05±4.88	15.66±6.72	13.09±5.56	15.33±6.47	56.76±16.71
25.0 – 29.9 (n=29)	11.93±5.57	9.41±5.65	12.14±5.55	15.69±7.22	12.97±6.07	14.79±6.57	62.07±16.67
30.0 and above (n=5)	15.40±3.36	10.60±6.47	13.80±6.76	18.80±4.87	13.40±7.70	15.40±7.54	46.40±14.43
p-value (F)	.448 (.889)	.923 (.160)	.612 (.605)	.772 (.373)	.861 (.250)	.252 (1.374)	.182 (1.638)
Number of siblings							
0 (n=16)	12.75±4.74	10.81±5.99	11.50±4.61	15.38±6.48	13.44±5.85	14.88±6.72	54.38±11.86
1 (n= 72)	12.51±4.88	10.14±5.58	12.86±4.66	16.97±5.97	13.93±5.26	16.86±5.58	55.81±17.18
≥2 (n= 110)	11.53±5.58	9.09±5.52	12.00±5.22	15.11±7.09	12.71±5.84	14.87±6.71	59.18±16.82
p-value (F)	.390 (.946)	.312 (1.172)	.424 (.861)	.178 (1.742)	.357 (1.036)	.107 (2.263)	.298 (1.218)
Place of birth							
Town/city (n=144)	12.13±5.16	9.87±5.69	12.22±5.04	16.06±6.40	13.18±5.65	15.90±6.38	55.17±15.15
District/Village (n=54)	11.61±5.60	8.93±5.26	12.41±4.83	15.13±7.41	13.30±5.67	14.78±6.31	63.96±18.79
p-value (t)	.542 (.610)	.291 (1.058)	.816 (-.233)	.383 (.875)	.898 (-.128)	.269 (1.108)	< .05* (-3.085)
Family status							
Together (n=171)	11.96±5.21	9.81±5.51	12.38±5.00	15.94±6.53	13.42±5.64	15.65±6.35	57.08±16.63
Divorced (n=14)	11.50±5.65	7.86±5.61	11.14±4.66	15.57±6.32	11.57±5.67	14.86±5.63	61.71±13.56
Death (n=13)	12.85±6.03	8.85±6.48	12.08±5.22	14.38±9.10	12.23±5.63	15.69±7.71	59.46±20.04
p-value (F)	.792 (.233)	.399 (.924)	.665 (.409)	.717 (.333)	.406 (.906)	.904 (.101)	.556 (.589)
Responsibility for financial support to the family							
Yes (n=11)	14.64±6.10	13.73±6.62	16.00±5.29	18.55±10.42	15.91±6.73	18.55±6.36	57.09±13.78
No (n=187)	11.83±5.19	9.37±5.44	12.05±4.88	15.65±6.40	13.05±5.55	15.42±6.34	57.59±16.83
p-value (t)	.086 (1.726)	< .05* (2.552)	< .05* (2.594)	.382 (.913)	.103 (1.640)	.114 (1.587)	.923 (-.097)
Last term's average							
AA (n=1)	14.00	14.00	20.00	17.00	12.00	24.00	73.00
BA (n=13)	11.15±5.93	9.00±5.80	13.85±5.44	15.85±6.19	13.77±6.04	14.62±6.90	59.85±18.69

BB (n=106)	11.74±5.51	9.76±5.65	12.36±5.11	15.45±6.85	13.27±5.62	15.84±6.32	57.08±15.63
CB (n=61)	12.67±5.03	9.92±5.59	12.46±4.61	16.93±6.38	13.84±5.48	16.21±6.23	57.98±17.63
CC (n=11)	10.36±3.44	7.64±5.20	9.09±3.94	12.64±7.45	9.55±5.87	11.36±6.49	60.09±18.66
Unknown (n=6)	13.83±5.12	8.00±5.33	10.00±4.60	16.17±6.49	11.50±5.68	13.50±5.09	49.83±19.17
p-value (F)	.625 (.699)	.718 (.577)	.086 (1.964)	.475 (.910)	.294 (1.235)	.139 (1.687)	.738 (.550)
Place of residence							
With family (n=11)	11.55±6.07	8.64±5.85	11.64±5.64	13.27±6.81	10.36±4.50	12.18±4.69	54.91±18.12
At home (n=128)	12.30±5.17	9.68±5.74	12.62±4.96	15.91±6.69	13.26±5.90	15.87±6.36	58.75±16.69
Hostel (n=59)	11.39±5.37	9.64±5.25	11.64±4.90	16.07±6.66	13.64±5.15	15.64±6.55	55.49±16.28
p-value (F)	.530 (.636)	.838 (.177)	.422 (.867)	.429 (.849)	.206 (1.591)	.183 (1.712)	.400 (.922)
Smoking							
Yes (n=85)	12.53±5.06	9.84±5.88	12.38±4.95	16.48±6.84	13.96±6.02	16.20±6.46	57.59±18.74
No (n=113)	11.58±5.41	9.44±5.36	12.19±5.02	15.30±6.54	12.65±5.29	15.14±6.29	57.55±14.96
p-value (t)	.208 (1.263)	.625 (.489)	.800 (.254)	.219 (1.233)	.103 (1.636)	.248 (1.159)	.987 (.017)
Alcohol consumption							
Yes (n=115)	12.48±5.11	10.06±5.61	12.69±4.83	16.82±6.35	13.90±5.44	16.46±6.24	56.34±17.32
No (n=83)	11.30±5.45	8.99±5.51	11.70±5.14	14.41±6.91	12.25±5.80	14.40±6.38	59.27±15.60
p-value (t)	.121 (1.556)	.183 (1.337)	.168 (1.383)	< .05* (2.537)	< .05* (2.050)	< .05* (2.274)	.223 (-1.222)
Substance addiction							
Yes (n=7)	11.29±5.91	10.71±5.44	10.29±8.52	14.71±11.34	11.71±7.83	12.00±7.64	56.43±18.80
No (n=191)	12.01±5.26	9.57±5.60	12.35±4.82	15.85±6.49	13.27±5.56	15.73±6.30	57.61±16.61
p-value (t)	.722 (-.357)	.596 (.531)	.548 (-.636)	.801 (-.263)	.476 (-.715)	.128 (-1.527)	.855 (-.184)
Working outside of school							
Yes (n=17)	11.29±5.17	10.12±5.92	12.18±6.17	16.29±7.94	12.88±6.19	13.71±7.28	63.29±17.28
No (n=181)	12.05±5.29	9.56±5.56	12.28±4.87	15.76±6.58	13.24±5.60	15.77±6.27	57.03±16.53
p-value (t)	.573 (-.564)	.697 (.391)	.934 (-.083)	.755 (.313)	.802 (-.252)	.201 (-1.282)	.138 (1.489)
History of psychiatric disease							
Present (n=40)	12.88±5.17	10.93±5.99	12.68±5.10	17.55±6.61	13.65±5.78	16.78±6.01	51.90±17.47
Absent (n=158)	11.76±5.29	9.28±5.44	12.17±4.95	15.37±6.65	13.10±5.62	15.30±6.44	59.00±16.17
p-value (t)	.233 (1.197)	.096 (1.674)	.568 (.572)	.065 (1.857)	.584 (.549)	.190 (1.314)	< .05* (-2.440)
Family history of psychiatric disease							
Present (n=54)	12.87±5.25	10.91±6.17	12.96±5.02	18.39±6.49	14.93±6.04	17.33±6.79	53.15±17.48
Absent (n=144)	11.65±5.26	9.13±5.29	12.01±4.95	14.84±6.52	12.57±5.36	14.94±6.10	59.22±16.07
p-value (t)	.148 (1.452)	< .05* (1.881)	.233 (1.197)	< .05* (3.418)	< .05* (2.660)	< .05* (2.379)	< .05* (-2.312)
Grade							
1 st (n=28)	9.64±5.47	7.89±4.57	9.71±4.50	14.18±6.47	11.50±4.72	12.96±6.27	59.00±13.42
2 nd (n=35)	12.29±5.43	9.23±5.57	11.54±4.80	15.97±6.20	13.17±5.70	15.31±6.24	58.20±20.79
3 rd (n=61)	12.38±4.31 [†]	10.57±5.35 [†]	12.80±4.66 [†]	16.36±5.71	13.66±5.01	16.74±5.65 [†]	56.44±15.80
4 th (n=38)	14.82±4.99 ^{††§}	11.89±5.82 ^{††§}	15.29±4.43 ^{††§}	18.53±6.80 [†]	15.42±5.19 [†]	17.97±6.94 [†]	54.84±17.59
5 th (n=36)	9.86±5.33 ^{§††}	7.28±5.38 ^{§††}	10.89±5.02 ^{††}	13.11±7.66 ^{§††}	11.50±6.91 ^{††}	13.47±5.97 ^{§††}	60.61±14.95
p-value (F)	< .001** (6.313)	< .05* (4.641)	< .001** (7.214)	< .05* (3.766)	< .05* (3.162)	< .05* (4.301)	.603 (.686)
The number of grade repetitions							
0 (n=176)	11.95±5.31	9.51±5.44	12.44±4.86	15.77±6.64	13.32±5.53	15.62±6.25	57.40±16.35
1 (n=20)	12.50±5.29	10.30±6.95	11.25±5.75	16.90±6.55	12.75±6.26	15.85±7.24	57.50±19.47
≥2 (n=2)	10.00±1.41	11.50±4.95	7.50±6.36	8.50±12.02	8.50±10.61	11.00±9.90	72.50±12.02
p-value (F)	.787 (.240)	.746 (.293)	.236 (1.454)	.232 (1.474)	.453 (.795)	.586 (.536)	.445 (.812)
Stressors							
Only education (n=72)	11.74±4.92	9.86±5.51	12.65±4.75	15.53±6.89	13.18±5.90	15.71±6.65	61.64±16.93

Only social (n=8)	9.25±6.86	4.00±3.02 [†]	9.13±5.14	8.88±6.15 [†]	9.50±5.86	12.00±5.45	64.63±20.64
Only others (n=8)	4.75±1.83 [†]	5.38±2.77 [†]	4.63±2.67 ^{†‡§}	9.25±3.69 [†]	7.63±0.52 [†]	10.88±5.72	64.13±8.66
Education and social (n=41)	11.59±4.89 [§]	8.68±4.75 [‡]	12.07±4.86 [§]	15.51±5.76 ^{‡§}	12.73±5.09 [§]	15.95±5.38 [§]	55.56±14.69
Education and others (n=17)	10.65±4.87 [§]	8.41±5.27 [‡]	11.82±4.19 [§]	14.94±6.03 ^{‡§}	13.94±5.96 [§]	14.59±6.86	58.53±18.67
Social and others (n=1)	14.00 [§]	3.00	8.00	11.00	9.00	9.00	47.00
All (n=51)	14.63±4.87 ^{†‡§†‡‡‡}	12.08±5.84 ^{†‡§†‡‡‡}	13.82±4.72 ^{‡§}	18.94±6.12 ^{†‡§†‡‡‡}	14.94±5.27 ^{‡§††}	16.92±6.41 ^{‡§}	51.18±15.62 ^{†‡§}
p-value (F)	< .001** (6.104)	< .001** (4.867)	< .001** (5.371)	< .001** (5.396)	< .05* (3.058)	.092 (1.849)	< .05* (2.731)
Overburdened exam schedule							
Yes (n=165)	12.38±5.09	10.05±5.60	12.84±4.93	16.47±6.59	13.77±5.75	16.24±6.41	57.31±16.73
No (n=33)	10.00±5.78	7.39±5.01	9.42±4.20	12.48±6.23	10.42±4.09	12.39±5.15	58.85±16.37
p-value (t)	< .05* (2.399)	< .05* (2.534)	< .001** (3.720)	< .05* (3.203)	< .05* (3.183)	< .05* (3.241)	.629 (-.484)
Dissatisfaction with exam criteria							
Yes (n=165)	12.53±5.17	10.05±5.68	12.87±4.86	16.44±6.71	13.75±5.62	16.26±6.44	57.55±17.02
No (n=33)	9.24±4.98	7.42±4.53	9.30±4.50	12.67±5.62	10.52±4.99	12.27±4.84	57.67±14.88
p-value (t)	< .05* (3.359)	< .05* (2.498)	< .001** (3.890)	< .05* (3.019)	< .05* (3.074)	< .05* (3.370)	.970 (-.038)
Dissatisfaction with the teaching method							
Yes (n=152)	12.89±5.11	10.20±5.74	12.95±4.95	16.73±6.54	13.83±5.62	16.10±6.46	56.70±16.78
No (n=46)	9.00±4.69	7.65±4.56	10.04±4.41	12.76±6.30	11.17±5.26	13.93±5.81	60.43±16.02
p-value (t)	< .001** (4.604)	< .05* (2.762)	< .001** (3.572)	< .001** (3.639)	< .05* (2.849)	< .05* (2.036)	.183 (-1.337)

* $p < .05$, ** $p < .001$, t: Independent Samples t-test, F: One-way ANOVA

†, ‡, §, ††, and ††† show the significant difference according to the item in the 1st, 2nd, 3rd, 4th, and 5th rows, respectively.

BMI: body mass index, DASS: Depression Anxiety Stress Scale, PHQ: Patient Health Questionnaire, GAD: Generalized Anxiety Disorder, CD-RISC: Connor-Davidson Resilience Scale

The frequencies of DAS severity levels among dental students were presented in Figure 1. According to the data obtained from females, it was observed that anxiety and stress levels were significantly higher than males ($p < .05$, for both). In addition, PHQ.9, GAD.7, PHQ.15 and CD-RISC values similarly showed significant differences compared to males. Significant differences were also found among places of birth; Participants born in a district/village reported higher resilience than participants born in a town/city ($p < .001$). Those with financial support responsibilities towards their families similarly showed significantly higher levels of anxiety and stress ($p < .05$, for both). The scale scores of participants who consumed alcohol were found to be higher than those who did not consume alcohol, but these scores were statistically significant only in the PHQ.9, GAD.7, and PHQ.15 scales ($p < .05$ for these scales). Among those who stated that they had a family history of psychiatric disease, a significant difference was found in the anxiety level (DASS-21) and the other scales ($p < .05$). In addition, it was observed that participants who reported a history of psychiatric illness both in themselves and their families showed less resilience ($p < .05$). All participants also reported high levels of DAS related to education (Table 1).

When the effect of the grades of all participants on the scores was evaluated, it was found that DAS levels increased towards the fourth-grade, with the highest levels being displayed in the fourth-grade. It was determined that all these levels decreased significantly in the fifth-grade. In addition, when DASS-21 was evaluated as three categories, statistically significant differences were obtained between the DAS severity levels of all participants in the different grades ($p < .001$ among all grades) (Figure 2). Accordingly, the 'extremely severe' level had the highest score in the depression and anxiety categories, and the 'severe' level had the highest score in the stress category.

When the correlations of DASS-21 categories with each other and with other scales were analyzed, it was seen that statistically significant results were obtained. Accordingly, the categories showed a positive correlation both with each other (Figure 3) and with the PHQ.9, GAD.7, and PHQ.15 scales showed a negative correlation with the CD-RISC scale (Figure 4).

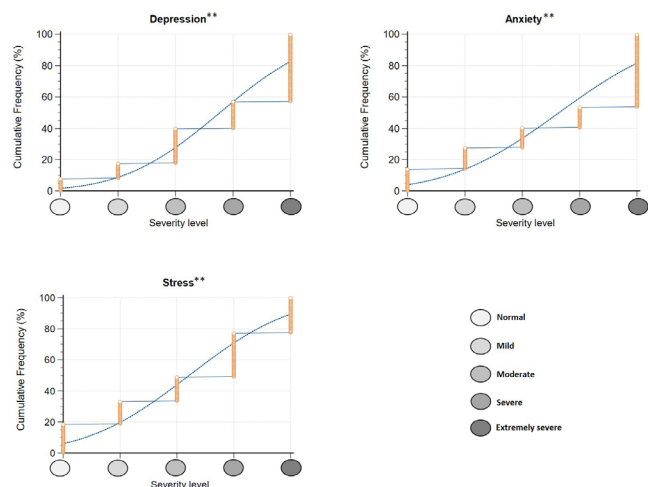


Figure 1. The frequencies of DAS severity levels among dental students. ** $p < .001$ among all levels

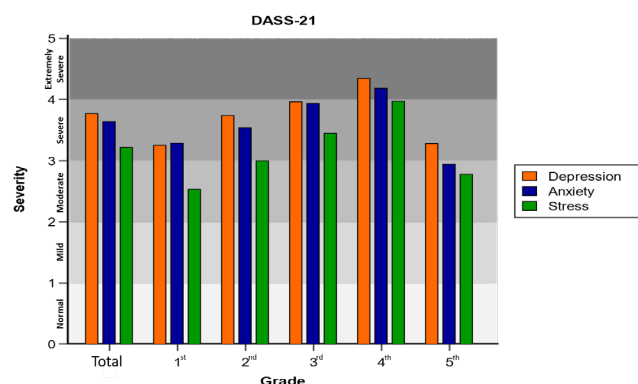


Figure 2. Comparison of participants' DAS levels according to their grades.

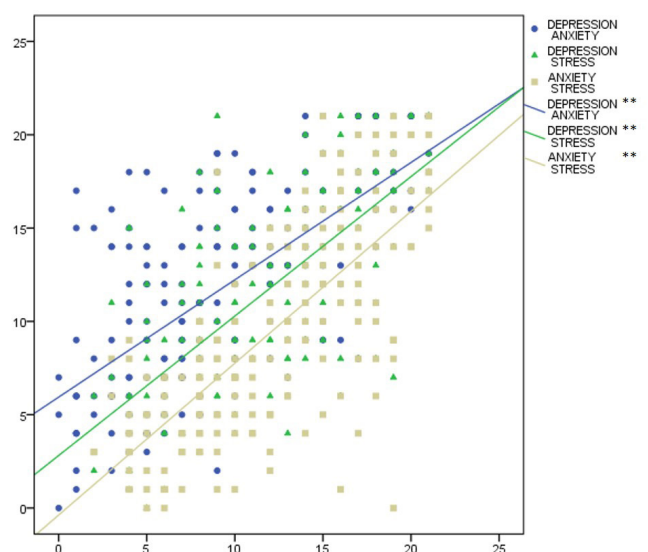


Figure 3. Correlation between DAS values. ** Correlation is significant at the .01 level.

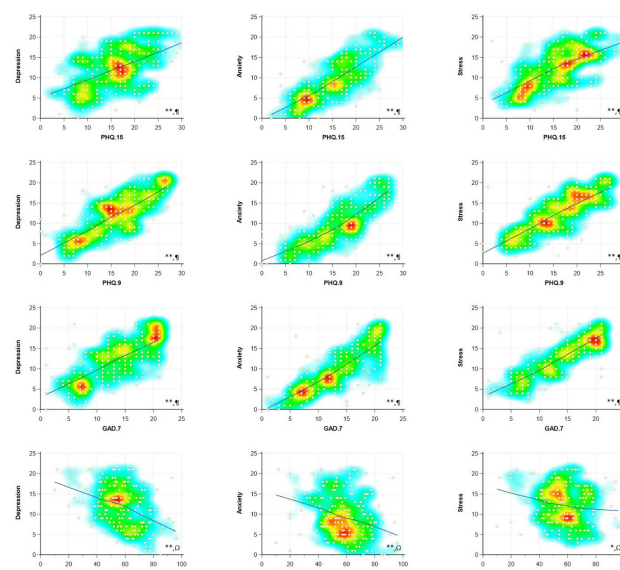


Figure 4. Correlation of DAS levels with the other evaluated scales. * $p < .05$; ** $p < .001$; ¶ rs (+); Ω rs (-)

4. DISCUSSION

Dentistry is one of the most stressful branches among healthcare professionals who work under challenging conditions. Reaching optimum academic knowledge in different topics in a limited period and being able to deal with the oral and dental concerns of patients immediately and efficiently are among the requirements of dental students to be responsible dentists (21). Additionally, dental schools are stressful due to their competitive nature (22). Therefore, the main purpose of this study was to determine the severity and possible factors that may affect DAS levels among dental students.

According to the results of our study, the severity levels of depression and anxiety, ranging from 'severe' to 'extremely severe', among dental students were recorded as 60.1% and 59.6%, respectively. The dental students participating in our study showed a higher prevalence of depression and anxiety than some previously reported rates while showing similar rates to the others. It is assumed that these different rates obtained from different studies are the result of environmental factors such as economic burden due to education and lack of familial support, as well as cultural differences in perception of stress or stressful situations (23). In a study conducted on dentistry students in Turkey, faculty and administration, workload, and students' perceptions of their self-efficacy were identified as the most stress-provoking factors (24). Additionally, certain comorbid medical conditions can also influence DAS scores. A recent study from Turkey reported a high prevalence of bruxism among dentistry students, with students who had bruxism showing higher DAS scores and more sleep-related problems compared to those without bruxism (25). Although the values obtained from the DASS-21 scale did not reach statistical significance, our findings indicated that students who consumed alcohol

had statistically higher depression, anxiety, and somatization scores according to the PHQ (Table 1). The presence of depression and anxiety, which are the most important mental disorders affecting productivity, negatively affects the improvement of health as well as the development of healthcare policies. Therefore, it is certainly expected that the efforts to deal with these disorders and their causes will provide a social benefit that cannot be ignored. Moreover, diagnosis and treatment of these disorders are possible as primary care (26).

Some mental disorders differ in prevalence according to gender and the predominance of disorders such as depression and anxiety in women has been identified (27). The findings of the current study showed that female dental students exhibited significantly higher levels of anxiety and stress than male students (Table 1). Although different findings on this subject were reported in the literature, studies mostly indicate higher levels of anxiety and stress in females (28,29). Consistent with our findings, some studies conducted among dentistry students in Turkey have reported higher scores for depression, anxiety, and stress in female students (24,30). Similar results have also been observed in other countries (31). In addition to the existing literature, our current study demonstrates that male dentistry students exhibit greater psychological resilience and report fewer somatic complaints compared to female students (Table 1). These results could be attributed to the higher likelihood of voicing concerns and emotions in women (32) or to the higher proportion of female students for this study. However, due to the importance of this issue, it is important to track possible environmental risk factors that lead to the gender gap, that is, changes in socioeconomic and cultural situations, and their effects on future symptoms in terms of psychopathologies in gender differences (33).

Psychological resilience refers to an individual's ability to cope with and adapt to adverse conditions. This is crucial for training well-rounded, successful health professionals capable of managing the various challenges they will encounter (34). One of our significant findings regarding psychological resilience is that students raised in urban settings and with a history of psychiatric illness exhibit lower resilience scores than those their counterparts (Table 1). When considering the entire sample, we observed that depression, anxiety, and stress subscale scores were all positively correlated with other measures of psychological well-being (PHQ-9, PHQ-15, and GAD-7), showing high statistical significance. Conversely, a significant negative correlation was found between these subscales and psychological resilience scores. As students' resilience decreases, DAS scores rise significantly (Figure 4). These findings underscore the importance of psychological resilience in relation to DAS levels among dental students.

Lack of financial support increases the likelihood of mental disorders in students (4). Mofatteh (35) stated that lack of financial support, low family income, and poverty are risk factors for DAS in developed and developing countries. Confirming this, in the current study, students who could not

receive any financial support and even had financial support responsibilities towards their families were observed to have high DAS values (Table 1). Such a heavy responsibility added to a difficult educational process is likely to cause mental disorders. Financial management can be a challenge for young students transitioning to independent lifestyles. Therefore, guiding students to achieve work-life balance is important for the quality of their education and mental health (35).

Studies conducted in Malaysia reported that the prevalence of depression and anxiety was higher in students with a family history of psychiatric illness (36,37). Similarly, in this study, higher anxiety values were found in students with a family history of psychiatric diseases (Table 1). McLaughlin et al. (38) suggested that individuals with generalized anxiety disorder have a higher rate of having relatives with anxiety problems than those without. These results were based on data obtained with self-reports. Additionally, the authors emphasize that a positive familial history of anxiety disorder may be a significant environmental etiologic factor for generalized anxiety disorder.

To become a dentist in Turkey, students have to complete a 5-year education. The first three years of this education include preclinical and the last two years include clinical training. Recently, Erdiç et al., in a large sample of dentistry students ($n = 791$), demonstrated that levels of depression, anxiety, and stress increase as students' progress through their academic years (30). Uraz et al. also reported similar findings (24). Accordingly, it was found that the DAS levels obtained from this study increased significantly as the years of education increased, but the highest value was in the fourth-grade and decreased significantly in the senior grade (Figure 2). Similarly, Telang et al. (39) stated that the most stressful period was the transition to clinical training. This is probably because real patients have replaced phantom mannequins used in training. Understanding real patients, each of whom is unique, in the best way possible, competing in the most appropriate diagnosis and treatment, meeting the minimum conditions of the relevant internship in a limited time, and briefly, keeping up with clinical conditions are the burdens of this transition period. We believe that in the final year, self-confidence and coping skills increase due to familiarity with clinical conditions, and therefore, there is a decrease in DAS levels related to clinical education. Another plausible factor that may help explain this situation could be recent policies implemented in our country. As mentioned above, insufficient financial support is associated with DAS scores. Recently, final-year students in medical and dental faculties in Turkey have begun receiving financial support at the level of the minimum wage. The significant reduction in DAS scores observed particularly among final-year students may be related to this financial support.

Finally, dental students exhibited higher DAS values on education-related stressors (Table 1). Similar results were noted for students who found the exam schedule overburdened and expressed dissatisfaction with the exam

criteria and teaching methods. The necessity of theoretical knowledge is indisputable, but the methods can be modified. For example, instead of gathering students in the classroom at certain hours, theoretical lessons can be given with asynchronous remote education and consultancy. In this way, they have the opportunity to listen to lessons efficiently at the time and place most suitable for them. Terlemez et al. (40) also emphasized the importance of interventions that will increase social support in educational programs to protect students from burnout during chronic stress and challenging educational processes. It is essential to transform academic advisory units, generally provided by faculty academic members and assumed to exist in most institutions, into a more active structure that assesses not only students' academic progress but also their social adjustment and stress factors. If needed, it would be appropriate to offer training on advisory skills to faculty academic members within the framework of educational development programs. Additionally, establishing social support units within institutions, ideally coordinated by a psychiatrist, to facilitate referrals when necessary is another crucial aspect. Ensuring the participation of student representatives in relevant academic committees to express their views on education and teaching methods will also make a valuable contribution. To foster a sense of belonging to the institution and provide financial support, involving students (not just for seniors but for all grade levels) in practical applications within the faculty, at levels appropriate to their responsibility, could be an important step. In return, a modest stipend (at least for students with financial need) could be offered. Psychological resilience, in relation to DAS among dentistry students, remains an area insufficiently explored in prior research. Studies indicate that interventions aimed at enhancing resilience among students could be effective (41). We anticipate that future studies will increasingly underscore the importance of this topic. Focusing on individual factors related to this issue, Uraz et al. reported that students who chose dentistry as their top preference in university entrance exams had lower stress levels and fewer health issues (24). This suggests that students who have clear goals and are committed to their chosen field may encounter fewer of these challenges. Other individual factors that might help reduce DAS levels include motivation to fulfill responsibilities, openness to seeking support when faced with stressors, and actively pursuing solutions.

In our study, we were limited to collecting data from dental students studying at a single academic institution in Turkey. Therefore, the results of our study might not be generalized. Future studies involving all institutions are needed to strengthen the validity of our results. Because the current study was a cross-sectional study assessing DAS levels over a specific period, we were not able to show changes over time. Additionally, a causal relationship could not be established. For this purpose, longitudinal studies with larger samples are needed in the future.

5. CONCLUSION

According to the findings of the current study, DAS levels and psychological resilience are too important to be ignored. To minimize these values in dental education, which is known to be challenging, the establishment of guidance within the institution, seminars, and regular monitoring can be considered both to protect the mental health of students as human beings and to indirectly have a positive effect on public health through its impact on the health system. Otherwise, quality in the treatment cannot be expected from a physician whose quality of life has been negatively affected. In this regard, institutions should consider it their duty to seek and offer solutions to this problem and give it at least as much importance as education.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Çanakkale Onsekiz Mart University, Graduate Education Institute (Approval date: 29.05.2023; Number: 2023-YÖNP-0400)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: RA, AT

Design of the study: RA, AT, HB, ŞG

Acquisition of data for the study: RA, EE

Analysis of data for the study: RA

Interpretation of data for the study: RA, ŞG

Drafting the manuscript: RA, HB

Revising it critically for important intellectual content: AT, ŞG, EE

Final approval of the version to be published: RA, AT, HB

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Urodynamic Findings of The Patients with Interstitial Cystitis/Bladder Pain Syndrome: A Single Tertiary Center Results

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Received: April 29, 2024

Accepted: May 15, 2025

ABSTRACT

Objective: Patients with interstitial cystitis/bladder pain syndrome (IC/BPS) exhibit a wide range of symptoms. Urodynamics-pressure flow study (UD-PFS) results may show that these patients have urgency, decreased bladder capacity, and pelvic pain worsening as the volume increases. UD-PFS examinations may contribute to analyzing the pathophysiology of lower urinary tract symptoms (LUTS). This study aimed to evaluate the demographic and clinical findings of IC/BPS patients and the results of UD-PFS examinations.

Methods: The data of 132 IC/BPS patients between 2010 and 2020 were examined retrospectively, and UD-PFS was applied to 63 patients whose LUTS did not benefit from medical treatment. The patients' clinical and demographic data and UD-PFS findings were evaluated separately.

Results: Of the patients who underwent UD-PFS, 7 were men, and 56 were women. The first urine sensation in UD was 74.0 ± 32.22 cc, and the maximum cystometric capacity was 288.4 ± 181.2 cc. Seven patients had a hypo-compliant bladder, and 42 had a normo-compliant bladder. In PFS, Qmax and maximum detrusor pressure in the voiding phase were 18.87 ± 8.21 mL/sec and 33.93 ± 14.78 cmH₂O, respectively. Stress urinary incontinence was detected in 7 patients. For detrusor function, neurogenic detrusor overactivity was detected in 18 patients, and normal UD-PFS was detected in 45 patients, whereas reflexive detrusor was not observed. Cystoscopy revealed Hunner's ulcer in 7 patients.

Conclusion: Urodynamic variables associated with early sensations, first urge, intense desire, and a reduced maximum cystometric capacity were significantly related to the severity of the IC/BPS symptoms. Urodynamic testing is not often a definitive diagnostic method for IC/BPS, although it may assist in the diagnosis process.

Keywords: Urodynamic examination, Pressure Flow Study, Bladder Pain Syndrome, Interstitial Cystitis

1. INTRODUCTION

Interstitial cystitis/bladder pain syndrome (IC/BPS) is a medical condition that is diagnosed based on clinical symptoms. These symptoms include increased frequency of urination, urgency, pain, pressure, or discomfort in the bladder. It is important to note that these symptoms are present without any other underlying pathological findings (1). It is a complex and hard-to-deal health issue with unknown pathology that affects approximately 10% to 15% of the female population (2). Urgency is the most common symptom of IC/BPS with an overactive bladder. It should prompt a referral to a provider with the requisite knowledge and expertise in this disease state.

Certain patients with IC/BPS exhibited distinct urodynamic characteristics, including sensory urgency and instability,

decreased bladder capacity, and pain during bladder filling at low volumes (3). However, there is limited literature regarding the urodynamic characteristics of patients with IC/BPS. In order to understand the pathophysiology of this disease, provide differential diagnosis, and be more precise in diagnosis, urodynamic-cystometric examinations and pressure flow studies (UD-PFS) provide clinical contributions. Although it is not recommended for all patients, it should be applied to selected patients with neurogenic bladder symptoms.

Urodynamics-PFS is not uniformly mandated for all patients with IC/BPS patients. It is particularly beneficial when the diagnosis is ambiguous, symptoms coincide with other

How to cite this article: Şahin MF, Akgül M, Doğan Ç, Malak A, Şeramet S, Sencer Köroğlu M, Orbeği O, Yazıcı CM. Urodynamic Findings of The Patients with Interstitial Cystitis/Bladder Pain Syndrome: A Single Tertiary Center Results. Clin Exp Health Sci 2025; 15: 290-294. <https://doi.org/10.33808/clinexphealthsci.1475656>

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urinary conditions (such as overactive bladder), or when first therapies are ineffective (4). Urodynamics-PFS results may differentiate IC/BPS from disorders like idiopathic overactive bladder. IC/BPS patients often have reduced bladder capacity and compliance and do not demonstrate involuntary bladder contractions, in contrast to those with an overactive bladder. Urodynamics-PFS may provide further insights to corroborate a diagnosis of IC/BPS, particularly in intricate cases, but it should be integrated with clinical data and other diagnostic modalities (5). Urodynamics-PFS can objectively assess bladder function alterations after intravesical therapies; nevertheless, its regular use for this purpose remains unestablished (6).

Based on these data, one can conclude that UD-PFS is not generally required for all patients with IC/BPS; nevertheless, it may serve as a valuable adjunct in complicated or ambiguous situations, especially when symptoms coincide with other urinary diseases. This study evaluated the demographic and clinical findings of IC/BPS patients with the UD-PFS examinations.

2. METHODS

The retrospective analysis included examining data from 132 patients with IC/BPS symptoms who received follow-up care at our clinic from 2010 to 2020. This study was conducted with the agreement of a local ethics committee (Tekirdağ Namık Kemal University, Non-interventional Clinical Trials Ethical Committee), under protocol number 2021.18.01.18. A written informed consent was obtained from participants (for the ones under age 18, a written informed consent was obtained from their parent/legal guardian/next of kin) to participate in the study. All procedures performed in this study followed the institutional and/or national research committee's ethical standards and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

The research excluded patients who did not meet the diagnostic criteria for IC/BPS or had other medical conditions that may account for their symptoms. All patients with sterile urine and with no abnormal physical examination (n:89) had a flexible cystoscopy under local anesthesia to rule out the possible etiology. UD-PFS was applied to 63 IC/BPS patients who did not benefit from the medical treatment of lower urinary tract symptoms (LUTS). The flowchart used to determine the patient group that underwent urodynamic evaluation is shown in Figure 1. Patients with early feeling of urgency, overactive bladder, or low bladder capacity had antimuscarinic therapy (Solifenacin succinate 5 mg daily) before urodynamics. Patients who did not benefit from this 1-month treatment were given an additional 1-month Mirabegron 50 mg combination and were followed up for three more months with dual therapy. Patients who did not benefit from the 3-month combination treatment were classified as treatment failure and were referred to urodynamics.

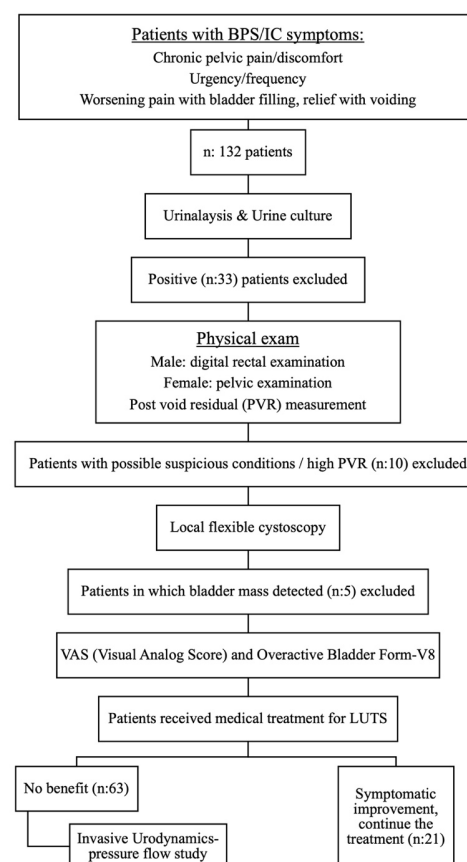


Figure 1. Study flowchart for urodynamics in BPS/IC patient group

The urodynamic investigations were conducted according to the guidelines recommended by the International Continence Society (ICS) (4). Patients were instructed to empty their bladders before the examination, and the first stage was to measure the postvoid residual (PVR) volume using a urethral catheter. Filling cystometry was then performed at 10 mL/min with saline solution or at reduced rates in cases of severe detrusor overactivity (DO) or known limited functional capacity. Following the urodynamic evaluation, a PFS was then performed. Following the pressure-flow study, the PVR was reevaluated with a urethral catheter. An expert in urodynamics evaluated all of the urodynamic traces. The study aimed to investigate the demographic characteristics (age, gender, follow-up period) and clinical data (incontinence, urgency) of the patients, as well as their urodynamic findings based on ICS guidelines (4). Specifically, the following parameters were examined separately: first urinary sensation of the filling bladder (mL), maximum cystometric capacity (mL), maximum detrusor pressures during the filling and voiding phases (cm H₂O), post-voiding residual volumes (mL), and pressure flow study parameters (Q_{max}, mL/sec, and PdetQ_{max}, cm H₂O).

3. RESULTS

A cohort of 63 individuals, including seven male (11.1%) and 56 (88.9%) females, underwent UD-PFS. The mean ages of the participants in the study were found to be 47.6 years, while

the average duration of follow-up was determined to be 49.4 months. Most patients had urgency symptoms (52.4%) and incontinence (66.7%). Seven individuals (7.9%) were found to have Hunner ulcers during cystoscopy, while others (92.1%) had normal bladder mucosal appearance. Table 1 presents the demographic information of the patients.

Table 1. Patient demographics of the BPS patients with UD examinations

Variable	Value
Age (mean $\pm$ SD)	47.6 $\pm$ 15.3
Gender (n, %)	
Male	7 (11.1%)
Female	56 (88.9%)
Follow up period (months) (mean $\pm$ SD)	49.4 $\pm$ 36.2
Body-Mass Index (BMI) (mean $\pm$ SD)	27.6 $\pm$ 3.8
Urgency (n, %)	
Yes	18 (28.6%)
No	45 (71.4%)
Urge Incontinence (n, %)	
Yes	16 (25.4%)
No	47 (74.6%)
Stress-Incontinence (n, %)	
Yes	7 (14.3%)
No	54 (85.7%)

SD: standard deviation, BPS: Bladder Pain Syndrome, BMI: Body Mass Index

The average first urinary feeling of the patients was 74.0 mL. Most individuals with IC/BPS had normal-compliant bladders, whereas 14 patients had a hypercompliant bladder. The average maximal cystometric capacities were 288.4 mL, and the post-voiding residual volumes were 22.57 mL. The detrusor pressure reached a maximum of 23.75 cm H₂O during the filling phase and 48.925 cm H₂O during the voiding phase. The maximum flow rate (Q_{max}) was 18.87 mL/sec. A total of 4 patients, constituting 6.3%, had obstruction during urinating. The patients' UD-PFS results are shown in Table 2.

Table 2. Urodynamic findings of the IC/BPS patients

Variable	Value
First urinary sensation (mL) (mean $\pm$ SD)	74.0 $\pm$ 32.22
First urge sensation (mL) (mean $\pm$ SD)	134.5 $\pm$ 34.56
Strong desire to void (mL) (mean $\pm$ SD)	245.8 $\pm$ 88.98
Maximum Cystometric Capacity (mL) (mean $\pm$ SD)	288.4 $\pm$ 181.2
Maximum Detrusor Pressure at filling (cm H ₂ O) (mean $\pm$ SD)	23.75 $\pm$ 19.15
Maximum Detrusor Pressure at voiding (cm H ₂ O) (mean $\pm$ SD)	48.25 $\pm$ 30.88
Compliance (n, %)	
Hypo-compliant	7 (11.1%)
Normo-compliant	42 (66.7%)
Hyper-compliant	14 (22.2%)
Post-voiding Residual Volumes (mL) (mean $\pm$ SD)	22.57 $\pm$ 18.45
Q _{max} (mL/sec) (mean $\pm$ SD)	18.87 $\pm$ 8.21
Detrusor pressure at maximum flow (cm H ₂ O) (mean $\pm$ SD)	33.93 $\pm$ 14.78

SD: standard deviation, n: 63, Q_{max}: maximum measured rate of flow

Urodynamic overactivity, decreased maximum cystometry capacity, and compliance disorder was detected in 21 of the patients who underwent urodynamics. These patients were treated by changing their medication or switching to intravesical botulinum toxin injection.

4. DISCUSSION

Interstitial cystitis/BPS is clinically diagnosed by the presence of urgency/frequency symptoms and bladder or pelvic discomfort. As clinicians and researchers, we still define, diagnose, and treat IC/BPS. Various studies have sought to investigate the urodynamic findings in patients with IC/BPS, aiming to understand the underlying mechanisms better and improve diagnostic accuracy and treatment strategies for this condition. However, urodynamics' usefulness in IC/PBS has been debated.

The urodynamic evaluation of the IC/BPS patients showed that frequent and small voiding is the predominant symptom. Teichman et al. (8) also found similar results. The lowered threshold for first feeling, initial desire, and awake bladder capacity aligns with bladder hypersensitivity, leading to urgency and frequent urination (8). Teichman et al. (8) found that maximum cystometric capacity (MCC) is lower than 300 mL, which is in correlation with our study. Detrusor overactivity was seen in 18% of the patients in this study, a lower percentage than ours. Individuals with IC/BPS and Hunner ulcers often experience increased frequency of urination and reduced amount of urine voided (9). Urodynamic measurements may not be necessary for diagnosis but reveal a consistent pattern of frequent voiding of tiny volumes in most individuals with interstitial cystitis (10). Interstitial cystitis/BPS should be included in the list of possible diagnoses for patients experiencing urgency, frequency, nocturia, dysuria, or pelvic pain and discomfort. Various clinical situations may need additional considerations and tests. Performing a urinalysis on all patients to rule out pyuria and hematuria and conducting a culture on any patient suspected of a urinary tract infection is crucial.

Urodynamic studies may assess bladder feeling, compliance, and capacity as the bladder fills. Detrusor contractility and uroflow rate may be assessed simultaneously. These examinations are beneficial for diagnosing voiding dysfunction, such as neuropathic bladder and bladder outlet blockage, in both men and women. The significance of urodynamic investigations in individuals with IC is uncertain (11). More randomized controlled studies are needed in this patient group. More recent research has been conducted. More needs to be done to examine the function of urodynamics in IC/PBS. Early research revealed that most patients with IC/PBS had first sensations quickly during UD-PFS (12). In their investigation, Perez-Marrero et al. (13) discovered bladder hypersensitivity (initial feeling <100 mL) in all 50 patients, similar to our study results. Steinkohl et al. (12) conducted a retrospective study of 41 patients with IC/PBS who had undergone UD. They discovered that all patients had "sensory instability," feeling the first urge or discomfort

when their bladder was filled to an average capacity of 74 mL.

The elimination of other pathologies and symptoms of urgency, frequency, pain, pressure, or discomfort during bladder filling is the main emphasis of the current paradigm for diagnosing IC/BPS (14). With an average symptom duration of 5 to 8 years before diagnosis, the absence of objective data in detecting IC/PBS often causes delays in diagnosis (1). On average, patients with IC/BPS have symptoms for five years before being diagnosed (15). The patient with IC/BPS usually suffers symptom progression, where the early-phase illness worsens with time. Some of the research reports that 8% of his adult patients had a history of urinary problems that began in childhood. Our study's relatively low age of disease onset also confirms this data.

Documentation of other significant lower urinary tract anomalies, such as detrusor instability and urge or stress urinary incontinence, is made easier with urodynamic examination. Although many diseases can cause bladder dysfunction (16), possible bladder effects may also occur in IC/BPS patients. Stress urinary incontinence has a substantial impact on both the physical and emotional well-being, as well as the overall quality of life, of affected individuals (17). Urodynamics may provide helpful, objective documentation of the lower urinary tract's reaction to different treatment procedures as IC/BPS research advances.

Studies investigating the relationship between PVR volume and LUTS are crucial for evaluating bladder emptying dynamics. A previous study demonstrated a significant association between the sensation of incomplete bladder emptying and PVR volume in women across all age groups. In contrast, this relationship was observed only in men over 60. The same study reported that PVR volume increased with age in men and that voiding symptoms and urgency were significantly correlated with higher PVR volumes (18). These findings support the role of PVR measurement in assessing IC/BPS patients and underscore the necessity of a comprehensive analysis of the voiding function.

Some of the study's limitations include the absence of a bladder diary to show the severity of IC/BPS, the retrospective and cross-sectional research design that restricts generalizability, and the limited sample size of patients that may lead to selection bias. Furthermore, urodynamic testing is a sensitive test that may be affected by several variables, such as patient stress and anxiety, and individual and environmental factors can also impact the results. Also, the IC/BPS patient group is diverse and has multiple clinical presentations. The fact that this was single-center research from a tertiary referral facility affected our results. The minimal sample size and intrinsic lack of statistical power prevented us from conducting multivariate analysis to investigate success and complication prediction more thoroughly. The literature indicates that even urology clinics with significant patient volumes could publish their findings with modest sample sizes. Other multicentric studies recording national data like ours will enhance national literature. Given this, the study's participant count

contributes substantial scientific data to the national data bank. Finally, one significant limitation might be the need for more assessment of the potential impact of urodynamic data on treatment choices and outcomes.

5. CONCLUSION

According to this research, urodynamic measures linked to early initial feeling, first urge, strong desire, and a lower MCC were substantially correlated with the severity of the symptoms. The urodynamic study is generally not a conclusive diagnostic tool for IC/BPS, but it may aid in the process. Nevertheless, we should be conscious that there are no definite diagnostic criteria for the disease.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study protocol was reviewed and approved by Tekirdağ Namık Kemal University, Non-interventional Clinical Trials Ethical Committee (Approval date: 26.01.2021; Number: 2021.18.01.18)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: MFŞ, MA, AM

Design of the study: MFŞ, MA

Acquisition of data for the study: MA, AM

Analysis of data for the study: AM, SŞ, MFŞ

Interpretation of data for the study: ÇD, MFŞ

Drafting the manuscript: SŞ, OÖ

Revising it critically for important intellectual content: MSK, OÖ

Final approval of the version to be published: MFŞ, MA, AM, ÇD, SŞ, OÖ, MSK, CMY

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Mediating Role of Mental Help-Seeking Attitude in the Effect of Mental Health Literacy on Mental Treatment: A Structural Equation Model

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Received: July 03, 2024

Accepted: May 23 2025

ABSTRACT

Objective: This study aims to display the mediating role of mental help-seeking attitude in the effect of mental health literacy (MHL) on mental treatment

Methods: This study conducted through a structural equation model. This research was carried out in line with the descriptive survey and relational screening model to determine the relationship between the variables. In this scope, the predictive relationship between MHL's effect on mental treatment and the mental help-seeking attitude was examined through a structural equation model. Data were obtained from 391 individuals through the Personal Information Form, the Mental Health Literacy Scale, and the Scale of Attitudes Toward Seeking Professional Psychological Help-Short Form.

Results: It was observed that MHL affected mental help-seeking attitude. It was determined that the mental help-seeking attitude does not affect the mental treatment. While the resource-oriented sub-dimension of the Mental Health Literacy Scale had a statistically significant effect on mental treatment behavior, this effect was not observed in the knowledge-oriented and belief-oriented sub-dimensions. Mental help-seeking attitude does not play a mediating role in the effect of MHL on mental treatment.

Conclusions: It was found that the help-seeking attitude develops in line with the MHL level increase. However, an increase in the level of MHL alone does not affect mental treatment. This indicates that other factors might also impact the mental treatment towards psychological problems.

Keywords: Mental health literacy, mental help-seeking attitude, mental treatment, structural equation model

1. INTRODUCTION

Mental disorders constitute a significant burden for all countries, with consequences in health, social, human rights and economic fields (1). Nearly 792 million (10.7%) people worldwide suffer from mental disorders (2). This figure is estimated to increase considering the adverse effects of traumatic experiences on mental health, such as pandemics or environments of conflict (3,4). In this case, early diagnosis of mental disorders and good management of the treatment process is becoming increasingly important. The importance of protecting mental health has also been recognized worldwide, and it has been stated in one of the nine sub-goals of Goal Three: Good Health and Well-being covered under the United Nations (UN) Sustainable Development Goals (5) that mental health should be improved. UN member states should conduct activities on society's mental

health to improve it. One of these efforts is to increase MHL. Healthcare professionals, especially those providing public health services, can do much to increase MHL (6).

The concept of MHL refers to the knowledge, abilities and beliefs related to the protection of mental health, recognition, and management of mental disorders (7-10). Various factors affect MHL, and one of these is its level. Increasing MHL is important in many aspects. For instance, MHL was determined to impact all health-promoting behaviors. Individuals with high levels of MHL tend to practice health-promoting behaviors more (11). It was reported that in line with the enhancement of MHL, social and health-related outputs would also improve, and thus, the burden of disease would decrease (7). Moreover, it was also determined that

How to cite this article: Albayrak S, Sönmez S, Öke Kaya P, Aşık E. Mediating Role of Mental Help-Seeking Attitude in the Effect of Mental Health Literacy on Mental Treatment: A Structural Equation Model. Clin Exp Health Sci 2025; 15: 295-301. <https://doi.org/10.33808/clinexphealthsci.1510141>

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increasing MHL improved university students' self-efficacy (12). However, MHL level is not at a sufficient level in general (6,13-15). It was determined that the MHL of Australian society is mostly satisfactory. Yet, there are deficiencies in recognizing and seeking professional treatment for some disorders, such as social phobia (16). Women's MHL level is higher than men's (6,15,17-19). MHL level decreases with increasing age (17) and increases with increasing educational level (19).

Health literacy levels might differ among those studying or working in health. MHL levels of the students studying health (pharmacy, medicine, and nursing) were determined to be alike (20). Similarly, it was found that the MHL levels of the doctors and nurses working in psychiatry clinics were also similar (21). However, it was established that the nurses who don't work on mental disorders do not have sufficient levels MHL (22). It was also noted that MHL could be affected by culture (21) and that despite numerous similarities, there are also differences in the MHL levels of the nursing students from different cultures (23). Among medical students, those who have experienced mental illness in their family, close friends or themselves show higher levels of MHL than those who have no experience of mental illness (18), and bisexuals and those with a history of mental disorder show higher levels of MHL than others (15).

The concept of MHL covers beneficial information for the individual's mental health, ways to prevent mental illnesses, recognition of mental disorders, effective methods to cope with mild-moderate problems individually, and psychological first aid skills necessary for the person and to help others (8,24). Moreover, MHL also means being active in the fields of protecting mental health, understanding mental problems and their treatments, decreasing stigmatization, and increasing mental help-seeking (25). Thereby, increasing MHL might help reduce stigmatization and early access to treatment (6,9,14).

The mental help-seeking attitude discussed under the subject of improving mental health refers to an individual's tendency to receive mental treatment or not (26). Besides the mental help-seeking attitude, other factors also affect mental treatment. Some studies carried out among high school and university students revealed that improving MHL increases mental treatment (7,27). Cultural features might also affect mental treatment. It might be asserted that the collectivistic culture plays an essential role in terms of mental treatment, and especially both stigmatization by society and self-stigmatizations prevent receiving mental treatment (6,28).

The number of studies in Turkey examining the relationship between MHL and mental help-seeking is rather limited. It is important to disclose the relationship between mental literacy and the mental help-seeking attitude, which is affected by many factors, such as culture, in the Turkish population.

This research aims to reveal the mediating role of the mental help-seeking attitude in the effect of MHL on mental treatment through the structural equation model (SEM). As a sub-objective, the research also aims to examine the effect of MHL on mental help-seeking attitude and the impact of mental help-seeking attitude on mental treatment.

Research hypotheses

In line with these objectives, the following hypotheses will be tested (Figure 1):

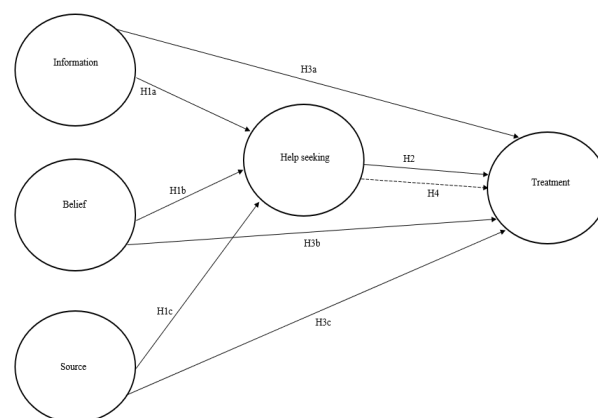


Figure 1. Research model.

H1: a) Knowledge, b) beliefs, and c) resource-oriented sub-dimensions of MHL affect the mental help-seeking attitude.

H2: Mental help-seeking attitude affects mental treatment.

H3: a) Knowledge, b) beliefs, and c) resource-oriented sub-dimensions of MHL affect the mental treatment.

H4: Mental help-seeking attitude has a mediating role in the effect of MHL on mental treatment.

2. METHODS

Permission granted by Kırıkkale University Ethics Committee (Approval date:10.03.20233 and Number: 2022.03.06) was obtained to verify the study's compliance with ethical considerations. The aim of the research was explained to the participants before answering the data collection tools. Volunteers filled out the data collection tools.

2.1. Design

This research was carried out in line with the descriptive survey and relational screening model to determine the relationship between the variables. The relational screening model helps to determine whether there is a relationship between variables and the direction of the relationship (29). Accordingly, the predictive relationship between MHL's effect on mental treatment and the mental help-seeking attitude was examined through a SEM. SEM is a statistical method testing the reciprocal and causal relationship between the

observed and latent variables on a single model (30). Data were collected between March and July 2022.

2.2. Participants

Data were collected through the convenience sampling method, a type of non-probability sampling method. In the scope of research, a survey was conducted with 408 individuals and 17 of the surveys were not included in the data set as they were not considered suitable for analysis. Thus, 391 surveys were included in the analysis.

2.3. Data collection

Data were obtained through the Personal Information Form, Mental Health Literacy Scale and Scale of Attitudes Toward Seeking Psychological Help-Short Form (ASPH-SF).

2.3.1. Personal Information Form

Personal Information Form covered questions aiming to identify the demographic characteristics of the participants, such as age, gender, and educational background. Besides, this part also covers questions (eight questions) on whether the participants or their close relatives experienced mental health problems and received professional mental health services.

2.3.2. Mental Health Literacy Scale

Mental Health Literacy Scale was developed by Jung et al. (31) and adapted to Turkish by Göktaş et al. (32). The scale consists of 22 items and has three dimensions: Knowledge-Oriented (ten questions), Belief-Oriented (eight questions), and Resource-Oriented (four questions). Total score that can be obtained on the scale is 0-22. An increase in the scores points out to higher levels of MHL. The total Cronbach alpha coefficient of the scale was found as .71 (31,32).

Scale of Attitudes Toward Seeking Psychological Help-Short Form (ASPH-SF)

ASPH-SF was developed by Türküm (33). The scale consists of 18 items. Questions are of five-point Likert type, and six questions are reversely scored. Evaluation is based on the total score, and the score that can be obtained on the scale is 18-90. In line with the increase in the total score on the scale, a positive attitude towards mental help-seeking also develops. Cronbach alpha coefficient for the whole scale is .88 (33).

2.4. Data Analysis

Data were analyzed in SPSS 22.0 and AMOS 21.0 programs. Descriptive statistics (frequency, percentage) and covariance-based SEM was used in the analyses. As in this research, SEM is frequently preferred in testing the mediating roles and has some advantages. Unlike regression analysis, in SEM, a dependent variable in the model might be an independent variable in another aspect. Moreover, SEM tests all these effects simultaneously. Actually, SEM is a two-level

multivariate analysis. Information on the structure of the scales is given at the first level, while information on the relationship between the variables is provided at the second level (34).

2.5. Research Model

In the research, while testing the mediating effect in SEM, sub-dimensions (knowledge-oriented, belief-oriented and resource-oriented) of the Mental Health Literacy Scale were taken as independent variables, ASPH-SF as the mediating variable and mental treatment as the dependent variable. In order to mention a mediating effect in SEM, the independent variable is required to affect the mediating variable, and the mediating variable affects the dependent variable. If the independent variable can affect the dependent variable without the mediating variable, and this effect is maintained when the mediating variable is included, then partial mediation is in question; if the independent variable cannot affect the dependent variable without the mediating variable and an effect is manifested when the mediating variable is included, then full mediation is in question (35). Before interpreting the significance of SEM's coefficients, the model goodness of fit values should meet the necessary conditions for the adequacy of the model. The model goodness of fit values obtained are expected to be $\chi^2 / df < 5$; CFI, NFI, IFI, TLI, GFI $> .90$ RMSEA, SRMR $< .80$ (35).

3. RESULTS

According to the research data, 60.9% of the participants were male, and 39.1% were female. In terms of their educational backgrounds, more than half of the participants had bachelor's degrees (52.2%). 36.1% of the participants were in the 18-28 age range, while 27.7% were in 29-39, 27.7% were in 40-50, and 20.5% in 51 and above. A great part of the participants (72.6%) stated not having experienced a mental problem they could not solve independently. 38.1% of the participants stated that in case of mental problems, they could share this with their parents, while 24.6% expressed that they could share this with their close friends. 69.8% of the participants declared that they had not received support from a mental health specialist until that day. While 58.1% of the participants expressed that their family members had not received support from a mental health specialist, 57.3% stated that the people in their close social spheres had received support from a mental health specialist (Table 1).

Figure 2 displays the SEM formed for testing the research hypotheses. The model goodness of fit values obtained from the SEM formed are as follows: $\chi^2 / df = 1.763$; CFI = .911; TLI = .903; IFI = .911; RMSEA = .044; SRMR = .052. After deciding that the model was sufficient with these values, the structure of the scales in the model was evaluated at the first level, and the items with factor loadings below .30 were removed from the model. Accordingly, two items in the Mental Health Literacy Scale and three items in ASPH-SF were not included in the scale.

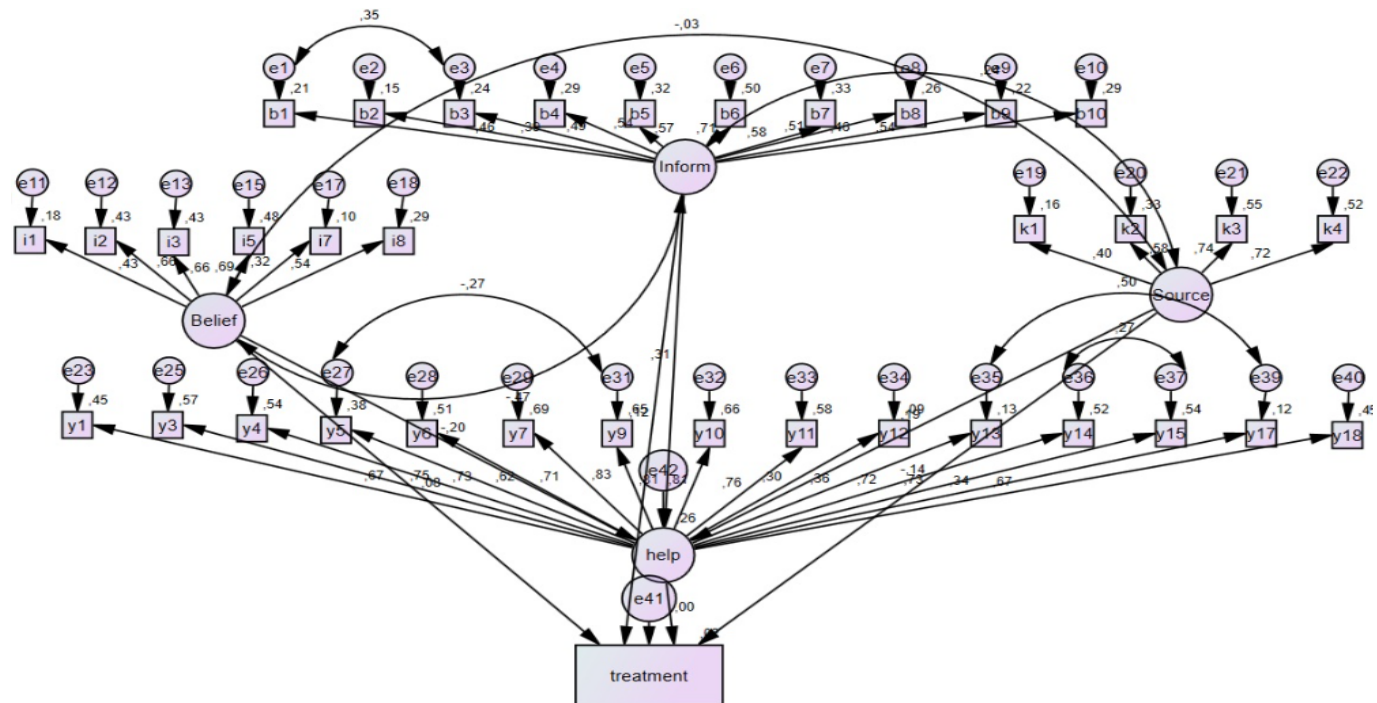


Figure 2. SEM results of research model.

Table 1. Descriptive statistics of sample group (n = 391)

Sex	n	%
Female	238	60.9
Male	153	39.1
Educational level		
Primary School-Middle School	18	4.6
High school	111	28.4
University	204	52.2
Master's degree and above	58	14.8
Age		
18-28	141	36.1
29-39	85	27.7
40-50	85	27.7
51 years and older	80	20.5
State of having mental problems		
Yes	107	27.4
No	284	72.6
Preferred people to sharing mental problems		
Parents	149	38.1
Children	16	4.1
Partner	60	15.3
Health worker (I know)	59	15.1
Close friend	96	24.6
I don't talk to anyone	11	2.8
Status of getting support from a mental health specialist		
Yes	118	30.2
No	273	69.8
Status of family members to get support from a mental health specialist		
Yes	163	41.7
No	228	58.3
Status of receiving support from a mental health specialist in the close social environment		
Yes	224	57.3
No	167	42.7

Table 2 displays the coefficients and significance levels obtained in SEM, used for the analyses. This part presents the results concerning the effects of the sub-dimensions of Mental Health Literacy Scale on the mental help-seeking attitude and the effects of the sub-dimensions of Mental Health Literacy Scale and mental help-seeking attitude on the mental treatment. Accordingly, it was observed that all sub-dimensions of MHL affect the mental help-seeking attitude ($p < .05$). H1a, H1b and H1c hypotheses were agreed on. It was determined that the mental help-seeking attitude did not affect the mental treatment ($p > .05$), and thus, the H2 hypothesis was rejected. Examining the effect of the sub-dimensions of MHL on mental treatment, it was detected that only the resource-oriented sub-dimension had a significant effect ($p < .05$), while the knowledge-oriented and belief-oriented sub-dimensions did not have a significant impact ($p > .05$). Accordingly, H3a and H3b were rejected, while H3c was agreed on.

Table 2. Path coefficients of SEM results

Dependent variable	Path	Independent variable	B Coefficient	Std. B	Standard error	t	p value
Help seeking	<---	Belief	-.252	-.197	.089	-2.824	.005
Help seeking	<---	Source	1.191	.193	.390	3.050	.002
Help seeking	<---	Information	.562	.308	.138	4.066	<.001
Treatment	<---	Help seeking	.003	.004	.044	.060	.952
Treatment	<---	Belief	.069	.077	.065	1.066	.286
Treatment	<---	Source	-.589	-.136	.285	-2.069	.039
Treatment	<---	Information	.151	.121	.097	1.594	.111

Key: SEM: Structural Equation Modelling, Std. B: Standardized B coefficient, Significant p value assessed at .05.

The presence of an indirect effect cannot be indicated since the ASPH-SF scale, which serves as the mediating factor in the model, does not affect the dependent variable, mental treatment. Moreover, Table 3 displays the coefficients and significance levels obtained concerning the mediating effect. Mental help-seeking attitude does not have a mediating role in the effect of MHL on mental treatment ($p > .05$). Accordingly, H4 hypothesis was rejected.

Table 3. Mediation results*

Variables	Total Effect			Direct Effect			Indirect Effect		
	Std. B	C. I.	p value	Std. B	C. I.	p value	Std. B	C. I.	p value
Help seeking	.004	-.122 .087	.908	-	-	-	-	-	-
Belief	.076	-.077 .193	.319	.077	-.079 .192	.290	-.001	-.015 .028	.940
Source	-.135	-.244 .256	.064	-.136	-.242 -.004	.085	.001	-.021 .016	.968
Information	.122	-.010 -.022	.115	.121	-.010 .283	.127	.001	-.040 .026	.888

Std. B: Standardized B coefficient; C. I.: Confidence intervals, *Dependent variable: Help Seeking Behavior (treatment)

4. DISCUSSION

This research addressed the mediating role of the mental help-seeking attitude in the effect of the MHL of the participants on their mental treatment. This research revealed that all sub-dimensions MHL affect the mental help-seeking attitude (H1 was agreed on). It was pointed out in research that MHL has both direct and indirect effects on mental help-seeking attitudes (9). In some study carried out in Germany among unemployed people, it was found that the Mental Health Literacy Scale as a whole has a significant positive relationship with the intention of mental help-seeking (37). People with low levels of MHL delay seeking mental help as they do not recognize the symptoms of the illness (7,17). It is known that especially the young tend to be late to seek mental help, and the reason for this is explained with the lack of knowledge among young people (7). However, MHL is an integral part of the early recognition of the symptoms and timely intervention for treating these disorders (14).

In some study, it was pointed out that despite high levels of mental help-seeking attitude, an individual might not equally tend to seek mental treatment in case of mental problems and thus, mental help-seeking attitude and mental treatment should be addressed separately (38). This research also revealed that MHL affects mental help-seeking attitude, but the mental help-seeking attitude does not affect mental treatment (H2 hypothesis was rejected). In future studies, it might be important to address the reasons why a person has the desire to seek mental treatment but does not receive it.

It was observed in this research that the resource-oriented sub-dimension of MHL affected the mental treatment, while the knowledge and belief-oriented sub-dimensions

had no effect (H3a and H3b were rejected, but H3c were agreed on). Those with low levels of MHL seek help at a later stage due to the fear of stigmatization, and this leads to progression of the disease and delayed treatment (7). While some research revealed no significant relationship between MHL and mental treatment (15), another study found a significantly positive relationship between MHL and mental treatment (37). This difference might be related to the scales measuring MHL. In the resource-oriented sub-dimension of the MHL scale used in this research, there are four questions evaluating the knowledge of where to apply when a person suffers from an illness (32). According to the results of this research, improving even this one aspect of MHL would enhance mental treatment. However, increasing knowledge and belief-oriented sub-dimensions might effectively increase knowledge of the disease and reduce stigmatizing attitudes. Studies indicate that decreasing stigmatizing attitudes enhances the desire to seek mental help and mental treatment (9,38). Stigmatizing attitudes are still an essential problem in terms of mental health. There are many studies on this subject (7,14,20,39,40). The results clearly show that the MHL of society, healthcare professionals and students to become healthcare professionals in the future should be increased to improve mental treatment.

5. CONCLUSION

MHL is essential for the early recognition of the symptoms and timely treatment of mental health disorders. This research established that MHL affects the mental help-seeking attitude, but the mental help-seeking attitude does not affect the mental treatment. Moreover, it was determined that the mental help-seeking attitude does not have a mediating role in the effect of MHL on mental treatment. On the other hand, the high level of resource-oriented (knowing where to receive mental help) sub-dimension of MHL positively affects mental treatment. It is crucial that research predicting the effective factors other than MHL and mental help-seeking attitude are conducted to determine the impediments to mental treatment. Thus, it can contribute to the improvement of mental health.

There were a few limitations in the research. The first of these may be the collection of data by the convenience sampling method, a type of non-probability sampling method. Although it was not a direct priority for the research, it would be better to use one of the probabilistic sampling methods. Researchers are advised to consider this issue. Another limitation is that the data was collected both online and face-to-face. We thought that this issue would not affect the research results. However, collecting data by face-to-face interview method could have helped the participants to be more careful.

Acknowledgements: We would like to thank all the participants for answering the questions sincerely.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Kırıkkale University, Noninvasive Clinic Ethics Committee (Approval date:10.03.20233 and Number: 2022.03.06)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: SA, EA

Design of the study: SS

Acquisition of data for the study: SA, SS, PÖK, EA

Analysis of data for the study: SS, PÖK

Interpretation of data for the study: SA, SS, PÖK, EA

Drafting the manuscript: SA, SS

Revising it critically for important intellectual content: SA

Final approval of the version to be published: SA, SS, PÖK, EA

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A Simple and Practical Method to Determine Amount of Rotation in Femoral Midshaft Derotational Osteotomy: Geometric Arc and Chord Formulas

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Received: May 7, 2024

Accepted: March 4, 2025

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ABSTRACT

Objective: Femoral derotational osteotomy is a surgical intervention that involves the derotation of the femur at certain sites to achieve the desired femoral anteversion angle. However, current intraoperative techniques measuring the degree of correction and adequately performing it is still insufficient to achieve the desired femoral anteversion angle. The aim of this study is to investigate whether the geometric arc and chord formulas are applicable to achieve the target femoral anteversion angle in mid-shaft femoral derotational osteotomy.

Methods: CT images of 20 femurs with excessive anteversion or retroversion deformities were retrospectively selected, and three-dimensional (3D) geometric models were obtained. 15° of femoral anteversion were chosen as the target angle. Geometric arc and chord formulas were separately applied on axial CT images at the mid-point of the femurs to calculate the degree of correction. Then, virtual mid-shaft femoral derotational osteotomy was performed, then post-op femoral anteversion angle was measured.

Results: There was no statistical difference between the postoperative measured anteversion angles and the targeted angle in all examples. The arc and the chord lengths were not statistically different which indicates both formulas can be used to estimate the degree of correction.

Conclusions: The arc and chord formulas provided an accurate target femoral anteversion angle. Using one of these formulas preoperatively can facilitate to achieve desired femoral anteversion angle without having the intraoperative measurements nor using any special equipment.

Keywords: Derotational osteotomy, femoral anteversion, geometric arc formula, femoral midshaft osteotomy

1. INTRODUCTION

Femoral version refers to the angle between the axis of the femoral neck and the axis of the femoral condyles in the transverse plane. Studies have shown that the normal femoral version in adults is typically in the range of 10-15 degrees of anteversion [1-3]. However, abnormal femoral versions can occur due to various reasons such as idiopathic factors, cerebral palsy (CP), or post-traumatic conditions like slipped capital femoral epiphysis (SCFE) [4, 5]. Untreated femoral versions can lead to several problems including labrum pathologies, gait disorders, coxarthrosis, hip and knee pain, and patellofemoral disorders [6-8]

Femoral derotation osteotomy needs to be performed to address femoral version issues which can be applied at proximal, diaphyseal and distal femur. Among these

techniques, midshaft femoral derotational osteotomy is often preferred due to its less invasive nature, stable fixation, and lower risk of complications [9, 10]. During the femoral derotation surgery, the distal femur fragment is rotated from the osteotomy site and fixed to the proximal part to achieve the desired femoral version angle. However, accurately determining the required amount of rotation to reach the target version angle is challenging, and it may not always be possible to achieve the precise femoral version angle.

Pre-operative calculation of the distal femur fragment rotation using the geometric arc and chord formulas on axial CT image can be useful to overcome this challenge. This method can also allow for easy access to the target femoral version angle without the need for additional measurements

How to cite this article: Ilgaroglu S, Ismailoglu AV, Shammadli Z,. A Simple and Practical Method to Determine Amount of Rotation in Femoral Midshaft Derotational Osteotomy: Geometric Arc and Chord Formulas. Clin Exp Health Sci 2025; 15: 302-307. <https://doi.org/10.33808/clinexphealthsci.1479692>

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during surgery which reduces the duration of the operation and minimizes the use of fluoroscopy. However, the reliability and validity of this approach are yet to be established. Therefore, this study aimed to investigate the applicability and reliability of the geometric arc and chord formulas to achieve the target femoral anteversion angle for midshaft femoral derotational osteotomy.

2. MATERIALS AND METHODS

2.1. Sample Size and Image Acquisition

Lower extremity computed tomographic (CT) angiography scans retrospectively obtained between October 2021 and January 2020 from 50 randomly selected patients were examined along with their clinical records. All collected CT images of femurs were included except the femurs whose femoral anteversion angle was between 10° and 15° . Patients with evidence of lower-extremity trauma, acetabular dysplasia, avascular necrosis of the femoral head, and femoral or pelvic implants were excluded.

A total of 20 femurs with excessive anteversion or retroversion deformities were selected from 20 patients (14 male and 6 female; 12 right and 8 left) with a mean age of 49 ± 16 (range: 20-76 years). Group 1 included 10 femurs with excessive anteversion deformity ranging between 18.2° and 46° and Group 2 included 10 femurs with retroversion deformity ranging between -9.7° and 3.7° determined by evaluating three-dimensional (3D) femur models. All scans were fully anonymized, and the study protocol was approved by University Research Ethics Board (No. 2019-17/27). DICOM format CT data of each CT scan were imported to Mimics software (version 21.0, Materialize, Leuven, Belgium) to reconstruct a three-dimensional geometric femur model and to perform measurements.

The CT scans were obtained with a Somatom Force device (Siemens Healthineers Global, Germany) using standard techniques at 100 kVp and 256 mAs, with a slice thickness of 0.5–0.9 mm and a resolution of 512×512 pixels (voxels approximately $0.7 \times 0.7 \times 0.5$ mm³).

2.2. Construction of Coordinate System

Establishing the femur-customized anatomical coordinate system was important for the validity of the measurements. Hence, after the reconstruction of the geometric femur model, an idealized coordinate system was reconstructed using specific femur bony landmarks to normalize the femur orientation. Two planes perpendicular to each other, representing the global Cartesian X-Y and X-Z planes were created. The X-Y plane (femur coronal plane) was created contacting the posterior-most prominent aspects of the lateral and medial femoral condyles and the greater trochanter, and the X-Z plane (femur horizontal plane) was created contacting the most distal aspects of the medial and lateral femoral condyles (Figure 1). The Y-Z plane (femur

sagittal plane) was created perpendicular to both X-Y and X-Z planes.

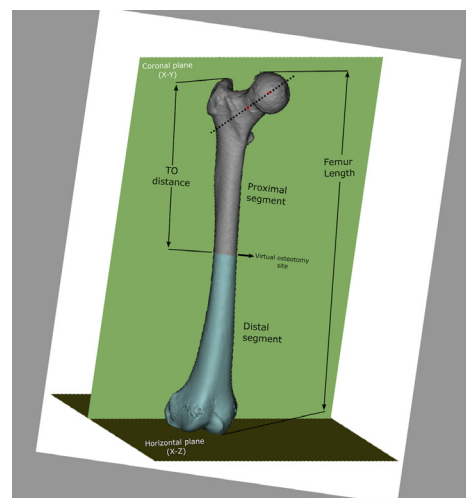


Figure 1. Virtually created 3D femur model and calculated TO distance

2.3. Measurement of Pre-op and Post-op Femoral Anteversion Angles

The reconstructed femur model was imported into the 3-Matic software (version 13.0, Materialise N.V., Belgium) in STL format, which geometry was triangle mesh to conclude the center of the femoral head and the neck more precisely and to avoid observer error. The surface of the head and the neck were marked using “Wave Bruch Mark” in the software and extracted from the reconstructed femur. Then, the point cloud model of the surface of the femoral head and the neck were exported as “.txt” extensions. A best-fit sphere that can fully contain the entire femoral head and just tangent to the femoral neck was defined using a least-squared approach on the point cloud model, and the center of the sphere was indicated on the 3D femur model. The center of the femoral neck was calculated via the center of gravity equation using the point cloud model and the center of the femoral neck was indicated on the 3D femur model.

The femoral neck axis was defined on a superior view of the 3D femur model as a line passing through the center of the femoral head and the center of the femoral neck. The pre-op femoral anteversion angle was measured as the angle formed by the femoral neck axis and a horizontal line (Figure 2). After measuring the pre-op femoral anteversion angle, the virtual mid-shaft femoral derotational osteotomy was performed. Then, a new femur-customized anatomical coordinate system was constructed for the virtually operated femur model, and the post-op femoral anteversion angle was measured in the same way as the measurement of pre-op femoral anteversion angle.

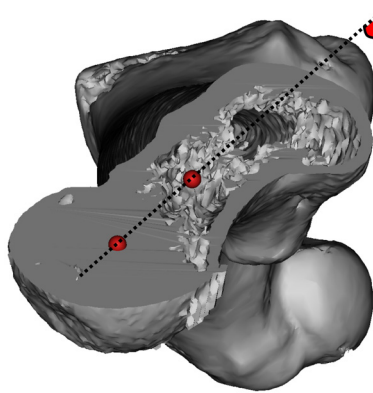


Figure 2. Determination of femoral anteversion

2.4. The Virtual Mid-Shaft Femoral Derotational Osteotomy

All data were measured in the MPR plane and then measurements were applied on the 3D femur model to perform the virtual mid-shaft femoral derotational osteotomy. The femur length was measured on the coronal CT image. After measuring the femur length, the mid-point of the femur was decided as the site of the mid-shaft femoral derotational osteotomy. During surgery, estimating the correct location of the mid-point of the femur is important to decide the level of the mid-shaft femoral derotational osteotomy. Therefore, the distance between the tip of the greater trochanter and the osteotomy site (TO-distance) was noted. The femur length and the TO-distance were also indicated on the 3D femur model in the X-Y plane (Figure 1).

The axial CT image at the virtual osteotomy site was viewed. The center of the medullary cavity was obtained by drawing an inner best-fit circle by indicating the lateral and medial boundaries of the medullary cavity on the axial CT image. An outer circle originated from the center of the medullary cavity and tangent to the lateral cortex of the femur was drawn (Figure 3). To perform the virtual osteotomy, the 3D femur was transversely cut using 3D Tools of Mimics software at the level of the osteotomy, and the femur separated to the proximal and the distal segments (Figure 1). The CT axial image of the osteotomy site was then embedded on the transversely cut surface of the 3D femur distal segment to confirm the correct location of the center of the medullary cavity and the state of the tangency of the outer circle (Figure 3).

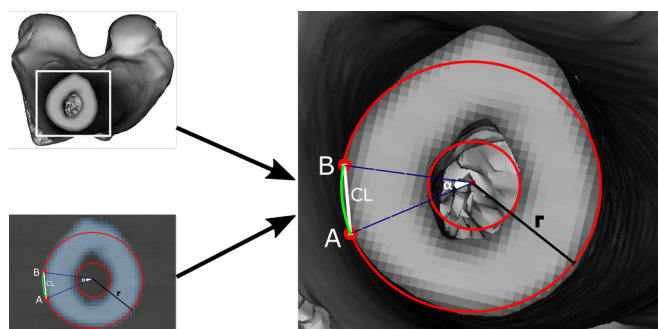


Figure 3 Finding the ideal circumference tangent to the lateral cortex using the best-fit circle and determining the guide points for the cortical distance (A-B distances)

The radius of the outer circle was noted (r) which was used for the geometric arc and chord formulas. The angle of 15° was chosen as the target femoral anteversion angle. In Group 1, the correction angle (α) was measured by subtracting the 15° from the pre-op femoral anteversion angle, while in Group 2, the correction angle (α) was measured by subtracting the pre-op femoral anteversion angle from the 15° . Arc is a segment of a curve distance between two points, and chord is a segment of a line joining two points on a curve. The arc length was calculated by using the geometric arc formula $[2\pi r(\alpha/360)]$ and the chord length by using the geometric chord formula $[2r\sin(\alpha/2)]$. The arc and the chord lengths, within the margins of the correction angle, indicated on the lateral cortex of the distal segment of the 3D femur with two points (A, B) (Figure 3). The distal segments of the Group 1 femurs were externally rotated about the center of the medullary cavity in the transverse plane from point A to point B to correct excessive femoral anteversion deformity and Group 2 femurs were internally rotated from point B to point A to correct femoral retroversion deformity (Figure 4). The distal and the proximal segments were then united to measure the post-op femoral anteversion angle.

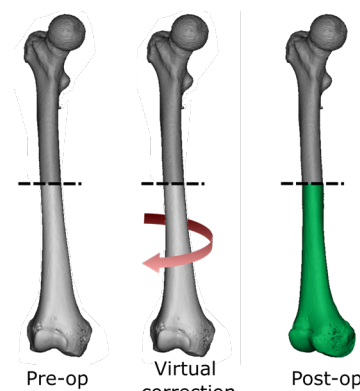


Figure 4. Implementation of virtual femoral derotation

2.5. Statistical Analysis

SPSS software (SPSS Inc, Chicago, IL) was used for statistical analyses. The variables were investigated using virtual and analytical methods to determine whether they were normally distributed. Descriptive statistics were provided as mean $\pm$ standard deviation. One sample t -test was used to compare the target femoral anteversion angle and the post-op femoral anteversion angle. Student's t -test was used to assess differences between right and left femurs. The differences between the arc length and the chord length were assessed with a paired t -test. A p -value of less than .05 was considered to show a statistically significant result.

3. RESULTS

The femur length and the TO-distance were measured to establish the location of the osteotomy site during surgery (Table 1). The calculated arc length and the chord length were presented in Table 2. The mean $\pm$ SD of the outer circle

radius (r) was 15 ± 1.5 (min 11.8, max 17.4). After performing the virtual rotation of the distal segment, post-op femoral anteversion angle was obtained and it was not statistically different from the target angle of 15° (Table 3). The mean $\pm$ SD difference between the post-op femoral anteversion angle and the target angle in Group 1 and Group 2 were 0.5 ± 1 , 0.7 ± 1.4 , respectively.

Table 1. Measured lengths to locate osteotomy site

Measurements	Mean (mm)	Standard Deviation $\pm$ (mm)	Minimum (mm)	Maximum (mm)
Femur length	439.2	37.6	363.1	507.7
TO-distance	204.3	19.5	170.7	241.6

TO-distance: the distance between the tip of the greater trochanter and the mid-shaft osteotomy site in the coronal plane

Table 2. Measured lengths to determine the amount of distal femoral segment rotation to achieve target angle

Measurements	Mean (mm)	Standard Deviation $\pm$ (mm)	Minimum (mm)	Maximum (mm)
Arc length	3.5	1.6	0.9	7.5
Chord length	3.5	1.6	0.9	7.4

Table 3. Measured Femoral Anteversion Angles ($^\circ$)

Group	Pre-op Angle (Min — Max)	Target Angle	Post-op Angle (Min — Max)	Difference
Group 1	26.2 ± 7.6 (18.2 — 46.0)	15	14.4 ± 1.0 (12.9 — 15.8)	0.5 ± 1.0
Group 2	-1.4 ± 4.1 (-9.7 — 3.7)	15	15.7 ± 1.4 (13.9 — 18.4)	0.7 ± 1.4

Note: Data are mean $\pm$ SD.

The arc length and the chord length were not statistically different ($p > .05$) (Table 2). Since the chord length is a linear measurement, it can be used as a reference line by drawing it on the outer lateral cortex of the femur during the mid-shaft femoral derotational surgery to determine the amount of the distal segment rotation.

There was no statistical difference between the right and the left femurs in any variables.

4. DISCUSSION

The striking finding of this study is that applying the preoperatively calculated cortical distance using the geometric arc or chord formula is a reliable method to achieve the desired femoral anteversion angle in virtual midshaft femoral derotation osteotomy. With this method, cortical distance between the points A and B, which represents the amount of bone to be rotated, can be easily calculated preoperatively on the axial CT and then, the calculated distance can be practically marked intraoperatively to achieve the targeted femoral anteversion. We observed no statistical difference between the arc and chord formulas for measuring the cortical distance (Table 2). Although the difference between chord and arc distances is theoretically expected to increase with the diameter of the circumference,

the radius of the femur's diaphysis in humans is too small for such a difference to occur [11]. Hence, even when a high degree of derotation (30-45 degrees) is required, there will be no statistical difference between these distances.

To the best of our knowledge, no study has been reported on human femurs to investigate the validity of arc/chord formula mathematically. In this study, we demonstrated how surgeons calculate the required cortical distance (chord length) to achieve desired femoral version angle preoperatively and then, how to implement the cortical distance on the femur during the surgery (Table-4). Moreover, intraoperative steps including the marking of cortical distance and performing the rotation are shown in Figure 5.

Table 4. Steps of determination of the degree of rotation using arc/chord formula to achieve target femoral anteversion angle

Preoperative steps	1. Decide the mid-shaft osteotomy site on the femur coronal CT image and measure the distance between the osteotomy site and the tip of greater trochanter (TO distance).
	2. Calculate arc length or chord length (cortical distance) using the formulas at osteotomy site on axial CT image as shown in the Figure 3.
Intraoperative steps	3. Locate the mid-shaft osteotomy site using TO distance.
	4. Expose the femur osteotomy site and mark the calculated arc or chord length (A-B line) on the lateral cortex (Figure 5).
	5. Cut the femur shaft and rotate the distal segment of the femur by the amount of the arc or chord length (Figure 5).

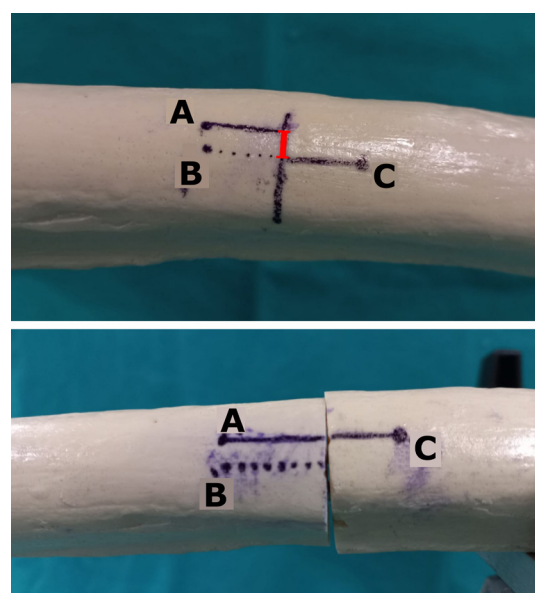


Figure 5. Marking the arc length on lateral cortex of osteotomy. Upper image: Preoperatively calculated chord length (cortical distance) is marked as a red line at osteotomy site between point A and B. Point C is also indicated on the distal segment of the femur in line with point B. Lower image: The distal segment is rotated by the amount of the chord length and the rotation is finished when the point aligns with point A.

Midshaft osteotomies are typically performed on the femur lateral cortex using a lateral approach. Hence, this study includes the calculations (best-fit circle tangent to the lateral cortex, guide points A and B) based on the lateral cortex of the midshaft femur. It is important to note that the femoral diaphysis does not have a perfect circular shape. Therefore, when drawing the outer best-fit circle during preoperative planning (Figure 3), the drawn circle on the axial CT must be in contact with the lateral cortex where marking of intraoperative cortical distance will be made (Figure 5). Thus, when drawing a circle whose center is at the midpoint of the femoral medulla, it is crucial to ensure that the circle aligns accurately with the lateral cortex of the femur (green arc in Figure 3). Otherwise, the calculations will yield different results. Since the midshaft region closely resembles – not perfectly – the tubular shape of the femur, it can be concluded that this method provides accurate results specifically at midshaft femur not at the distal or proximal femur.

There is no clear information in the literature regarding the optimal location for performing midshaft osteotomy. In this study, we calculated the midpoint of the femur based on femur length and decided midshaft osteotomy site. Then, we determined the distance between the tip of greater trochanter and midpoint of the femur, TO distance (Trochanter to Osteotomy), calculating which is especially important to match the preoperatively decided osteotomy site on the femur during the surgery. Since the tip of the greater trochanter can be easily found during the surgery, using a tape or a metal tape with fluoroscopy can be a practical method to obtain TO distance and the correct midpoint osteotomy site.

Various suggestions and technical skills for controlling femoral rotation can be found in the literature [12-19]. Some of these authors traditionally recommend using Steinmann pins on the proximal and distal segments to control rotation and then measuring the angle between these wires using a goniometer, triangular guide, or visual estimation after derotation [12, 14-16, 18, 19]. However, these methods primarily require surgical experience. Additionally, the use of fluoroscopy is necessary for the application of guide transmission pins or K-wires, which are used for rotation, exposing the patient to radiation. Sterile goniometers or triangular guides are also required. In the absence of these materials or if their sterility is compromised during the operation, it can lead to prolonged surgical time and potential difficulties. On the other hand, the preoperative calculation method described in this study offers significant convenience and confidence during surgery.

In two studies, smartphones were used to determine rotation [13, 17]. However, implementing these methods requires additional hardware such as a smartphone, a specialized app, and equipment to mount the smartphone. Moreover, using these methods is more likely to compromise the sterility of the surgical site. The installation of these instruments and their alignment with the femur can also lengthen the operation time. Although there is no information available about the learning curve for these methods, it can be inferred that they require substantial surgical experience.

The technique described in this study based on preoperative calculations on the axial CT does not require any additional materials or calculations during the surgery which can further facilitate the operation. Furthermore, since the markings are made with a mini-open incision over the lateral cortex, there is no need for fluoroscopy during the derotation phase. It is also likely that even surgeons with limited surgical experience can achieve success with this practical method.

We believe that the geometric arc/chord method can also be applied to the human humerus bone since its shaft is also tubular-shaped [11]. By using this method, nail fixation, which is a less invasive approach, can be preferred for derotation osteotomies in adult patients with CP or for treating humeral malrotations. However, the suitability of this method for human humerus derotation osteotomy needs to be thoroughly researched.

However, this study has its limitations. We conducted the study on a 3D reconstructed bone model, although it may be more advantageous to perform the method on cadavers. Furthermore, the success of the application of this method in intraoperative experiences also requires it to be evaluated. However, this study proved that mathematically calculation of the cortical distance and performing it on the virtual femurs is a reliable method to achieve desired femoral anteversion angle. Additionally, we used software which includes best-fit circle tool to calculate cortical distance. Surgeons who intend to use this method should consider the requirement of having such software having specific tools.

Hereby, the geometric arc and chord method is a reliable approach for midshaft derotation osteotomies, effectively addressing rotational issues of the femur. This method allows surgeons to achieve the desired femoral version without the need for intraoperative measurements or additional radiation exposure.

Acknowledgements: Samir Ilgaroglu, Abdul Veli Ismailoglu

**These two authors contributed equally to this work and considered as co-first authors.*

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Acibadem University, Noninvasive Clinic Ethics Committee (Approval date: 2019; Number: 2019-17/27).)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: SI

Design of the study: SI, AVI

Acquisition of data for the study: SI, ZS

Analysis of data for the study: AVI

Interpretation of data for the study: ZS

Drafting the manuscript: SI, AVI, ZS

Revising it critically for important intellectual content: SI, AVI, ZS

Final approval of the version to be published: SI, AVI, ZS

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The Effect of Histamine H4 Receptor Antagonist JNJ7777120 on Experimental Ulcer Models in Rats

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Received: July 08, 2024

Accepted: March 21, 2025

ABSTRACT

Objective: Gastric ulcer, one of the common diseases of the gastrointestinal system, affects more than 5% of the population of the world. Gastric ulcer occurs when the balance between mucosal damage mechanisms and mucosal protection mechanisms is disrupted. Helicobacter pylori infection, alcohol use, nonsteroidal anti-inflammatory drugs (NSAIDs), and stress are among the most common causes of gastric ulcers. Factors such as disruption of microcirculation, decreased mucus production, inhibition of gastric mucosal prostaglandin synthesis, and gastric acidity are involved in the pathogenesis of ulcers. It has been suggested that histamine H4 receptors, mostly found on mast cells, dendritic cells, basophils, eosinophils, and T cells, are principally responsible for inflammatory reactions. This study aims to investigate the gastroprotective effect of the H4 receptor antagonist, JNJ7777120 (JNJ), on experimental ulcer models.

Methods: In this study, the possible protective effects of JNJ (10 mg/kg s.c.) were investigated by creating experimental ulcer models with indomethacin (40 mg/kg i.g.), ethanol (1 ml 96% i.g.), and lipopolysaccharide (LPS) (1 mg/kg/day, i.p. for 3 days) in Sprague Dawley rats. Macroscopic scoring, histopathological examinations, and biochemical analyses were performed on the stomach samples obtained to evaluate the protective effect of JNJ. Ulcer index and levels of COX-1, SOD, NF-κB, TNF-α, catalase, and caspase were measured.

Results: In ethanol – and indomethacin-induced ulcer groups, JNJ treatment was found to significantly reduce ulcer formation in the stomach. In the groups treated with LPS, gastric damage, and gastritis occurred, but the preventive effect of JNJ on ulcer formation was not determined.

Conclusions: JNJ has a gastroprotective effect for ulcers. In future studies, it will be useful to test different doses to investigate the protective effect of JNJ on gastric damage caused by LPS.

Keywords: JNJ7777120, histamine antagonists, ulcer, LPS, indomethacin, ethanol

1. INTRODUCTION

Gastric ulcer, affecting 5% of the world population, is a common disease related to the gastrointestinal tract. Therefore, prevention and treatment are important. In the mechanism of ulcer formation, there is a disturbed balance of external factors and intrinsic defense mechanisms. These factors include psychological stress, nonsteroidal anti-inflammatory drugs (NSAIDs), alcohol, and Helicobacter pylori (*H. pylori*) infection; cell protective effect intrinsic factors contain cell regeneration, mucus, mucosal blood flow, prostaglandins and nitric oxide (NO) (1). Ethanol causes stomach ulcers as an outcome of an imbalance of gastric protective factors. Studies have found that free lipid peroxidation and reactive

oxygen species (ROS) play a role in ethanol-induced ulcer pathogenesis. ROS inhibit many antioxidants such as catalase (CAT), superoxide dismutase (SOD) and malondialdehyde (MDA) and increases the proinflammatory cytokines like tumor necrosis factor-alpha (TNF-α), interleukin-1, and 6 (IL-1, IL-6) (2-4). The most common and undesired side effect of NSAIDs is stomach injury. Complications of peptic ulcers occur up to five times more frequently among those taking NSAIDs (5). Indomethacin causes more stomach damage than other NSAIDs (6). NSAID-induced gastric ulcers occur due to damage to mucosal and vascular endothelial cells by active radicals and reduced blood flow. Indomethacin causes

How to cite this article: Kaltuş Z, Harmancı N, Eroğlu E, Özatik O, Yildirim E. The Effect of Histamine H4 Receptor Antagonist JNJ7777120 on Experimental Ulcer Models in Rats. Clin Exp Health Sci 2025; 15: 308-315. <https://doi.org/10.33808/clinexphealthsci.1512347>

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damage to the gastric mucosa and inhibits cyclooxygenase (COX) by limiting the synthesis of prostaglandins (7).

LPS can increase the production of many cytokines; the resulting inflammatory response can lead to organ damage. Gastrointestinal inflammation, hemorrhage and mucosal damage, and serious adverse effects on the stomach may occur in diffuse inflammation. In the stomach, histamine release, increased gastric acid, back-diffusion, and reduction in defense factors, including oxyradical formation and/or glutathione, can lead to gastric bleeding and damage (8). Studies show that increased TNF- α production is inhibited in vivo by treatment with histamine receptor (H4R) antagonists (JNJ777120), and this treatment also prevents LPS-induced inflammation and organ damage in mice (9). In the study conducted by Hung et al., it was observed that there was a significant correlation between gastric histamine secretion and lipid peroxide levels in rats administered LPS. It has also been shown that histamine release from gastric mucosa and oxyradical production plays an important role in hemorrhagic ulcer formation. As a result of the disruption of the gastric mucosal barrier, leakage of stomach acid into the mucosa can lead to histamine release (8). H4R ligand has great selectivity for histamine receptors (10, 11). In humans and rodents, H4R expression has been detected in human colon cancer cells, intestinal epithelial cells, submucosa, and different gastrointestinal tract cell types by immunohistochemistry (12). Therefore H4R antagonists are new anti-inflammatory and anti-allergic drugs under development. It has been observed that H4R is effective in the inflammatory process by mediating the chemotaxis of mast cells, dendritic cells, and eosinophils (13). The H4R antagonist JNJ has been reported to significantly block neutrophil infiltration in a peritonitis rat model. In parallel, its protective effect has been reported in the intestinal inflammation model (11).

This study aimed to investigate the protective effect of JNJ against gastric ulcers caused by indomethacin, ethanol, and LPS.

2. METHODS

2.1. Animals

Forty-nine adult male Sprague Dawley rats (6-8 weeks, 150-200 g) were kept in cages within a controlled environment with 12/12 light-dark cycles and a temperature of $24 \pm 1^\circ\text{C}$. Rats were taken to the laboratory one week before the start of the experiment to acclimate to the work environment, and they were placed, and access to water was allowed until one hour before the experiments. All experiments conducted during the study were performed after the approval by the Local Ethical Committee of Eskişehir Osmangazi University for Animal Experimentation (723-1/2019).

The forty-nine rats were divided into seven groups ($n = 7$): (i) Control group (saline, i.p.), (ii) Ethanol control group [(1 ml 96%, intragastric (i.g.)), (iii) Ethanol + JNJ [10 mg/kg, subcutaneous (s.c.)] group, (iv) Indomethacin group (40 mg/kg), (v) Indomethacin + JNJ (10 mg/kg, s.c.) group,

(vi) LPS serotype (O26:B6) 1 mg/kg/day (i.p.), (vii) LPS serotype (O26:B6) (1 mg/kg/day) + JNJ (10 mg/kg/day) for 3 consecutive days.

After fasting the animals for 24 hours and withholding water for 1 hour, JNJ was administered subcutaneously to investigate its protective effects against gastric damage.

2.2. Drugs

JNJ was purchased from BLDPHARM (BLD Pharmatech Ltd., China); LPS from Sigma Chemical Co. (St. Louis, Mo, USA); indomethacin and ethanol from Merck (Darmstadt, Germany; ketamine (Ketalar® 50 mg/10 mL) from Pfizer (Istanbul, Türkiye); and (Rompun® 23.32 mg xylazine (Rompun® 23.32 mg/ml) from Bayer (Istanbul, Türkiye).

2.3. Experimental Design

E. coli-LPS induced ulcer: LPS serotype was administered 1 mg/kg i.p. for three consecutive days and animals were terminated by cervical dislocation under anesthesia five hours after the last dose. In previous studies, various doses were used in LPS-induced gastric ulcer models. Based on these studies, we selected a dose of 1 mg/kg for our study (8).

Ethanol-induced ulcer: 96% ethanol was administered in a 1 ml volume via oral gavage. Two hours after ethanol administration, animals were terminated by cervical dislocation under ketamine and xylazine anesthesia (14).

Indomethacin-induced ulcer: Indomethacin was administered 40 mg/kg i.g. Under anesthesia, they were executed by cervical dislocation five hours after indomethacin was administered (15, 16).

JNJ was given s.c. 1 h before ethanol and indomethacin administrations and 30 minutes before LPS administration (17).

After stomach cutting along the greater curvature, gastric tissue was separated from fundus and corpus parts and stored at -80°C until CAT, SOD, TNF- α , COX-1, NF- κB and caspase levels were determined. Additionally, samples were taken from the stomach fundus region for histological evaluation.

2.4. Microscopic Evaluation of the Gastric Damage

Samples from the fundus and corpus region were fixed in a 10% formalin solution, and paraffin blocks were obtained using routine histological techniques. Then the blocks were cut at a thickness of 5 micrometers, stained with hematoxylin-eosin, and then PAS and evaluated with light microscopy. Ulcer evaluation was performed according to the following scoring (18): 0: No lesions (normal stomach), 1: hyperemia, 2: hemorrhagic spots, 3: gastritis in a weak degree, 4: moderate gastritis, 5: erosive gastritis, 6: severe damage to mucosa and submucosa. Ulcer index (UI) was measured by using the following formula: $\text{UI} = \frac{\text{UN} + \text{US} + \text{UP}}{10}$. Where UI= Ulcer Index; UN = average number of ulcers per animal; US = average number of severity score; UP = percentage of animals with ulcers (19)

2.5. Biochemical assays

2.5.1. Preparation of Gastric Homogenate

Gastric tissue was isolated and then collected in cold phosphate buffered saline (PBS) solution. Subsequently, these samples were homogenized using an ultrasonic homogenizer and centrifuged at 15,000 rpm for 15 minutes. The supernatant was removed and stored at -80°C .

2.5.2. Determination of Total Protein Content, Gastric CAT, SOD, TNF- α , COX-1, NF- κB and Caspases

Firstly, protein determination was made in gastric tissue homogenate supernatants (milligrams of protein). Total protein concentration was measured by a rat total protein Enzyme-Linked Immunosorbent Assay (ELISA) kit. Absorbance was measured at 450 nm using a microplate reader, according to the colorimetric method (BioTec ELX800). Then, each well was proportioned according to the amount of protein, and data were expressed as gastric CAT, SOD, TNF- α , COX-1, NF- κB , and caspases levels per milligrams of total protein. Evaluation of antioxidant enzyme (CAT, SOD) and TNF- α , COX-1, NF- κB , and caspase (play a role in apoptosis) levels were measured using the appropriate ELISA kits. SOD and CAT were supplied by Cayman Chemical (Ann Arbor, Mich., USA). TNF- α , COX-1, caspase, and NF- κB ELISA kits were purchased from USCNC (Wuhan USCNC Business Co., Ltd., China).

2.6. Statistics

SPSS (v15.0, Chicago, IL, USA) software program was used for statistical evaluations. The normality of data distribution was assessed by the Shapiro-Wilk test. Kruskal-Wallis test was applied for comparison of biochemical parameters. All data are shown as mean $\pm$ standard error of the mean (SE). Differences were considered significant when $P < .05$.

3. RESULTS

3.1. Macroscopical Findings

In the macroscopic examination of the ethanol-induced ulcer group, severe dark red submucosal hemorrhagic areas of various sizes associated with submucosal thickening were observed (Figure 1a). In the ethanol + JNJ group, hemorrhagic areas were less, and mucosal edema was observed (Figure 1b). Similar to the ethanol group, severe dark red submucosal hemorrhagic areas of various sizes, associated with submucosal thickening, were observed in the indomethacin-induced ulcer group (Figure 1c). Hemorrhagic vascular responses were occasionally present in the indomethacin + JNJ group (Figure 1d). Hemorrhagic vascular reactions and submucosal edema were observed in the LPS and LPS + JNJ groups (Figures 1e and 1f). The control group shows healthy color gastric mucosa with normal mucosal thickening (Figure 1g).

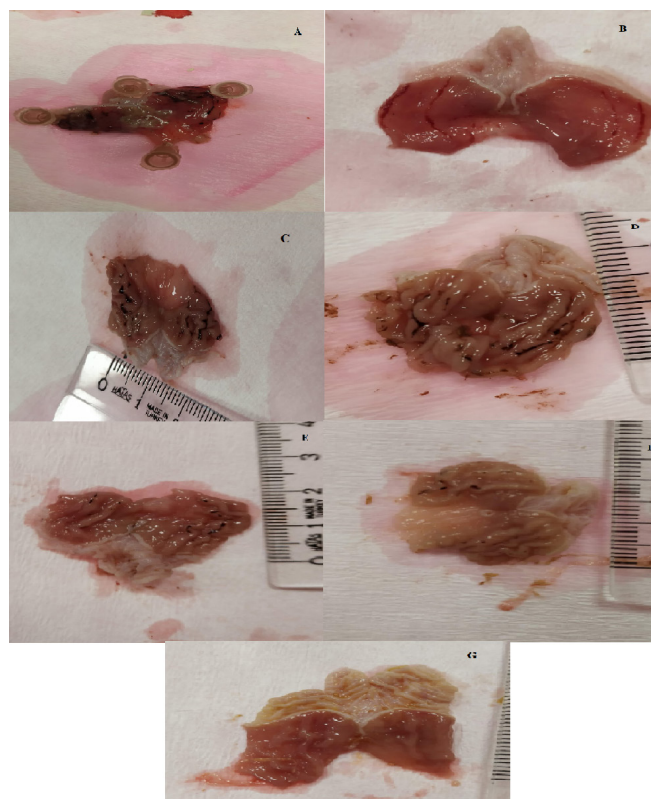


Figure 1. Macroscopic aspects of gastric mucosa. Ethanol (A), Ethanol+JNJ (B), Indomethacin group (C), Indomethacin+JNJ (D), LPS (E), LPS+JNJ (F), Control group (G) ($n=7$).

3.2. Severity of Gastric Damage at Microscopic Level

In the histopathological examination, mild hyperemia was determined in only 2 rats in the control group. In other rats, normal histological structures were detected. Severe mucosal damage and erosive gastritis, hyperemia, and edema in the submucosa layer were observed in the ethanol-induced ulcer groups. Weak and moderate gastritis findings and partial edema in the submucosa layer were observed in the ethanol + JNJ group. Significant gastritis and severe damage were detected in the indomethacin-administered group. Stomach histology was observed to be close to normal in the indomethacin + JNJ group. Only 2 animals had mild hemorrhagic areas, and 3 animals had mild hyperemia. Weak and moderate gastritis was observed in the LPS group. Histological findings of animals in the LPS + JNJ group consist of hemorrhagic spots and mild gastric findings (Table 1, Figures 1 and 2).

Table 1. Ulcer Index in Experimental Groups. Data are expressed as mean $\pm$ SEM. $^{**}p < .01$ compared to control group. $^{\#}p < .05$, $^{##}p < .01$ compared to its own control group. ($n=7$).

	Ulcer index
Control	0.28 ± 0.18
Ethanol	$5.42 \pm 0.20^{**}$
Ethanol+JNJ	$3.00 \pm 0.31^{\#}$
Indomethacin	$4.85 \pm 0.26^{**}$
Indomethacin+JNJ	$1.00 \pm 0.31^{##}$
LPS	$3.10 \pm 0.20^{**}$
LPS+JNJ	2.71 ± 0.18

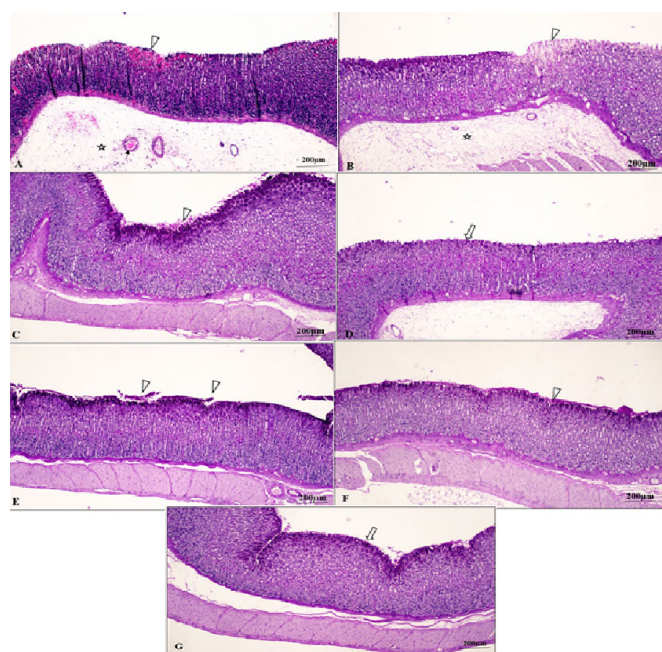


Figure 2. Histological examination of gastric tissues. Epithelial tissue ($\Rightarrow$). Severe mucosal damage and erosive gastritis ($\triangleright$), hyperemia ($\rightarrow$) and edema in the submucosa layer ($\star$) were observed in the ethanol group (A). Weak and moderate gastritis findings ($\triangleright$) and partial edema in the submucosa layer ($\star$) were observed in the ethanol+JNJ group (B). Significant gastritis and severe damage were detected in the indomethacin group ($\triangleright$) (C). Stomach histology was observed to be close to normal in the indomethacin+JNJ group ($\Rightarrow$) (D). Weak and moderate gastritis was observed in the LPS group ($\triangleright$) (E). Moderate gastric findings were observed in the stomachs of the LPS+JNJ group ($\triangleright$) (F). Control group (G). (scale bar: 200µm, PAS+ HE) (n=7).

3.3. Biochemical Results

In our study, biochemical results support the histological findings. When comparing caspase levels between the groups, a significant decrease in caspase levels was observed in the ethanol – and indomethacin-induced ulcer models treated with JNJ, compared to their respective ulcer groups ($p<.001$ and $p<.01$) (Figure 3). CAT levels were examined; a significant increase was found in the ethanol and indomethacin-induced ulcer groups treated with JNJ compared to both their control groups and the main control group ($p<.05$) (Figure 4). TNF- α levels were significantly decreased in the ethanol – and indomethacin-induced ulcer groups treated with JNJ compared to the control groups ($p<.05$ and $p<.01$) (Figure 5). When SOD levels were compared, a statistically significant increase was observed in the JNJ-applied indomethacin-induced ulcer group compared to the control group ($p<.01$) (Figure 6). When the ethanol – and indomethacin-induced ulcer groups treated with JNJ were compared with the control groups, NF- κ B levels were determined to be significantly lower in these groups (Figure 7). No significant changes in COX-1 levels were observed in either the ulcer or treatment groups (Figure 8).

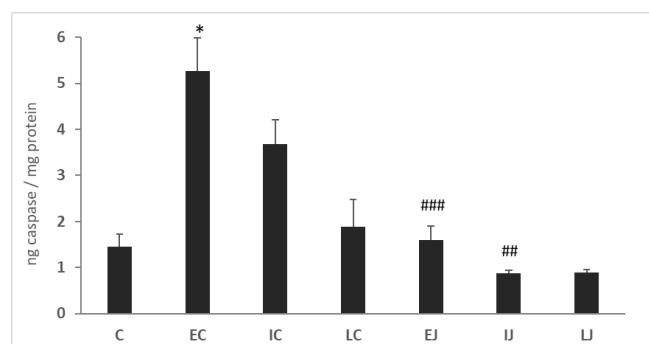


Figure 3. Effects of JNJ on caspase levels in ethanol, indomethacin and LPS-induced gastric ulcer tissue (Each data means $\pm$ SEM, C: Control. EC: Ethanol control. IC: Indomethacin control. LC: LPS control. EJ: Ethanol+JNJ. IJ: Indomethacin+JNJ. LJ: LPS+JNJ. Significance is indicated as follows *: $P<.05$ vs control group, ##, $P<.01$, ###, $P<.001$ vs their own control group) (n=7).

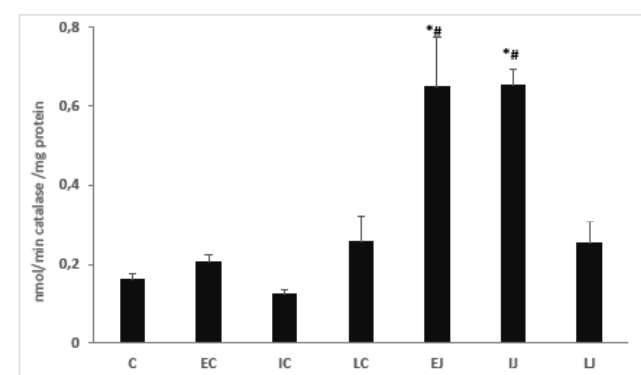


Figure 4. Effects of JNJ on catalase levels in ethanol, indomethacin and LPS-induced gastric ulcer tissue (Each data means $\pm$ SEM, C: Control. EC: Ethanol control. IC: Indomethacin control. LC: LPS control. EJ: Ethanol+JNJ. IJ: Indomethacin+JNJ. LJ: LPS+JNJ. Significance is indicated as follows *: $P<.05$ vs control group, #, $P<.05$ vs their own control group) (n=7).

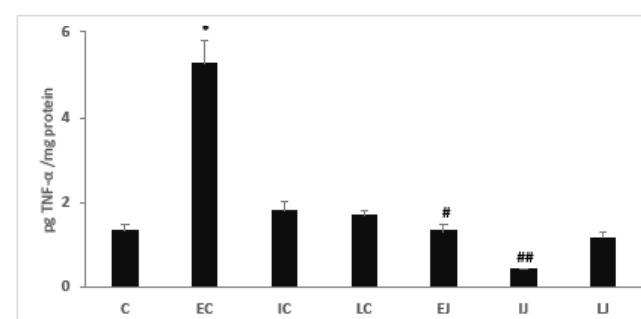


Figure 5. Effects of JNJ on TNF- α levels in ethanol, indomethacin and LPS-induced gastric ulcer tissue (Each data means $\pm$ SEM, C: Control. EC: Ethanol control. IC: Indomethacin control. LC: LPS control. EJ: Ethanol+JNJ. IJ: Indomethacin+JNJ. LJ: LPS+JNJ. Significance is indicated as follows *: $P<.05$ vs control group, #, $P<.05$, ##, $P<.01$ vs their own control group) (n=7).

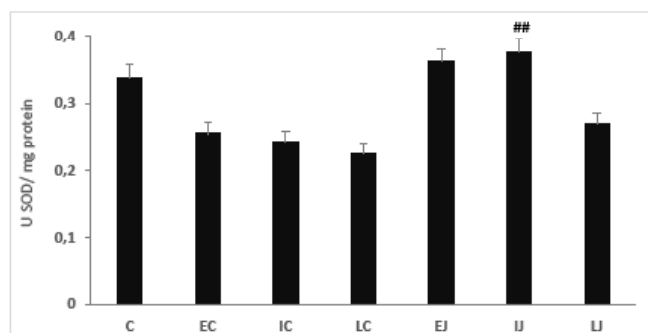


Figure 6. Effects of JNJ on SOD levels in ethanol, indomethacin and LPS-induced gastric ulcer tissue (Each data means $\pm$ SEM, C: Control. EC: Ethanol control. IC: Indomethacin control. LC: LPS control. EJ: Ethanol+JNJ. IJ: Indomethacin+JNJ. LJ: LPS+JNJ. Significance is indicated as follows ^{##}; $P < .01$ vs their own control group) ($n=7$).

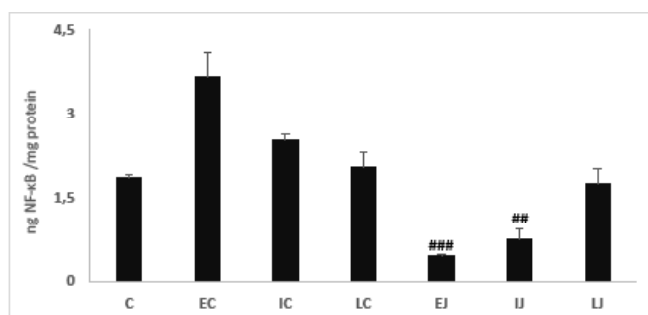


Figure 7. Effects of JNJ on NF-κB levels in ethanol, indomethacin and LPS-induced gastric ulcer tissue (Each data means $\pm$ SEM, C: Control. EC: Ethanol control. IC: Indomethacin control. LC: LPS control. EJ: Ethanol+JNJ. IJ: Indomethacin+JNJ. LJ: LPS+JNJ. Significance is indicated as follows ^{##}; $P < .01$, ^{###}; $P < .001$ vs their own control group) ($n=7$).

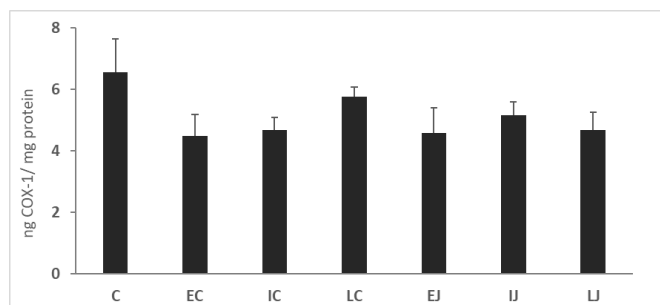


Figure 8. Effects of JNJ on COX-1 levels in ethanol, indomethacin and LPS-induced gastric ulcer tissue. (Each data means $\pm$ SEM, C: Control. EC: Ethanol control. IC: Indomethacin control. LC: LPS control. EJ: Ethanol+JNJ. IJ: Indomethacin+JNJ. LJ: LPS+JNJ) ($n=7$).

4. DISCUSSION

Gastric ulcer is a common disease that is difficult to prevent and manage (20). In support of histological results in our study, JNJ had gastroprotective effects against indomethacin and ethanol-induced ulcer groups. The results of other studies also support this protective effect. A protective effect of JNJ has been seen in some studies about models

of intestinal inflammation in rats. This protective effect was supported by Gabriella Coruzzi et al. on mice with ulcers formed with indomethacin and betanecol (21). In our study, we also demonstrated this protective effect for ethanol-induced ulcers. In a study by Pini et al., it was demonstrated that JNJ reduced caspase, TNF- α , and IL-1 parameters (22).

In our study, while there was a significant decrease in caspase, TNF- α , and NF-κB levels in the JNJ + NSAID-induced ulcer group, a significant increase was observed in CAT and SOD levels. However, COX 1 levels did not change. In the study by İpek et al., CAT and SOD levels decreased in the indomethacin-induced ulcer group and increased in the treatment group, like our results (23). When gastric tissues obtained from indomethacin groups were examined, mucosal and epithelial damage and disruption of mucosal glands were observed. Also, increased stomach acid has an impact on the pathogenesis of drug-induced stomach ulcers (1). The lipid peroxidation, leukocyte infiltration, and upregulation of adhesion molecules are involved in the pathogenesis of NSAID-induced ulcers. At the same time, it increases gastric damage concerning such as SOD, CAT, glutathione (GSH), MDA, and cytokines. Indomethacin causes erosions in the gastroduodenal system through inhibition of COX and associated prostaglandin synthesis and overexpression of polymorphonuclear leukocytes (24, 25). In another rat study, it seemed that indomethacin remarkably increased the caspase-3 mRNA expression level (26).

Ethanol causes the release of superoxide anions and hydroperoxide free radicals. These free radicals play a role in the ulceration mechanism in the stomach (27). As observed in human and animal models, ethanol penetrates the gastric mucosa producing lesions with extensive edema, bleeding, and inflammatory cell infiltration (28). In our study, gastritis was observed in the ethanol + JNJ7 group, which was weak and moderate in comparison to the ethanol group. This indicates a significant protective effect. It was determined that antioxidant markers such as SOD and CAT were increased in animals treated with JNJ, while TNF- α was significantly reduced compared to the ethanol-induced ulcer group. Some studies support these findings and have shown that gastric ulcer caused by ethanol is closely related to oxidative stress and inflammation (2, 29). JNJ reduced the increase in NF-κB levels due to ethanol and indomethacin administration. Additionally, it was determined that JNJ administration also reduced the increase in caspase levels. It has been shown in a study that the decrease in caspase levels may be related to the gastric protective effect (30). Previous studies have observed that ethanol exposure causes ROS formation and stomach damage and increases antioxidant enzymes to protect the stomach (31). Similar to other studies showing that JNJ increases SOD activity, an increase was observed in our study, but this increase was not statistically significant (32).

LPS administration has been shown to trigger the inflammatory process and increase the gene expression of cytokines in animal models of ulcers. With this, a model similar to H. pylori-induced ulcer is developed (33). In our study, we applied the

LPS dose as 1 mg/kg. In a study conducted using LPS doses of 1, 3, or 10 mg/kg, significant changes in ulcerogenic effects were observed at the 1 mg/kg dose. A significant increase in blood coagulation time and leukocyte numbers, important markers of sepsis, has previously been demonstrated in rats treated with LPS (1-3 mg/kg) (8). *E. coli* LPS, which mimics *H. pylori* ulcer, was used in the study of Rajagopal et al. While stress + LPS was used in this study, we used a higher dose of LPS than applying stress in our study (33). We detected hemorrhage and gastritis in the groups that we gave LPS. There was no significant change in biochemical results in this group. No significant decrease was detected in ulcer scoring of the LPS + JNJ group. LPS induces a cytokine pattern with increased TNF- α levels. TNF- α signaling has been shown to induce increased production of NF- κ B and IL-8. Similarly, NF- κ B and TNF- α have also been shown to be strongly associated with *H. pylori*-associated gastric inflammation (34). Konturek et al. showed that bacterial endotoxin impairs ulcer healing by decreasing gastric mucosal blood flow, increasing the expression and secretion of proinflammatory cytokines IL-1 β and TNF- α , and decreasing antiapoptotic BCL-2. It was determined that the deterioration in ulcer healing due to LPS was accompanied by decreased gastric blood supply at the edge of the ulcer and apoptosis caused by LPS. In the same study, it was observed that LPS caused a significant increase in plasma IL-1 and TNF- α values, while there was no considerable change in COX-1 (35). In our study, areas with weak gastritis findings and hemorrhagic areas were detected histologically in the group given LPS. LPS is known to play a role in ulcer pathogenesis by causing microscopic damage to the gastric epithelium, decreased gastric acid secretion, duodenogastric bile reflux, or inhibition of gastric emptying (36). In a study of Hung et al., functions of histamine receptors and oxyradicals in acid-induced gastric bleeding and exacerbation of gastric ulcers were investigated by measuring changes in the acid lumen, mucosal permeability of LPS to electrolytes, and histamine concentrations. Results of previous reports suggest that several different etiopathogenesis mechanisms are involved in LPS-induced gastric injury. Immunohistochemical studies have shown the presence of H4R expression in different parts of the intestine. Moreover, the level of TNF- α increased by LPS has been shown to be reduced by H4 receptor blockers (9). Indeed, studies investigating the effects of JNJ on various gastrointestinal injury models in rodents have clearly demonstrated the role of H4R in gastrointestinal inflammation and ulcerogenesis (17, 21).

In our study, there was a decrease in TNF- α level in the LPS + JNJ group, but no statistically significant decrease was detected. This could arise from a few different factors. TNF- α levels fluctuate over time in response to LPS. If the levels are measured at a time point after the peak, they might not show a significant increase. The peak of TNF- α secretion typically occurs within 1–2 hours post-LPS exposure, after which levels may decline depending on the severity of the inflammatory response (38).

On the other hand, the dose of LPS used can significantly influence TNF- α production. Higher doses tend to elicit more

robust inflammatory responses, while lower doses may not produce the same magnitude of TNF- α release (39).

5. CONCLUSION

In summary, the current study evaluated JNJ and confirmed that it has a gastroprotective effect on ethanol and indomethacin-induced gastric mucosal damage. The value of JNJ has been recognized, which may have a potential for preventing gastric injury. Administering JNJ at different doses and investigating the mechanisms underlying its gastroprotective effect in greater detail may provide significant contributions to the literature.

The study's evaluation of JNJ's protective effect on LPS-induced ulcers was limited by the lack of different dose assessments.

Acknowledgements: We would like to thank Eskişehir Osmangazi University for providing access to academic databases.

Funding: This study was supported by Eskişehir Osmangazi University Scientific Research Project Coordination Unit (Project number: 202011035).

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by the Local Ethical Committee of Eskişehir Osmangazi University for Animal Experimentation (723-1/2019).

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: ZK, EY

Design of the study: ZK, EY

Acquisition of data for the study: ZK, NH, EE

Analysis of data for the study: ZK, NH, EE, OÖ

Interpretation of data for the study: ZK, NH, EE, OÖ

Drafting the manuscript: ZK, NH, EE

Revising it critically for important intellectual content: EE

Final approval of the version to be published: EE, ZK, EY, OÖ, NH

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Clinical Pharmacist's Input in Identification and Resolution of Drug-Related Problems in the Neonatal and Pediatric Intensive Care Units

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Received: July 8, 2024

Accepted: May 9, 2025

ABSTRACT

Objective: Patients in the pediatric intensive care unit (PICU) and neonatal intensive care unit (NICU) are at high risk for drug-related problems (DRPs). It is crucial to assess pharmacotherapy with the active involvement of clinical pharmacist (CP). The study aims to investigate the effect of CPs in identifying and resolving DRPs in the NICU and PICU settings.

Method: This study with a retrospective and prospective design was conducted within the timeframe of October 2020 – August 2021 at the NICU (n=200) and PICU (n=200) of a university-affiliated state hospital in Türkiye. The Pharmaceutical Care Network Europe (PCNE) Classification V9.1. was used for classifications of the DRPs. DRPs identified by the CP and the regarding intervention proposals were communicated with the attending physician.

Results: A total of 1247 DRPs were identified for all patients. The median (interquartile range [IQR]) number of DRPs per patient was 3 (1-6) for the pediatrics and 1 (0-1) for the neonates (p<.001). The most frequently observed DRPs in the prospective part of this study were 'drug selection' (41%) in the PICU, while it was 'dose selection' (34%) in the NICU.

Conclusion: The study findings demonstrate role of the CPs in the NICU and PICU settings in identifying and resolving DRPs.

Keywords: Clinical pharmacist, drug-drug interactions, drug-related problems, neonatal intensive care unit, pediatric intensive care unit

1. INTRODUCTION

The Pharmaceutical Care Network Europe (PCNE) defines 'drug-related problems (DRPs)' as events or circumstances involving drug therapy that actually or potentially interferes with desired health outcomes (1). The risk of developing DRPs is higher in pediatric patients than in adults since there is a higher rate of off-label drug use and pharmacokinetic and pharmacodynamic properties of drugs are affected by age-specific characteristics such as physiological immaturity and weight changes (2-4). In a cohort study, potential adverse drug events (ADEs) were found to be three times higher in pediatrics than in adults, and a significantly higher rate of potential ADEs was reported in neonates in the neonatal intensive care unit (NICU) (5). DRPs may worsen the clinical outcomes of the patient, prolong hospital stays, lead to the emergence of new complications and increase morbidity, mortality and healthcare costs (6, 7). Although the risk of DRPs is high in the NICU and pediatric intensive care unit (PICU), most DRPs are predictable and preventable (8, 9).

Despite this high risk, studies conducted in the NICU and PICU on clinical pharmacists' (CPs) involvement in the identification and resolution of DRPs remain limited. It is emphasized in the literature that the most common DRPs detected by CPs in the NICU and PICU are generally related to drug selection and/or dose selection (10-12). Additionally, issues such as lack of pediatric oral dosage forms, drug administration through enteral feeding tubes, interactions between enteral or parenteral nutrition solutions and administered drugs, potential drug-drug interactions (pDDIs), and intravenous drug incompatibilities are frequently observed (13-15). Studies from India, Brazil, and United States revealed that CPs working in collaboration with the multidisciplinary team identified DRPs in the NICU and PICU and contributed to the reduction of ADEs and prescription-related costs with their interventions (7, 16, 17). CPs play a critical role in optimizing pharmacotherapy by providing recommendations on dose adjustments based on patients' hepatic and renal function, selecting appropriate dosage forms,

How to cite this article: Ay ZY, Bayraktar S, Sancar M, Büyükkayhan D, Apikoglu Ş. Clinical Pharmacist's Input in Identification and Resolution of Drug-Related Problems in the Neonatal and Pediatric Intensive Care Units. Clin Exp Health Sci 2025; 15: 316-323. <https://doi.org/10.33808/clinexphealthsci.1512167>

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modifying drug administration routes (e.g., continuous infusion and bolus administration), preventing medication duplication, discontinuing or introducing medications, monitoring pDDIs, and conducting therapeutic drug monitoring, thereby reducing or preventing DRPs (10, 12).

In Türkiye, studies revealing the positive impact of CPs in the identification and resolution of DRPs in adult ICUs and pediatric wards exist (18, 19); however, to our current knowledge, there is a lack of such studies conducted in the NICU and PICU. The study aims to investigate the impact of a CP in the identification and resolution of DRPs in the NICU and PICU, through a two-phase (retrospective and prospective) study design.

2. METHODS

2.1. Study Design

This study with a bi-directional (retrospective and prospective) design was conducted within the timeframe of October 2020 – August 2021 at the NICU and PICU of a university-affiliated state hospital in Türkiye. It was granted ethical approval by the Ethics Committee of Marmara University, Institute of Health Sciences, Noninvasive Clinic Ethics Committee (Approval date 16.03.2020; Number: 41). Before starting the study, legal guardians of neonatal and pediatric patients were informed, and their written and verbal consents were obtained.

2.2. Study Population

Sample size was calculated via an online calculator at a confidence level of 80% and a margin of error of 5%. Population proportions were considered as 9.07% for the neonates, which was the NICU admission rate reported in the literature (20) and as 15.5% for the pediatric patients, which was the prevalence of PICU admission rate among hospitalized children reported in the literature (21). The minimum number of subjects to be included was calculated as 55 for the neonates and 86 for the pediatric patients. Therefore, it was planned to include 100 patients in each group.

The inclusion criteria were being under 18 years of age, staying in the NICU and PICU for at least 24 hours, and receiving at least 1 medication. The study excluded patients who were prescribed solely blood products, parenteral nutrition, electrolytes, oxygen therapy, vitamin and mineral supplements, diagnostic agents, as well as those with admitted less than 24 hours and those without any prescribed medications.

For the retrospective part, the first retrospectively consecutive 100 patients meeting the inclusion criteria from the NICU (n=100) and the PICU (n=100) were included in the study. The retrospective patient groups were aimed to serve as control groups of the study groups. All data of the retrospective patient groups were gathered from the hospital records.

For the prospective part, the first prospectively consecutive 100 patients meeting the inclusion criteria and whose parents after being informed about the study gave their consent, from the NICU (n=100) and the PICU (n=100) were included in the study.

Retrospective NICU and PICU patients were assigned as ‘Control Group N and ‘Control Group P’, respectively, and prospective NICU and PICU patients participating in the study were assigned as ‘Study Group N and Study Group P’, respectively.

2.3. Data Collection

Data such as age, gender, weight, diagnosis, length of stay in the NICU or PICU were recorded for each patient. The International Statistical Classification of Diseases and Related Health Problems version 11 (WHO-ICD 11) was used for recording the diagnosis of the patients.

A comprehensive list of all medications (including prescription and non-prescription medications; nutritional and herbal supplements) was created for each patient. Clinical and medication-related information such as the dosage form of the medication or for how long and for which indication the medication has been used were obtained from the patient records. Data on routine laboratory test results and daily medication orders throughout the patients’ hospitalization period were gathered right after the daily ICU rounds. The age of the neonate patients was expressed as ‘last menstrual period (LMP) – based gestational age’ in terms of weeks.

2.4. Interventions

In this study, the CP (ZYA; Ph.D. candidate) actively worked in the NICU and PICU and closely followed up with the patients from their admission to discharge or demise. In the prospective part, CP attended medical rounds in the NICU and the PICU 3-5 days per week, during which patients were assessed based on treatment effectiveness, treatment safety, drug selection, drug formulation, dose determination, and treatment duration.

Evidence-based guidelines, and databases such as UpToDate®, Micromedex®, and Medscape® were used as up-to-date resources for identifying DRPs. Lexidrug™ database was used for the identification of pDDIs. Lexidrug™ D-level interactions (i.e., DDIs necessitating consideration of therapy modification) and X-level interactions (i.e., DDIs necessitating avoidance of combination) were considered pDDIs.

Using the Turkish version of the PCNE Classification for Drug-Related Problems V9.1 patients’ current treatments were assessed for the presence of any potential and/or manifest DRPs. For each patient, the number of administered drugs, the presence and characteristics of DRPs were recorded and analyzed. Following discussions with the attending physician, it was decided that off-label drug use would not be classified as a DRP, and therefore, off-label drug use was not recorded under the category “C1.2 (No indication for drug)” in the DRP list. The presence of pediatric polypharmacy, defined as the simultaneous use of two or more drugs by a patient for more than one day, a definition commonly used in the pediatric population, was also recorded and analyzed (22). The CP communicated with the attending physician regarding the DRPs she identified as well as intervention proposals for the resolution of each DRP. Due to

the setting of the study, no intervention was proposed at the patient level.

2.5. Data Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), Version 11.5 (SPSS Inc., Chicago, IL). According to the results of the Kolmogorov-Smirnov test, it was determined that continuous variables showed non-normal distribution. Data for continuous variables were presented using median (interquartile range [IQR]) values. Differences between two groups were compared using the Mann Whitney U test, which is used for nonparametric data. Differences between four groups were compared using the Kruskal Wallis H test. Whether the presence of different clinical conditions posed a risk for DRPs was determined using the Odds ratio. A p value <.05 was considered statistically significant.

3. RESULTS

A total of 400 patients were included in the study (Study Group P [n=100]; Control Group P [n=100]; Study Group N [n=100]; Control Group N [n=100]). In table 1 presents major clinical and medication-related patient characteristics.

Table 1. Major clinical and medication-related patient characteristics

Patient Characteristics	Study Group P (n=100)	Control Group P (n=100)	p	Study Group N (n=100)	Control Group N (n=100)	p
Age (months); median (IQR)	34.50 (10.25-100.50)	27 (10.00-149.25)	NS	-	-	-
Gestational age (weeks); median (IQR)	-	-	-	38 (37-39)	38 (35-39)	NS
Male gender; n (%)	52 (52)	56 (56)	NS	57 (57)	56 (56)	NS
Length of hospital stay (day); median (IQR)	3 (2-6)	5 (2.0-11.5)	.008	8 (6.00-11.75)	7 (5.00-9.75)	NS
Number of drugs used; median (IQR)	7 (4-12)	10 (6-14)	.005	4 (3-5.75)	4 (3-5)	NS
Number of drug-related problems; median (IQR)	2 (1-5)	3 (2-6)	.018	0.5 (0-1)	1 (1-2)	< .001
Mechanical ventilation; n (%)	58 (58)	67 (67)	NS	52 (52)	35 (35)	.015

Study Group P: prospective pediatric intensive care unit patients; Control Group P: retrospective pediatric intensive care unit patients; Study Group N: prospective neonatal intensive care unit patients; Control Group N: retrospective neonatal intensive care unit patients; NS: non-significant

The median (IQR) age of all pediatric patients was 30.50 (10.00-127.75) months and 54% of them were male. The control and

study groups had similar age and gender distributions ($p>.05$, for both). The two most frequently reported diagnoses in the PICU were diseases of the respiratory system (45% of Control Group P and 38% of Study Group P), and diseases of the nervous system (21% of Control Group P and 14% of Study Group P) ($p>.05$, for both). The median (IQR) length of hospital stay was 4 (2.00-7.75) days and the median (IQR) number of drugs used was 8 (5-13) for PICU patients. The median (IQR) length of hospital stay and the median (IQR) number of drugs used were higher for the control group ($p<.05$, for both). Polypharmacy was observed in 92% of PICU patients in the prospective part and 97% of PICU patients in the retrospective part ($p>.05$).

The median (IQR) age of all neonate patients was 38 (36-39) weeks and 56.5% of them were male. The control and study groups had similar age and gender distributions ($p>.05$, for both). The most frequently reported diagnoses in the NICU were certain conditions originating in the perinatal period such as lower respiratory tract infection, asphyxia, bronchopulmonary dysplasia, low birth weight, hypoxic ischemic encephalopathy, congenital anomaly, congenital pneumonia, meconium aspiration, polycythemia, jaundice, septicemia, thrombocytopenia, transient tachypnea of the newborn and urinary tract infection of the newborn (94% of Control Group N and 96% of Study Group N) ($p>.05$). The median (IQR) length of hospital stay was 7 (6-10) days and the median (IQR) number of drugs used was 4 (3-5) for NICU patients. The median (IQR) length of hospital stay and the median (IQR) number of drugs used were similar for the study and the control groups ($p>.05$, for both). Polypharmacy was observed in 100% of NICU patients in the prospective and retrospective part.

Of all patients, 80.25% had at least one DRP, and pDDIs were observed in 25.5% of all patients.

A total of 1247 DRPs were detected across all groups. 2 (1-5) for the Study Group P and 3 (2-6) for the Control Group P ($p<.05$) whereas it was 0.5 (0-1) for the Study Group N and 1 (1-2) for the Control Group N ($p<.001$) were the median (IQR) numbers of DRPs per patient. The causes of the DRPs are classified in Table 2.

Interventions were proposed to the physicians for 95.5% ($n=447/468$) of the DRPs in Study Group P and 91.5% were accepted; while interventions were proposed for 88.7% ($n=86/97$) of the DRPs in Study Group N and all were accepted. Proposed interventions for Study Group P were mostly about other interventions (such as monitoring drug treatment, storage conditions, etc.) [32.7%], formulation change [22.4%], and changing the instructions for use [16.3%]; while for Study Group N these were mostly about dosage change [26.7%], other interventions [23.3%], and starting a new drug [21%] as detailed in Table 3.

The most drugs causing DRPs in the PICU were fentanyl (13.73%), midazolam (6.16%), levetiracetam (5.88%), ampicillin (3.78%) and ampicillin-sulbactam (3.64%). The most common drugs causing DRPs in the NICU were vitamin D (44.56%), ampicillin (8.07%), gentamicin (8.07%), cefotaxime (4.56%) and vancomycin (4.21%).

For 400 patients, 389 pDDIs of which 6.4% were contraindicated were identified. (Table 4).

Table 2. Causes of the drug-related problems (n=100, for each group)

Causes	Study P n (%)	Control P n (%)	p	Study n (%)	Control n (%)	p
1. Drug selection						
C1.1 Inappropriate drug according to guidelines/formulary	8 (1.7)	6 (1.2)	NS	1 (1)	1 (0.6)	NS
C1.2 No indication for drug	7 (1.5)	4 (0.8)	NS	2 (2.1)	2 (1.2)	NS
C1.3 Inappropriate combination of drugs or drugs and herbal medications or drugs and dietary supplements	136 (29.1)	240 (46.8)	.033	7 (7.2)	12 (7.1)	NS
C1.4 Inappropriate duplication of therapeutic group or active ingredient	1 (0.2)	0	NS	0	0	NS
C1.5 No or incomplete drug treatment in spite of existing indication	40 (8.5)	24 (4.7)	NS	16 (16.5)	6 (3.6)	.024
C1.6 Too many different drugs/active ingredients prescribed for indication	0	1 (0.2)	NS	0	0	NS
2. Drug form						
C2.1 Inappropriate drug form/formulation (for this patient)	96 (20.5)	143 (27.9)	.008	10 (10.3)	16 (9.5)	NS
3. Dose selection						
C3.1 Drug dose too low	22 (4.7)	13 (2.5)	NS	19 (19.6)	27 (16)	NS
C3.2 Drug dose of a single active ingredient too high	19 (4.1)	5 (1)	.028	4 (4.1)	92 (54.4)	< .001
C3.3 Dosage regimen not frequent enough	30 (6.4)	31 (6)	NS	10 (10.3)	7 (4.1)	NS
C3.4 Dosage regimen too frequent	6 (1.3)	1 (0.2)	NS	0	1 (0.6)	NS
4. Treatment duration						
C4.1 Duration of treatment too short	2 (0.4)	0	NS	0	0	NS
C4.2 Duration of treatment too long	11 (2.4)	0	.002	0	0	NS
5. Dispensing						
C5.1 Prescribed drug not available	23 (4.9)	8 (1.6)	NS	6 (6.2)	4 (2.4)	NS
C5.2 Necessary information not provided or incorrect advice provided	1 (0.2)	0	NS	2 (2.1)	0	NS
6. Drug use process						
C6.1 Inappropriate timing of administration or dosing intervals by a health professional	15 (3.2)	35 (6.8)	NS	3 (3.1)	0	NS
C6.2 Drug under-administered by a health professional	3 (0.6)	1 (0.2)	NS	2 (2.1)	0	NS
C6.3 Drug over-administered by a health professional	0	1 (0.2)	NS	2 (2.1)	0	NS
C6.4 Drug not administered at all by a health professional	8 (1.7)	0	.044	6 (6.2)	1 (0.6)	NS
C6.6 Drug administered via the wrong route by a health professional	2 (0.4)	0	NS	0	0	NS
8. Patient transfer related						
C8.1 Medication reconciliation problem	4 (0.9)	0	.044	0	0	NS
9. Other						
C9.1 No or inappropriate outcome monitoring (incl. TDM)	24 (5.1)	0	.001	0	0	NS
C9.2 Other cause; specify	10 (2.1)	0	.007	7 (7.2)	0	.044
Total number of DRPs	468	513		97	169	
C: cause; DRP: drug-related problem; NS: non-significant; TDM: therapeutic drug monitoring						

Table 3. Analysis of interventions in study groups

The planned interventions	Study Group P	Study Group N
	n (%)	n (%)
I0.1 No intervention	21 (4.5)	11 (11.3)
I1.3 Intervention proposed to prescriber	12 (2.6)	0
I1.4 Intervention discussed with prescriber	3 (0.6)	0
I3.1 Drug changed to ...	2 (0.4)	1 (1)
I3.2 Dosage changed to ...	43 (9.2)	23 (23.7)
I3.3 Formulation changed to ...	100 (21.4)	10 (10.3)
I3.4 Instructions for use changed to ...	73 (15.6)	12 (12.4)
I3.5 Drug paused or stopped	24 (5.1)	2 (2.1)
I3.6 Drug started	44 (9.4)	18 (18.6)
I4.1 Other intervention (specify)	146 (31.2)	20 (20.6)
Total number of DRPs	468	97

DRP: drug-related problem; I: intervention

Table 4. The most common D-level and X-level potential drug-drug interactions

PICU		NICU	
D-Level (n)	X-Level (n)	D-Level (n)	X-Level (n)
fentanyl-midazolam (58)	acetazolamide – topiramate (4)	fentanyl-midazolam (7)	fluconazole-domperidone (1)
fentanyl-levetiracetam (40)	desmopressin-dexamethasone (3)	fluconazole-midazolam (3)	
fentanyl-ketamine (26)	desmopressin – furosemide (2)	amikacin – vancomycin (3)	
fentanyl-propofol (14)	desmopressin – hydrocortisone (2)		
dexmedetomidine – midazolam (11)	topiramate-zonisamide (2)		

D-level: interactions necessitating consideration of therapy modification, according to Lexidrug™; X-level: contraindicated to use interacting drugs concomitantly, according to Lexidrug™; PICU: pediatric intensive care unit; NICU: neonatal intensive care unit

Table 5. Factors that increase the risk of DRP in the pediatric intensive care unit

	Odds Ratio of having at least one DRP	95% Confidence Interval		p
		Lower	Upper	
Antibiotic use	15.027	5.703	39.590	< .001
Polypharmacy*	28.833	6.953	119.563	< .001
Mechanical ventilation	11	3.590	33.708	< .001

*Presence of a minimum of two drugs in the treatment regimen; DRP: drug-related problem

In Study Group P number of DRPs was correlated with length of hospital stay ($r=0.637$; $p<.001$), number of drugs used ($r=0.835$; $p<.001$), and number of pDDIs ($r=0.640$; $p<.001$). In Study Group N number of DRPs was correlated with the number of drugs used ($r=0.448$; $p<.001$), and the number of pDDIs ($r=0.283$; $p<.001$); whereas it was not significantly correlated with length of hospital stay ($p>.05$).

For all patients in the study, age (day) was correlated with the number of DRPs ($r=0.413$; $p<.001$). However, when each group was evaluated separately, there were no significant correlations between the number of DRPs and age. DRPs were more common in the pediatric group than in neonates ($n=981$ vs. $n=266$, respectively; $p<.001$). The median (IQR) number of DRPs was 3 (1-6) for the pediatric patients and 1 (0-1) for the neonate patients ($p<.001$).

DRP risk in PICU patients increased with the presence of antibiotic use, polypharmacy, and mechanical ventilation (Table 5). No significance was noted for NICU patients concerning the same factors.

4. DISCUSSION

Although many studies analyze CP's input in the identification and resolution of DRPs in patients hospitalized in the general pediatric ward, only a limited number of such studies have been conducted in the NICU and PICU settings (17, 23-25). As far as we know, our study is the first one aiming to assess the CP's input in identifying and intervening in the DRPs encountered in the NICU and PICU settings in Türkiye.

In our study DRPs were more common in the pediatric group than in the neonates ($p<.001$). The median number of DRPs per patient was 3 for the Control Group P and 1 for the Control Group N. Tawhari et al (26) reported the number of DRPs per patient as 1.9 in the PICU and 0.9 in the NICU. In another one, the number of DRPs per patient was determined 2.5 in the PICU, 1.4 in the NICU, and 1.6 in the pediatric ward (27). A systematic review indicated an increased occurrence of medication errors in the PICU in comparison to the NICU (28). Similar results were recorded in studies from United Kingdom and Saudi Arabia, showing that DRP risk in children is higher in the PICU than in other services and that DRP incidence, as well as the number of DRPs per patient, is higher in the PICU than in other services and NICU (8, 29). In contrast, DRPs were more common in newborns in Ethiopia than in other age groups (30). The rationale behind this increased rate of DRPs in the PICU compared to the NICU can be attributed to the higher number of medications administered to the PICU patients. A study conducted in Saudi Arabia, similar to this study, found that the probability of DRPs in PICU was higher than in NICU and that the incidence of DRPs increased proportionally with the number of medications (29). This may be attributed to the more complexity of medication regimens in the PICU compared to the NICU.

The number of DRPs per patient in the retrospective part of our study was higher than that was calculated for the prospective part for both the pediatric and neonatal patients.

This may be explained by a possible Hawthorne effect that might be caused by the presence of the CP in the PICU and NICU; healthcare professionals might have behaved more cautiously knowing they were being watched (31).

The most frequently observed DRPs and their rates in the prospective part of this study were in agreement with those reported from other studies where 'drug use process' (32.6%) and 'dose selection' (30.8%) were the most common causes of DRPs in the NICU (30) and, 'dose selection' and 'drug selection' in pediatrics (29).

Similarly, studies conducted at the NICU, PICU, and general pediatric service found out that 'drug selection' and 'dose problems' were the most frequently observed DRPs (25.5-27.5%, 34.2-50.7%, respectively) (11, 27). In another study conducted in the NICU, the most common causes of DRPs which were 'dose selection' (72.1%) and 'drug selection' (14%) were reported with about twice the frequency that we observed (27). The main reason for the DRPs caused by dose selection was that the drug doses remained at the sub-dose as the body weight of the newborns changed within a few days after birth.

In this study, 'too low drug dose' (19.6%) and 'no/incomplete drug treatment in spite of existing indications' (16.5%) were the most common causes of DRPs in the prospective NICU patients, while it was 'inappropriate combination of drugs' (29.1%) and 'inappropriate drug form/formulation' (20.5%) in the prospective PICU patients. This is similar to the finding that the most DRP causes in the general pediatric ward were an 'inappropriate combination of drugs' (69%) and 'no or inappropriate outcome monitoring' (10%)(19). In another study conducted in the NICU, the 3 most frequently observed DRPs were 'wrong drug administered' (14.4%), 'prescription error' (13.8%), and 'drug dose too low' (13.5%) (26). In another study conducted in NICU, PICU, and general pediatrics, the 2 most common DRPs were 'inappropriate drug form' (13.6%) and 'no drug treatment in spite of existing indication' (12.6%)(29).

In pediatrics, as the number of drugs used by patients increases, the risk of DRP may also increase(25, 29). In our PICU patients, DRP risk was increased by 29-fold by the presence of polypharmacy; this was similar to the results of a pediatric study where polypharmacy increased DRP risk by 32-fold (19).

In our study, the most common pDDIs in the PICU were related to the concomitant use of fentanyl-midazolam, fentanyl-levetiracetam, and fentanyl-ketamine. Like our results, in a pediatric study in the literature phenobarbital, diazepam, and hydrocortisone were among the drugs causing the majority of pDDIs (32). Interactions involving these groups of drugs are common due to the high need for opioid analgesics, anesthesia, and seizure monitoring in intensive care conditions.

Since our study was conducted in the intensive care setting, interventions were not performed at the patient level as in other studies in the literature (8, 33, 34).

In our study, the majority of the proposed interventions (91.5% for PICU, 100% for NICU) were accepted by the physicians similar to the high acceptance rates reported in other studies (24, 25, 35, 36). In studies conducted in the general pediatric service, the acceptance rates of interventions ranged from 81% to 97% (23, 34), while Jafarian et al. reported a lower acceptance rate (59.2%) in their study conducted in the NICU, PICU, and general pediatrics (27).

Although this novel study is one of the first studies from Türkiye reporting the results of CP's involvement in the NICU and PICU healthcare teams through identification and intervention regarding DRPs, it has some limitations. As this was not a randomized controlled trial, the real impact of the CP on the resolution or prevention of DRPs could not be assessed. Additionally, the severity and preventability of DRPs could not be assessed. As the study was carried out in a single center, the results of the study may not be generalized. The possibility that the Hawthorne effect is a type of human behavioral reactivity in which individuals change an aspect of their behavior in response to their awareness could also be considered one of the limitations of the study. In the future, multicenter studies employing a randomized controlled trial design with larger patient populations should be conducted to assess the long-term impact of CPs in the NICU and PICU.

5. CONCLUSION

The study findings demonstrate the potential of CPs in the NICU and PICU settings to identify and resolve DRPs. Physicians' high acceptance rate of the CP's intervention proposals suggests that involvement of the CP in the healthcare team can make a positive contribution to the success of the treatment. Additionally, the results of the study are anticipated to inform decision-makers in the future, guiding the implementation of formal policies to ensure the inclusion of CPs in the NICU and PICU.

Acknowledgements: We would like to thank to the staff of University of Health Sciences Istanbul Haseki Training and Research Hospital for their support.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Marmara University, Institute of Health Sciences, Noninvasive Clinic Ethics Committee (Approval date 16.03.2020; Number:41)

Peer-review: Externally peer-reviewed

Author Contributions:

Research idea: ZYA, SA

Design of the study: ZYA, SA, DB

Acquisition of data for the study: ZYA, SB

Analysis of data for the study: ZYA, MS

Interpretation of data for the study: ZYA, SA

Drafting the manuscript: ZYA

Revising it critically for important intellectual content: ZYA, SA, MS

Final approval of the version to be published: ZYA

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Mediterranean Diet as an Adjunct Therapy in Bacterial Vaginosis Treatment: A Randomized Controlled Trial

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Received: August 14, 2024

Accepted: May 25, 2025

ABSTRACT

Objective: Vaginitis is a common and treatable condition in women. However, bacterial vaginosis (BV) may be resistant to treatment despite the use of antibiotics. This study aimed to determine the effect of the Mediterranean diet on the treatment of BV.

Methods: This randomized controlled trial was designed to investigate the impact of the Mediterranean diet on BV treatment. Demographic data, body mass index (BMI), menopausal status, presence of diabetes mellitus, medical history, average three-day food intake, and treatment outcomes during follow-up examinations were recorded. Patients who were advised to follow the Mediterranean diet and adhered to it (Group 1) were compared with those in the control group who did not follow a dietary intervention (Group 2). Additionally, patients were categorized based on the persistence of BV following treatment.

Results: The study included 64 patients who were advised to follow the Mediterranean diet and complied with it, and 64 patients who received no dietary recommendation. The mean age of participants was 49.32 ± 10.53 years. The treatment-resistant group had higher rates of elevated BMI ($>30 \text{ kg/m}^2$), history of vaginal surgery, history of vaginitis, and non-adherence to the Mediterranean diet compared to the treatment-responsive group ($p < .05$). Multivariate analysis revealed that high BMI (≥ 30), diabetes mellitus, recurrent vaginitis, and not adhering to the Mediterranean diet were statistically significant risk factors for treatment-resistant vaginitis.

Conclusion: The Mediterranean diet enhances the effectiveness of BV treatment. High BMI, diabetes mellitus, and a history of recurrent vaginitis are significant risk factors for treatment-resistant bacterial vaginosis.

Keywords: Bacterial vaginosis, treatment, Mediterranean diet

1. INTRODUCTION

Vaginosis is a highly prevalent condition among women. It encompasses a range of disorders that cause distressing vaginal symptoms such as burning, itching, abnormal discharge, unpleasant odor, dryness, and dyspareunia [1–4]. The causes of vaginosis include fungal, bacterial, and protozoal infections, chemical irritants, medications, tumors, and hormonal changes [5,6]. Different types of vaginosis occur depending on the causative agent, with bacterial vaginosis (BV) being one of the most common. BV is estimated to account for 10–30% of vaginal infections, affecting approximately 13 million women globally [7–10]. If left untreated, BV can lead to serious health complications, including cervical and ovarian cancers, infertility, chronic pelvic pain, and ectopic pregnancy [10].

Previous research has demonstrated a relationship between dietary habits and the development of BV [12–14]. Risk factors for vaginitis include obesity, physical inactivity, consumption of sugary and acidic beverages, excessive alcohol intake, insufficient vitamin C, stress, sleep disturbances, and antibiotic use [15]. Diet plays a critical role in vaginal health. High intake of fruits and vegetables increases dietary fiber and supplies non-digestible oligosaccharides, prebiotics, and other functional carbohydrates that support intestinal and vaginal health [16,17]. Functional foods, probiotics, and prebiotics have also been shown to help treat vaginal inflammation.

Micronutrient deficiencies—particularly in vitamins A, C, D, E, and beta-carotene—can increase susceptibility to BV and

How to cite this article: Tazeoğlu A, Gecgil Demir E. Mediterranean Diet as an Adjunct Therapy in Bacterial Vaginosis Treatment: A Randomized Controlled Trial. Clin Exp Health Sci 2025; 15: 324-332. <https://doi.org/10.33808/clinexphhealthsci.1533219>

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often reflect inadequate fruit and vegetable consumption. Recently, researchers have found that nutrient-dense diets significantly reduce the likelihood of bacterial infections. Regular consumption of fresh fruits and vegetables is associated with a reduced risk of vaginitis [18]. Betaine, found in vegetables like spinach, has also been linked to vaginal health; reduced betaine intake correlates with an increased risk of molecular-BV, according to Tuddenham et al. [19]. Moreover, high consumption of refined sugar has been shown to negatively impact vaginal health, increasing vulnerability to fungal infections. A balanced diet—rich in fresh vegetables and fruits, and low in processed and sugary foods—is recommended for maintaining vaginal health [20–22].

The Mediterranean diet (MD), characterized by high consumption of fruits, vegetables, whole grains, legumes, fish, and low intake of processed foods, is considered a model of healthy eating. Women's health is a cornerstone of development, particularly in low – and middle-income countries [21]. The human microbiota, which is closely influenced by dietary patterns, plays a crucial role in health and disease. Studies across diverse populations show that strong adherence to the MD correlates with reduced incidence of chronic conditions such as cancer, metabolic syndrome, cardiovascular and neurodegenerative diseases, type 2 diabetes, non-alcoholic fatty liver disease, and allergies [23]. Furthermore, MD adherence is associated with improved quality of life, psychological well-being, and metabolic health [24].

In recent years, improved dietary habits have been linked to declining gastric cancer rates worldwide. For instance, in Southern Italy—where the MD is prevalent—and other Mediterranean countries like France and Greece, cancer mortality rates are lower than in Northern Italy and other non-Mediterranean regions, although the exact reasons for this remain under investigation [25].

While BV is commonly treated with vaginal tablets, creams, antibiotics, and antiparasitic drugs, these treatments are not always effective [26]. Therefore, incorporating nutritional therapy alongside medical treatment could provide greater benefits. This study aimed to evaluate the impact of the Mediterranean diet as a complementary intervention to standard medical treatment in patients diagnosed with vaginitis.

2. METHODS

A randomized controlled study was designed to investigate the effect of the Mediterranean diet on the treatment of vaginitis in patients diagnosed with BV and receiving medical treatment. The study was carried out in collaboration between the Gynecology and Obstetrics Clinic and the Diet Clinic. The patient group with bacterial vaginosis was randomly divided into two: diet and control groups (Figure 1).

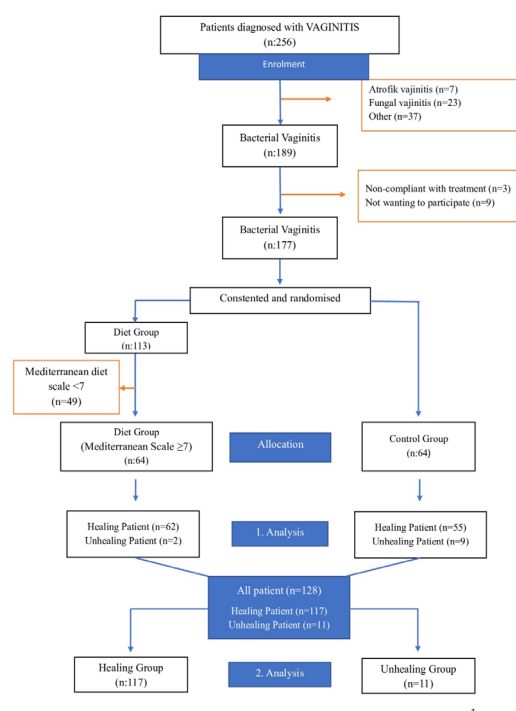


Figure 1: Patient Selection

The inclusion criteria for the study were; having been diagnosed with vaginitis, agreeing to participate in the study, not having used antibiotics or probiotics in the last 3 months, not being pregnant or breastfeeding. Individuals with mental illness, special diet, immune system diseases and those who had given birth in the last 6 months were excluded from the study. Patients (n=256) diagnosed with BV (n=189) and receiving medical treatment were randomly divided into two groups: diet and control. Medical treatment was administered to both groups. Excluded from the study were: 7 patients with vaginal atrophy, 23 with fungal vaginitis, 37 with different diagnoses upon symptom examination, 3 who discontinued treatment after study initiation, and 9 who withdrew voluntarily (Figure 1). Patients in the diet group were those who had been diagnosed with BV, received medical treatment, were recommended a Mediterranean diet, adhered to it based on the Mediterranean Diet Adherence Questionnaire, and returned for a follow-up visit after two weeks. Control group patients were those who had been diagnosed with BV, received medical treatment, and returned for a follow-up visit but were not given any dietary recommendations. After the control visit, patients were classified as either successfully or unsuccessfully treated and compared accordingly.

Patients' sociodemographic data (age, gender, marital status, duration of education, and employment status) were recorded. Educational status was grouped based on duration (≤ 12 and > 12 years), and employment status was categorized as employed or unemployed. The Mediterranean diet has no time limit and is considered a lifestyle. Its effects typically begin two weeks after initiation, lowering the inflammatory index of the diet [27]. For this reason, a re-evaluation was

performed after two weeks of dietary intervention. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Osmaniye Korkut Ata University Science, Scientific Research, and Publication Ethics Committee (Approval Number: 2022/8/1). Written informed consent was obtained from all participants. The study is registered at <https://clinicaltrials.gov/> with the identifier NCT05828498.

2.1. Recommended Diet Protocol

The total energy needs of randomly selected participants were calculated by a dietitian using the Harris-Benedict method [28], and a personalized Mediterranean diet plan was created. Only individuals not on any prior diet were included. Those who had dieted in the past year or were currently on a diet were excluded. The diet plan was followed for two weeks and tailored to individual eating habits. Meals were distributed across breakfast, lunch, dinner, and two snacks. While meal frequency could be adjusted based on individual preferences, the diet pattern and caloric intake remained constant. The control group received only medical treatment, without any dietary guidance.

The traditional Mediterranean diet emphasizes plant-based foods (fruits, vegetables, whole grains, legumes, nuts, and seeds); minimally processed, seasonal, and locally grown ingredients; fresh fruit for dessert; moderate consumption of dairy (mainly cheese and yogurt); 0–4 eggs per week; low to moderate fish and poultry; limited red meat; and moderate wine consumption with meals [26] (Figure 2). The MD is rich in antioxidants such as beta-carotene, vitamins B, C, and E, folic acid, polyphenols, and other phytochemicals. It has been extensively studied for its role in chronic disease prevention and management [29]. The diet plan was thoroughly explained to participants.

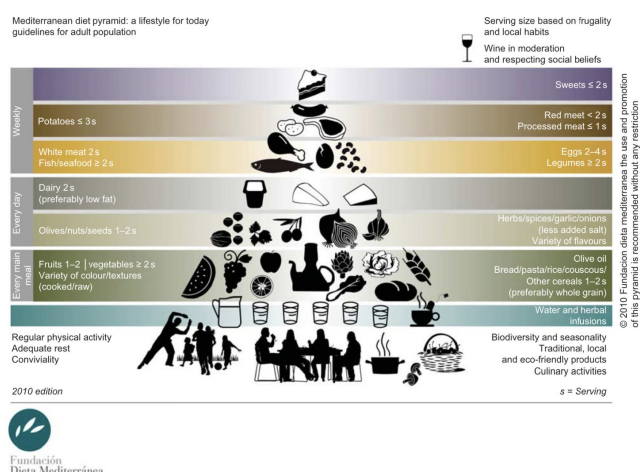


Figure 2: The Mediterranean diet pyramid [18].

2.2. Data Collection

Demographic data (age, gender), anthropometric measurements, presence of comorbid diseases, menopausal

status, diabetes mellitus (DM), medical history, average three-day food intake (2 weekdays, 1 weekend), and treatment outcomes were recorded. Additional information regarding birth history, delivery method, vaginal surgery, and history of vaginitis was obtained.

2.3. Anthropometric Measurements

Body weight (kg), height (cm), and total body and abdominal fat percentages were measured. Weight was assessed using a 100g-sensitive standard scale, and height was measured using a Harpenden Stadiometer. BMI was calculated using the formula: $\text{weight}/\text{height}^2$. Body composition was assessed using the Tanita device, which measures fat, muscle mass, and fat-free mass across five regions via bioelectrical impedance analysis (BIA). Obesity was defined as BMI ≥ 30 kg/m² according to WHO standards [30].

2.4. Nutrient Consumption Analysis

Patients were instructed to keep a food diary before their follow-up visit. To ensure accuracy, visual aids of portion sizes (e.g., tea glass, bowl, spoon sizes) were provided. Data from food diaries were analyzed using the BEBIS software. Daily energy intake (kcal), macronutrient distribution, and fiber intake were calculated, and protein sources were categorized as animal or plant-based. The frequency of vegetable, fruit, and grain consumption was recorded.

2.5. Mediterranean Diet Compliance Questionnaire

Adherence to the Mediterranean diet was assessed using the Mediterranean Diet Adherence Scale. This 14-question tool evaluates aspects such as type and amount of oil, frequency of fruit and vegetable intake, red meat, wine, legumes, fish, nuts, and olive oil-based tomato sauce consumption. Each question is scored 0 or 1 based on consumption. A score >7 was considered indicative of good adherence and used to determine inclusion in the diet group [31].

2.6. Diagnosis and Treatment of Bacterial Vaginosis

BV diagnosis was made by an obstetrician-gynecologist. When needed, diagnosis was confirmed via vaginal culture and microbiological testing. Treatment was administered using oral or vaginal antibiotics (metronidazole or clindamycin), based on physician preference.

2.7. Power Analysis

A clinically significant difference was assumed to be half a standard deviation (Cohen's d) between patients on and off the Mediterranean diet. Based on a power of 0.80 and a Type I error of 0.05, the required sample size per group was 64. Sample size calculation was performed using G*Power.

2.8. Ethics Committee Approval

The study protocol was reviewed and approved by the Scientific Research and Publication Ethics Committee of Osmaniye Korkut Ata University (Decision Number: 2022/8/1-168). Written informed consent was obtained from all participants prior to inclusion in the study.

2.9. Statistical Analysis

Continuous data were presented as mean $\pm$ standard deviation; ordinal data as median with minimum and maximum values; and categorical data as frequencies and percentages. Student's t-test and Mann-Whitney U test were used for comparisons between two independent groups. The Chi-square test assessed relationships between categorical variables. Logistic regression analysis with backward and enter methods was conducted to evaluate treatment-resistant vaginitis risk. A p-value $<.05$ was considered statistically significant. Analyses were performed using MedCalc and www.e-picos.com.

3. RESULTS

In total, 256 patients were diagnosed with vaginitis in the Obstetrics and Gynecology Clinic. Of these, bacterial vaginosis (BV) was identified in 189 patients (73.8%). Twelve patients with BV declined participation and were therefore excluded from the study. Among the remaining 177 patients, 113 were provided with counseling regarding the Mediterranean diet. Of these, 49 patients (42.5%) were excluded due to a Mediterranean Diet Adherence Scale (MDAS) score below 7. The remaining 64 patients (57.5%) who adhered to the Mediterranean diet (MDAS ≥ 7) were included in the dietary intervention group (Group 1). The control group (Group 2) consisted of 64 patients who received standard medical treatment without any dietary intervention.

All participants were female, with a mean age of 49.32 ± 10.53 years. In terms of marital status, 39 patients (30.5%) were single and 89 (69.5%) were married. Educational attainment was ≤ 12 years in 76 patients (59.4%) and >12 years in 52 patients (40.6%). Employment status was nearly balanced, with 67 patients (52.3%) employed and 61 (47.7%) unemployed. There were no statistically significant differences between the two groups in terms of age, marital status, educational level, or employment status ($p>.05$).

Demographic and clinical characteristics are presented in Table 1 and 2. There were no statistically significant differences between the groups regarding age, body mass index (BMI), total body fat percentage, abdominal fat percentage, menopausal status, presence of diabetes mellitus (DM), obstetric history, delivery method, history of vaginal surgery, or previous episodes of vaginitis ($p>.05$).

Nutritional analysis revealed that the mean daily energy intake was significantly lower in Group 1 (27.58 ± 9.19 kcal/kg/day) compared to Group 2 (31.12 ± 8.27 kcal/kg/day; $p = .02$). The proportion of energy derived from carbohydrates was also significantly lower in Group 1 ($63.18 \pm 15.82\%$) than in Group 2 ($76.41 \pm 13.43\%$; $p<.001$). Daily protein intake did not differ significantly between groups ($p = .16$); however, the proportion of protein derived from plant-based sources was significantly higher in Group 1 (72.35%) compared to Group 2 (31.75%) ($p<.001$).

Mean daily fiber intake was significantly greater in Group 1 (22.92 ± 5.53 g/day) than in Group 2 (17.93 ± 4.84 g/day; $p<.001$). Regarding daily food consumption frequencies, Group 1 consumed significantly more vegetables [5 (3–7) vs. 3 (2–6) portions/day], fruits [3 (1–5) vs. 2 (1–3) portions/day], and cereals [7 (3–9) vs. 3 (1–4) portions/day] than Group 2 (all $p<.001$).

Following treatment, treatment-resistant vaginitis persisted in 2 patients (3.1%) in Group 1 and in 9 patients (14.1%) in Group 2, indicating a significantly higher rate of resistance in the control group ($p<.05$).

Table 1. Anthropometric measurements and food consumption distribution of patients

	All patient (n=128)	Group 1 (n=64)	Group 2 (n=64)	p value	test value	Cohen's d	Average Difference	95% Confidence Interval
	X $\pm$ SD	X $\pm$ SD	X $\pm$ SD					
Age(year)	49.32 $\pm$ 10.53	48.11 $\pm$ 9.97	50.53 $\pm$ 11.02	.19*	-1.303	0.23	2.42	-1.22 to 6.06
BMI (kg/m ²)	27.95 $\pm$ 6.72	27.81 $\pm$ 5.81	28.09 $\pm$ 6.23	.79*	-0.263	0.05	0.28	-1.81 to 2.37
Total body fat (%)	34.87 $\pm$ 8.76	33.79 $\pm$ 8.33	35.94 $\pm$ 7.27	.12*	-1.556	0.28	2.15	-0.56 to 4.86
Abdominal region fat (%)	36.29 $\pm$ 10.52	35.57 $\pm$ 9.11	37.12 $\pm$ 10.05	.36*	-0.914	0.16	1.55	-1.77 to 4.87
Energy (kcal/kg/day)	29.35 $\pm$ 9.47	27.58 $\pm$ 9.19	31.12 $\pm$ 8.27	.02*	-2.291	0.4	3.54	0.51 to 6.57
Carbohydrate consumption (%)	69.78 $\pm$ 14.39	63.18 $\pm$ 15.82	76.41 $\pm$ 13.43	<.001*	-5.10	0.9	13.23	8.15 to 18.31
Protein (g/day)	0.88 $\pm$ 0.31	0.84 $\pm$ 0.29	0.91 $\pm$ 0.27	.16*	-1.413	0.25	0.07	-0.03 to 0.17
Vegetable protein (%)	52.05 $\pm$ 10.37	72.35 $\pm$ 10.07	31.75 $\pm$ 9.87	<.001*	23.035	-4.07	-40.6	-44.05 to -37.15
Animal protein (%)	47.95 $\pm$ 10.37	27.65 $\pm$ 10.07	68.25 $\pm$ 9.87	<.001*	-23.035	4.07	40.6	37.15 to 44.05
Fiber (g)	20.43 $\pm$ 5.83	22.92 $\pm$ 5.53	17.93 $\pm$ 4.84	<.001*	5.432	-0.96	-4.99	-6.79 to -3.19

Group 1: Mediterranean Diet, Group 2: Control, * Independent t test.

Table 2. Demographic data and food consumption distribution of patients

	All patient (n=128)	Group 1 (n=64)	Group 2 (n=64)	p value	test value	Dependency Coefficient (Cohen's ω)
	Median (min-max)	Median (min-max)	Median (min-max)			
Vegetable consumption (portion/day)	4 (2-7)	5 (3-7)	3 (2-6)	< .001*	6.461	-
Fruit consumption (portion/day)	2 (1-5)	3 (1-5)	2 (1-3)	< .001*	3.228	-
Grain consumption (portion/day)	4 (1-9)	7 (3-9)	3 (1-4)	< .001*	7.455	-
	n (%)	n (%)	n (%)			
Marital status						
Single	39 (30.5)	21 (32.8)	18 (28.1)	.57**	0.332	5.1
Married	89 (69.5)	43 (67.2)	46 (71.9)			
Education status						
≤12	76 (59.4)	35 (54.7)	41 (64.1)	.28**	1.166	9.5
>12	52 (40.6)	29 (45.3)	23 (35.9)			
Working status						
Yes	67 (52.3)	37 (57.8)	30 (46.9)	.22**	1.535	10.9
No	61 (47.7)	27 (42.2)	34 (53.1)			
Menopausal period						
premenopause	45 (35.2)	24 (37.5)	21 (32.8)	.58**	0.308	4.9
postmenopause	83 (64.8)	40 (62.5)	43 (67.2)			
BMI						
<30	93 (72.7)	43 (67.2)	50 (78.1)	.17**	1.927	12.3
≥30	35 (27.3)	21 (32.8)	14 (21.9)			
Diabetes Mellitus	54 (42.2)	29 (45.3)	25 (39.1)	.47**	0.513	6.3
Vaginal operation history	9 (7.1)	5 (7.8)	4 (6.2)	.73**	0.120	3.1
Birth history	114 (89.1)	59 (92.2)	55 (85.9)	.26**	1.283	10.0
Birth method						
Vaginal	92 (71.9)	44 (68.8)	48 (75)	.43**	0.618	7.0
C/S	36 (28.1)	20 (31.2)	16 (25)			
Vaginitis history	67 (52.3)	31 (48.4)	36 (56.3)	.38**	0.783	7.8
Vaginitis clinic continuing after treatment	11 (8.6)	2 (3.1)	9 (14.1)	.03**	4.203	17.7

Group 1: Mediterranean Diet, Group 2: Control, * Mann Whitney-U test, ** Chi square test.

Table 3. Clinical data of treatment-resistant and susceptible patients after bacterial vaginitis treatment

	All patient (n=128)	Successful Group (n=117)	Failed Group (n=11)	p value	test value	Dependency Coefficient (Cohen's ω)
	n (%)	n (%)	n (%)			
Menopausal period						
premenopause	45 (35.2)	42 (35.9)	3 (27.3)	.57*	0.328	5.1
postmenopause	83 (64.8)	75 (64.1)	8 (72.7)			
BMI						
<30	93 (72.7)	89 (76.1)	4 (36.4)	.005*	7.977	25.0
≥30	35 (27.3)	28 (23.9)	7 (63.6)			
Diabetes Mellitus	54 (42.2)	45 (38.5)	9 (81.8)	.005*	7.748	24.6
Vaginal operation history	9 (7.1)	7 (5.9)	2 (18.2)	.006*	2.292	13.4
Vaginitis history	67 (52.3)	57 (48.7)	10 (90.9)	.04*	7.174	23.7
Birth history	114 (89.1)	105 (89.7)	9 (81.8)	.42*	0.649	7.1
Birth method						
Vaginal	92 (71.9)	85 (72.6)	7 (63.6)	.53*	0.404	5.6
C/S	36 (28.1)	32 (27.4)	4 (36.4)			
Diet						
Normal diet	64 (50)	55 (47.1)	9 (81.8)	.03*	4.873	19.5
Mediterranean	64 (50)	62 (52.9)	2 (18.2)			

Group 1: Mediterranean Diet, Group 2: Control, * Chi square test.

Participants were further categorized into two outcome groups: successful ($n = 117$; 91.4%) and unsuccessful ($n = 11$; 8.6%) based on treatment response. No significant differences were observed between these groups in terms of menopausal status, birth history, or delivery method ($p > .05$). However, the unsuccessful treatment group had significantly higher rates of obesity ($\text{BMI} > 30 \text{ kg/m}^2$), presence of DM, prior vaginal surgery, a history of vaginosis, and non-adherence to the Mediterranean diet ($p < .05$; Table 3).

Multivariate logistic regression analysis revealed that high BMI ($\geq 30 \text{ kg/m}^2$) was significantly associated with treatment resistance ($\text{OR} = 5.56$, 95% CI: 1.52–20.41, $p < .05$). Similarly, presence of diabetes mellitus ($\text{OR} = 7.21$, 95% CI: 1.49–34.85, $p < .05$), history of vaginosis ($\text{OR} = 10.53$, 95% CI: 1.31–84.88, $p < .05$), and non-adherence to the Mediterranean diet ($\text{OR} = 5.07$, 95% CI: 1.05–24.49, $p < .05$) were found to be independent risk factors for persistent vaginitis. However, a history of vaginal operation was not significantly associated with treatment failure ($\text{OR} = 3.49$, 95% CI: 0.63–12.89, $p > .05$) (Table 4).

Table 4. Relationship between treatment-resistant vaginitis and clinical data

	Odds ratio	%95 confidence interval (Lower – Upper)	p value
Body Mass Index	5.56	1.52 – 20.41	< .05
Diabetes Mellitus	7.21	1.49 – 34.85	< .05
Vaginal Operation History	3.49	0.63 – 12.89	> .05
Vaginitis History	10.53	1.31 – 84.88	< .05
Diet	5.07	1.05 – 24.49	< .05

4. DISCUSSION

Women's health constitutes a cornerstone of development and societal progress, particularly in low – and middle-income countries. If left untreated, vaginitis can result in severe complications, including uterine, cervical, and ovarian cancers, infertility, chronic pelvic pain, and ectopic pregnancy [10]. The findings of this study demonstrate that adherence to the Mediterranean diet—characterized by a high intake of vegetables, fruits, nuts, legumes, seafood, and olive oil—significantly enhances the therapeutic response in patients with bacterial vaginosis (BV). As such, the incorporation of nutritional therapy into vaginitis treatment protocols holds considerable promise from a public health perspective.

An inverse correlation was observed between the incidence of vaginitis and adherence to a healthy diet, sufficient physical activity, and psychological well-being. These lifestyle components have been consistently associated with improved vaginal health outcomes [32]. The Mediterranean diet was recognized by the United Nations Educational, Scientific and Cultural Organization (UNESCO) in 2010 as a model dietary pattern that promotes health and longevity [33]. The improved treatment response observed in the intervention group (Group 1) aligns with the findings of Parsapour et al.,

who reported that health-promoting lifestyle interventions positively influence women's health [21].

Notably, the Mediterranean diet is distinguished by its high consumption of plant-based foods and limited intake of dairy products [34]. In this study, participants in Group 1 exhibited significantly higher consumption of vegetables, fruits, and protein-rich foods compared to the control group. These dietary components—particularly fresh fruits and vegetables—are rich sources of vitamins and minerals essential for maintaining vaginal health. Nutrients such as phytosterols, vitamins C and E, beta-carotene, and calcium may exert protective effects through antioxidant mechanisms that reduce cellular proliferation [35]. Zodzika et al. demonstrated that vaginal administration of ascorbic acid improved vaginal pH and microflora composition [36]. Furthermore, consistent with the present findings, previous research has shown that reduced sugar and dairy intake, coupled with increased fruit and vegetable consumption, contributes to the effective management of vaginitis [37]. Additionally, trace elements such as iron and zinc have been implicated in modulating immune function, particularly mucosal immunity—a relationship that appears to be mediated by dietary diversity [38]. Therefore, the Mediterranean diet, due to its nutritional richness and variety, may serve as an effective dietary strategy for managing vaginitis.

Weight management, maintenance of an optimal body mass index (BMI), and stress regulation are also critical factors in the effective management of vaginitis. Nyirjesy et al. reported a higher prevalence of BV symptoms—such as irritation, itching, and abnormal vaginal discharge—among obese individuals compared to those with normal BMI values [39]. The Mediterranean diet, which provides a minimum of 14 grams of dietary fiber per 1000 kilocalories—approximately twice the fiber content of a typical Western diet—contributes to weight control, improved gut microbiota, and reduced serum cholesterol and insulin levels [40]. In alignment with these findings, the current study identified elevated BMI as a risk factor for vaginitis.

Additionally, the presence of diabetes mellitus (DM) was identified as another risk factor. While some studies have found no direct association between elevated HbA1c levels and BV, borderline HbA1c values have been significantly associated with BV [41]. It is worth noting that in both the current and referenced studies, the impact of antihyperglycemic medications on vaginal microbiota was not examined. Given the potential modulatory effects of these drugs, future research should aim to isolate and assess their specific contributions.

Vaginitis is not confined to women of reproductive age but is also prevalent among postmenopausal women. The decline in estrogen levels during menopause reduces glycogen stores in vaginal epithelial cells, leading to diminished lactobacilli populations, which rely on glycogen for sustenance. These hormonal changes are accompanied by an elevated vaginal pH, reduced skin elasticity, and a decrease in vaginal secretions, collectively contributing to increased vulvovaginal discomfort

and a predisposition to infections [39]. Although the altered hormonal milieu in postmenopausal women increases susceptibility to BV, menopausal status does not appear to significantly influence treatment outcomes [42]. Moreover, comparative studies examining treatment responses between premenopausal and postmenopausal women remain scarce. In the present study, no significant difference in treatment efficacy was observed between these two groups.

The Mediterranean diet is rich in mono- and polyunsaturated fatty acids, as well as polyphenols and antioxidants, and has been shown to exert beneficial effects on the composition of the gut microbiota [43]. Fava et al. reported that adherence to the Mediterranean diet increased the abundance of *Lactobacillus*, *Bifidobacterium*, and *Prevotella* species, while reducing *Clostridium* populations [44]. It is hypothesized that the favorable response to treatment observed in Group 1 may be attributable, in part, to the prebiotic properties of dietary fiber, which modulate the vaginal microbiota.

The overarching aim of this study was to enhance women's health and mitigate the adverse effects of vaginitis through dietary intervention. Given the potential to reduce both disease burden and healthcare costs, the implementation of nutritional therapy—specifically, adherence to the Mediterranean diet—may constitute a cost-effective and sustainable approach for the management of BV [45]. However, the present study did not fully account for confounding variables such as psychological stress, physical activity, and comorbid health conditions, which may have influenced the findings. One of the primary strengths of this study lies in the homogeneous distribution of participants in Groups 1 and 2 with respect to anthropometric parameters, including body mass index (BMI), total body fat, and abdominal fat at baseline. Additionally, most previous studies in this field have predominantly focused on women of reproductive age (15–49 years). However, vaginitis is not exclusive to younger women; it is also frequently observed in postmenopausal women. Notably, in the present study, 65% of the participants were postmenopausal, which is a valuable contribution toward broadening clinical awareness and tailoring treatment strategies for this demographic group. Besides, our findings suggest that diet can serve as a complementary approach to conventional medical treatment in the management of BV. Considering the rise in antibiotic resistance, lifestyle-based interventions may offer an effective and sustainable solution to enhance treatment efficacy, particularly in high-risk populations. Importantly, no significant differences were observed between the intervention and control groups in terms of sociodemographic or baseline clinical characteristics, supporting the conclusion that the improved outcomes were primarily attributable to dietary adherence. Accordingly, future longitudinal studies are warranted to validate these results and to assess the long-term feasibility and clinical efficacy of dietary interventions, while systematically controlling for such confounding factors.

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anthropometric parameters, including body mass index (BMI), total body fat, and abdominal fat at baseline. Additionally, most previous studies in this field have predominantly focused on women of reproductive age (15–49 years). However, vaginitis is not exclusive to younger women; it is also frequently observed in postmenopausal women. Notably, in the present study, 65% of the participants were postmenopausal, which is a valuable contribution toward broadening clinical awareness and tailoring treatment strategies for this demographic group.

Despite contributing to a broader understanding of the association between the Mediterranean diet and vaginitis, the study has several limitations. First, dietary intake was assessed using a three-day food intake diary and a Mediterranean Diet Adherence Scale. Since these instruments are based on self-reported data, the potential for recall bias and reporting inaccuracies must be acknowledged. Since individuals could not be followed up verbatim during the dietary intake questionnaire, we used information provided by individuals in the intake records. Monitoring and recording their intake verbatim would eliminate this limitation. Second, the medication status of patients with diabetes mellitus (DM) was not assessed. This omission represents a limitation, as anti-hyperglycemic medications may affect the composition of the vaginal microbiota. Secondly, the medication status of patients with diabetes mellitus (DM) was not assessed. This omission represents a limitation, as anti-hyperglycemic medications may influence the composition of the vaginal microbiota. Finally, The short follow-up duration did not allow assessment of long-term treatment outcomes.

5. CONCLUSION

This study demonstrates that adherence to the Mediterranean diet may improve treatment success and reduce resistance in bacterial vaginosis. These findings underscore the potential role of dietary interventions as adjunctive therapies in managing BV, especially in patients with obesity, diabetes, or recurrent infections. Future studies with larger sample sizes and randomized controlled designs are needed to confirm these results, explore the long-term effects, and elucidate the underlying biological mechanisms.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Osmaniye Korkut Ata University, Noninvasive Clinic Ethics Committee (Approval date: 01 / 08 / 2022; Number: 168)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: AT

Design of the study: AT

Acquisition of data for the study: AT

Analysis of data for the study: AT, EGD

Interpretation of data for the study: EGD

Drafting the manuscript: AT

Revising it critically for important intellectual content: AT, EGD

Final approval of the version to be published: AT, EGD

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The Effects of Music Listening on Pain, Anxiety, and Quality of Life in Patients with Chronic Low Back Pain

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Received: September 19, 2024 **Accepted:** June 20, 2025

ABSTRACT

Objective: The aim of this study was to investigate the effects of music listening on pain, anxiety and quality of life in Chronic Low Back Pain (CLBP) patients.

Methods: This randomized controlled trial included 60 patients aged 30-50 with CLBP. Participants were randomly assigned to either a control group receiving standard physiotherapy or a music group receiving the same physiotherapy accompanied by music listening. Pain intensity, anxiety levels, and quality of life were assessed using the Visual Analogue Scale (VAS), Beck Anxiety Inventory (BAI), and SF-36, respectively, at baseline and after a 4-week intervention.

Results: Both groups showed significant reductions in pain and anxiety post-intervention, with more pronounced improvements in the music group ($p < .05$). The music group also demonstrated significant enhancements in physical function, emotional role, and pain perception on the SF-36 ($p < .05$), while other subscales showed no significant changes ($p > .05$).

Conclusion: Music listening, as an adjunct to conventional physiotherapy, effectively reduces pain and anxiety while improving certain aspects of quality of life in CLBP patients. These findings support the inclusion of music therapy as a complementary approach in the management of chronic pain.

Keywords: Physical Therapy, Low back pain, Music

1. INTRODUCTION

Low back pain (LBP) is one of the leading causes of disability worldwide. According to the World Health Organization (WHO), 619 million people worldwide will suffer from LBP in 2020 (1). Due to population growth and ageing, the number of people with LBP is expected to reach 843 million worldwide by 2050 (2). Low back pain leads to loss of working days and is an economic burden on societies. Low back pain is therefore an important public health problem (3).

Low back pain is classified according to the duration of symptoms as acute (<6 weeks), subacute (6-12 weeks) and chronic (>12 weeks). Acute low back pain usually resolves spontaneously and lasts less than 6 weeks. However, in some patients the pain may recur after the acute phase and progress to chronic low back pain (4).

The treatment programme for low back pain should be planned according to the patient's symptoms. The main aim of treatment is to improve function and reduce pain. However, it is important for the patient to avoid situations that may trigger symptoms in the future and to adopt a healthy lifestyle (5).

Treatment options include patient education, pharmacological treatment, physiotherapy and rehabilitation approaches, minimally invasive applications, passive modalities and surgical treatment approaches. The first step in treatment is usually conservative management. The most commonly used conservative treatment is exercise (6). Studies show that exercise is effective in relieving low back pain, improving functionality, increasing muscle endurance and flexibility, reducing the risk of pain recurrence, and improving quality of

How to cite this article: Torlak MS, Ünüvar BS, Tüfekçi O, Gerçek H, Dursun B. The Effects of Music Listening on Pain, Anxiety, and Quality of Life in Patients with Chronic Low Back Pain. Clin Exp Health Sci 2025; 15: 333-339. <https://doi.org/10.33808/clinexphealthsci.1552871>

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life. Physical activity has also been reported to reduce anxiety symptoms and improve emotional and psychological status (7, 8).

One of the alternative methods of pain management is music therapy. Music is one of the oldest and most deeply rooted forms of expression in human history. It has been used for therapeutic purposes in many cultures since ancient times (9). It has a powerful effect on the emotional states of individuals. Music listening is a method used for individuals to achieve emotional relaxation by listening in the background without actively participating in the music (10). Studies have found that music therapy improves general mood of people, reduces perceived pain and decreases anxiety levels. Patients receiving music therapy have been shown to have better outcomes than those receiving standard care alone (11). It is thought that music therapy can improve people's quality of life by reducing pain levels and the need for medication, and by controlling stress and anxiety (12).

Although there are studies in the literature that indicate the positive effects of listening to music on health, there are no studies on CLBP. This study aims to investigate the effects of music listening on low back pain, anxiety and quality of life. The results of the study will inform the integration of alternative and complementary health approaches by understanding the contribution of music to the psychological and physical health of individuals and how it can be used in treatment processes.

2. MATERIAL AND METHOD

2.1. Patients

The study was conducted in a private hospital between March 2024 and August 2024. The study included 60 volunteer patients, aged between 30-50 years, who were diagnosed with chronic low back pain by a physical medicine and rehabilitation physician. Patients were randomly divided into control (n=30) and music groups (n=30). Patients with low back pain for more than 3 months and pain intensity of 5 or more on a visual analogue scale (VAS) were included in the study. Patients who regularly took painkillers or antidepressants and cortisone, those with serious chronic conditions, and those who had spinal surgery were excluded from the study.

2.2. Randomization

The trial was designed as a single-blind, randomised, prospective trial. Two different treatment options for randomisation were created on a computer by a statistician and numbered from largest to smallest by placing them in envelopes. Sixty patients were divided into two groups using the sequential randomisation method. The person administering the treatment opened the envelopes in turn and applied the treatment in the envelope according to the number of patients. The different physiotherapists performed the conventional physiotherapy and these physiotherapists

were not changed during the treatment. It was not possible to blind the physiotherapist and the patients. However, the outcome assessor who assessed the clinical measures was unaware of the type of treatment. The Consolidated Standards of Reporting Trials (CONSORT) diagram for participant recruitment is shown in Figure 1.

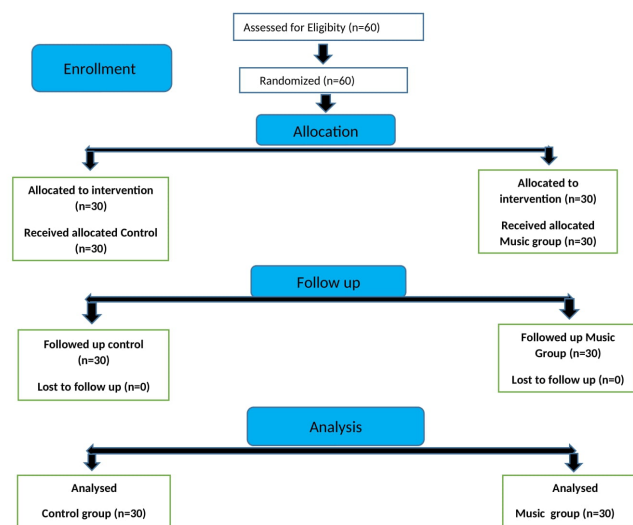


Figure 1. Study Flow

2.3. Ethical Consideration

The study was approved by the ethics committee of KTO Karatay University Faculty of Medicine, non-drug and non-medical device research. (Protocol No:2023/042). The study was registered on ClinicalTrials.gov (number: NCT06263803). All patients were given verbal and written information about the study and signed an informed consent form. The trial was conducted in accordance with the ethical principles of the Declaration of Helsinki. Participants gave their informed consent to be included in this study.

2.4. Treatment

Participants in the control group received a classic physiotherapy programme 5 days a week for 4 weeks. This programme included transcutaneous electrical stimulation (TENS) for 20 minutes, hot pack for 20 minutes and ultrasound for 5 minutes (13). For the participants in the music group, Pachabel's Canon in D major (20 min) and Mozart's Sonata for Two Pianos in D, KV 448 (25 min) were played during the classical physiotherapy session, without external sounds (max 70 dB through headphones). These two music parts were chosen because there is evidence that they have a positive effect on cognitive function and reduce anxiety (14, 15).

In addition, participants in both groups were given a patient-specific home exercise programme by a specialist physiotherapist. The exercise programme developed by Koumantakis et al (2005) was used for participants in all groups (16). The programme aims to increase the strength and flexibility of the abdominal, erector spinae, gluteal,

quadriceps and hamstring muscles. The programme begins with lumbar and pelvic stretching and warm-up exercises, followed by strengthening exercises. Participants completed the programme 3 times a day for 4 weeks, doing 10 repetitions of each exercise.

2.5. Outcomes

At the beginning and end of the study, participants' anxiety levels were measured using the Beck Anxiety Scale (BAS), pain intensity using the Visual Analogue Scale (VAS), and quality of life using the SF-36 scale.

The BAS is a 4-point Likert-type scale consisting of 21 items scored from 0 to 3, with raw scores ranging from 0 to 63. The higher the total score, the more anxious the person. BAI scores are categorised as minimal anxiety (0 to 7), mild anxiety (8 to 15), moderate anxiety (16 to 25) and severe anxiety (30 to 63) (17).

VAS is a practical and easy-to-use scale for subjective assessment of pain. A 100 mm straight line is used for measurement. The patient is asked to mark the intensity of the felt pain on this line. On the line, '0' means no pain and '100' means unbearable pain (18).

The SF-36 assesses a person's general health. It consists of a total of 36 questions assessing two basic parameters (mental and physical) and eight sub-parameters (emotional functioning, physical functioning, physical role, social functioning, mental health, general health, vitality and pain). Each parameter can be scored from zero to 100 points. High scores indicate good quality of life (19).

2.6. Sample Size

The sample size calculation was done using a G*power analysis software Version 3.0.10 (G*Power, Franz Faul, Universitat Kiel, Germany). It was calculated according to the previous study examining the effect of conventional physiotherapy on chronic low back pain (20). VAS scores were used to estimate the sample size. The analysis indicated that thirty participants for each group were enough to detect a large Cohen's effect ($d = 0.75$) with an alpha error probability of 0.05 and a power of 80%.

2.7. Statistical Analysis

Statistical Package for the Social Sciences software version 29 (IBM Corp., Armonk, NY, USA) statistical package program was used to evaluate the data. Descriptive statistics (mean, standard deviation, number and percentile) were given for categorical and continuous variables. The conformity of the variables to normal distribution was examined using the Shapiro-Wilk test and histogram method. In the comparison

of paired groups, the Independent Samples t Test was used for the data fitting the normal distribution and the Mann-Whitney U test was used for the data not fitting the normal distribution. Chi-Square test was used to compare categorical data. Within comparison, Wilcoxon test was used due to the fact that the data did not fit the normal distribution. The formula $r = z/\sqrt{N}$ was used to determine the effect size. Statistical significance level $p < 0.05$ was accepted.

3. RESULTS

The study included 60 participants, 32 men and 28 women, aged 44.58 ± 9.41 years, with a mean BMI of 25.85 ± 3.79 kg/m². The demographic information of the participants is shown in Table 1.

Table 1. Demographic data of participants

	Music (n=30) X $\pm$ SD / n(%)	Control (n=30) X $\pm$ SD / n(%)	t / X ²	p
Age	46.97 $\pm$ 8.34	42.20 $\pm$ 9.94	2.011	.051a
BMI	24.96 $\pm$ 2.64	26.75 $\pm$ 4.55	1.977	.066 a
Gender				
Male	15 (50,0)	17 (56.7)	.268	.605 b
Female	15 (50,0)	13 (43.3)		

n: number, X: mean, SD: standard deviation, %: percentage, BMI: body mass index; t: Independent Sample t Test, X²: Chi-Square, $p < .05$

Participants' pain ($p = .584$), anxiety ($p = .538$) and quality of life scores were similar before the study (Table 2).

Table 2. Participants' pain, anxiety and quality of life scores

	Music (n=30) X $\pm$ SD	Control (n=30) X $\pm$ SD	Z	p
VAS	7.76 $\pm$ 1.07	7.83 $\pm$ 0.59	.547	.584
BAS	11.33 $\pm$ 7.14	10.03 $\pm$ 6.86	.615	.538
SF36				
Physical Functioning	43.17 $\pm$ 26.01	54.17 $\pm$ 28.80	1.483	.138
Physical role	36.67 $\pm$ 35.19	31.67 $\pm$ 39.89	.756	.449
Emotional role	37.77 $\pm$ 42.65	23.33 $\pm$ 37.29	1.515	.130
Vitality	34.67 $\pm$ 19.21	37.83 $\pm$ 17.05	.668	.504
Mental	50.80 $\pm$ 18.04	57.87 $\pm$ 19.33	1.119	.263
Social	57.08 $\pm$ 23.37	60.42 $\pm$ 25.44	.479	.632
Pain	43.83 $\pm$ 17.95	34.41 $\pm$ 17.61	1.969	.049*
General	57.50 $\pm$ 17.31	51.00 $\pm$ 21.94	1.106	.269

n: number, X: mean, SD: standard deviation, VAS: visual analog scale, BAS: Beck Anxiety Scale, Z: Mann-Whitney U test, $p < 0.05$

In the music group, pain ($p < .001$, $Z = 4.822$, $r = 0.88$) and anxiety ($p = .001$, $Z = 3.308$, $r = 0.60$) values decreased after the application. Similarly, in the control group, pain ($p < .001$, $Z = 4.821$, $r = 0.88$) and anxiety ($p = .002$, $Z = 3.173$, $r = 0.57$) decreased after the study (Table 3).

Table 3. within-group comparison before and after the study

	Music (n=30) X ± SD	Z	p	Control (n=30) X ± SD	Z	p
VAS before	7.76 ± 1.07	4.822	<.001**	7.83 ± 0.59	4.821	<.001**
VAS after	3.20 ± 1.32			3.40 ± 1.59		
BAS before	11.33 ± 7.14	3.308	.001**	10.03 ±6.86	3.173	.002**
BAS after	9.30 ± 6.12			6.93 ± 5.84		
SF36						
Physical Functioning before	43.17 ± 26.01	4.189	<.001**	54.17 ± 28.80	0.736	.462
Physical Functioning after	58.50 ± 28.29			57.50 ± 26.84		
Physical role before	36.67 ± 35.19	2.362	.018*	31.67 ± 39.89	1.779	.075
Physical role after	54.17 ± 35.41			46.67 ± 40.86		
Emotional role before	37.77 ± 42.65	2.047	.041*	23.33 ± 37.29	2.754	.006**
Emotional role after	52.22 ± 42.61			46.67 ± 47.63		
Vitality before	34.67 ± 19.21	1.572	.116	37.83 ± 17.05	2.120	.034*
Vitality after	37.33 ± 18.23			43.83 ± 17.35		
Mental before	50.80 ± 18.04	0.922	.357	57.87 ± 19.33	0.017	.986
Mental after	54.00 ± 16.76			58.40 ± 15.42		
Social before	57.08 ± 23.37	0.458	.647	60.42 ± 25.44	1.872	.061
Social after	56.77 ± 23.64			67.08 ± 21.64		
Pain before	43.83 ± 17.95	2.957	.003**	34.41 ± 17.61	4.143	<.001**
Pain after	53.41 ± 18.19			54.83 ± 21.51		
General before	57.50 ± 17.31	0.626	.531	51.00 ± 21.94	3.327	.001**
General after	57.83 ± 16.85			57.67 ± 22.19		

n: number, X: mean, SD: standard deviation, VAS: visual analog scale, BAS: Beck Anxiety Scale, Wilcoxon, $p < 0.05$

When SF36 and its sub-parameters were evaluated before and after the study in the music group, Physical function ($p < .001$, $Z = 4.189$, $r = 0.76$), Physical role ($p = .018$, $Z = 2.362$, $r = 0.43$) Emotionality ($p = .041$, $Z = 2.047$, $r = 0.37$) and pain ($p = .003$, $Z = 2.957$, $r = 0.53$) increased, while no change was observed in Vital ($p = .126$, $Z = 1.572$, $r = 0.28$), Mental ($p = .357$, $Z = 0.922$, $r = 0.16$) Social ($p = .647$, $Z = 0.458$, $r = 0.08$) and General ($p = .531$, $Z = 0.626$, $r = 0.11$) parameters (Table 3).

In the control group, when SF36 and its sub-parameters were evaluated before and after the study, Emotional ($p = .006$, $Z = 2.754$, $r = 0.50$), Vital ($p = .034$, $Z = 2.120$, $r = 0.38$), Pain ($p < .001$, $Z = 4.143$, $r = 0.75$) and General ($p = .001$, $Z = 3.327$, $r = 0.60$)

increased, while no change was observed in Physical function ($p = .462$, $Z = 0.736$, $r = 0.13$), Physical role ($p = .075$, $Z = 1.779$, $r = 0.43$), Mental ($p = .986$, $Z = 0.017$, $r = 0.01$) and Social ($p = .061$, $Z = 1.872$, $r = 0.34$) parameters (Table 3).

The participants' post-test pain ($p = .812$, $Z = 0.238$) and anxiety ($p = .108$, $Z = 1.609$) values were similar between the groups (Table 4).

Post-test SF36 ($p = .964$, $Z = 0.045$) and Physical Functioning ($p = .929$, $Z = 0.089$), Physical role ($p = .449$, $Z = 0.757$), Emotionality ($p = .582$, $Z = 0.550$), Vitality ($p = .186$, $Z = 1.324$), Mental ($p = .598$, $Z = 0.527$), Social ($p = .110$, $Z = 1.600$) and Pain ($p = .846$, $Z = 0.194$) subparameters were similar between groups (Table 4).

Table 4. Between group comparison of post-test pain, anxiety and quality of life scores

	Music (n=30) X ± SD	Control (n=30) X ± SD	Z	p
VAS	3.20 ± 1.32	3.40 ± 1.59	0.238	.812
BAS	9.30 ± 6.12	6.93 ± 5.84	1.609	.108
SF36				
Physical Functioning	58.50 ± 28.29	57.50 ± 26.84	0.089	.929
Physical role	54.17 ± 35.41	46.67 ± 40.86	0.757	.449
Emotional role	52.22 ± 42.61	46.67 ± 47.63	0.550	.582
Vitality	37.33 ± 18.23	43.83 ± 17.35	1.324	.186
Mental	54.00 ± 16.76	58.40 ± 15.42	0.527	.598
Social	56.77 ± 23.64	67.08 ± 21.64	1.600	.110
Pain	53.41 ± 18.19	54.83 ± 21.51	0.194	.846
General	57.83 ± 16.85	57.67 ± 22.19	0.045	.964

n: number, X: mean, SD: standard deviation, VAS: visual analog scale, BAS: Beck Anxiety Scale, Mann Whitney U, $p < 0.05$

4. DISCUSSION

This study aimed to investigate the effects of music listening on low back pain (LBP), anxiety, and quality of life in patients with chronic low back pain (CLBP). The findings reveal that integrating music listening into a conventional physiotherapy regimen significantly reduces pain and anxiety levels, while also improving certain aspects of quality of life, particularly physical function, emotional role, and pain perception. These results contribute to the growing body of evidence supporting the use of music therapy as a complementary treatment modality in managing chronic pain conditions. The significance of these findings lies in the ability of music therapy to address multiple dimensions of well-being in a holistic manner, providing both physical and psychological benefits, which is essential for comprehensive patient care.

The study demonstrated a significant reduction in pain levels in both the music and control groups, as measured by the Visual Analogue Scale (VAS). However, the reduction in pain was more pronounced in the music group. This aligns with existing literature that suggests music has a powerful analgesic effect. Research indicates that music can reduce the perception of pain by engaging cognitive

and emotional pathways that modulate pain sensitivity (21-23). The mechanism through which music achieves this effect may involve the activation of the brain's reward centers and the release of endogenous opioids, which help diminish pain perception (24-26). This is consistent with findings from Cepeda et al. (2013) who reported that music therapy is effective in reducing the intensity of pain in various patient populations, including those with chronic pain (27). These observations suggest that music therapy could be a particularly effective tool in pain management by addressing both the physiological and emotional aspects of pain, thereby offering a more comprehensive approach to patient treatment.

Anxiety levels, as measured by the Beck Anxiety Inventory (BAI), also decreased significantly in both groups, with the music group showing a more substantial reduction. The anxiolytic effects of music are well-documented, with studies suggesting that music can induce relaxation and reduce stress by lowering cortisol levels and stabilizing autonomic nervous system responses (28, 29). In this study, the reduction in anxiety observed in the music group could be attributed to the calming effects of classical music, particularly the selected pieces by Pachelbel and Mozart, which have been shown to have positive effects on cognitive function and mood regulation (30-31). These findings are supported by other research that highlights the role of music in improving psychological well-being and reducing anxiety in clinical settings (32-34). The implications of these results are significant because they demonstrate that music therapy not only alleviates anxiety but also enhances cognitive and emotional stability, which are critical for the overall well-being of patients suffering from chronic pain conditions.

Quality of life, as assessed by the SF-36, showed significant improvements in physical function, emotional role, and pain in the music group. These findings are important because they suggest that music listening not only alleviates physical symptoms but also enhances psychological and emotional well-being. The improvement in physical function is particularly noteworthy, as it indicates that music therapy may contribute to better overall physical health and greater engagement in daily activities (35). This is consistent with the study by Bradt et al. (2007), which found that music therapy significantly improved physical and emotional outcomes in patients with chronic conditions (36). The improvement in these quality of life metrics underscores the potential of music therapy to serve as an effective adjunct to traditional physiotherapy, providing a more holistic approach to improving patient outcomes by addressing both the physical and emotional dimensions of chronic pain.

However, it is important to note that some SF-36 subscales, such as vitality, mental health, social functioning, and general health, did not show significant changes in either group. This could be due to the relatively short duration of the intervention or the specific characteristics of the patient population. Previous studies have shown that longer-term music interventions may be required to observe significant

changes in these dimensions of quality of life (37). This finding suggests that while short-term interventions can yield positive results in some areas, a more extended duration of music therapy might be necessary to achieve broader improvements in overall quality of life, particularly in aspects related to mental and social health.

The findings of this study have several clinical implications. First, they support the inclusion of music listening as a complementary therapy in the management of CLBP. Given the low cost, ease of implementation, and minimal side effects, music therapy can be readily integrated into existing treatment protocols to enhance patient outcomes. Second, the study highlights the potential for music therapy to address both physical and psychological aspects of chronic pain, making it a holistic approach to pain management. These implications are particularly relevant in clinical practice, where the need for effective, non-invasive, and cost-effective treatment options is increasingly recognized, and where integrating music therapy could lead to more comprehensive and patient-centered care.

Despite the promising findings, this study has some limitations. The sample size was relatively small, which may limit the generalizability of the results. Additionally, the study duration was short, and the long-term effects of music therapy on pain, anxiety, and quality of life were not assessed. Future research should consider larger sample sizes and longer follow-up periods to better understand the sustained impact of music therapy on chronic pain conditions. These limitations highlight the need for continued research to validate and expand upon the findings of this study, ensuring that music therapy is appropriately tailored and applied to achieve the best possible outcomes for patients with chronic pain.

Implications for physical therapy practice

In this study, positive effects of listening to music were observed in patients with chronic low back pain. As this method is cheap and easy to use, we recommend that it be added to physiotherapy sessions. In addition, this inexpensive method may have a positive effect on the cost of treatment.

5. CONCLUSION

In conclusion, this study provides evidence that music listening can significantly reduce pain and anxiety while improving certain aspects of quality of life in patients with chronic low back pain. These findings suggest that music therapy may be a valuable addition to conventional treatment strategies for CLBP, offering a non-invasive, cost-effective, and easily accessible method to enhance patient care. The integration of music therapy into clinical practice could provide a more holistic approach to managing chronic pain, ultimately leading to better patient outcomes and improved quality of life.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by the ethics committee of KTO Karatay University Faculty of Medicine, non-drug and non-medical device research. (Approval date: 22.12.2023 Number: 2023/042).

Peer-review: Externally peer-reviewed.

Author Contribution

Research idea: MST

Design of the study: MST, BSU

Acquisition of data for the study: OT, BD

Analysis of data for the study: HG

Interpretation of data for the study: HG, BD

Drafting the manuscript: BSU, OT, HG

Revising it critically for important intellectual content: MST, BSU, OT

Final approval of the version to be published: MST, BSU, OT, HG

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The Effect of Sleep Quality on Happiness in Elderly Individuals

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Received: September 20, 2024 **Accepted:** June 18, 2025

ABSTRACT

Objective: Sleep problems are commonly seen in elderly people. This study was planned to determine the effect of sleep quality on happiness in elderly people.

Method: The study was conducted with 306 elderly people. Data were collected with Personal information form, Pittsburgh Sleep Quality Index and Oxford Happiness Questionnaire-Short Form.

Results: The mean sleep quality score of the elderly people was 7.91 ± 3.65 . The mean happiness score of the elderly people was 24.00 ± 4.88 . There was a relationship between sleep quality scores and happiness scores of elderly people ($r = -0.44$; $p < .001$). Sleep quality was a predictor of approximately 20% of the happiness level of elderly people ($\beta = -.442$; $p < .001$).

Conclusion: This study reveals that sleep quality is poor in elderly people and it is one of the predictor of happiness. Nurses caring for elderly people should implement initiatives to ensure the sleep hygiene of elderly people.

Keywords: Elderly, sleep quality, happiness, nursing

1. INTRODUCTION

One of the basic and vital needs for protecting and maintaining health is sleep. Sleep is effective on mental functions such as emotion, thought, behavior, memory and physical functions such as circulation and digestion. Unfortunately, some goals, such as high status and income, lead to sleep being ignored today (1,2). However, studies on sleep draw attention to the fact that inadequate or poor quality sleep is one of the major health problems, that quality sleep is associated with subjective well-being, and that quality of life decreases as sleep quality decreases (1-6).

Although sleep is necessary for the health of all age groups, there are changes in sleep duration depending on age. The amount of sleep required decreases from childhood to adulthood. There is a change in circadian rhythm and sleep-wake phases with aging and that elderly people cannot adequately produce sleep due to some physiological reasons. Additionally, medical and psychiatric disorders, medication side effect, primary sleep disorders, behavioral habits disrupt sleep quality in the elderly (7). It is showed by studies that chronic health problems lead to sleep problems in the elderly. Thichumpa et al. (2018) reported in their study that moderate depression reduces sleep quality in the elderly (8). Qin et al. (2022) found in a study in which they followed elderly individuals for 2 years that high body

mass index, physical health problems and depression lead to poor sleep quality (9). Zhang et al. (2022) proved that sleep quality is an important mediator between chronic diseases and depressive symptoms (10). On the other hand, there is a misconception in society that sleep problems are a natural consequence of aging. This situation causes sleep quality in elderly people to be underestimated and sleep problems to be ignored (1,2). However, poor sleep quality and daytime sleepiness increase fatigue in elderly people and negatively affect daily living (11,12). Researches suggests that sleep problems lead to serious negative physical, social and mental consequences in elderly people (1,13-15).

Today, successful aging policies aim to ensure that elderly people go through the aging process more happily, positively and satisfied with their lives. Health conditions play an important role in the successful aging (16). It has been known that physical or mental health problems reduce the happiness of people (17-19). A study conducted with people over the age of 65 shows that elderly people who do not feel "well" physically and mentally have low levels of happiness. Similarly, elderly people with low social support have low levels of happiness (20). The other study conducted with people over the age of 60 found that anxiety, social phobia, depression, disability and frailty

How to cite this article: Temel M, Dilek F. The Effect of Sleep Quality on Happiness in Elderly Individuals. Clin Exp Health Sci 2025; 15: 340-346. <https://doi.org/10.33808/clinexphealthsci.1553613>

increased unhappiness (21). It has been determined that health is the first important factor in the perception of happiness of 82 percent of elderly people in Turkey (22).

Detection and treatment of sleep problems in elderly people is important in terms of maintaining both their physical and mental health. In order for elderly people to have an active, healthy and successful old age, it is necessary to maintain that their healthy lifestyle habits like adequate sleep. Nurses are primary health care personnel who will support elderly people in this regard.

Although there are studies on sleep problems of elderly people in nursing literature, the relationship between sleep quality and perception of happiness has not been adequately evaluated. In this study, it was aimed to examine the effect of sleep quality on happiness in elderly people. The data to be obtained will contribute the practices in elderly care nursing and aging policies

Research questions;

What is the sleep quality level of the elderly people?

What is the happiness level of the elderly people?

Is there a relationship between sleep quality and happiness levels of the elderly people?

Does sleep quality affect happiness in elderly people?

2. METHODS

2.1. Study Design

This study is cross-sectional and correlational design.

2.2. Sample and Setting

This study was conducted with face-to-face interviews with elderly people in their home between November 2021-January 2022. The universe of the study consists of people aged 60 and over living in a city province. The elderly population of city in 2020 is 98.066 people (23). The sample size of the study was determined as a minimum of 267 people using the Raosoft Sample Size Calculation Program ($\alpha=0.05$, $\beta=0.90$) (<http://www.raosoft.com/samplesize.html>). The sample consisted of 306 elderly people who volunteered to participate in the study. People with a psychiatric diagnosis, those using psychotropic medication, those experiencing chronic pain, those experiencing loss in the last 6 months, and those with communication problems were excluded from the study.

2.3. Instruments

Personal information form: It consists of a total of ten questions developed by the researchers questioning the socio-demographic characteristics of elderly people.

Pittsburgh Sleep Quality Index (PSQI): It was improved by Buysse et al. (1989) to determine sleep quality, sleep disturbance and severity. PSQI evaluates sleep quality in the last one month. 19 questions of the 24-question are answered by the patient himself/herself and the scoring of the scale is based on these questions. The other 5 questions are answered

by the patient's spouse or chum and are used only for clinical information and are not included in the rating. The scale has 7 sub-dimensions. These are sleep quality, daytime dysfunction, sleep latency, habitual sleep efficiency, sleep disturbance, use of sleep medication, sleep duration. Each sub-dimension is rated between 0-3, and the total scale score is calculated with the total of the sub-dimension scores. Scores that can be received from the scale change between 0-21. High scores signify poor sleep quality, and a total score bigger than 5 is interpreted as "poor sleep quality". The Cronbach's alpha value of the original scale was 0.83 (24). The Turkish validity and reliability study of the scale was executed by Ağargün et al. (1996) and Cronbach's alpha value was detected to be 0.80 (25). Cronbach's alpha value was found to be 0.80 in this study.

Oxford Happiness Questionnaire-Short Form (OHQ-SF): The scale was initially enhanced by Argyle, Martin and Crossland (1989) as a 4-point likert-type scale with 29 items (26). The scale was later revised by Hills and Argyle (2002) and transformed into a 6-point Likert-type Oxford Happiness Questionnaire, and an 8-item brief form of the scale was also developed in the same study (27). The Cronbach's alpha coefficient of the original version of the OHQ-SF was calculated as 0.76 (28). The unidimensional scale was adapted into Turkish by Doğan and Akıncı-Çötök (2011) and was designed as 7 questions in 5-point Likert type. The minimal score that can be obtained in the Turkish version of the scale is 7, and the supreme score is 35. High scores obtained from the scale signify a high level of happiness. The Cronbach's alpha coefficient of the Turkish version of the OHQ-SF was detected to be 0.74 (29). Cronbach's alpha value was found to be 0.75 in this study.

2.4. Statistical Analysis

Statistical analysis of the data was done with SPSS 22.0 package program (IBM Inc., Chicago, IL, USA). The suitability of the data to normal distribution was tested by Kolmogorov-Smirnov test, kurtosis and skewness values. Descriptive statistical methods and comparative analysis methods were used in the evaluation. Student t test and One Way Anova test was used for group benchmarking of normally distributed quantitative data. The relationships between variables were analyzed with Pearson Correlation Analysis for normally distributed data and Spearman's Correlation Analysis for non-normally distributed data. Simple linear regression analysis was applied to determine whether sleep quality was a predictor of "happiness". Statistical significance was putative as $p<0.05$.

2.5. Ethical Statement

Approval for this study was received by the Non-Interventional Clinical Research Ethics Committee of Medical Faculty of one university with reference number 28/09/2021 (2021.236.09.22). Since the participants were not under any institutional care and the interviews were conducted in their own homes, institutional permission was not required. The participants were informed about the research and their written informed consent was received showing that they voluntarily participated in the study.

3. RESULTS

Table 1 presents the descriptive characteristics of the participants. The mean age of the participants was 69.81 ± 7.02 years, 54.2% were female and 77.5% were married. 53% of the participants were retired and 65.7% had an middle socioeconomic level. Slightly more than half of them had at least one chronic disease and were taking medication.

Table 1. Descriptive characteristics of the elderly people (n=306)

Variables		n	%
Age ($X \pm SD = 69.81 \pm 7.02$) (min-max=60-98)	60-69	175	57.2
	70-79	91	29.7
	80 +	40	13.1
Gender	Female	166	54.2
	Male	140	45.8
Education status	Literate	51	16.7
	Primary and secondary	217	70.9
	High school and university	38	12.4
Marital status	Married	237	77.5
	Single	69	22.5
Children	Yes	289	94.4
	No	17	5.6
Employment status	Employed	17	5.6
	Retired	163	53.3
	Unemployed	126	41.2
Income status	Low	91	29.7
	Middle	201	65.7
	High	14	4.6
Status of living	Alone	56	18.3
	Living with family	250	81.7
Chronic Illness	Yes	169	55.2
	No	137	44.8
Drug use	Yes	165	53.9
	No	141	46.1

The mean OHQ-SF score of the elderly people was 24.00 ± 4.88 and their happiness level was found to be moderate. The mean PSQI score of the elderly people was 7.91 ± 3.65 . According to the cut-off score of the scale, 82.7% of the elderly people had poor sleep quality. According to the PSQI subscale scores, the highest score was found in the sleep disturbance subscale (1.66 ± 0.61) and the lowest score was found in the use of sleeping medication subscale (0.29 ± 0.73) (Table 2).

Table 2. Elderly People' Sleep Quality and Happiness Scores

Variables	Mean	SD	Median	Minimum	Maximum
OHQ-SF	24.08	4.88	24.00	9	35
Total PSQI	7.91	3.65	7	2	20
PSQI-sleep quality	1.11	0.66	1	0	3
PSQI-sleep latency	1.30	0.89	1	0	3
PSQI-sleep duration	1.38	1.15	1	0	3
PSQI-habitual sleep efficiency	1.21	1.32	1	0	3
PSQI-sleep disturbance	1.66	0.61	2	0	3
PSQI-use of sleeping medication	0.29	0.73	0	0	3
PSQI-daytime dysfunction	0.92	0.86	1	0	3

*PSQI: Pittsburgh Sleep Quality Index; OHQ-SF: Oxford Happiness Questionnaire-Short Form

In Table 3, happiness and sleep quality scores of elderly people were compared according to descriptive characteristics. A statistically significant difference was found in both sleep quality scores and happiness scores according to gender, working status, economic status, chronic illness and constant drug use ($p < .05$).

Table 3: Happiness and sleep quality according to descriptive characteristics of elderly people

Variables	OHQ-SF		Total PSQI	
	Mean $\pm$ SD	Test/p	Mean $\pm$ SD	Test/p
Age				
60-69	24.26 $\pm$ 4.98	F: 0.701 p: .497	7.76 $\pm$ 3.65	F: 1.866 p: .156
70-79	24.12 $\pm$ 4.65		7.73 $\pm$ 3.61	
80 and over	23.25 $\pm$ 4.99		8.95 $\pm$ 3.68	
Gender				
Female	23.53 $\pm$ 5.19	t: -2.189 p: .029	8.37 $\pm$ 3.76	t: 2.456 p: .015
Male	24.75 $\pm$ 4.42		7.35 $\pm$ 3.45	
Education status				
Literate	22.64 $\pm$ 4.86	F: 2.834 p: .060	8.39 $\pm$ 3.56	F: 0.545 p: .581
Primary and secondary	24.30 $\pm$ 4.72		7.83 $\pm$ 3.66	
High school and over	24.76 $\pm$ 5.53		7.71 $\pm$ 3.76	
Marital status				
Married	24.06 $\pm$ 4.99	t: -0.165 p: .869	7.92 $\pm$ 3.60	t: 0.146 p: .884
Single	24.17 $\pm$ 4.53		7.85 $\pm$ 3.84	
Children				
Yes	23.95 $\pm$ 4.88	t: -1.923 p: .055	7.82 $\pm$ 3.62	t: -1.815 p: .071
No	26.29 $\pm$ 4.44		9.47 $\pm$ 3.92	
Status of living				
Alone	24.19 $\pm$ 4.70	t: 0.183 p: .855	7.76 $\pm$ 4.06	t: -0.325 p: .745
With family	24.06 $\pm$ 4.93		7.94 $\pm$ 3.56	
Employment status				
Employed (1)	24.52 $\pm$ 4.54	F: 3.112 p: .046 * 2>3	6.76 $\pm$ 3.94	F: 4.399 p: .013 *2<3
Retired (2)	24.68 $\pm$ 4.74		7.48 $\pm$ 3.51	
Unemployed (3)	23.26 $\pm$ 5.02		8.61 $\pm$ 3.70	
Income status				
Low (1)	20.35 $\pm$ 4.68	F: 10.127 p: .000 *1<2;1<3;2<3	10.07 $\pm$ 4.10	F: 5.181 p: .006 *1>3
Middle (2)	23.64 $\pm$ 4.44		8.12 $\pm$ 3.53	
High (3)	25.64 $\pm$ 5.35		7.09 $\pm$ 3.68	
Chronic illness				
Yes	23.23 $\pm$ 4.95	t: -3.470 p: .001	8.55 $\pm$ 3.93	t: 3.452 p: .001
No	25.14 $\pm$ 4.60		7.12 $\pm$ 3.11	
Drug use				
Yes	23.17 $\pm$ 4.99	t: -3.602 p: .000	8.59 $\pm$ 3.95	t: 3.598 p: .000
No	25.15 $\pm$ 4.55		7.11 $\pm$ 3.09	

t: Student's t-test; F: One-Way ANOVA test; * Bonferroni test; OHQ-SF: Oxford Happiness Questionnaire Short Form; PSQI: Pittsburgh Sleep Quality Index

Table 4 presents the happiness scores of the participants according to sleep quality. It was determined that the happiness level of elderly people with poor sleep quality was also lower ($p < .01$).

Table 4. Happiness scores of elderly people according to sleep quality

	n	%	OHQ-SF		
Sleep quality			Mean $\pm$ SD	t*	p
PSQI < 5 (good sleep quality)	53	17.3	27.13 $\pm$ 4.22	5.195	p< .01
PSQI > 5 (poor sleep quality)	253	82.7	23.45 $\pm$ 4.78		

OHQ-SF: Oxford Happiness Questionnaire Short Form; PSQI: Pittsburgh Sleep Quality Index; *t: Student's t-test

Table 5 presents the relationship between sleep quality scores and happiness scores of elderly people ($p < .01$). According to PSQI, high scores from the scale indicate low sleep quality. In this study, it was found that as the sleep quality of elderly people increased, their happiness level also increased.

Table 5. Relationship between sleep quality and happiness scores of elderly people

		PSQI SQ	PSQI SL	PSQI SDu	PSQI SE	PSQI SDi	PSQI USM	PSQI DD	PSQI Total
OHQ-SF	r	-0.382*	-0.214*	-0.152*	-0.226*	-0.342*	-0.198**	-0.378*	-0.442*
	p	.000	.000	.008	.000	.000	.000	.000	.000

OHQ-SF: Oxford Happiness Questionnaire Short Form; PSQI: Pittsburgh Sleep Quality Index *Pearson correlation **Spearman's correlation

In addition, simple linear regression analysis was used to define the impact of sleep quality on happiness (Table 6). The model in the analysis was found to be significant ($F=73.946$; $p < .001$). As per the results of the analysis, it was found that sleep quality determined approximately 20% ($R^2=0.196$) of the happiness level of elderly people ($\beta=-.442$; $p < .001$).

Table 6. Effects of sleep quality on happiness

Parameter	B	Std.error	Beta	t	p	95% CI
Constant	28,764	0,599		48,030	$p < .001$	27,586 29,943
PSQI Total	-0,591	0.069	-0,442	-8,599	$p < .001$	-0,726 -0,456

$R=0,442$; $R^2=0,196$; $F=73,946$; $p < .001$

*PSQI: Pittsburgh Sleep Quality Index

4. DISCUSSION

In this study, sleep quality of elderly people was evaluated with PSQI. According to the mean PSQI score (7.91 ± 3.66), it can be said that the sleep quality of the elderly people participating in the study was poor. When other studies in this field are examined, it is seen that the mean PSQI score of the elderly is greater than 5 and therefore their sleep quality is evaluated as poor (8,10,30,31,32). In different studies, it is reported that there are sleep problems ranging from 30% to 70% among elderly people (8,9,12,32,33). In this study, when the PSQI cut-off score was considered, sleep quality was found to be poor in a large part of the elderly people, 82.7%. This result indicated that sleep problems in the elderly are more common than thought and should be taken into attention. Zhang et al. (2023) reported that 2.5% of elderly people had seriously sleep problems that required treatment (31). Thichumpa et al. (2018) reported that 9.4% of elderly people used sleeping pills (8). In our study, It was determined that the deterioration in sleep quality of elderly people was mostly in the sub-dimensions of sleep disturbance, sleep duration and sleep latency, respectively. The use of sleeping pills was low. This may indicate that although the majority of the elderly participating in this study have sleep problems, they do not take their sleep problems seriously and do not consult a physician.

According to the results we obtained from this study; it can be said that elderly people are moderately happy. In Turkey

life satisfaction surveys, the highest happiness rates were obtained from the population over the age of 65. The life satisfaction level of elderly people in Turkey was determined to be 56-57% in the last few years (34). According to our study results, the happiness levels of elderly people are found to be at a moderate level, which supports the national results. Zhang et al. (2023), it is stated that the happiness rates of Chinese older adults are similar to our country (31). Similarly, in one study conducted in Brazil and the other study conducted in Turkey, the happiness level of elderly people was found to be moderate level and above (20,21). Today's elderly people are called the baby-boomer generation. This generation is known as a resilient group despite the difficulties they experienced when they were born and grew up. It is stated that this generation is more optimistic, calm, has low expectations and is therefore happier compared to other generations (35). The results of the study may be related to this situation.

In this study, the relationship between socio-demographic characteristics of elderly people and sleep quality and happiness was evaluated. It was found that female elderly people had worse sleep quality. Similar results with our study are found in the literature (8,9,13,36). In the present study, it was found that the sleep quality of the elderly who retired from a job and the elderly with good economic status was better. Similarly, Li et al. (2020) reported in their study that sleep quality was worse in the elderly with low income (13). Lack of income and financial difficulties may minds of the elderly busy and lead to sleep problems. It is also supported by other studies that chronic health problems lead to sleep problems in the elderly (8,9,10,36). In this study, sleep quality was devised to be worse in elderly people with chronic diseases and continuous medication use. This may be related to the fact that problems such as pain, drug intake or drug side effects cause sleep interruption.

The relationship between health and happiness is more clearly seen in the elderly population (17,21,37) According to the Turkey Satisfaction Survey (2023), it was found that health came first among the sources of happiness in elderly people (34). In addition, Zhang et al (2022) stated that chronic diseases increase depressive symptoms in the elderly (10). It is thought that reasons such as frequent health problems in the elderly and relatively limited access to treatment reduce the subjective well-being of the elderly (37,38). In this study, the presence of chronic disease was investigated without making a distinction between mental or physical health problems. The happiness levels of the elderly with chronic diseases and who constantly use medication for this reason are lower supports the literature.

In this study, the happiness level of female elderly was found to be lower. states that, happiness level of female elderly is lower and this may be due to the fact that mental problems are more common in female elderly. Unlike these data, there are also studies indicating that female elderly are happier or that the level of happiness does not differ according to gender (38,39). In the present study, it was found that the retired

elderly were happier than the elderly who were not involved in working life. Similarly, the elderly with better economic status were also happier. Retirement provides a regular income for the elderly to make a living. Being financially secure in old age may cause many needs such as receiving health care, nutrition, and paying bills and therefore to feel happier (38).

The relationship between health and happiness is more clearly seen in the elderly population (18,21,37). Zhang et al. (2022) stated that chronic diseases increase depressive symptoms in the elderly (10). That reasons such as frequent health problems and relatively limited access to treatment reduce the subjective well-being of the elderly (37,38). In this study, it was found that the happiness level of elderly with poor sleep quality was lower. Additionally, there was a correlation between sleep quality and happiness. It was also found that sleep quality was one of the determinants of happiness. In the literature; it is indicated that the happiness levels of the elderly with insomnia symptoms are lower and the life satisfaction of the elderly is directly affected by sleep quality (6,40). Reflections of sleep problems in elderly people can occur as depression and anxiety symptoms (8,41). Deterioration in sleep quality also increases the risk of cognitive dysfunction in the elderly (14). This situation negatively reflects on the daily life activities and social life of the elderly due to reasons such as loss of attention, interest and concentration and causes a decrease in the quality of life of the elderly people (42). Sleep quality can play a mediating role between different variables. It has also been found that sleep quality is a mediator between life satisfaction and mental health, as well as between chronic diseases and depressive symptoms (10,31).

The results of the study were evaluated only on the data of the elderly people who participated in the study. Sleep quality and happiness data are based on subjective evaluations of elderly people. On the other hand, other variables that may affect happiness in elderly people were not taken into account in this study.

Therefore, this research results cannot be generalised to all elderly people and care should be taken when interpreting data.

5. CONCLUSION

According to the data obtained from this study; sleep quality is low in elderly people. This situation is also reflected negatively in the happiness perceptions of elderly people. Today, concepts such as active aging, healthy aging, successful aging have started to be adopted in the field of elderly health. In this context, various approaches are applied to ensure that the elderly are happy, peaceful, healthy, independent and involved in social life. Evaluating the sleep quality of elderly people, improving sleep quality and providing treatment of sleep problems should be a part of these approaches. The process can be started by raising awareness of elderly people and caregivers about sleep quality and sleep hygiene. Nurses

working in the field of elderly health should play the most important role in this regard.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Tekirdağ Namık Kemal University, Noninvasive Clinic Ethics Committee (Approval date: 28.09.2021; Number 2021.236.09.22)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: MT, FD

Design of the study: FD, MT

Acquisition of data for the study: MT, FD

Analysis of data for the study: MT, FD

Interpretation of data for the study: MT, FD

Drafting the manuscript: MT, FD

Revising it critically for important intellectual content: MT, FD

Final approval of the version to be published: MT, FD

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Emergency Department Physicians' Knowledge, Attitudes, and Behaviors Regarding Antimicrobial Use, Resistance, and Stewardship: A Cross-Sectional Study

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Received: October 11, 2024

Accepted: June 19, 2025

ABSTRACT

Objective: Antimicrobial resistance (AMR) is a global public health threat. In our country, emergency departments, where antibiotics are most frequently prescribed, have limited data regarding physicians' knowledge, attitudes, and behaviors related to antibiotic use (AMU), AMR, and antibiotic stewardship (AMS).

Methods: A cross-sectional survey was conducted among emergency department (ED) physicians in a major city in western Turkey. The online survey assessed their knowledge, attitudes, and behaviors regarding AMU, AMR, and AMS. The internal consistency of the questionnaire was validated with a Cronbach's alpha of 0.77.

Results: Among the 141 participating physicians, 54.6% were assistants, 34.0% specialists, 7.09% faculty members, and 4.26% general practitioners. The median knowledge score was 90.0 [Q1; Q3: 80.0; 100], and 69.5% had good knowledge, but a lack of knowledge about antimicrobial agents' (AMA) pharmacology was observed. The median attitude score was 59.4 [Q1; Q3: 56.2; 68.8], and 48.2% had correct attitudes. Wrong attitudes were observed in the AMA administration. The median behavior score was 53.0 $\pm$ 16.6, with 53.9% of physicians exhibiting appropriate behavior regarding the use of AMA. The most important factors affecting behavior were patient insistence and errors in empirical AMA administration. A positive correlation was observed between attitudes and behaviors ($r = 0.397$, $p < .001$), and it was found that the level of knowledge wasn't reflected in behaviors.

Conclusions: Our results showed that although physicians working in EDs have high levels of knowledge about AMU, AMR, and AMS, this knowledge isn't reflected in attitudes and behaviors. To increase the effectiveness of AMS programs, special education programs that shape attitudes and behaviors and public awareness are needed.

Keywords: Antimicrobial Stewardship; Emergency Service, Hospital; Health Knowledge, Attitudes, Practice; Anti-Infective Agents; Drug Resistance, Bacterial

1. INTRODUCTION

Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi, and parasites evolve to resist medications, making infections harder to treat and increasing the risk of severe disease and death (1). In the United States, over 2.8 million AMR infections occur annually, with the CDC reporting more than 35,000 deaths in 2019 (2). It has been projected that AMR could cause 10 million deaths per year by 2050 (3). The World Health Organization (WHO) has identified AMR as an urgent issue requiring a global, coordinated response (4).

The overuse of antimicrobial agents (AMAs), inappropriate prescribing, extensive agricultural use, and limited new antibiotic development are key factors driving AMR (5).

Inappropriate prescribing is often linked to inexperienced physicians, diagnostic challenges, and patient interference (6). Physicians' knowledge, attitudes, and behaviors (KAB) regarding antimicrobial use (AMU) are crucial for controlling AMR and ensuring the success of antimicrobial stewardship programs (AMS-P) (7).

Antimicrobial stewardship (AMS) is a coordinated program that promotes appropriate AMU, improves patient outcomes, reduces AMR, and limits the spread of multidrug-resistant infections (8). It systematically educates and supports healthcare professionals in following evidence-based guidelines for AMA prescribing. Studies show that AMS programs enhance

How to cite this article: Korkmaz İ, Korkmaz ÖE. Emergency Department Physicians' Knowledge, Attitudes, and Behaviors Regarding Antimicrobial Use, Resistance, and Stewardship: A Cross-Sectional Study. Clin Exp Health Sci 2025; 15: 347-356. <https://doi.org/10.33808/clinexphealthsci.1565284>

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healthcare professionals' awareness and knowledge of AMR and AMU, leading to better prescribing practices (9).

In Turkey, national action plans and guidelines aligned with WHO recommendations have been developed to combat AMR. The Prescription Information System (PIS) analyzes physicians' prescriptions and provides feedback. Medication production, distribution, and disposal processes are closely monitored, and AMAs are prescription-only. Hospital infection control committees, led by infectious disease specialists and trained nurses, oversee AMA use and monitor resistant bacteria. Despite these efforts, healthcare costs related to AMR in Turkey remain high, and the country faces a potential economic loss of \$220 billion to \$1.4 trillion by 64 2050 due to high antibiotic resistance (10,11).

Physicians working under heavy workloads, such as in emergency departments (EDs), may be more prone to unnecessary AMA use due to patient pressure, potentially undermining the effectiveness of the AMS program. This study aimed to evaluate the KAB of ED physicians regarding AMU, AMR, and AMS. The findings will provide valuable insights to enhance AMS programs and develop strategies to combat AMR, serving as a guide for planning and implementing interventions to reduce AMR in healthcare delivery.

2. METHODS

2.1. Study Design

This study is an observational descriptive study with a cross-sectional design. Between September 2024 and October 2024, 141 physicians consisting of general practitioners, assistants, specialists, and faculty members working in the EDs of hospitals (private, public, university, and education and research hospitals) located in the 3rd metropolitan area in western Turkey were included. The survey was distributed via online forms to a group of physicians in all hospitals across the province, who were then asked to forward it to their colleagues. Data collection lasted 7 days and concluded after 10 consecutive days with no new responses. The minimum required sample size was calculated as 97 participants, based on a 95% confidence interval ($Z=1.96$), an expected prevalence rate ($p=0.5$), and a margin of error ($d=0.1$). No sampling was conducted, as the aim was to reach the entire population. Ethics committee approval was obtained. (Date: 21/08/2024; Decision No. 2024/100)

2.2. Data Collection Tool

The survey was conducted in three stages. In the first stage, a systematic search of the PubMed, ScienceDirect, Google Scholar, and SCOPUS databases was performed for literature published from 2020 onwards using search terms such as "Antimicrobial stewardship," "knowledge, attitude, behavior," "physician," and "antimicrobial resistance." Six relevant studies were identified (12–17). The CDC's "Core Elements of Antibiotic Stewardship" and the 'WHO Bacterial Priority Pathogens List, 2024' reports were also analyzed (18,19).

Survey questions were developed based on these sources. The final survey consists of four sections: (i) demographic information, including sociodemographic and occupation-related details and AMR/AMS training status; (ii) a knowledge section with 10 multiple-choice questions assessing correct knowledge of AMU, AMR, and AMS (score range: 0-10); (iii) an attitude section with 8 questions using a 5-point Likert scale to evaluate views and beliefs on AMU and AMR (score range: 8-40); and (iv) a behavior section with 8 questions using a 5-point Likert scale to assess prescribing and usage behaviors concerning AMAs (score range: 8-40). Attitude responses ranged from "certainly agree" to "certainly disagree," and behavior responses from "never" to "always," with scores adjusted for positive or negative wording. Although a single survey instrument was used, it was structured into three distinct sections specifically designed to assess knowledge, attitudes, and behaviors following methods used in prior validated studies. Each section had its own scoring system and was independently evaluated.

In the second stage, a pilot test was conducted with 20 physicians to assess the survey's clarity. The data from the pilot test were not included in the main study. Feedback was used to refine the questions for clarity before distribution. Physicians were provided with a direct line to the research team via mobile phone for any survey-related questions, and the survey took approximately 10-15 minutes to complete. In the third stage, before data analysis, calculations were made to convert the KAB scores into a general score ranging from 0 (worst) to 100 (best): $\text{Total score} = [(\text{obtained score} - \text{minimum possible score}) / (\text{maximum possible score} - \text{minimum possible score})] \times 100$.

The survey's internal consistency was assessed using Cronbach's alpha, resulting in a coefficient of 0.77 (95% CI: 0.72-0.82 using the Duhachek method). This indicates that the survey has excellent internal consistency and is a reliable tool for evaluating the relevant topic. The full questionnaire is provided as Supplementary Material.

2.3. Statistical Analysis

Statistical analyses were performed using the R programming language (Version 2024.04.1+748). The Kolmogorov-Smirnov test assessed data normality. For normally distributed data, mean and standard deviation were calculated, while median, Q1, and Q3 were reported for non-normally distributed data. Descriptive statistics analyzed demographic data using the "dplyr" and "psych" packages. Pearson and Spearman correlation tests examined the relationships between KAB scores. The effects of demographic variables on these scores were assessed using the Kruskal-Wallis test or one-way ANOVA, depending on the distribution of the data. The impact of training was evaluated using the independent samples T-test or Mann-Whitney U test. Correlation analyses were conducted with the "Hmisc" package, and comparative analyses were performed using the "stats" package. Visualizations were created with the "ggplot2" package. A p-value of $< .05$ was considered statistically significant.

3. RESULTS

3.1. Sociodemographic, Occupational, and Education Information

A total of 141 physicians participated in the study. The median age was 31 years (Q1-Q3: 28.0-37.0), with 59.6% male (n=84) and 40.4% female (n=57). Of the participants, 54.6% were assistants (n=77), 34.0% were specialists (n=48), 7.09% were faculty members (n=10), and 4.26% were general practitioners (n=6). Employment duration was 0-5 years for 50.4% (n=71), 6-10 years for 20.6% (n=29), 11-15 years for 11.3% (n=16), and 16 years or more for 17.7% (n=25). Most worked in education and research hospitals (75.2%, n=106), followed by state hospitals (17.7%, n=25), private hospitals (3.55%, n=5), and university hospitals (3.55%, n=5).

Patient load during a 24-hour shift was: 45.4% saw 51-100 patients (n=64), 29.8% saw 0-50 (n=42), 17.0% saw 101-149 (n=24), and 7.80% saw ≥150 patients (n=11). The number of AMA prescriptions written during a shift was: 33.3% wrote 0-10 prescriptions (n=47), 25.5% wrote 11-20 (n=36), 22.0% wrote ≥30 (n=31), and 19.1% wrote 21-29 prescriptions (n=27) (Table 1).

Table 1. Demographic and Occupational Characteristics of Emergency Department Physicians (n=141)

Parameters	n(%)
Age (years) (median [Q1;Q3])	31.0 [28.0;37.0]
Gender	
Male	84 (59.6%)
Female	57 (40.4%)
Profession Title	
Assistant	77 (54.6%)
Specialist	48 (34.0%)
Faculty Member	10 (7.09%)
General Practitioner	6 (4.26%)
Employment duration	
0-5 years	71 (50.4%)
6-10 years	29 (20.6%)
11-15 years	16 (11.3%)
≥ 16 years	25 (17.7%)
Hospital	
Education Research Hospital	106 (75.2%)
State Hospital	25 (17.7%)
Private Hospital	5 (3.55%)
University Hospital	5 (3.55%)
Total number of patients seen in a 24-hour shift	
0-50	42 (29.8%)
51-100	64 (45.4%)
101-149	24 (17.0%)
≥150	11 (7.80%)
Number of prescriptions containing AM written during a 24-hour shift	
0-10	47 (33.3%)
11 – 20	36 (25.5%)
21-29	27 (19.1%)
≥30	31 (22.0%)
AMA: Antimicrobial agent	

Of the physicians, 60.3% (n=85) had received training on AMU and AMR, while 39.7% (n=56) had not. Additionally, 24.8% (n=35) had AMS training, while 75.2% (n=106) had not. Furthermore, 64.5% (n=91) felt their AMA therapy education in medical school was sufficient (Table 2).

Table 2. Antimicrobial Use and Resistance Training Status of Emergency Department Physicians (n=141)

Parameters	n(%)
History of AMR training	
Have	85 (60.3%)
None	56 (39.7%)
History of AMS training	
Have	35 (24.8%)
None	106 (75.2%)
Finding the AMA education received at the medical faculty adequate	
Yes	91 (64.5%)
No	50 (35.5%)
AMR:Antimicrobial resistance, AMS: Antimicrobial stewardship, AMA: Antimicrobial agent	

3.2. Knowledge

In the knowledge section, the median overall score for physicians was 90.0 [Q1; Q3: 80.0; 100]. Of the participants, 69.5% (n=98/141) had good knowledge, while 30.5% (n=43/141) had poor knowledge. Physicians demonstrated a high level of knowledge about the place of AMU (99.3%), the causes of AMR (99.3%), and the purpose of AMS programs (100%). Their understanding of the consequences of AMA overuse (97.9%) and the transmission routes of resistant bacteria (92.9%) was also strong.

Knowledge of empirical antibiotics (87.2%) and the de-escalation strategy (83.0%) was substantial, and they correctly identified priority pathogens 75.2% of the time. However, knowledge about broad-spectrum AMAs was lower, at 56.0%. The distribution of correct and incorrect responses to the knowledge questions is illustrated in Figure 1.

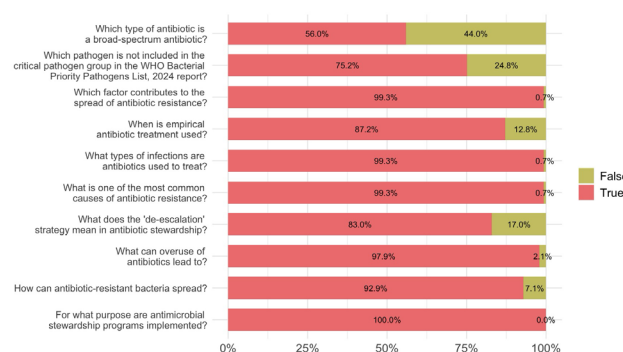


Figure 1. Percentage of emergency department physicians answering knowledge questions correctly and incorrectly regarding antimicrobial use, antimicrobial resistance, and antimicrobial stewardship.

3.3. Attitudes

A total of 62.4% (n=88/141) avoided prescribing AMAs based on patient requests. However, 72.3% (n=102/141) believed that patients would obtain AMAs from another physician if they did not prescribe them. The majority (96.5%, n=136/141) believed in the importance of public education on the proper use of AMAs. While 44.0% (n=62/141) supported using broad-spectrum AMAs in case of uncertainty, 59.6% (n=84/141) emphasized the need for a definitive diagnosis before prescribing. Most physicians (71.7%, n=101/141) felt that AMAs could be initiated in suspected bacterial infections without waiting for microbiological results. Additionally, 86.5% (n=122/141) considered AMAs unsafe and did not support their widespread use. Finally, 73.0% (n=103/141) expressed a desire for further education to combat AMR more effectively (Figure 2).

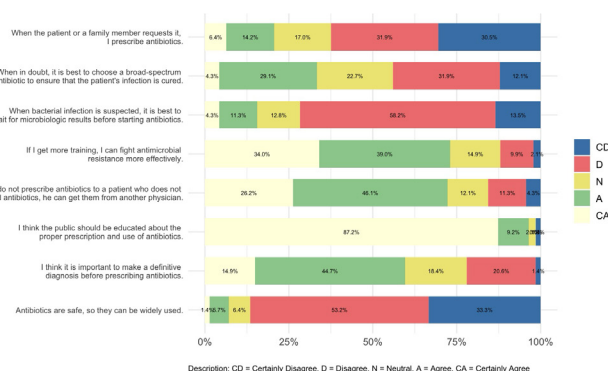


Figure 2. Attitudes of emergency department physicians on the use of AMA: Distribution of opinions on education, diagnosis, and patient requests

3.4. Behaviors

In the behavior section, physicians had a mean score of 53.0 ± 16.6 . More than half (53.9%, n=76/141) exhibited correct behavior when administering AMA treatment. A significant portion (60.3%, n=85/141) reported sometimes prescribing AMAs based on patient requests to avoid conflicts, while 21.3% (n=30/141) never fulfilled such requests. Only 20.6% (n=29/141) regularly followed clinical guidelines when prescribing AMAs.

While 66% (n=93/141) sometimes or often preferred broad-spectrum AMAs to prevent potential complications, 39.0% (n=55/141) primarily preferred narrow-spectrum AMAs. Nearly all physicians (92.2%, n=130/141) provided education about prescribed AMAs whenever possible. A small percentage (5%, n=8/141) never considered bacterial resistance mechanisms before prescribing. While 26.9% (n=38/141) always reviewed the patient's past culture results before empirical AMA treatment, 17.0% (n=24/141) never did so. Most physicians (70.2%, n=99/141) were cautious to prevent unnecessary AMA use (Figure 3).

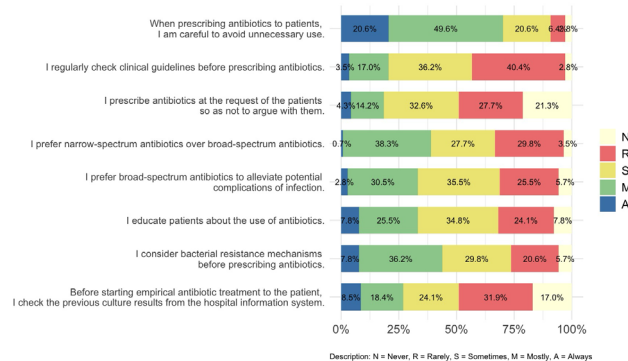


Figure 3. Emergency physicians' AMA use behaviors: unnecessary use, guideline follow-up and approaches to patient requests

3.5. Correlations between Knowledge Attitude and Behavior Scores

There is a weak, statistically insignificant positive correlation between physicians' knowledge and attitudes ($r=0.114$, $p=.174$) and a very weak negative correlation between knowledge and behavior ($r=-0.038$, $p=.646$). There is a statistically significant ($r=0.397$, $p<.001$) moderate positive correlation between attitudes and behaviors (Table 3).

Table 3. Correlations between Knowledge, Attitudes and Behaviors of Emergency Physicians

Variables	s	p value
Knowledge vs Attitude	0.114	.174
Attitude vs Behavior	0.397	< .01*
Knowledge vs Behavior	-0.038	.646

s: spearman correlation coefficient, * $p<.005$ statistically significant

3.6. Factors Related to Knowledge, Attitudes, and Behaviors

Knowledge scores were similar across profession titles. Faculty members had slightly higher attitude scores, but the difference was not statistically significant ($p=.232$). Behavior scores of specialists and faculty members were higher than those of general practitioners and residents, but the difference was not statistically significant ($p=.109$). There was no significant difference in knowledge scores based on the employment duration ($p=.229$). Physicians with ≥ 16 years of employment had higher attitude scores, though the difference was not statistically significant ($p=.140$). Similarly, physicians with 11-15 years and ≥ 16 years of employment had higher behavior scores than those with ≤ 10 years, but the difference was not statistically significant ($p=.063$) (Table 4).

No significant differences were found in knowledge and attitude scores between physicians trained in AMU, AMR, and those who were not. Although behavior scores were higher among those who received training, the difference was not statistically significant ($p=.350$). Similarly, no significant differences were observed in knowledge and attitude scores between those who received AMS training. While behavior scores were higher among trained physicians, this difference was also not statistically significant ($p=.319$) (Table 5).

Table 4. Comparison of Knowledge, Attitude, and Behavior Scores Based on Profession Title and Duration of Employment: Associated *p*-Values and Effect Sizes (Eta Squared)

	Knowledge		Attitude		Behavior	
	Median (Q1;Q3)	p value η^2 *	Median (Q1;Q3)	p value η^2 *	Mean $\pm$ SD	p value η^2 *
Profession title						
Practitioner	90 (90;97.5)	.873	59.4 (57; 61.7)	.232	51.6 $\pm$ 16.6	.109
Assistant	90 (80;100)	-0.01*	59.4 (53.1; 65.6)	0.00*	50.4 $\pm$ 14.2	0.04*
Specialist	90 (80;100)		62.5 (56.2; 75)		57.2 $\pm$ 17.4	
Faculty member	90 (82.5;97.5)		68.8 (60.9; 68.8)		57.9 $\pm$ 21.2	
Employment duration						
0-5 years	90 (80;100)	.229	59.4 (54.7; 65.6)	.140	50.7 $\pm$ 14.3	.063
6-10 years	90 (90;100)	0.00*	62.5 (59.4; 68.8)	0.01*	52.1 $\pm$ 15.2	0.05*
11-15 years	90 (80;92.5)		57.8 (53.1; 69.5)		56.6 $\pm$ 18.5	
≥ 16 years	90 (80;100)		68.8 (59.4; 75)		60.2 $\pm$ 18.9	

* η^2 : Eta Squared , effect size between groups**Table 5.** History of AMR and AMS Training: Comparison of Knowledge, Attitude, and Behavior Scores with Associated *p*-Values and Effect Sizes (Rank-Biserial Correlation and Cohen's *d*)

	Knowledge		Attitude		Behavior	
	Median (Q1;Q3)	p value r_B *	Median (Q1;Q3)	p value r_B *	Mean $\pm$ SD	p value Cohen's d^{**}
History of AMR training						
Yes	90 (80;100)	.501	59.4 (56.1;65.6)	.270	54.1 $\pm$ 15.1	.350
No	90 (80;100)	0.056*	62.5 (56.2; 69.5)	0.092*	52.1 $\pm$ 17.7	0.123**
History of AMS training						
Yes	90 (80;100)	.964	59.4 (56.2; 71.9)	.744	56.1 $\pm$ 15.8	.319
No	90 (80;100)	0.003*	59.4 (56.2;68.8)	0.027*	52.4 $\pm$ 16.2	0.229**

* r_B : Rank-Biserial Correlation and **Cohen's *d* = effect size between groups

AMR:Antimicrobial resistance, AMS: Antimicrobial stewardship

4. DISCUSSION

National and International AMS programs are vital in combating AMR, but identifying the most effective interventions for each country or setting is challenging. Evaluating the knowledge and awareness of AMR among those who prescribe and dispense AMAs is crucial for developing national strategies and ensuring the success of AMS programs. Our study is significant as it evaluates the KAB of physicians in EDs, where AMAs are frequently used and prescribed, providing valuable feedback to policymakers and implementers regarding AMU, AMR, and AMS.

Studies showing high levels of knowledge among physicians regarding AMU and AMR emphasize the importance of comprehensive education and continuous medical training. Taborda et al. reported that physicians with adequate university training were more conscientious in their AMU practices (20). AMS programs in hospitals also enhance knowledge and promote appropriate AMU (21). Salsgiver et al. found that ED physicians often felt inadequate when selecting antibiotics under pressure and expressed a need for more AMS training, highlighting post-prescription review and feedback as valuable interventions (22). In our study, 69.5% of physicians had good knowledge of AMU, AMR, and AMS. Nearly everyone was aware of the causes and consequences of AMR, transmission routes for resistant bacteria, and the purpose of AMS programs. More than half had knowledge of

empirical AMU and de-escalation strategies, but knowledge of broad-spectrum AMAs was lower. These findings suggest that while physicians have good awareness of AMU, AMR, and AMS, there are gaps in their AMA pharmacology knowledge. Since most participants were assistants with 0-5 years of experience, refreshing basic AMA knowledge during specialty training or in the final year of medical school could enhance AMU knowledge and aid in combating AMR.

Patient pressure and emphasis on patient satisfaction is one of the main reasons for inappropriate AMA prescribing (23). Sirota et al. showed that patient expectations heavily influence physicians' prescribing decisions (24), and Ashworth et al. found that the volume of AMA prescriptions strongly predicts overall patient satisfaction (25). In our study, only 48.2% of physicians exhibited attitudes consistent with AMS programs. This low percentage appears to be due to patient persistence and a lack of patient education. While physicians recognize that prescribing based on demand is inappropriate, they believe patients will obtain the medication elsewhere if denied. Detailed examination and patient education could help mitigate this issue.

EDs, with their high patient volumes and limited consultation times, make it difficult to dissuade patients from unnecessary AMU. Our study also found that over 80% of physicians do not consider AMAs safe and believe their widespread use

is inappropriate, yet they feel compelled to prescribe them to avoid conflict with patients. As a result, physicians agree that public education is crucial for effectively combating AMR. Miller et al. demonstrated that providing patients with information about the potential harms of AMAs significantly reduced their likelihood of requesting them (26). Public education is vital in reducing AMR, but AMR is a complex concept that can be difficult for patients to understand, with comprehension varying by education level and health literacy. To raise AMR awareness across all levels of society, comprehensive educational initiatives and supportive health policies are needed.

When selecting empirical AMA therapy, it is crucial to assess the severity of the infection and the timing of intervention. In life-threatening conditions like septic shock, rapid action can significantly reduce mortality (27). However, in more stable patients, a “wait and see” approach may effectively reduce unnecessary AMA use, especially in upper respiratory tract infections (28). In our study, more than half of the physicians stated that it is important to administer AMAs without waiting for microbiological results in cases of suspicion. However, some physicians believe it is wrong to prescribe antibiotics without a definitive diagnosis. The best approach depends on the patient’s condition. Additionally, rapid microbiological diagnostic kits can help quickly distinguish between infection and inflammation, identifying the causative agent and making them valuable tools in the fight against AMR.

In our study, 54% of physicians demonstrated appropriate behavior when selecting and prescribing AMAs. While they are generally conscientious about AMA use, they sometimes yield to patient demands. Inconsistent adherence to clinical guidelines contributes to confusion, especially in choosing between broad and narrow-spectrum AMAs. In some cases, an AMA initiated by one physician is altered by another before completion. To address these issues, ongoing education is necessary, as highlighted in the literature (12,17,22,29,30). Regular training sessions, improved access to current guidelines, and the development of national/regional guidelines with up-to-date local surveillance data could enhance awareness and promote more consistent and effective AMA management, thereby reducing AMR and unnecessary AMU.

Studies show that while healthcare workers are well-informed about AMR, their behavior is also influenced by social norms, attitudes, and beliefs (31). Despite high levels of knowledge, external pressures, time constraints, and structural issues often prevent translating knowledge into appropriate behavior (32). Chatterjee et al. found that knowledge alone may not strongly influence behavior, highlighting the importance of attitudes in clinical practice (33). Other studies similarly emphasize that attitudes significantly impact clinical behaviors and AMS protocol implementation (34).

In our study, consistent with the literature, we found a weak relationship between knowledge and behavior but a strong, statistically significant correlation between attitude and behavior. High knowledge levels do not always lead to

correct behavior, especially in EDs, where patient care is intensive, time is limited, and healthcare violence is common. These conditions may shape physicians’ behaviors, such as prescribing unnecessary AMAs due to patient pressure or choosing broad-spectrum AMAs to avoid repeat visits. While AMS programs can improve knowledge and behavior, policymakers should also focus on improving working conditions for physicians and raising public awareness.

In our study, knowledge levels regarding AMU, AMR, and AMS did not differ by professional rank or experience. However, specialists and faculty members scored higher in attitude and behavior compared to assistants and general practitioners. While increased professional experience appeared to positively influence attitudes and behaviors, the effect was not statistically significant, likely due to individual differences, workload, burnout, and personal or economic factors. Similar findings have been reported in other studies, showing that faculty members generally exhibit higher knowledge, attitudes, and behaviors (34). In our study, those who received AMU and AMR training had higher behavior scores, though not statistically significant. While educating physicians can improve knowledge, behavior is not solely driven by knowledge; its practical application in daily practice is crucial. Therefore, alongside raising awareness of AMU, AMR, and AMS, strategies to foster positive attitudes should be developed.

Our study has several limitations. Since it was conducted in a specific geographic region, the results may not fully represent the knowledge, attitudes, and behaviors of all physicians. Voluntary participation could have led to volunteer bias, with more interested physicians being more likely to participate. Additionally, as a survey-based study, participants may have provided socially acceptable responses rather than reflecting their actual behaviors. Additionally, although behaviors and attitudes are ideally assessed through observational or longitudinal methods, cross-sectional surveys with well-structured items have been widely used in previous literature to assess self-reported behaviors and attitudes, which was also the approach in our study.

Our study’s strength is the high internal consistency of the survey, as demonstrated by a strong Cronbach’s alpha value. This suggests that the survey accurately measured knowledge, attitudes, and behaviors.

5. CONCLUSION

In conclusion, although emergency department physicians possess good knowledge of AMU, AMR, and AMS, this does not consistently translate into their attitudes and behaviors. Barriers such as patient demands, inadequate health policies, and the need to manage a high patient load hinder the practical application of this knowledge. Physicians may struggle to stay updated with guidelines, often relying on outdated knowledge from medical school.

Our findings suggest that improving AMS program effectiveness requires addressing not only education but also attitudes and behaviors. Training programs tailored to

high-pressure environments like EDs, where patient pressure is significant, may be beneficial. More importantly, raising public awareness about AMR and reducing non-critical visits to emergency departments should be a primary focus of health policy.

Acknowledgements: We are grateful to the healthcare workers who participated in this study.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: Ethics committee approval was obtained from Izmir City Hospital, Turkey (Date: 21/08/2024; Decision no: 2024/100).

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: İK, ÖEK

Design of the study: İK, ÖEK

Acquisition of data for the study: İK, ÖEK

Analysis of data for the study: ÖEK

Interpretation of data for the study: İK, ÖEK

Drafting the manuscript: İK, ÖEK

Revising it critically for important intellectual content: İK, ÖEK

Final approval of the version to be published: İK, ÖEK

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Supplementary Material

The questionnaire used in this study, including all knowledge, attitude, and behavior items, is available as Supplementary Material.

Demographic Information

Age: _____

Gender: _____

Professional Title:

Assistant
Specialist
Faculty Member
General Practitioner

Years of Professional Experience:

0–5 years
6–10 years
11–15 years
16 years and above

Type of Hospital:

Education Research Hospital
State Hospital
Private Hospital
University Hospital

Number of Patients Seen per 24-Hour Shift:

0–50
51–100
101–149
150

Number of Antimicrobial Prescriptions Written per 24-Hour Shift:

0–10
11–20
21–29
≥30

Have you received education on antimicrobial resistance (AMR) and use (AMU)?

Have / None

Have you participated in any antimicrobial stewardship (AMS) program?

Have / None

Do you think the antimicrobial education you received during medical school was sufficient to prescribe correctly?

Yes / No

Knowledge Section (Multiple Choice)

What types of infections are antibiotics used to treat?

- A) All types of infections
- B) Bacterial infections**
- C) Viral infections
- D) Fungal infections
- E) Parasitic infections

What is one of the most common causes of antibiotic resistance?

- A) Overuse of antibiotics**
- B) Correct dosing of antibiotics
- C) Sale of antibiotics without a prescription
- D) Inappropriate use of antibiotics
- E) Natural mutation of bacteria

Which factor contributes to the spread of antibiotic resistance?

- A) Adhering to hygiene rules
- B) Inappropriate use of antibiotics**
- C) Regular vaccination
- D) Proper use of antibiotics
- E) Use of antibiotics only for bacterial infections

What can overuse of antibiotics lead to?

- A) Decreased treatment effectiveness**
- B) Faster recovery
- C) Fewer side effects
- D) Complete eradication of the infection
- E) Strengthening of the immune system

For what purpose are antimicrobial stewardship programs implemented?

- A) To increase antibiotic use
- B) To reduce antibiotic resistance**
- C) To encourage over-the-counter use of antibiotics
- D) To prolong antibiotic treatment duration
- E) To increase the cost of antibiotics

Which type of antibiotic is a broad-spectrum antibiotic?

- A) Penicillin
- B) Amoxicillin/Clavulanic acid**
- C) Erythromycin
- D) Amikacin
- E) Metronidazole

How can antibiotic-resistant bacteria spread?

- A) Only through direct contact
- B) Only from animals to humans
- C) Through person-to-person contact and contaminated surfaces**
- D) Only during surgical procedures
- E) Through airborne transmission

When is empirical antibiotic treatment used?

- A) When a definitive diagnosis is made
- B) After bacterial culture results are obtained
- C) When the physician suspects a bacterial infection**
- D) When antibiotic resistance is detected
- E) When the infection is known to be viral

What does the 'de-escalation' strategy mean in antibiotic stewardship?

- A) Not initiating antibiotic treatment
- B) Shifting from broad-spectrum to narrow-spectrum antibiotics**
- C) Increasing the antibiotic dose
- D) Using antibiotics prophylactically

Which pathogen is not included in the critical pathogen group in the WHO Bacterial Priority Pathogens List, 2024 report?

- A) Carbapenem-resistant Enterobacterales
- B) Third-generation cephalosporin-resistant Enterobacterales
- C) Rifampicin-resistant Mycobacterium tuberculosis
- D) Macrolide-susceptible Streptococcus pneumoniae**

Attitude Section (5-Point Likert Scale)

When the patient or a family member requests it, I prescribe antibiotics.

Strongly Agree (1), Agree (2), Neutral (3), Disagree (4), Strongly Disagree (5)

If I do not prescribe antibiotics to a patient who does not need antibiotics, he can get them from another physician.

Strongly Agree (1), Agree (2), Neutral (3), Disagree (4), Strongly Disagree (5)

I think the public should be educated about the proper prescription and use of antibiotics.

Strongly Agree (5), Agree (4), Neutral (3), Disagree (2), Strongly Disagree (1)

When in doubt, it is best to choose a broad-spectrum antibiotic to ensure that the patient's infection is cured.

Strongly Agree (1), Agree (2), Neutral (3), Disagree (4), Strongly Disagree (5)

When bacterial infection is suspected, it is best to wait for microbiologic results before starting antibiotics.

Strongly Agree (5), Agree (4), Neutral (3), Disagree (2), Strongly Disagree (1)

If I get more training, I can fight antimicrobial resistance more effectively.

Strongly Agree (5), Agree (4), Neutral (3), Disagree (2), Strongly Disagree (1)

Antibiotics are safe, so they can be widely used.

Strongly Agree (1), Agree (2), Neutral (3), Disagree (4), Strongly Disagree (5)

I think it is important to make a definitive diagnosis before prescribing antibiotics.

Strongly Agree (5), Agree (4), Neutral (3), Disagree (2), Strongly Disagree (1)

Behavior Section (5-Point Likert Scale)

I prescribe antibiotics at the request of the patients so as not to argue with them.

Never (5), Rarely (4), Sometimes (3), Mostly (2), Always (1)

I regularly check clinical guidelines before prescribing antibiotics.

Never (1), Rarely (2), Sometimes (3), Mostly (4), Always (5)

I prefer broad-spectrum antibiotics to alleviate potential complications of infection.

Never (5), Rarely (4), Sometimes (3), Mostly (2), Always (1)

I prefer narrow-spectrum antibiotics over broad-spectrum antibiotics.

Never (1), Rarely (2), Sometimes (3), Mostly (4), Always (5)

I educate patients about the use of antibiotics.

Never (1), Rarely (2), Sometimes (3), Mostly (4), Always (5)

I consider bacterial resistance mechanisms before prescribing antibiotics.

Never (1), Rarely (2), Sometimes (3), Mostly (4), Always (5)

Before starting empirical antibiotic treatment to the patient, I check the previous culture results from the hospital information system.

Never (1), Rarely (2), Sometimes (3), Mostly (4), Always (5)

When prescribing antibiotics to patients, I am careful to avoid unnecessary use.

Never (1), Rarely (2), Sometimes (3), Mostly (4), Always (5)

Predictive Factors for Non-sentinel Lymph Node Metastasis of Breast Cancer

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Received: October 20, 2022

Accepted: May 29, 2025

ABSTRACT

Objective: The indications for axillary dissection after sentinel lymph node biopsy (SLNB) in breast cancer (BC) is gradually decreasing, even for selected patients with positive SLNB. Increased predictability of Non-sentinel lymph node (Non-SLN) metastasis could prevent unnecessary axillary dissection and even eliminate the need for SLNB. In this study we aimed to investigate the clinical and the pathological factors that affect Non-SLN metastasis.

Methods: Early breast cancer patients who underwent SLNB between 2013 and 2018 were retrospectively included in the study. Patients were divided into 3 groups; Group-1 SLNB negative patients, Group-2 SLNB positive but Non-SLN negative patients and Group-3 both SLNB and non-SLN positive patients. Groups were compared in terms of demographic data, tumor size, SLN size, Ki-67 percentages, and hormone receptor status.

Results: Seventy-six (36.4%) out of 206 patients had positive SLNB. Non-SLN metastases were detected in 33 (42.7%) patients. Mean tumor size found significantly higher in Group 3 (Group-1, 2 and 3 respectively; 20.5±9.7mm, 21.9±9.3mm, 25.1±9.5mm; p<.01). The mean SLN size was significantly bigger in Group-3 (Group-1, 2 and 3 respectively, 13.1±5.6mm, 13.9±8.2mm, 16.8±6.5mm; p<.01). Rate of patients with Ki-67 index higher than 14% was 84.3% in Group-3, 59.1% in Group-2 and 49.2% in Group-1(p<.01). A statistically significant difference was not detected between the groups in terms of hormone receptor status.

Conclusion: Tumor size, SLN size and Ki-67 percentages have importance in predicting the presence of Non-SLN metastasis in BC patients. These factors should also be taken into account for the management of the axillary metastasis and adjuvant treatment for BC.

Keywords: Breast cancer, Non-sentinel lymph node, Lymph node metastasis

1. INTRODUCTION

The assessment of lymph node metastasis is crucial for staging, prognosis and treatment of breast cancer (BC). In the 20th century, axillary lymph node dissection (ALND) was an irreplaceable part of breast cancer surgery. With the help of radiological improvements and screening programs, BC surgery has evolved from radical resections with axillary dissection to breast-conserving surgeries and SLNB's.

The increased risk of wound infections, seroma, axillary paresthesia, brachial plexus injury, and lymphedema causes surgeons to continue questioning the necessity of ALND [1]. Emerging studies on the idea have revealed that ALND can be avoided in a selected number of patients. Even though SLNB has become the standard practice in clinically node-negative patients, the requirement for axillary dissection has been

decreasing. According to the ACOSOG Z0011 criteria axillary dissection can be averted even in the presence of metastatic sentinel nodes. The ACOSOG Z0011 randomized clinical trial showed no difference in 10-year overall survival between SLNB alone and ALND in T1 and T2 tumors with whole breast irradiation [2]. Studies comparing SLNB with ALND have shown that SLNB accurately identifies axillary metastases with less morbidity in patients with unifocal, node negative tumors less than 3 cm [3].

Nowadays the necessity of SLNB is a matter of discussion and predicting the presence of SLN and Non-SLN metastases in the axilla is important for planning the adjuvant treatment options for patients. The SLNB positivity is expected to be 30% in early stage BC patients. Only 30-40% of these patients

How to cite this article: Özemer İA, Aydemir MA, Tigrel LZ, Baysal H. Predictive Factors for Non-sentinel Lymph Node Metastasis of Breast Cancer. Clin Exp Health Sci 2025; 15: 357-361. <https://doi.org/10.33808/clinexphealthsci.1190227>

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present with Non-SLN metastasis [4,5,6]. As surgeons are moving further away from axillary dissections it is gaining importance to determine risk factors for Non-SLN metastasis. The purpose of this study was to investigate the risk factors for Non-SLN metastasis.

2. METHODS

2.1. Patient selection

Clinical and radiological node negative breast cancer patients who underwent breast-conserving surgery or mastectomy with SLNB at Istanbul Medeniyet University, Department of General Surgery between 2013 and 2018 were investigated retrospectively. Axillary dissection was performed routinely to all patients who had metastatic SLN after SLNB between 2013 and 2018 in our department. Patients who underwent neoadjuvant chemotherapy and patients with metastatic disease, multi-centric tumors, prior axillary surgery and per-operatively unidentified sentinel lymph node were excluded from the study. Two-hundred and six histologically confirmed invasive breast cancer patients, aged between 18 and 80 years, were included in the study. All patients provided written informed consent. The study was approved by the Ethics Committee of İstanbul Medeniyet University Göztepe Prof. Dr. Süleyman Yalçın City Hospital (Approval date: 30.12.2014; Number: 2014/0200)

2.2. Sentinel lymph node biopsy

All participating patients underwent SLNB. Immediately after the induction of anesthesia 2-4 ml of methylene blue dye was injected to the subareolar area of the patients. Eight minutes after the injection of blue dye sentinel lymph nodes were excised through axillary incision. Frozen section examination was applied to all patients. The SLNs were then assessed intraoperatively via frozen section examination and subsequently cut into 2-mm serial sections for staining with standard hematoxylin and eosin. Presence of metastasis and size of the metastatic deposit was evaluated. Axillary dissection was performed in cases of macro-metastasis (metastasis ≥ 2 mm) detected in sentinel lymph nodes.

2.3. Data Analysis

Patients were divided into three groups according to the pathological examination of their sentinel and non-sentinel lymph nodes. Group-1 consisted of patients with negative SLNB, Group-2 consisted of patients with positive SLNB results and negative Non-SLN. Group-3 consisted of patients with positive SLNB and positive Non-SLN. Patients' histopathological results of frozen sections, tumor and axillary dissection materials were reviewed. Tumor type, tumor size, SLN metastasis status, number of SLNs removed, SLN frozen section results, SLN paraffin-embedded section results, size of SLN, axillary dissection status, Non-SLN metastasis status, number of metastatic lymph nodes and total number of

removed lymph nodes were assessed. For evaluating tumors according to Estrogen Receptor (ER), Progesterone Receptor (PR), Human epidermal growth factor receptor-2 (HER-2) and Ki-67 expressions, immunohistochemical analysis were performed for all patients. The Allred scoring system was used to evaluate ER and PR status [7]. Ki-67 percentages of each group were assessed according to the cut-off values of; 14% defined by 2011 St Gallen consensus and 20% suggested by majority of panelists of 2013 St Gallen consensus. Statistical analyses were performed comparing Ki-67 percentages by these cut-off values [8, 9].

2.4. Statistically Analysis

SPSS software version 20.0 (SPSS Inc., Chicago, IL) was used to analyze the data of this study. Descriptive statistics was applied in relevant parameters. Distributions of the numerical variables were examined by histograms and Shapiro-Wilk test. Where appropriate, comparisons of categorical variables were performed using the chi-squared test and continuous variables with median or mean values were compared using the Mann-Whitney U and Kruskal-Wallis tests. Spearman's rho correlation coefficient was used for the correlation analysis between the parameters. The results were reviewed in the confidence interval of 95%, and the value $p < .05$ was considered statistically significant.

3. RESULTS

Between 2013 and 2018 a total of 206 BC patients who underwent SLNB for clinically node negative breast cancer were included in the study. The patients' mean age was 55.4 ± 12.5 years. Demographic data of the patients are shown in Table-1. Histologic subtypes of BC were invasive ductal carcinoma in 176-patients (85.4%), invasive lobular carcinoma in 15 patients (7.3%), papillary carcinoma in 9 patients (4.4%), and mucinous carcinoma in 6 patients (2.9%). SLNB results were negative for metastasis in 130 (63.1%) patients (Group-1) and positive for 76 patients. Out of 76 patients with positive SLNB's, 44 (21.4%) patients Non-SLN were negative (Group-2) and 32 (15.5%) patients Non-SLN were positive (Group-3). There was no significant difference between the groups in terms of age (Group-1: 55.2 ± 12.7 , Group-2: 56.6 ± 14.1 and Group-3: 53.3 ± 8.4 years, $p = .322$).

The mean tumor size of the patients was found to be 21.5 ± 9.7 mm. We compared the tumor sizes of the groups, and it was found that the tumor sizes of the patients in Group-3 (25.1 ± 9.5 mm) were significantly ($p < .05$) higher than the other groups (Group-1: 20.5 ± 9.7 mm; Group-2: 21.9 ± 9.3 mm) (Table-1). Comparison of Group 2 and 3 according to tumor size also had statistically significant difference ($p < .05$) (Table-2).

The mean SLN size of patients was 13.8 ± 6.4 mm. The mean SLN size was 13.1 ± 5.6 mm in Group-1, 13.9 ± 8.2 mm in Group-2 and 16.8 ± 6.5 mm in Group-3. There was a statistically significant difference between groups in terms of SLN size ($p < .05$) (Table-1). When Group 2 and 3 were compared to determine the effect of lymph node size on

non-SLN metastasis, SLN size was statistically significantly higher in Group-3 ($p<.05$) (Table-2).

Table-1: Demographic, clinical and histopathological data of patients with breast cancer.

	Group-1 n=130	Group-2 n=44	Group-3 n=32	Total n=206	p value
	Mean±Sd	Mean±Sd	Mean±Sd	Mean±Sd	
Age ^a	55.2±12.7	56.6±14.1	53.3±8.4	55.4±12.5	.322
Tumor size (mm) ^a	20.5±9.7	21.9±9.3	25.1±9.5	21.5±9.7	.003**
Ki-67 Proliferation Index ^a	19.2±20.4	19.4±17.3	22.2±12.3	19.7±18.7	.017*
Sentinel lymph node size (mm) ^a	13.1±5.6	13.9±8.2	16.8±6.5	13.8±6.4	.004**
	n(%)	n(%)	n(%)	n(%)	
Tumor side ^b					
– Right	68 (52.3)	17 (38.6)	16 (50)	101 (49.1)	.290
– Left	62 (47.7)	27 (61.4)	16 (50)	105 (50.9)	
Surgical technique ^b					
– Breast-conserving Surgery	92 (70.8)	30 (68.2)	23 (71.9)	145 (70.4)	.929
– Mastectomy	38 (29.2)	14 (31.8)	9 (28.1)	51 (29.6)	
Ki-67 Proliferation Index (%) ^b					
– >14%	64 (49.2)	26 (59.1)	27 (84.3)	116 (56.3)	.001**
– <14%	66 (50.8)	18 (40.9)	5 (15.7)	90 (43.7)	
Lymphovascular invasion ^a					
– Positive	58 (44.6)	25 (56.8)	21 (65.6)	104 (50.5)	.661
– Negative	72 (55.4)	19 (43.2)	11 (34.4)	102 (49.5)	
Estrogen receptor status ^b					
– Positive	110 (84.6)	37 (84.1)	29 (90.2)	176 (85.4)	.514
– Negative	20 (15.4)	7 (15.9)	3 (9.8)	30 (14.6)	
Progesterone receptor status ^b					
– Positive	97 (74.6)	33 (75)	29 (90.2)	159 (77.2)	.143
– Negative	33 (25.4)	11 (25)	3 (9.8)	47 (22.8)	
HER-2 status ^b					
– Positive	41 (31.5)	12 (27.3)	8 (25)	61 (29.6)	.706
– Negative	89 (68.5)	32 (72.7)	24 (75)	145 (70.4)	
Triple negative patients	6 (4.6)	2 (4.5)	2 (6.7)	10 (4.9)	.944

^a Kruskal-Wallis test ^b Pearson Chi-square test * $p<.05$ ** $p<.01$

The Ki-67 percentages of the groups were 19.2±20.4 for Group-1, 19.4±17.3 for Group-2 and 22.2±12.3 for Group-3. The mean value of Ki-67 proliferation index was statistically significantly higher in Group-3 ($p<.05$). Groups were compared according to Ki-67 cut-off value of 14%. Out of 116 patients with Ki-67 results $\geq 14\%$, 64 (49.2%) had negative SLN (Group-1), 26 (59.1%) had positive SLNB (Group-2) and 27 (84.3%) had positive non-SLN (Group-3). The number of patients with Ki-67>14% was significantly higher in Group-3 ($p<$

.001) (Table-1). When we compared Group-2 and Group-3 to evaluate the effect of Ki-67 proliferation index on Non-sentinel lymph node metastasis, we found a significant difference between these two groups. Group-3 had higher values in terms of both the mean Ki-67 and the number of patients with higher than 14% cut-off (Table-2).

Table-2: Comparison of the histopathological factors between Group-2 and Group-3.

	Group-2 n=44	Group-3 n=32	p value
	Mean±Sd	Mean±Sd	
Tumor size (mm) ^a	21.9±9.3	25.1±9.5	.027*
Ki-67 Proliferation Index ^a	19.4±17.3	22.2±12.3	.062
Sentinel lymph node size (mm) ^a	13.9±8.2	16.8±6.5	.018*
	n(%)	n(%)	
Ki-67 Proliferation Index (%) ^b			
– >14%	26 (59.1)	27 (84.3)	.017*
– <14%	18 (40.9)	5 (15.7)	

^a Mann-Whitney U test ^b Pearson Chi-square test * $p<.05$ ** $p<.01$

Immunohistochemical analysis for the ER status of tumors revealed positive results for 110 (84.6%) patients in Group-1, 37 (84.1%) patients in Group-2 and 29 (90.2%) patients in Group-3. PR status for each group was determined positive in 97 (74.6%), 33 (75%) and 29 (90.2%) patients for Groups-1, 2 and 3, respectively. The number of patients with positive HER-2 expression was found 41 (31.5%) in Group-1, 12 (27.3%) in Group-2 and 8 (25%) in Group-3. Number of “triple negative (TN)” patients was 6 (4.6%) in Group-1, 2 (4.5%) in Group-2 and 2 (6.7%) in Group-3. Immunohistochemical analysis results did not show statistically significant difference between the groups (Table-1).

4. DISCUSSION

Axillary management of patients with newly diagnosed BC has undergone many practical changes in the last few decades with the impact of oncological treatment outcomes. Sentinel lymph node biopsy has replaced routine axillary lymph node dissection for the staging of clinically node-negative BC patients [10]. The presence and number of metastatic axillary lymph nodes are the most important factors that determine treatment options such as radiotherapy, axillary dissection and chemotherapy for BC patients. All BC patients with clinically negative axilla should be offered SLNB to provide information for node staging and relevant treatment decisions. According to ACOSOF 20011 [11,12] and AMAROS [13] trials there are no difference in terms of survival in BC patients with proven 1 or 2 positive sentinel lymph nodes who underwent SLNB with whole breast irradiation and those who underwent ALND. American Society of Clinical Oncology clinical practice guideline [14] does not recommend ALND for early BC patients with one or two SLN metastasis who will undergo whole-breast radiotherapy. NSABP-B32 trial revealed no statistically significant differences between patients who underwent ALND and those who had SLNB in terms of overall survival, disease-free survival, and regional control [10].

Therefore, today axillary dissection can be abandoned in this selected patient group. Among these selected patients with SLN metastasis, only 40-60% have Non-SLN metastasis [14-16]. During their study, Mikami et al [17] observed Non-SLN metastasis in 35% of their patients with metastatic SLN. Our patient group had Non-SLN metastases in 32 (42.1%) of 76 patients with SLN metastasis which is consistent with the literature. Thus, more than half of the patients underwent ALND without a therapeutic benefit. All these results emphasize the importance of the predictability of metastases in non-SLN for the choice of treatment options in BC patients.

In light of the previous studies, today axillary dissection is not performed in selected patients with positive SLNB results. Therefore, we designed this study between 2013 and 2018, to investigate the results of patients who underwent axillary dissection because of positive SLNB results. Various studies have been conducted to predict the Non-SLN metastasis, most of them questioned scoring systems based on the number of metastatic SLN. Van la Parra et al [18] revealed that >1 metastatic SLN, ≤ 1 non-metastatic SLN, the ratio of metastatic SLN $>50\%$, tumor size, lymphovascular invasion, extra-capsular extension and size of metastatic lymph node were factors predicting presence of the Non-SLN metastasis. Maimaitiali et al [19] found that ≥ 3 metastatic SLN and lymphatic invasion were associated with Non-SLN metastasis. Mikami et al [17] showed in their study that patients who had ≥ 2 metastatic SLN, ≤ 1 non-metastatic SLN and $>12\%$ Ki-67 index significantly higher risk of Non-SLN metastasis.

Our study demonstrated that tumor size, SLN size, and Ki-67 proliferation index $>14\%$ were statistically significant to predict Non-SLN metastasis in early BC patients. Consistent with the previous studies, we did not detect any significant relation between the molecular subtypes and hormone receptor status and non-SLN metastasis.

Factors mentioned above have been assessed by various nomograms, but have not been able to generate a suitable nomogram to predict Non-SLN metastasis [20-25]. As the number of clinical studies to predict non-SLN metastasis increases, it will be possible to create nomograms with high accuracy.

In order to create a homogeneous cohort in our study, patients who had neoadjuvant chemotherapy, metastatic disease, multi-centric tumors, or prior axillary surgery excluded from the study. This study has some limitations such as small number of cases and its retrospective nature.

5. CONCLUSION

Tumor size, SLN size and Ki-67 proliferation index higher than 14% are seen as significant factors in predicting Non-SLN metastasis in early-stage BC patients. In light of our study we advise the use of these factors together with the criteria defined by previous studies to diagnose Non-SLN metastasis. These factors should also be taken into account during the axillary management and adjuvant treatment for BC.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of İstanbul Medeniyet University Göztepe Prof. Dr. Süleyman Yalçın City Hospital (Approval date: 30.12.2014; Number: 2014/0200)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: IAO

Design of the study: IAO

Acquisition of data for the study: MAA, HB, LZT

Analysis of data for the study: IAO, HB

Interpretation of data for the study: IAO, HB

Drafting the manuscript: IAO

Revising it critically for important intellectual content: IOA, MAA, LZT, HB

Final approval of the version to be published: IAO, MAA, LZT, HB

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Relationship Between Perceived Stress and Anxiety in Patients Undergoing Coronary Angiography

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Received: October 28, 2024

Accepted: May 19, 2025

ABSTRACT

Objective: This study was conducted to determine the relationship between perceived stress and anxiety levels in patients undergoing coronary angiography (CAG).

Methods: A descriptive-observational study design was conducted in a single center in Turkey with 190 patients.

Results: The mean age of the participants was 61.2 ± 12.4 , 68.4% were male, 64.2% were primary school graduates and 56.3% had angiography for the first time. It was found that having a family history of heart disease and receiving information for angiography affected stress status, while education level, income status, and access to intervention-oriented information from health professionals affected anxiety. It was found that there was a positive low and significant relationship between Perceived Stress level and trait anxiety levels, while there was no relationship between state anxiety levels.

Conclusions: Perceived stress and anxiety levels were found to be moderate in patients who underwent CAG. For this reason, health workers need to plan interventions to reduce the stress and anxiety in patients.

Keywords: Anxiety, coronary angiography, stress.

1. INTRODUCTION

Coronary Artery Disease (CAD) is a condition that occurs as a result of the deterioration of the nutrition of the heart muscle. In some individuals, it may progress more rapidly and appear in the 30s, while in others it may remain silent until the ages of 50s and 60s (1-3). Early diagnosis of atherosclerosis and early identification of risky lesions have an important place in the reduction of cardiovascular diseases. A clinical history, physical examination, and electrocardiogram for diagnosing CAD are important tools for diagnosing coronary heart disease and informing decision-making, however, the only absolute way to evaluate coronary heart disease is CAG (Coronary Angiography) (4-7). CAG is a procedure performed with radiopaque material given by entering the coronary arteries through a catheter entered through the brachial or femoral artery (8,9). Although it provides many benefits in the diagnosis of coronary artery disease, it can lead to physical problems such as bleeding, hematoma, pain, nausea, and vomiting as well as psychological problems. Infarction,

arrhythmia, vascular complications, hypersensitivity, and inflammatory and hemodynamic problems also increase the stress and anxiety levels of patients due to fear (10,11).

Stress can be defined as a response to a stimulus or external situation. The effects of stress on individuals can vary widely. It is widely believed that stress is closely linked to the development of cardiovascular disease (12-15). Individual responses to stressful situations complicate the determination and categorization of stress levels and their implications for health. Numerous techniques and instruments have been developed to identify and quantify stress levels. Perceived stress (PS) offers a more realistic measure than objective stress levels, making it a better predictor of health (12,16,17). Perceived stress can also play a role in anxiety. Anxiety is defined as an emotional state in which an individual experiences uneasiness or worry in response to a perceived or real threat. It is evaluated as situational and persistent anxiety. State anxiety is a temporary

How to cite this article: Youssouf AM, Arslan S. Relationship Between Perceived Stress and Anxiety in Patients Undergoing Coronary Angiography. Clin Exp Health Sci 2025; 15: 362-367. <https://doi.org/10.33808/clinexphealthsci.1575268>

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emotional state, while persistent anxiety is a lifelong pattern of anxiety as a personality trait (18). It is a warning sign that warns of impending danger and allows the individual to take measures to deal with this threat (19-21). Research has shown that people who will undergo a CAG procedure are exposed to performing the procedure on the heart as a vital organ, wondering how the results of the procedure will be revealed, feeling pain and insecurity (22,23). The healthcare providers should focus on the patient's psychological activity and cognitive process to relieve the patient's stress and anxiety (24). Very little is known about the anxiety levels of patients undergoing CAG during different hospital stages. Identifying such characteristics can help providers identify patients at high risk for anxiety. It is important to create this awareness in healthcare providers so that providers can prevent or respond to the patient's anxiety. Therefore, the study was conducted to determine the relationship between perceived stress with anxiety levels and the factors affecting perceived stress in patients undergoing coronary angiography.

Research Questions

- 1) What are the perceived levels of stress and anxiety in patients undergoing coronary angiography?
- 2) Do the perceived stress situations of the patients who underwent coronary angiography change according to their socio-demographic and disease characteristics?
- 3) Is there a relationship between the perceived stress levels and anxiety levels of patients undergoing coronary angiography?

2. METHODS

2.1. Study Permissions and Ethical Statement

In order to conduct the research, the ethics committee approval was obtained from the Ethics Committee of a University (Decision No: 2022/248). Informed consent was obtained from the patients included in the study. In all stages of the study, the STROBE checklist were followed.

2.2. Study design

This is a descriptive observational study.

2.3. Participants and sample size

The research was carried out between August and October 2022 in the Department of Cardiology. According to a calculation the sample size required for moderate effect size (0.15), 95% power and 13 independent variables were determined as 190.²⁵ Those who are confirmed to undergo coronary angiography, who are over 18 years old, who speak and understand Turkish, and who volunteer to participate in the study are included in the study. Those with previous or ongoing psychological or psychiatric conditions such as major depressive disorder, generalized anxiety disorder or dementia were excluded from the study.

2.4. Instruments

Patient Information Form: A form consisting of sociodemographic and clinical questions was used in the study. Whereas, disease characteristics questions are as follows: the presence of chronic disease, previous angiography status, information status for the intervention, status of receiving information about angiography, if so, from whom, and status of receiving social support during the procedure.

Perceived Stress Scale (PSS): The scale was assess the extent to which certain situations in a person's life are stressful (26). The "PSS" was adapted to Turkish society and determined to be appropriate by Eskin et al., (27) in 2013 by conducting a validity and reliability study. In the study of Eskin et al. (2013), the Cronbach alpha internal consistency coefficient of the scale was 0.84, and the test-retest reliability was 0.87. In this study, the reliability value was found to be 0.64.

The State-Trait Anxiety Inventory (STAI): The Persistent Anxiety Inventory was developed in 1970 (28). It is a 4-pack type inventory that the individual can answer on his own, easy to apply, and consists of 20 questions. There are direct and inverted statements in the inventory. There are 7 inverted statements (items 1, 6, 7, 10, 13, 16 and 19) in the Inventory of Persistent Anxiety (29). The test reliability method found 0.71 to 0.86. In this study, Cronbach's alpha value was found as 0.81 for the state anxiety inventory, and 0.73 for the trait anxiety inventory.

2.5. Data collection procedure

The data were collected by the researchers between August and October 2022 by interviewing the patients face-to-face after permission was granted by the ethics committee and the institution.

2.6. Statistical analysis

The data were analyzed using the IBM SPSS Statistics User V 26. In the analysis of the data obtained as a result of the research, number, percentage, mean and standard deviation were used for descriptive statistics. Student's t-test was used to compare the paired group with normal distribution, and the Kruskal Wallis test was used to compare more than two groups that did not fit the normal distribution. If the variance analysis result was significant, multiple comparisons were made with Bonferroni test. Pearson correlation analysis were used in the analysis of the data obtained as a result of the research. The effect size was obtained with Cohen's d. $p < .05$ was considered the statistical significance level.

3. RESULTS

The sociodemographic data of the participants are presented in Table 1. The mean age of the participants in the study was 61.2 ± 12.4 years, 68.4% were male. The patients participants

in the study was 64.2% were primary school graduates, and 65.8% had a moderate income perception.

Table 1. Distribution of sociodemographic characteristics of patients (n:190)

Properties	Number	%
Gender		
Female	60	31.6
Male	130	68.4
Marital status		
Single	18	9.5
Married	172	90.5
Education		
Illiterate	23	12.1
Primary school graduate	122	64.2
High school and above	45	23.7
Profession		
Working	90	47.4
Nonoperating	100	52.6
Income		
Good	24	12.6
Middle	125	65.8
Bad	41	21.6
The presence of chronic diseases		
Yes	98	51.6
No	92	48.4
Family history of heart disease		
There is	107	56.3
No	83	43.7
	X	± SD
	Median	(Min-Max)
Average age	61.21	± 12.4
	50.0	18-80

The patients' characteristics of angiography intervention presented in Table 2. Of the participants, 56.3% reported that they had angiography for the first time, 52.1% received information about CAG, and 41.6% received information from health professionals. It was found that the social support during the procedure was mostly provided by the spouse and children.

When the PSS score distribution according to sociodemographic characteristics was examined, the mean score of those without a family history of heart disease was higher than those with a family history of heart disease ($p < .05$). It was found that the mean score of income status perception of the STAI-S was statistically significant and that the difference was between the groups with medium income status perception ($p < .05$). It was found that the mean scale score of those whose income perception was in the middle group was lower than those whose income perception was in the good and bad groups. It was found that the average score of the educational status of the trait anxiety level was statistically significant, and the score was low for those with high school education and above compared to illiterate and primary school graduates. It was found that the average level of trait anxiety decreased as the education level increased ($p < .05$) (Table 3).

Table 2. Distribution of patients' characteristics of angiography intervention (n:190)

Properties	Number	%
Number of Angiography		
First	107	56.3
Two and more	83	43.7
Information about angiography		
Yes	99	52.1
No	91	47.9
Place of education (n:99)		
Health worker	79	41.6
Friend/Relative/Social Media	20	10.6
Status of receiving social support during the procedure		
No	6	3.2
Wife	89	46.8
Children	89	46.8
Friends	6	3.2
Total	190	100

Table 3. PSS according to sociodemographic characteristics and STAI level distribution

Properties	PSS	STAI-S	STAI-T
Gender			
Female	31.18±6.31	43.31±5.14	51.65±5.76
Male	31.35±6.02	44.44±5.31	48.80±5.32
t:	-0.178	-1.376	3.331
p:	.483	.752	.432
Marital status			
Single	29.50±8.36	44.00±5.82	49.00±5.69
Married	31.48±5.82	44.09±5.22	49.77±5.61
t:	-1.317	-.075	-.559
p:	.145	.267	.618
Education			
Illiterate ^a	30.95±5.27	45.08±5.29	52.34±4.42
Primary ^b	31.40±6.22	43.94±5.01	50.13±5.51
Highschool-above ^c	31.20±6.29	43.97±5.96	47.20±5.58
KW:	0.130	0.935	14.832
p:	.937	.627	.001
			(a, b) > c
Income status perception			
Good ^a	32.00±5.10	45.87±5.68	48.54±6.59
Middle ^b	31.11±6.51	43.17±5.02	49.33±5.55
Bad ^c	31.46±5.40	45.82±5.17	51.51±4.84
KW:	0.357	11.525	6.190
p:	.837	.003	.145
		(a, c) > b	
The presence of chronic diseases			
Yes	30.59±6.15	43.41±5.42	50.23±5.69
No	32.05±5.98	44.80±5.03	49.14±5.49
t:	-1.658	-1.822	1.345
p:	.754	.299	.463
Family history of heart disease			
There is ^a	31.06±6.80	44.04±5.31	49.41±5.42
No ^b	31.60±5.08	44.14±5.24	50.08±5.85
t:	-.600	-.127	-.819
p:	.043	.746	.913
	b > a		

PSS: Perceived Stress Scale, STAI: State Trait Anxiety Inventory, STAI-S: State Trait Anxiety Inventory-State, STAI-T: State Trait Anxiety Inventory-Trait, t: independent sample t-test, KW: Kruskal Wallis.

The score distribution of the PSS according to the intervention characteristics is examined in Table 4. The mean score of those who did not receive information about angiography was higher than the mean score of those who received information ($p < .05$). When the distribution of scores of the State Anxiety Inventory according to intervention features was examined; the mean score of those who received information about the intervention from healthcare professionals was higher than those who received information from friends/relative/social media ($p < .05$).

According to the Pearson correlation analysis, there is a low and significant relationship between the PS level and the trait anxiety levels of the patients in a positive direction, and there is no relationship between the state anxiety levels (Table 5).

Table 4. PSS according to angiography intervention characteristics and STAI level distribution

Properties	PSS	STAI-S	STAI-T
Number of Angiography			
First	31.77±6.21	44.81±4.92	49.98±5.49
Two and more	30.68±5.93	43.15±5.58	49.34±5.77
t:	1.221	2.169	0.769
p:	.895	.191	.632
Information about angiography			
Yes	31.18±4.83	45.14±5.36	48.96±5.19
No	31.42±7.26	42.94±4.95	50.50±5.95
t:	-.278	2.925	-1.897
p:	.000	.492	.107
Where he studied (n:99)			
Health worker	31.56±4.74	45.21±4.89	48.97±4.94
Friend/Relative/ Socialmedia	29.65±5.00	44.85±7.07	48.95±6.23
t:	1.598	0.271	0.019
p:	.397	.029	.067

PSS: Perceived Stress Scale, STAI: State Trait Anxiety Inventory, STAI-S : State Trait Anxiety Inventory-State, STAI-T: State Trait Anxiety Inventory-Trait, t: independent sample t-test, KW: Kruskal Wallis. t: independent sample t-test.

Table 5. The relationship between the patients' PSS and STAI levels

Variables	1	2	3
PSS	-	r=0.124 p=.088	r=0.218 p=.002**
STAI-S	r=0.124 p=.088	-	r=.144 p=.048*
STAI-T	r=0.218 p=.002**	r=0.144 p=.048*	-

PSS: Perceived Stress Scale, STAI: State Trait Anxiety Inventory, STAI-S : State Trait Anxiety Inventory-State, STAI-T: State Trait Anxiety Inventory-Trait, r: Pearson Correlation.

*Correlation is significant at the .05 level (2-tailed),

**Correlation is significant at the .01 level (2-tailed),

4. DISCUSSION

In the study conducted to patients who underwent CAG, it was determined that the anxiety levels of the patients before

angiography were moderate level (44.08±5.27). In the study of Yel et al. (2020) (30) it was reported that the mean of the patients' state anxiety level was 42.5±6.3 and the mean of trait anxiety level was 46.3±6.0. In the study conducted by Moradi & Adib (2015), (31) it was shown that the mean score of the patients was 40.38±8.16 1.5 hours before the CAG. In the literature, patients undergoing CAG have been reported to be prone to stress and even panic even because they sign a consent form before the procedure (32). The variability in the rates obtained from the study may have been because the anxiety level of the patients before angiography, the causes of anxiety, the cultural and individual characteristics of the patients, and the reasons for concern differed according to the individuals.

While it was found that patients who did not receive information perceived the PS status higher, the level of state anxiety of those who received the information from health workers was found to be high. In the studies of Özdemir et al. (2015) (33) it was determined that all patients were given care before CAG and that patients experienced moderate anxiety before and after CAG. In the study conducted by Ho et al., it was reported that the emotional support provided to the patients by the nurses and the levels of post-counseling anxiety reached the lowest level compared to the previous period (34). In a meta-analysis of the effectiveness of nurse briefing patients and their families (35), was shown that informing them effectively reduced anxiety. In our study, the fact that the status anxiety level of those who received information from health workers was significant suggested that detailed information was given in these studies and that the target group in our study received on-foot information in general care.

It was found that those with a medium income perception had lower anxiety levels than those with low and high income perception. In the study conducted by Yel et al. (2020) (30) it was found that with the increasing income level of patients undergoing CAG, the level of pain, physical function, energy, and physical role limitations increased and the level of trait anxiety decreased. The researcher concluded that the average score of the trait anxiety level was lower in patients with high educational status, while low education level is associated with more anxiety. In the study conducted by Delewi et al. (2017) (36) post-procedure anxiety level were found to be higher in patients with low education levels than in both medium and highly-educated patients.

It was found that there was a low positive correlation between the PS mean scores of the patients evaluated before CAG and their State-Trait Anxiety levels. In a study conducted by Moradi & Adib (2015) (31) it was found that in patients who underwent CAG, the condition and trait anxiety level of the patients increased as the angiography time approached, the highest level of condition and trait anxiety was just before angiography, and the anxiety of the patients returned to almost the initial level after angiography. It has been reported that patients experience moderate trait anxiety before and after the angiography procedure and that the long waiting

time before the angiography procedure increases the anxiety level because the state anxiety of patients is not due to angiography (33). One study also emphasizes the importance of including patients in a well-organized preparatory program to control the high anxiety levels experienced by cardiac patients undergoing cardiac catheterization (37). Most patients awaiting angiography may experience fear, anxiety, and other unpleasant emotional experiences in which they do not have sufficient information about the medical procedure performed.

4.1. Limitations of Study

Our study had several limitations. The fact that the research was conducted in a single center posed a limitation on the generalizability of the findings. The current anxiety levels of the patients were not assessed through a structured clinical interview based on self-report. Other external factors affecting individuals' stress levels during that period were not investigated. Lastly, although the presence of a previous psychiatric disorder was set as an exclusion criterion, relying on participants' self-reports for this information was considered a limitation.

5. CONCLUSION

According to the findings, it was found that the mean scores of PS and anxiety in the patients were moderate and affected by some variables. It was found that there was a positive low and significant relationship between Perceived Stress levels and trait anxiety levels. For this reason, health workers need to plan interventions to reduce the stress and anxiety in patients.

Acknowledgments: We extend our appreciation to the patients who willingly participated in the research, providing valuable insights and data.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Necmettin Erbakan University, Noninvasive Clinic Ethics Committee (Approval date: 2022; Number:248)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: AMY, SA

Design of the study: AMY, SA

Acquisition of data for the study: AMY, SA

Analysis of data for the study: AMY, SA

Interpretation of data for the study: AMY, SA

Drafting the manuscript: AMY

Revising it critically for important intellectual content: SA

Final approval of the version to be published: AMY, SA

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Performance Evaluation of the Semi-automated Urine Analyser DFI R-600S

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Received: November 12, 2024 Accepted: April 14, 2025

ABSTRACT

Objective: The major considerations of the urine analysis performed in laboratories are to obtain a fast and accurate test result. Increasing number of instruments and methods have been developed for making it possible. The aim of this study is to compare the performance of the DFI R600S with that of the Roche Cobas U411.

Methods: Five hundred thirty three freshly obtained out – and in-patient routine urine samples collected. We conducted an analysis using results from urine dipstick tests that measure ten parameters: glucose, protein, bilirubin, urobilinogen, pH, specific gravity, ketones, red blood cells, nitrite, and leukocytes. Both analyzers were utilized in the process, followed by a microscopic examination of the urinary sediment.

Results: It was determined that the pH and specific gravity tests showed poor concordance, while the remaining tests exhibited moderate to very good concordance between the manual microscopic method and the individual devices.

Conclusions: The semi-automated test strip analyzer DFI R600S offers low cost, easy to use and reliable first level screening method for urinalysis but it is important to be aware of conditions produce false-positive or false-negative results of the urine dipstick.

Keywords: Urine analysis, dipstick, urine microscopy, Roche Cobas U411, DFI R600S

1. INTRODUCTION

Urine is a biological fluid produced and excreted from the body and urinalysis can give us useful information about the presence or absence of kidney and other diseases (1). In routine laboratory, it is very practical, available and cost-effective test for monitoring and treatment of the disease. In this analysis three different methods are used to assess the appearance, concentration, and content of urine: a visual *exam*, a dipstick *test* and a *microscopic exam* (2).

In pathological conditions urine composition varies in kind and quantities. Urine dipstick test is a chemical analysis of urine by multi-parameter pads allows a determination of the complete urine status. The chemical changes of urine can indicate various diseases, such as renal disease, liver disease, and some metabolic disorders (3). The strips change color based on the presence and concentration of certain substances like erythrocytes, leukocytes, nitrites, proteins, specific gravity, glucose, ketones, bilirubin, urobilinogen and pH (4). Urine test strip is an inexpensive, simple and non-invasive procedure.

Microscopic examination of urine sediment is considered as gold standard method for urine sediment analysis in the course and management of disorders, because the urine strip tests may not detect microscopic elements such as casts,

crystals, yeast, parasites, spermatozoa or rare cell types in the urine is a reflection of changes that take place in the kidney (2). A complete urine analysis includes microscopic examination, allowing for the detection of these elements.

The aim of this study was to determine the performance of a urine test strip analyzer DFI R-600S with Roche Cobas U411 currently used in our laboratory. In this study we also compare the results of the urine analysis performed with dipsticks, to the results obtained with the microscopic examination and to evaluate the dipstick performances.

2. METHODS

2.1. Sample

Five hundred thirty three freshly obtained out – and in-patient routine urine samples which were submitted to our laboratory between 1 September 2024 and 15 September 2024 were included. Routine diagnostic urinalysis, including both strip and microscopic analysis, was performed on fresh urine specimens within one hour of receipt, following the Clinical Laboratory Standards Institute GP16-A3 guidelines (5). The study was approved by the Ethics Committee of the Zonguldak Bulent Ecevit University (Approval date: 04.09.2024 Number2024/15)

How to cite this article: Can M, Güven B, Adıbelli F, Altunsoy E. Performance evaluation of the semi-automated urine analyser DFI R-600S. Clin Exp Health Sci 2025; 15: 368-372. <https://doi.org/10.33808/clinexphealthsci.1583681>

Table 1. Characteristic of Analyzers and Strips

Parameter	Roche Cobas U411	DFI R-600S
Method	Reflectance photometer	Reflectance photometer
Measuring system (Wavelengths)	470 nm, 555 nm, 620 nm	460, 550, 650 nm
Throughput (strips per hour)	600	600
Memory	1000 sample results	5,000 samples results
Size (mm) and weight (kg)	424x339x260 and 11.7 kg	360 x 330 x 240 mm and 5.7 kg
Printer	Thermal printer	Thermal printer
Strip name	Combur 10	DUS
RBC measurement principle	Activity measurement of pseudoperoxidase in hemoglobin	Activity measurement of pseudoperoxidase in hemoglobin
WBC measurement principle	Activity measurement of esterase in leukocytes	Activity measurement of esterase in leukocytes
Nitrite measurement principle	Griess reaction	Griess reaction
Protein measurement principle	Protein error of a pH indicator	Protein error of a pH indicator
Specific gravity measurement principle	Cation extraction	Cation extraction
Glucose measurement principle	Glucose-oxidase/oxidase reaction	Glucose-oxidase/oxidase reaction
Ketones measurement principle	Legal's nitroprussid reaction	Legal's nitroprussid reaction
Bilirubin measurement principle	Diazo reaction	Diazo reaction
pH measurement principle	Double pH indicator	Double pH indicator
Urobilinogen measurement principle	Ehrlich's reaction	Ehrlich's reaction

2.2. Analyzers

The urine test strip analyzer Roche Cobas U411 (Roche, Basel, Switzerland) and R-600S (DFI Co, Gyeongsangnam-do, Korea) were used for semiquantitative measurement of analytes in human urine and commercially available control materials according to the manufacturer's instruction. Calibration, maintenance, and bilevel (normal and abnormal) urine quality control procedures for all devices were completed to ensure they were prepared to provide patient results before the study. Table 1 presents the general characteristics of the analyzers and the strips. The sensitivity of the Urine Test Strips of the manufacturer were shown at Table 2.

Table 2. The sensitivity of the Strips

Parameter	Roche Combur 10	DFI DUS
RBC	5 – 10 Ery/ μ l	10 – 15 Ery/ μ l
WBC	20 – 25 Leu/ μ l	20 – 25 Leu/ μ l
Nitrite	0.05 – 0.07 mg/dl	0.05 – 0.10 mg/dl
Protein	8 – 12 mg/dL	15-30 mg/dL
Glucose	30 – 40 mg/dl	75-125 mg/dl
Ketones	3 – 6 mg/ dl	5-10 mg/ dl
Bilirubin	0.4 – 0.6 mg/dl	0.8-1.0 mg/dl

2.3. Manual Microscopic Analysis

Urine samples were first assayed semiautomated urine analyzers than 10 mL urine samples were centrifuged (NF 400, Nuve, Turkey) at 400 $\times$ g for 5 minutes and examined by manual microscopy. The supernatant was discarded. The precipitate was resuspended in the test tube, then 20 μ L of the precipitate was taken on a glass slide and covered by coverslips. All microscopic examination (DMLS, Leica, Japan)

results were completed by two laboratory expert, and the mean values were calculated.

2.4. Statistical Analysis

All statistical calculations were performed with SPSS Statistics 18.0 (Statistical Package for Social Sciences version 18.0, IBM Corporation, Armonk, NY, USA). Erythrocytes and leukocytes were classified semi-quantitatively (0–5, 6–10, 11–20, >20 cell/HPF). The semi-quantitative elements were also classified as positive or negative, positive results being those exceeding the cutoff values, defined as 5/HPF for leukocytes and erythrocytes. We calculated the exact match concordance rate (%) and concordance rate (%) with ± 1 grading difference rates (%) between Cobas U411 and R-600S. Cohen's kappa coefficient (κ) was calculated for concordance between the methods and the values of the Cohen's kappa coefficient are characterized as poor (0–0.21), fair (0.21–0.40), moderate (0.40–0.60), good (0.61–0.80), and very good (0.81–1.00) agreement, respectively (6).

3. RESULTS

3.1. Red Blood Cell

The kappa coefficient between manual microscopy and Cobas U411 was moderate ($\kappa = 0.464$) with an exact match concordance rate of 65% and a ± 1 rank match concordance rate of 84%. The kappa coefficient between manual microscopy and R-600S was moderate ($\kappa = 0.438$) with an exact match concordance rate of 62% and a ± 1 rank match concordance rate of 92% (Figure 1).

[illegible]

Figure 1. Cross Tabulation of Urine Dipstick Parameters

3.2. Leucocyte

The kappa coefficient between manual microscopy and Cobas U411 was moderate ($\kappa = 0.472$) with an exact match concordance rate of 66% and a ± 1 rank match concordance rate of 90%. The kappa coefficient between manual microscopy and R-600S was good ($\kappa = 0.533$) with an exact match concordance rate of 73% and a ± 1 rank match concordance rate of 90% (Figure 1).

3.3. Nitrite

The kappa coefficient between Cobas U411 and DIF 600 was very good ($\kappa = 0.842$) with an exact match concordance rate of 97% and a ± 1 rank match concordance rate of 100% (Figure 1).

3.4. Protein

The kappa coefficient between Cobas U411 and DIF 600 was moderate ($\kappa = 0.407$) with an exact match concordance rate of 47% and a ± 1 rank match concordance rate of 82% (Figure 1).

3.5. Glucose

The kappa coefficient between Cobas U411 and DIF 600 was moderate ($\kappa = 0.587$) with an exact match concordance rate of 87% and a ± 1 rank match concordance rate of 96% (Figure 1).

3.6. Ketone

The kappa coefficient between Cobas U411 and DIF 600 was very good ($\kappa = 0.806$) with an exact match concordance rate of 92% and a ± 1 rank match concordance rate of 99% (Figure 1).

3.7. Bilirubin

The kappa coefficient between Cobas U411 and DIF 600 was good ($\kappa = 0.781$) with an exact match concordance rate of 90% and a ± 1 rank match concordance rate of 98% (Figure 1).

3.8. Urobilinogen

The kappa coefficient between Cobas U411 and DIF 600 was very good ($\kappa=0.807$) with an exact match concordance rate of 93% and a ± 1 rank match concordance rate of 100% (Figure 1).

3.9. pH

The kappa coefficient between Cobas U411 and DIF 600 was poor ($\kappa = 0.138$) with an exact match concordance rate of 39% and a ± 1 rank match concordance rate of 50% (Figure 1).

3.10. Specific gravity

The kappa coefficient between Cobas U411 and DIF 600 was poor ($\kappa = 0.095$) with an exact match concordance rate of 11% and a ± 1 rank match concordance rate of 49% (Figure 1).

4. DISCUSSION

A good analytical and diagnostic accuracy were recommended for urinalysis. Our study confirmed that the combination of chemical strip analysis and sediment microscopic analysis reliably distinguishes normal from positive samples, based on the concordance between the manual method and the two instruments.

The dipstick test for hematuria is a sensitive and rapid but nondiagnostic screening test (7). The decreased urine specific gravity (below 1.010) and increased pH (above 7.0) may result in hemoglobin release and microscopy can fail to detect urinary red blood cells (8). In our study group we don't have any dipstick hematuria without microscopic hematuria. Some dipstick tests should also check the urinary ascorbic acid to predict potential false-negative results (9). In contrast to the COBAS U411, test strips used in DFI R600S have an ascorbic acid pad. In 26 sample ascorbic acid result positive and seven of them in DFI R600 S and two of them in COBAS U411 demonstrated false negative microscopic hematuria. Also hemoglobinuria, myoglobinuria, menstrual blood, concentrated urine, strenuous exercise and strong oxidizing agents (soaps, detergents, sodium hypochlorite, hydrogen peroxide) are influenced the red blood cell pad (8) and cause differences in results between microscope and dipstick. Therefore, dipstick hematuria should be verified by microscopic examination to confirm the presence of red blood cells.

In sediment analysis both urine analyzers showed sufficient performance for leucocyte in comparison to manual microscopy. The dipstick test gives false results for leukocyte count because of possible causes, such as elevated glycosuria, proteinuria, bilirubinuria, some oxidizing drugs or vitamin C (10). In 28 urine sample DFI R600S results were negative and the COBAS U411 results were positive, in 30 urine sample the COBAS U411 results were negative and the DFI R600S results were positive and in 5 samples both analyzer were negative when compared to microscopy contained a large amount of glucose or protein. The presence of glucose or protein may lead to false-negative results by reducing the sensitivity of the reaction to leukocyte esterase. In 3 urine sample DFI R600S results were positive and the COBAS U411 results were negative, in 14 urine sample the COBAS U411 results were positive and the DFI R600S results were negative and in one samples both analyzer were positive when compared

to microscopy contained a large amount of bilirubin or urobilinogen. The presence of bilirubin or urobilinogen may lead to false-positive results due to the color of the urine.

In our study we found very good match concordance between urine analyzers in nitrite. Causes of false-negative nitrite results include a short time between urine collection and testing, urine pH below 6.0, organisms that further reduce nitrite to ammonia, blood, dilute urine, proteinuria, glycosuria, presence of urobilinogen, and certain medications such as ascorbic acid (11). False-positive nitrites can occur with contaminated urine specimens, exposure to air, and the use of phenazopyridines (12). The DFI R600S showed false negatives in seven cases and false positives in ten cases, particularly involving large amounts of blood, proteinuria, or glycosuria. Hence, a positive nitrite result is very likely to indicate a true urinary tract infections.

Proteinuria is defined as urinary protein excretion of greater than 150 mg per day. The dipstick method is most sensitive to albumin. Hematuria, alkaline urine pH, high urine specific gravity and antibiotics such as penicillin or sulfonamides can give false positive results and non albumin urinary proteins and low urine specific gravity can give false negative results (13). Our results showed good level of agreement, only for negative protein results. The dipstick test has a high negative predictive value for proteinuria and can identify individuals at risk of rapid kidney function decline (14). It has the advantage of ruling out overt proteinuria with a spot urine sample, eliminating the need for specially collected samples. Additionally, due to its simplicity and low cost, the dipstick test can still be used as a primary screening method (15). If a subsequent dipstick test result is positive, work up should undergo a quantitative measurement of protein excretion, which can be done with a 24-hour urine specimen.

Glucose appears in urine when plasma glucose concentration exceeds the renal threshold. Fasting urine glucose measurement may not be suitable for diabetes screening, as plasma glucose levels may not be high enough to cause significant glycosuria. The potential of glycosuria for diabetes screening has been underestimated, and urine glucose measurement is not recommended due to its low sensitivity (16). While urine glucose can be used for mass screening, it cannot reflect fluctuations in blood glucose levels, unlike blood glucose measurements (17-18).

Dipstick testing showed acceptable performance for detection of glucose in comparison with Roche Cobas U411. Urine dipstick tests are inexpensive, non-invasive and easy to use to obtain additional information about a patient's condition. Urine dipsticks detect the presence of acetoacetate in urine by a colorimetric reaction with nitroprusside. In current clinical practice, ketosis is frequently tested using a urine dipstick that measures acetoacetate concentrations but although it detects severe ketosis, it is not successful in moderate to mild levels (19). Our results showed very good concordance for clinical usage.

Bacteria in the gut metabolize conjugated bilirubin by removing the glucuronic acid, after which bilirubin is reduced to the colorless pigment urobilinogen by bilirubin reductase, through the action of intestinal microflora (20). Most urobilinogen is excreted in the feces, small quantities of urobilinogen is transported by the blood into the kidneys and found in normal urine, The goal of urine bilirubin screening is to potentially reveal a pathologic liver or gall bladder condition early, before jaundice is apparent (13). Comparing the urinary bilirubin result with the urobilinogen result may assist in distinguishing between red cell hemolysis, hepatic disease, and biliary obstruction (13). In the case of bilirubin and urobilinogen, similar results were observed for both reagent and dipstick measurement This suggests that both methods are similarly useful for assessment bilirubin and urobilinogen presence in urine.

The pH test area contains indicators which change colour between pH 5 and pH 9. Wesarachkitti B et found poor concordance level of approximately 40% was obtained for pH between Sysmex UX-2000 vs Cobas 6500 (21). Single dipstick pH measurements have been shown to produce an unacceptable rate of clinically significant deviation [22]. Based on our chemical strip performance evaluation in this study, the concordance rate for strip pH was not satisfactory too. Differences for strip parameters might be due to altered chemical design of pads, the calibration of readers for optical absorbance or interferences. The most accurate method to measure urine pH is the use of a glass electrode (23). Urine specific gravity generally gives useful information about the patient's hydration status and the concentrating ability of kidneys. The DFI R600S gave poor results when compared to Roche Cobas U411. The results observed for specific gravity were very similar with highly consistent observations by Tanaka et al. (24).

This present study may have some limitations. First, some parameters such as protein, glucose, ketones, bilirubin, specific gravity and pH were not measured with other methods. Second, we did not compare dipstick results to a reference of *urine culture*. Third, we couldnt classify patients according to their symptoms that may potentially affect the observed results and such results should be interpreted with caution. Therefore, future studies are recommended which can better address the limitations seen in our findings.

5. CONCLUSION

To the best of our knowledge this is the first study evaluating the performance of DFI R600S by comparing that with Cobas U411 and microscopy analysis. Both systems have satisfactory agreement with microscopic exam. We only find inconsistencies for pH and specific gravity between analyzers. In conclusion the semi-automated test strip analyzer DFI R600S offers low cost, easy to use and reliable first level screening method for urinalysis but it is important to be aware of the limitations of the urine dipstick.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Zonguldak Bülent Ecevit University, Noninvasive Clinic Ethics Committee (Approval date: 04.09.2024 Number2024/15)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: MC, BG

Design of the study: MC, BG

Acquisition of data for the study: MC, BG, AF, EA

Analysis of data for the study: MC, BG, AF, EA

Interpretation of data for the study: MC, BG, AF, EA

Drafting the manuscript: MC

Revising it critically for important intellectual content: MC

Final approval of the version to be published: MC, BG, AF, EA

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Evaluating the Clinical Performance of Highly Filled Injectable Composite and Condensable Universal Composite Restorations: A One-Year Randomized Clinical Trial

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Received: November 28, 2024 **Accepted:** March 2, 2025

ABSTRACT

Objective: Composite materials are constantly renewed and developed. Recently, injectable composite materials with filler ratios similar to condensable composites have been made available to clinicians. The purpose of this randomized controlled clinical trial was to evaluate the one-year clinical performance of Class II restorations performed with injectable and condensable universal composite resins.

Methods: The study involved 71 patients (45 female, 26 male) and 140 restorations. It used G-aenial Universal Injectable (GCI; GC, Tokyo, Japan), G-aenial A'CHORD (GCA; GC, Tokyo, Japan), Tetric Prime (TP; Ivoclar Vivadent, Lichtenstein), Filtek Ultimate (FU; 3M ESPE, St. Paul, MN, USA) universal composites, and the Clearfil SE Bond (Kuraray Noritake Dental, Japan) self-etch adhesive system. Restorations were evaluated and scored according to modified USPHS criteria at baseline, six months, and one year. Cochran Q and Fisher-Freeman-Halton tests were used for statistical analysis ($p < .05$).

Results: At the end of the first year, no significant differences over time were observed in any parameter within any material group ($p > .05$). The study's materials were compared, showing statistically similar results ($p > .05$).

Conclusion: This study found that all materials, including the injectable universal composite, demonstrated similar and successful clinical performance at the end of the first year.

Keywords: Class II restoration, clinical evaluation, high-fill injectable, universal composite resin

1. INTRODUCTION

Composite resins' high aesthetic properties, ability to allow minimally-invasive cavity design, and improved mechanical and physical properties have increased their popularity today (1). Due to aesthetic and possible toxic concerns, amalgam has been abandoned in many countries, and composite resins have become the primary materials for restoring posterior teeth (2–4).

Composite resins have made remarkable advances in recent years and are available in various forms (5–8). Universal composites offer clinicians a wide range of applications thanks to their functional durability in the posterior region, and the high degree of polishability and aesthetic properties required to imitate natural tooth tissue in the anterior region (9,10).

Choosing the appropriate composite material for restoring posterior teeth requires balancing many requirements. Mechanical and physical properties affect the restorations' life, such as fracture resistance, optimized elastic modulus,

low solubility, and low polymerization shrinkage. At the same time, it must fulfill aesthetic properties such as color stability, optimum polishability, and long-term preserved anatomical form (11). In addition, technical precision is also critical in the use of composite materials. While the clinical survival of restorations not made under appropriate conditions decreases, secondary caries may also occur (12,13). These disadvantages have shown the need to produce materials that are easy to apply and mechanically and physically resistant (14).

In recent years, second-generation flowable composites with a high filler ratio entitled "high filler flowable composite" (HFFC) or "high filler injectable composite" (HFIC), have been introduced to the market. These materials have been reported to have reduced polymerization shrinkage/stress and improved mechanical properties. The aim is to simplify the application and shorten the time spent on the restoration

How to cite this article: Gürses M, Ünlü N. Evaluating the Clinical Performance of Highly Filled Injectable Composite and Condensable Universal Composite Restorations: A One-Year Randomized Clinical Trial. Clin Exp Health Sci 2025; 15: 373-379. <https://doi.org/10.33808/clinexphealthsci.1592696>

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step with these composites (14,15). In addition, due to their increased physical and mechanical properties, manufacturers recommend using HFICs as permanent restoration materials even in areas that will receive chewing loads (16).

Filtek Ultimate conventional universal composite (CUC), preferred in our study, has been widely used in dentistry for many years (17–19). However, G-aenial A'CHORD, Tetric Prime and G-aenial Universal Injectable composite materials considered in the study are relatively new, and studies on them are limited (9,20–23). We have yet to find a study in the literature comparing the clinical performance of HFIC and CUCs in posterior restorations. Clinical follow-up studies are needed in which these materials, that provide ease of application and are thought to reduce technical sensitivity, are investigated together with CUCs.

This study evaluated the clinical performance of Class II restorations performed with one HFIC and three CUCs at baseline, 6 months, and 1st year according to modified USPHS criteria (United States Public Health Service criteria) (24). The study's null hypothesis was that there is no difference in the clinical performance of Class II restorations performed with HFIC and CUCs.

2. METHODS

2.1. Ethical approval and protocol registration

The T.R.Ministry of Health, Turkish Pharmaceuticals, and Medical Devices Ethical Committee approved this prospective clinical trial (2022/152). Participants were informed of the objectives and content of the study, and voluntary consent forms were signed. This clinical trial was registered at ClinicalTrials.gov under the registration number NCT06346756.

2.2. Trial design, settings, and location of data collection

The study was a single-blind (patient) randomized controlled clinical study. It was conducted in the Restorative Dentistry Department Clinic of Selçuk University.

2.3. Participant recruitment and randomization

Participants were selected from patients who applied to the Restorative Dentistry Clinic of the Faculty of Dentistry of Selçuk University and met the inclusion criteria for the study. Table 1 presents the inclusion and exclusion criteria for patients to be included in the study. A total of 71 patients (45 female, 26 male) aged between 18 and 50 years, and involving 140 restorations were included in the study.

The patients included in the study had at least two and a maximum of four posterior approximal caries. At least two different restorative materials were used in each patient. The study used well-sealed envelopes containing material information to determine which restoration material would be applied to the teeth.

Table 1. Inclusion and exclusion criteria.

Inclusion Criteria	Exclusion Criteria
A patient presenting with;	1) poor oral hygiene status
1) over 18 years of age	2) those with severe or chronic periodontitis
2) a normal periodontal status and good general health	3) absence of adjacent and antagonist teeth
3) proximal caries that similar size on premolar and molar teeth	4) potential behavioural problems (e.g. bruxism)
4) cavity width not exceeding ½ of the intercuspal distance	5) allergy to any product used in the study
5) teeth that were vital	6) exposure of the pulp during cavity preparation
6) teeth in contact with the opposing tooth and subjected to normal occlusal forces	7) systemically unhealthy
7) attend follow-up appointments	8) pregnant and lactating women

2.4. Sample size calculation

The study calculated the sample size based on the difference between the groups' initial, 6-, and 12-month clinical success rates. The minimum sample size for determining the statistical difference with a significance level of 5%, a statistical power of 80%, and an effect size of 0.30 (moderate) was 31 restorations in each group. Considering the potential for patients to discontinue follow-up, the number of restorations in each group was determined to be 35.

2.5. Restoration Procedures

A single practitioner (M.G.) performed all cavity preparations and restorations. A rubber dam (heavy – 0.25 mm, Sanctuary Dental, Malaysia) was used for isolation purposes. Operative procedures and restoration processes were performed under local anesthesia if necessary (Ultracain, Sanofi aventis, Germany). In cavity preparation enamel tissue was removed in cavity preparation with a high-speed aerator and green band diamond round burs under water cooling (Green band, NO:12C, SWS-MDT, Turkey). Class II cavities were prepared according to the boundaries of the carious tissue. Necrotic and infected dentin were removed using a low-speed micromotor with tungsten carbide burs (ISO size 014-016, Meisinger, Neuss, Germany). All cavity margins were finished in sound enamel tissue. After cavity preparation was completed, the cavities were washed and dried. Proximal contacts were achieved using a metallic matrix (Tofflemire Contoured Matrices, Kerr/USA) and wooden wedges (Sycamore Interdental Wood Wedge, Kerr/USA).

In the study, G-aenial A'CHORD (GCA), Tetric Prime (TP), Filtek Ultimate Universal (FU), and G-aenial Universal Injectable (GCI) composite resins, and a Clearfil SE Bond adhesive system were used. Adhesive systems and composite resins were applied according to the manufacturer's instructions. The types, contents, and manufacturer's instructions for the materials used in the study are shown in Table 2. The adhesive system and composite resins were polymerized with a Valo LED light device (1000 mW/cm², Ultradent, South Jordan, UT, USA). After removing the matrix band from the tooth, the light was applied for 20 seconds on the buccal and palatal/lingual surfaces. The power of the light device was checked with a radiometer (Hilux Curing Light Meter, Benlioğlu Dental, Turkey) every ten applications.

Table 2. Materials used in the study.

Product Name	Composition	Mode of Application
Clearfil SE Bond Kuraray Noritake Dental, Japan (self-etch adhesive system)	Primer: 10-Methacryloyloxidodecyl dihydrogen phosphate (10-MDP), 2-Hydroxyethyl methacrylate (HEMA), hydrophilic aliphatic dimethacrylate, dl-camphorquinone, N,N-diethanol-p-tolidine, water. Bond: 10-Methacryloyloxidodecyl dihydrogen phosphate (MDP), Bisphenol A diglycidyl methacrylate (Bis-GMA), 2-hydroxyethyl methacrylate (HEMA), hydrophobic aliphatic dimethacrylate, dl-camphorquinone, N,N-diethanol-p-tolidine, colloidal silica.	The primer is applied to the cavity for 20 seconds, dried with air for 5 seconds, and light-cured for 10 seconds after applying the bonding agent.
G-aenial A'CHORD GC/ Tokyo, Japan (high viscous classic)	Monomers: UDMA, TEGDMA, BisMEPP Filler (wt%): Glass-filler (barium glass) and fumed silica organic filler (fumed silica) (82 wt%).	2 mm layers are placed in the cavity, each layer is light-cured for 20 seconds.
Tetric Prime Ivoclar Vivadent/Lichtenstein (high viscous classic)	Monomers: Bis GMA, UDMA, Bis-EMA Filler (wt%): Ba-Al-Silicate glass, copolymer, mixed oxide, ytterbium trifluoride (79–80%).	2 mm layers are placed in the cavity, each layer is light-cured for 20 seconds.
Filtek Ultimate Universal 3M ESPE, St. Paul, MN, USA (high viscous classic)	Monomers: Bis-GMA, UDMA, TEGDMA, bis-EMA, PEGDMA Filler (%wt): Silica filler and zirconia filler (76.5%).	2 mm layers are placed in the cavity, each layer is light-cured for 20 seconds.
G-aenial Universal Injectable GC/ Tokyo, Japan (high filler injectable)	Monomers: UDMA, bis-EMA, methacrylate monomers Filler (wt%): Silica and barium glass (69%).	2 mm layers are placed in the cavity, each layer is light-cured for 20 seconds.

Contacts in occlusion and articulation were controlled with double-sided articulating paper and adjusted where necessary. Yellow-band diamond burs (Meisinger Dental Burs, Hager & Meisinger GmbH, Germany) were used to remove premature contacts, make occlusal adjustments, and shape interproximal areas. Finishing and polishing procedures were performed using rubbers (Dentsply/Canada) and discs (Sof-Lex™ 3M ESPE, USA) with micromotor under water cooling. The rubber dam was removed. After the procedures were completed, patients were given oral hygiene motivation.

2.6. Clinical Evaluation of Restorations

In this study, calibration training was given to two dentists who participated as evaluators before the study was conducted. After the restorations were placed, patients were called for follow-up at one week (baseline), six months, and one year. Dental mirrors, probes, floss, bitewing radiographs, and intraoral photographs were used to clinically evaluate the restorations. The restorations were evaluated for retention, color match, marginal discoloration, marginal adaptation, surface texture, secondary caries, anatomical form, and postoperative sensitivity by double-blind and calibrated by two experienced dentists according to modified USPHS criteria. Cohen's Kappa coefficient was used for interobserver reliability. If there were discrepancies between the observers' evaluations, both observers re-evaluated the restorations, and consensus was reached before the patients were left (25,26). Restorations were scored as Alpha, Bravo, and Charlie. Clinical examination was performed using a dental mirror, probe, and floss.

2.7. Statistical Analysis

Statistical analyses were performed using R version 4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) statistical software. The change rates of GCA, TP, FU, and GIC restorations were examined over time with the Cochran Q test according to the modified USPHS criteria. Alpha score rates for the study's materials at the same measurement time were compared with the Fisher-Freeman-Halton test. The significance value was determined as $p < .05$.

3. RESULTS

Our study evaluated 140 restorations in 71 patients (45 female, 26 male). The distribution of restorations according to composite materials and teeth is shown in Table 3. Follow-up appointments were carried out on the 7th day, 6th month, and 1st year after the restorations were performed. All patients attended their control appointments. The clinical evaluation of Class II restorations according to the Modified USPHS criteria is shown in Table 4.

Table 3. Distribution of composite materials according to teeth.

MATERIAL	Premolar	Molar	TOTAL
G-aenial A'CHORD	18	17	35
Tetric Prime	18	17	35
Filtek Ultimate Universal	19	16	35
G-aenial Universal Injectable	20	15	35

Table 4. Baseline, six-months and one-year clinical evaluation of restorations.

USPHS Criterion	Baseline			Six months			One year		
	A	B	C	A	B	C	A	B	C
Retention									
GCA	35	0	0	35	0	0	35	0	0
TP	35	0	0	35	0	0	35	0	0
FU	35	0	0	35	0	0	35	0	0
GCI	35	0	0	35	0	0	35	0	0
Color match									
GCA	35	0	0	35	0	0	35	0	0
TP	35	0	0	35	0	0	35	0	0
FU	35	0	0	35	0	0	35	0	0
GCI	35	0	0	35	0	0	35	0	0
Marginal discoloration									
GCA	35	0	0	35	0	0	35	0	0
TP	35	0	0	35	0	0	35	0	0
FU	35	0	0	35	0	0	35	0	0
GCI	35	0	0	35	0	0	35	0	0
Marginal adaptation									
GCA	35	0	0	35	0	0	34	1	0
TP	35	0	0	35	0	0	35	0	0
FU	35	0	0	35	0	0	34	1	0
GCI	35	0	0	35	0	0	32	3	0
Secondary caries									
GCA	35	–	0	35	–	0	35	–	0
TP	35	–	0	35	–	0	34	–	1
FU	35	–	0	35	–	0	35	–	0
GCI	35	–	0	35	–	0	35	–	0
Surface texture									
GCA	35	0	0	35	0	0	35	0	0
TP	35	0	0	34	1	0	34	1	0
FU	35	0	0	35	0	0	35	0	0
GCI	35	0	0	35	0	0	35	0	0
Anatomical form									
GCA	35	0	0	35	0	0	35	0	0
TP	35	0	0	35	0	0	35	0	0
FU	35	0	0	35	0	0	35	0	0
GCI	35	0	0	35	0	0	35	0	0
Postoperative sensitivity									
GCA	35	0	0	33	2	0	35	0	0
TP	35	0	0	35	0	0	35	0	0
FU	35	0	0	35	0	0	35	0	0
GCI	35	0	0	35	0	0	35	0	0

Abbreviation: USPHS, US Public Health Service; A, Alpha; B, Bravo; C, Charlie; GCA, G-aenial A'CHORD; TP, Tetric Prime; FU, Filtek Ultimate Universal; GCI, G-aenial Universal Injectable.

3.1. Evaluation of Restorations

At the end of the first year, no significant differences over time were observed in any parameter within any material group (Figure 1) ($p > .05$). In the GCA group, postoperative sensitivity was observed in two teeth at six months. However, these complaints disappeared in patients at the one-year evaluation. In one GCA, one FU, and three GCI restorations scored as Bravo in the marginal adaptation parameter at one year, and excess composite resin at the finishing margins was corrected with yellow-band diamond burs and polished. In the TP group, at one year, secondary caries was diagnosed in one

restoration. Although there was no loss in the overall form of the restoration, decay was detected on a bite-wing radiograph. The restoration was renewed with GCA. In the 6th month and 1st year, one TP restoration scored as Bravo in the surface texture parameter. The study's materials were compared, and statistically similar results were observed ($p > .05$).

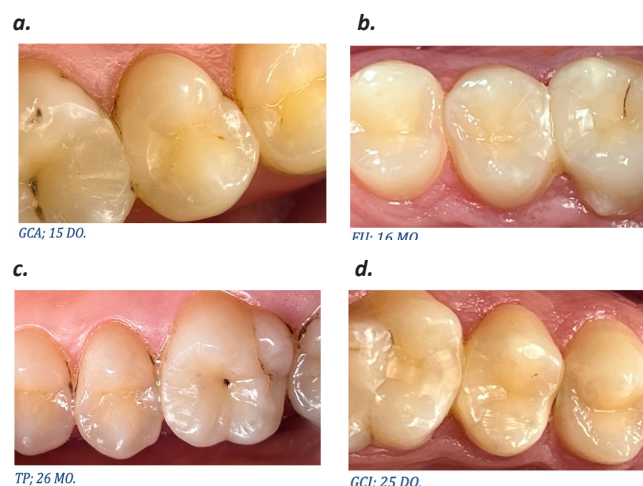


Figure 1. Restorations that scored as Alpha from all parameters at one year: a. 15 DO restorations performed with GCA, b. 16 MO restorations performed with FU, c. 26 MO restorations performed with TP, and d. 25 DO restorations performed with GCI.

4. DISCUSSION

This study presents a one-year clinical follow-up of Class II restorations restored with one HFIC (GCI) and three CUCs (GCA, FU, TP). The study's results led to an acceptance of the null hypothesis. At the end of the first year, HFIC and CUCs' clinical performances were comparable and successful.

FU has been a preferred material in clinical routine for many years. The literature includes both in vitro and clinical studies of this material (18,27–29). The study presenting the clinical follow-up of FU and a bulk-fill composite in Class II restorations reported that both materials showed successful clinical performance at 12 months (17). These results are compatible with those of our study. However, in the sixth year of the same study, the marginal adaptation and marginal coloration rate of FU showed a significant increase compared to the initial situation (18). Based on these data, it seems that long-term clinical follow-ups are necessary to determine the effects of a dynamic environment such as that found in the mouth on materials.

The literature lacks long-term clinical follow-up studies of GCA, TP, and GCI composites, which are relatively new materials. In vitro studies examining materials' physical and mechanical properties are also limited (9,20,21,30).

In an in vitro study, Class II cavities prepared in extracted primary and permanent molars were restored with TP, an HFIC, and a bulk-fill composite. The marginal integrity of the restorations was examined before and after mechanical

loading. No significant difference was observed in the marginal compliance of the TP after mechanical loading (30). It is not possible to directly compare the results of our study with those of this study. However, in our study, all TP restorations were scored as Alpha in the marginal adaptation parameter in the first year.

In another study, the surface roughness and microhardness values of GCI and four different HFFC (Filtek Supreme Flowable, 3M; Estelite Universal Flow, Tokuyama; Omnichroma Flow, Tokuyama; Filtek Universal Restorative, 3M) materials were investigated after brushing. It has been reported that the surface roughness values of all materials increased, and the microhardness values decreased after brushing. The lowest microhardness values were observed in GIC (31). Properties such as surface roughness, microhardness, and the wear behavior of thin occlusal veneers made with GIC and two different HFICs (Beautifil Injectable, Shofu; Sonicfill-2, Kerr) were compared in vitro with resin-based CAD/CAM material (Ceresmart, GC). The materials were subjected to thermomechanical loading in a chewing simulator. The study reported that GIC showed the least wear and was more durable than Ceresmart. In addition, other HFICs were reported to undergo degradation after thermomechanical loading (20). While GIC showed the lowest microhardness values in one study (31), it was reported as the material with the highest wear resistance in another study (20). The fact that the materials compared with GIC in the studies are entirely different may affect the results. During the restoration phase of our work, notes were taken and recorded for each material. It has been noted that in restorations made with GIC, more restorative material is removed from the surface during the polishing stage than other materials. This situation is parallel to the low microhardness data in Canyurt's study (31). In the first year, the results of our research showed that GCI showed very successful clinical performance. The marginal adaptation of only three restorations was scored as Bravo. Excess composite material that exceeded the restoration-tooth boundary was corrected in these restorations at the control appointment. The high fluidity of the material may be a factor in exceeding the tooth-restoration limit.

In the SEM study, simulated gastric acid was applied to GCA, and four different composite materials (Omnichroma, Tokuyama; Vittra Unique, FGM; Charisma Diomand One, Kulzer; Neo Spectra ST, Dentsply; Nova Compo C, Imicryl) and their surface roughness and microhardness changes were examined. On the 7th day of acid application, the roughness values of all materials were found to be acceptable. On the 14th day, a significant difference was observed in all materials' roughness and microhardness values. However, on the 14th day, the surface roughness values of GCA were reported to be clinically acceptable (21). Gürkan et al.'s study (9) compared the physical properties of GCA, FU, and three universal composites (Estelite Asteria, Tokuyama; Charisma Dimond, Kulzer; Neo Spectra ST HV, Dentsply). The results indicated that GCA showed the lowest surface roughness and microhardness values. While FU shows the highest microhardness values, it is just below those of

Charisma Dimond, which shows the highest values in surface roughness. GCA and FU showed similar values in terms of color change and translucency examination. In addition, in the SEM images of the study, the smoothest surface was observed in GCA (9). In our study, all GCA restorations scored as Alpha for parameters such as color change, marginal discoloration, marginal adaptation, and surface texture that can be affected by surface roughness.

The study detected secondary caries in only one TP restoration in the first year mark in the case of one patient whose oral hygiene was found to be inadequate. The patient was given oral hygiene motivation, and the restoration was renewed. Postoperative sensitivity was observed in two GCA restorations at six months. However, no symptoms or pathology were found in these restorations at the 1-year follow-up. Short-term and spontaneously-resolving postoperative sensitivity may be associated with periodically increasing bruxist forces in patients.

In line with these data, although in vitro studies have an important place in determining materials' physical and mechanical properties, they should be supported by clinical findings. Since the literature does not appear to exist for clinical follow-up of GCA, TP, and GCI materials, we could not compare our study's results clinically. Therefore, we think our study's results are valuable.

There are several limitations in our study. First of all, more than one year is needed to determine the clinical behaviour of the materials. Long-term clinical follow-up of this study is planned in the future. Additionally, split-mouth randomization was not applied in our study. It is quite challenging to include patients in whom four restorative materials can be applied split-mouth. Since materials without clinical follow-up were used in the study, it was planned for individuals with good oral hygiene and have small approximal caries. Studies evaluating the clinical performance of these materials in individuals with high caries risk patients and cavities with high material loss are also required.

5. CONCLUSION

G-aenial Universal Injectable, G-aenial A'CHORD, Tetric Prime, and Filtek Ultimate universal composites showed similar and successful clinical performance. In addition, G-aenial Universal Injectable, a high filler injectable composite, can be considered an alternative to conventional universal composites in the restorations of Class II posterior cavities.

Acknowledgements: We thank Dr. Hakan Serin, a biostatistician, for the statistical analysis.

Funding: This clinical research was supported by Selcuk University Scientific Research Projects Institution (Project no: 21112010).

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: The Turkish Republic Ministry of Health, Turkish Pharmaceuticals, and Medical Devices Ethical Committee approved this prospective clinical trial (2022/152).

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: N.Ü., M.G.

Design of the study: N.Ü., M.G.

Acquisition of data for the study: M.G., N.Ü.

Analysis of data for the study: M.G., N.Ü.

Interpretation of data for the study: M.G., N.Ü.

Drafting the manuscript: M.G., N.Ü.

Revising it critically for important intellectual content: M.G., N.Ü.

Final approval of the version to be published: M.G., N.Ü.

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A Comparative Analysis of Obesity Prejudice, Orthorexia Nervosa, and Fatphobia Among Nutrition and Dietetics Students, Clinical Dietitians, and General Population

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Received: November 29, 2024 **Accepted:** May 21, 2025

ABSTRACT

Objective: Weight-related biases, including orthorexia nervosa, fatphobia, and obesity prejudice, are significant social and health issues, particularly within nutrition-related fields. This study aimed to compare these biases among nutrition and dietetics students, clinical dietitians, and the general population.

Methods: This cross-sectional study, conducted between May and July 2024, included 837 participants comprising 301 nutrition and dietetics students (mean age: 19.9 ± 7.5 years), 227 clinical dietitians (mean age: 30.2 ± 9.0 years), and 309 individuals from the general population (mean age: 24.4 ± 7.5 years). Orthorexic tendencies were assessed using the ORTO-11 scale, attitudes toward body weight were measured by the Fatphobia Scale, and obesity-related stigma was evaluated using the GAMS-27 Obesity Prejudice Scale.

Results: Significant differences were observed in orthorexia nervosa tendencies, fatphobia, and obesity prejudice across the groups. Nutrition and dietetics students had the highest orthorexic tendencies, while clinical dietitians had the lowest orthorexic tendencies among the groups ($F=90.114$, $p<.001$). Fatphobia scores were highest in the general population (41.8 ± 5.8), with clinical dietitians scoring the lowest (36.9 ± 4.4 ; $F=88.577$, $p<.001$). Obesity prejudice was also significantly greater in the general population (79.8 ± 9.6 ; $F=14.958$, $p<.001$). Correlational analysis indicated a positive association between ORTO-11 scores and fatphobia in clinical dietitians ($r=0.313$, $p<.001$), suggesting that lower orthorexic tendencies are linked to stronger fatphobic attitudes within this group.

Conclusions: In conclusion, these results show the need to integrate targeted education into nutrition programs to promote balanced and flexible dietary health. Further research is essential to develop effective strategies addressing weight bias.

Keywords: Orthorexia nervosa, fatphobia, obesity prejudice, nutrition education, weight stigma

1. INTRODUCTION

The rise in global obesity rates has highlighted both the associated health risks and the social stigma faced by individuals with obesity. Weight bias, which often appears as negative attitudes, stereotypes, and discrimination, is prevalent in various areas of life, including employment, education, and healthcare (1-3). In addition to its psychosocial dimensions, recent evidence suggests that dietary behavior also has measurable effects on metabolic and inflammatory outcomes in individuals with obesity, underscoring the clinical importance of weight-related attitudes (4). Research shows that individuals with obesity frequently encounter stigma and mistreatment, leading to significant psychological distress, reduced quality of healthcare, and worsened health outcomes (5). Within healthcare settings, weight bias can lead to disparities in care, diminishing empathy and resulting

in poorer health experiences for individuals with higher body weights (1). Addressing weight stigma is crucial for creating a more equitable healthcare environment and improving outcomes for individuals with obesity (6, 7).

Orthorexia nervosa and fatphobia have received increasing attention as specific forms of weight-related bias, particularly in health and nutrition contexts. Orthorexia nervosa (ON) and fatphobia are two forms of bias related to body weight. ON involves an intense focus on eating only “healthy” foods, often leading to restrictive eating patterns and anxiety around food choices (8). Although ON is not officially classified as an eating disorder, it shares similarities with other forms of disordered eating and has been associated with negative impacts on physical and psychological well-being (8, 9).

How to cite this article: Bodur M, İpek MN, Tümren G, Mammadova N. A Comparative Analysis of Obesity Prejudice, Orthorexia Nervosa, and Fatphobia Among Nutrition and Dietetics Students, Clinical Dietitians, and General Population. Clin Exp Health Sci 2025; 15: 380-386. <https://doi.org/10.33808/clinexphealthsci.1593283>

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Research suggests that ON tendencies appear more common among those in health-related fields, where nutrition knowledge may encourage rigid attitudes toward food (10-12). The term “fatphobia” is used to describe negative attitudes towards body fat. These attitudes are often based on social beliefs that equate low body weight with good health and moral worth (13). Fatphobic attitudes may lead to stigmatizing behaviors and discriminatory practices, contributing to social exclusion and mental health challenges for individuals with higher body weights (2, 14). Together, orthorexia nervosa and fatphobia contribute to weight bias by promoting restrictive standards for body image and health, which may also influence attitudes within healthcare settings (2, 15).

Professionals in the field of nutrition and dietetics, including students and clinical dietitians, are uniquely positioned to impact public attitudes toward body weight due to their expertise in dietary health. However, research suggests that they are not protected from biases such as obesity stigma, ON and fatphobic attitudes, which can affect their interactions with clients and patients (16, 17). Nutrition students, in particular, may be at increased risk for orthorexia due to their focus on dietary health and “clean eating” ideologies, while clinical dietitians may develop more balanced views through professional exposure and experience in working with a range of body types (18, 19). Understanding the prevalence of these attitudes within and outside the nutrition field is critical for identifying areas for educational and professional interventions to reduce weight bias in healthcare. Therefore, the aim of this study is to evaluate the presence of prejudice towards obesity, orthorexia nervosa tendencies, and fatphobia among nutrition and dietetics students, clinical dietitians, and the general population.

2. METHODS

This cross-sectional study, conducted in Ankara, Turkey, between May and July 2024, aimed to compare obesity prejudice, orthorexia nervosa tendencies, and fatphobia among nutrition and dietetics students, clinical dietitians, and individuals from the general population, aged 20 to 65 years. In the power analysis conducted to determine the required sample size, differences in the Obesity Prejudice Scale scores between groups were considered the primary outcome. Based on a Type I error (α) of 0.05, a study power (β) of 0.85, and an effect size of 0.15, the required sample size was calculated as 271 participants per group. To account for potential dropouts or other unforeseen circumstances, the target sample size was set at 840 participants. This study was approved by the Ethics Committee of Ankara University (56786525-050.04.04/1356448).

2.1. Study Design and Sample Recruiting

The inclusion and exclusion criteria are shown in Table 1. No additional criteria were applied.

Table 1. Inclusion and exclusion criteria for participant recruiting

	Undergraduate Dietetic Students (S)	Clinical Dietitians (C)	General Population (G)
Inclusion Criteria	• Being a 1st or 2nd-year student in the Nutrition and Dietetics Department • Willingness to participate in the study	• Having graduated from a Nutrition and Dietetics Department at a university in Turkey and currently working in Ankara, • Having graduated at least 2 years ago, • Being actively employed, • Working in a position that involves direct patient contact, such as a clinic, hospital, or polyclinic.	• Having no formal education related to nutrition, • Not having followed any dietary treatment, • Not having any diagnosed chronic illness by a doctor.
Exclusion Criteria	• Being a 3rd or 4th-year student or a postgraduate student in the Nutrition and Dietetics Department • Not willing to participate in the study	• Not being actively employed, • Not willing to participate in the study, • Not working in a position involving direct patient contact, such as a clinic, hospital, or polyclinic.	• Not willing to participate in the study, • Having received any education related to nutrition or having any course on healthy eating in the formal curriculum.

2.2. Sociodemographic Characteristics

Participants were asked about their age, sex, educational level, and smoking status. Anthropometric measurements were performed following standard procedures, with height measured in the Frankfurt plane and weight obtained using a body composition analyzer (Omron) (20). Physical activity levels were assessed using a 24-hour diary, recording time spent in sleep, light, moderate, and vigorous activities. PAL was calculated as (activity time $\times$ MET) / 24, classifying participants as “sedentary” (PAL 1.40–1.69), “moderately active” (PAL 1.70–1.99), or “highly active” (PAL > 2.0) (21).

2.3. Ortorexia Nervosa

The Orthorexia Nervosa Scale–15 (ORTO-15), developed by Donini et al., is a 15-item self-assessment tool designed to evaluate orthorexia nervosa tendencies. It assesses behaviors related to food selection, purchasing, preparation, and consumption based on individuals’ perceptions of healthy eating (22). Responses are rated on a 4-point Likert scale, with lower scores indicating a higher risk of orthorexia nervosa. A Turkish validity and reliability study of the ORTO-15 was conducted by Arusoğlu et al., resulting in the ORTO-11 version (23). This version includes 11 items with strong factor loadings.

Table 2. Sociodemographic characteristics of the participants

Sociodemographic Characteristics	Students (S) (n=301)		Clinical Dietitians (C) (n=227)		General Population (G) (n=309)		F/ χ^2 p
Age, years ($\bar{x} \pm SD$)	19.9 $\pm$ 7.5 ^a		30.2 $\pm$ 9.0 ^b		24.4 $\pm$ 7.5 ^c		154.623 < .001**
	S	%	S	%	S	%	
Gender							
Male	65	15.9	36	21.6	73	23.6	4.978
Female	236	84.1	191	78.4	236	76.4	.083
Smoking Status							
Yes	49	18.1	41	83.7	70	77.3	4.231
No	252	81.9	186	16.3	239	22.7	.121
Marital Status							
Single	301	100.0	130	57.3	251	81.2	156.618
Married	0.0	0.0	97	42.7	58	18.8	< .001**
Education Level							
High School	301	100.0	0	0	90	27.8	252.619
Associate degree	0.0	0.0	1	0.4	38	12.3	< .001**
Bachelor degree	0.0	0.0	172	75.8	160	51.8	
Graduate degree	0.0	0.0	54	23.8	21	6.8	
PAL values ($\bar{x} \pm SD$)	1.85 $\pm$ 0.22		1.83 $\pm$ 0.21		1.85 $\pm$ 0.22		2.825 .467
Physical Activity Levels							
Sedentary	73	24.3	48	21.1	90	29.1	14.555
Moderate	124	41.2	106	46.7	138	44.7	.024*
Heavy	104	34.6	73	32.1	81	26.2	
BMI (kg/m ²) ($\bar{x} \pm SD$)	22.23 $\pm$ 3.11 ^a		22.20 $\pm$ 3.34 ^a		23.12 $\pm$ 4.10 ^b		6.226 < .001**
BMI categories							
Underweight	33	11.0	15	6.6	27	8.7	19.133
Normal	221	73.4	177	78.0	199	64.4	< .001**
Overweight/Obese	47	15.6	35	15.4	83	26.9	

The table presents the sociodemographic characteristics of the participants across three groups: Students (S), Clinical Dietitians (C), and General Population (G). Continuous variables are reported as mean $\pm$ standard deviation ($\bar{x} \pm SD$) and analyzed using one-way ANOVA (F-values). Different letters in the same row indicate statistically significant differences ($p < .05$) based on ANOVA results. Categorical variables are presented as frequencies and percentages (n, %) and analyzed using Pearson's chi-square (χ^2) test. Statistical significance is indicated as follows: * $p < .05$, ** $p < .01$.

2.4. Obesity Prejudice Scale

The Obesity Prejudice Scale consists of 27 items in a 5-point Likert format to identify individuals' prejudices towards obese people. The scale was developed to measure obesity-related prejudices (24). It is rated as 'strongly agree', 'agree', 'neutral', 'disagree', and 'strongly disagree'. Positive items (2, 4, 7, 10, 11, 14, 15, 17, 20, 22, 25, 27) are scored from 5 to 1, starting from 'strongly agree', while negative items (1, 3, 5, 6, 8, 9, 12, 13, 16, 18, 19, 21, 23, 24, 26) are reverse-scored from 1 to 5. The total score range for the 27-item scale is between 27 and 135. The scale is categorized into three levels: prejudice-free (≤ 68 points), prejudice-prone (68.01-84.99 points), and prejudiced (≥ 85 points), with higher scores indicating greater levels of prejudice (24).

2.5. Fatphobia Scale

The Fatphobia Scale, developed by Robinson et al. (1993), measures individuals' attitudes towards obesity (25). The Turkish validity and reliability study of the Fatphobia Scale was

conducted by Koçak et al. (2005) (26). The scale comprises 14 items rated on a five-point Likert scale, with the total score calculated by dividing the sum of item responses by 14; higher scores (closer to five) indicate stronger fatphobic attitudes, while lower scores (closer to one) reflect weaker fatphobic attitudes.

2.6. Statistical Analyses

In this study, the data collected were analyzed using the SPSS statistical software package. Categorical variables, such as gender and educational status, were expressed as counts (percentages). The normality of data distribution was assessed through visual methods (histogram) and hypothesis tests (Kolmogorov-Smirnov and Shapiro-Wilk tests). Data conforming to a normal distribution were reported as mean $\pm$ standard deviation, whereas non-normally distributed data were expressed as median $\pm$ interquartile range. Differences between groups in continuous numerical variables were analyzed using one-way analysis of variance (ANOVA), followed by post hoc comparisons

with Bonferroni correction to adjust for multiple testing. A p -value of less than 0.05 was considered statistically significant in all analyses.

3. RESULTS

The sociodemographic characteristics of the study participants, including students (S), clinical dietitians (C), and the general population (G), are summarized in Table 2. The mean ages of the groups were significantly different ($F = 154.623$, $p < .001$), with students averaging 19.9 ± 7.5 years, clinical dietitians 30.2 ± 9.0 years, and the general population 24.4 ± 7.5 years. The majority of participants across all groups were female, with 84.1% of students, 78.4% of clinical dietitians, and 76.4% of the general population being women, though the gender distribution did not differ significantly ($\chi^2 = 4.978$, $p = .083$).

Smoking status also showed no significant difference across groups ($\chi^2 = 4.231$, $p = .121$), with the highest rates among clinical dietitians (18.1%) and the lowest among students (18.1%). Marital status significantly varied between groups ($\chi^2 = 156.618$, $p < .001$), with all students being single (100%), compared to 42.7% of clinical dietitians and 18.8% of the general population being married. Educational levels differed significantly ($\chi^2 = 252.619$, $p < .001$): all students had completed high school, 75.8% of clinical dietitians held a bachelor's degree, and in the general population, 51.8% had a bachelor's degree while 27.8% had completed high school.

In terms of physical activity levels, a significant difference was observed ($\chi^2 = 14.555$, $p = .024$), with 34.6% of students, 32.1% of clinical dietitians, and 26.2% of the general population categorized as heavily active. However, when physical activity was evaluated using estimated PAL values derived from MET-based calculations, no statistically significant differences were found between the groups ($F(2, 825) = 0.76$, $p = .467$), indicating that overall physical activity levels were relatively comparable despite categorical differences. BMI values differed significantly between groups ($F = 6.226$, $p < .001$), with mean BMI values of 22.23 ± 3.11 for students, 22.20 ± 3.34 for clinical dietitians, and 23.12 ± 4.10 for the general population. The majority of participants in all groups were classified as having a normal BMI, with 73.4% of students, 78.0% of clinical dietitians, and 64.4% of the general population in this category ($\chi^2 = 19.133$, $p < .001$).

The main results of the study, including ON, Fatphobia, and Obesity Prejudice scores among students, clinical dietitians, and individuals from the general population, are presented in Table 3. Statistically significant differences were observed in ON scores between groups ($F = 90.114$, $p < .001$). Students had the highest ON scores (29.4 ± 2.1), indicating lower orthorexic tendencies, whereas clinical dietitians had the lowest scores (25.9 ± 3.8), reflecting a greater inclination toward orthorexic behaviors. The general population's scores (26.1 ± 4.1) were intermediate, suggesting a moderate level of orthorexic tendencies.

Fatphobia scores also differed significantly among the groups ($F = 88.577$, $p < .001$). The general population showed

the highest fatphobia scores (41.8 ± 5.8), reflecting more negative attitudes toward body weight. In contrast, clinical dietitians (36.9 ± 4.4) and students (37.4 ± 3.8) reported lower levels of fatphobia, with clinical dietitians having the least stigmatizing attitudes.

Obesity Prejudice scores differed significantly among groups as well ($F = 14.958$, $p < .001$). The general population showed the highest levels of obesity prejudice (79.8 ± 9.6), while students (76.2 ± 7.2) and clinical dietitians (76.6 ± 8.9) had comparatively lower scores, suggesting more neutral or less biased attitudes.

Furthermore, the categorical distribution of obesity prejudice levels revealed statistically significant differences ($\chi^2 = 33.263$, $p < .001$). The general population had the highest proportion of individuals classified as having high bias (53.0%), while clinical dietitians had the largest proportion with low bias (43.7%). Students were predominantly classified in the moderate bias category (38.8%). These results indicate that weight-related bias is most pronounced in the general population, whereas clinical dietitians tend to hold more inclusive attitudes.

Table 3. Comparison of orthorexia nervosa, fatphobia, and obesity prejudice scores among nutrition and dietetics students, clinical dietitians, and general population

Scales	Students (S) (n=301)	Clinical Dietitians (C) (n=227)	General Population (G) (n=309)	F P
Orthorexia Nervosa (ON) ($\bar{x} \pm SD$)	29.4 $\pm$ 2.1 ^a	25.9 $\pm$ 3.8 ^b	26.1 $\pm$ 4.1 ^b	90.114 <.001**
Fatphobia ($\bar{x} \pm SD$)	37.4 $\pm$ 3.8 ^a	36.9 $\pm$ 4.4 ^a	41.8 $\pm$ 5.8 ^b	88.577 <.001**
Obesity prejudice scores ($\bar{x} \pm SD$)	76.2 $\pm$ 7.2 ^a	76.6 $\pm$ 8.8 ^a	79.8 $\pm$ 9.6 ^b	14.958 <.001**
Obesity prejudice classification				χ^2 / p
Low bias	27 (38.0)	31 (43.7)	13 (18.3)	33.263 / <.001**
Moderate bias	245 (38.8)	162 (25.6)	225 (35.6)	
High bias	29 (21.6)	34 (25.4)	71 (53.0)	

The F and p -values indicate the significance of group differences. Different superscript letters (a, b) denote statistically significant differences between groups as determined by post hoc analysis ($p < .05$). The chi-square test was used for the classification of obesity prejudice levels.

The correlation matrix presented in Figure 1 and Supplementary table 1 summarizes the relationships between age, BMI, ON scores, Fatphobia scores, and Obesity Prejudice scores among the groups. A significant positive correlation between age and BMI was observed in all groups, with the strongest association found in the general population ($r = 0.456$, $p < .001$), followed by clinical dietitians ($r = 0.273$, $p < .001$) and students ($r = 0.224$, $p < .001$). These results suggest that older individuals tend to have higher BMI values, particularly within the general population. Among clinical dietitians, ON and Fatphobia scores were positively correlated ($r = 0.313$, $p < .001$), indicating that greater orthorexic tendencies may be linked to stronger fatphobic attitudes.

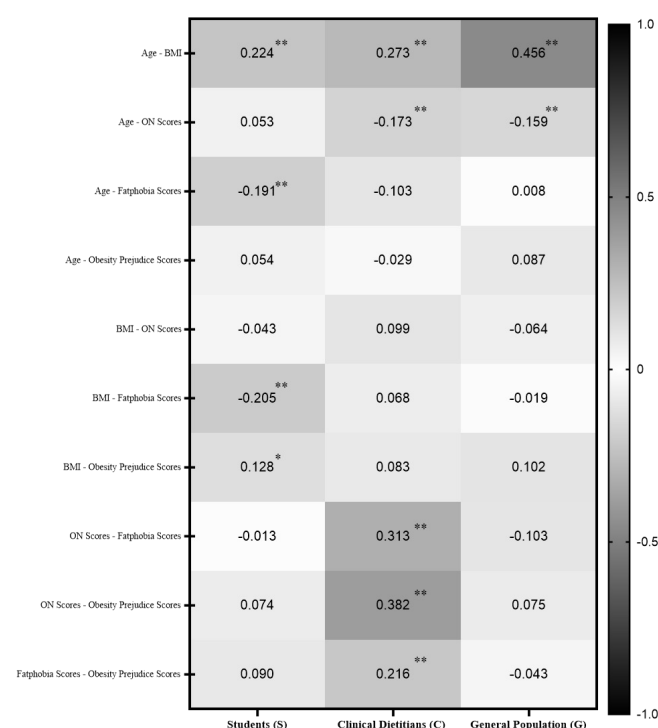


Figure 1. Correlation matrix of age, bmi, orthorexia nervosa (on) scores, fatphobia scores, and obesity prejudice scores among groups (students, clinical dietitians, and general population)

BMI: Body Mass Index, ON: Orthorexia Nervosa, FAT: Fatphobia Scores, OBP: Obesity Prejudice Scores, S: Students, C: Clinical Dietitians, G: General Population, p: Probability Value, r: Correlation Coefficient, * $p < .05$; ** $p < .001$

Negative correlations were observed between age and ON scores in both the general population ($r = -0.159$, $p < .001$) and clinical dietitians ($r = -0.173$, $p < .001$), suggesting that orthorexic tendencies tend to decrease with age. In the student group, BMI was negatively correlated with overall scale scores ($r = -0.205$, $p < .001$), implying that students with higher BMI may exhibit lower adherence to the measured constructs. Additionally, among clinical dietitians, a significant positive correlation was found between ON and Obesity Prejudice scores ($r = 0.382$, $p < .001$), suggesting that greater orthorexic tendencies may be associated with higher levels of obesity prejudice. A small but significant positive correlation between BMI and Obesity Prejudice scores was also noted in students ($r = 0.128$, $p < .05$), indicating a slight trend toward increased weight-based bias among those with higher BMI.

4. DISCUSSION

This study examined obesity prejudice, orthorexia nervosa (ON) tendencies, and fatphobia across three groups: nutrition and dietetics students, clinical dietitians, and the general population. Findings reveal substantial differences among these groups. Clinical dietitians had the highest ORTO-11 scores, reflecting the lowest orthorexic tendencies. However, nutrition students scored the lowest on the ORTO-11

scale, indicating greater orthorexic tendencies. The general population scored between these two groups, suggesting moderate orthorexic tendencies. These results suggest that both professional training and exposure to diverse body types may influence attitudes toward food and body weight, potentially moderating orthorexic tendencies and weight bias.

The increased orthorexic tendencies among nutrition and dietetics students are consistent with previous studies that suggest individuals within nutrition-focused academic environments are more likely to adopt rigid dietary behaviors, especially when body image concerns are also present (16, 17, 27). Nutrition students may face pressure to follow strict dietary practices, which can sometimes lead to obsessive eating behaviors (8, 28). This pressure may be influenced by the concept of “clean eating,” which focuses on avoiding certain foods to maintain purity. Research suggests that this approach can increase anxiety about food choices and promote restrictive eating habits (29, 30). The emphasis on dietary perfection that is often present in nutrition education may unintentionally encourage such behaviours by promoting a rigid attitude towards food. However, recent findings from a Turkish sample suggest that this association may not always be straightforward. In a cross-sectional study conducted among dietitians, although orthorexic tendencies and abnormal eating attitudes were found to be moderately correlated, the authors concluded that nutrition education alone may not necessarily lead to disordered eating patterns (31). To prevent the development of disordered eating patterns among students, nutrition education programmes could include lessons on the importance of flexibility and balance in healthy eating.

Fatphobia and obesity prejudice were most pronounced in the general population, as reflected in higher scores on the fatphobia and obesity prejudice scales compared to clinical dietitians and nutrition students. These findings are aligned with research suggesting that societal norms equate thinness with health and attractiveness, reinforcing negative stereotypes and biases toward individuals with higher body weights (32, 33). The prevalence of fatphobia in society is frequently exacerbated by the presentation of body fat in the media and the establishment of cultural ideals that associate body fat with notions of undesirability or moral inferiority. This, in turn, gives rise to weight-based stigma in a multitude of social contexts, including healthcare, employment, and personal relationships (34, 35). Such biases have been shown to negatively impact the mental health and quality of life of individuals with obesity, leading to increased levels of anxiety, depression, and body dissatisfaction (36, 37). Public health campaigns that challenge harmful weight stereotypes and emphasize the acceptance of body diversity may therefore be beneficial in reducing fatphobia and improving social attitudes toward individuals of all body types.

Clinical dietitians showed more balanced attitudes with the highest ORTO-11 scores, indicating lower orthorexic tendencies, and relatively lower levels of fatphobia and obesity prejudice compared to the general population. This pattern aligns with studies suggesting that professional exposure and training in nutrition may cultivate empathy and a more

comprehensive understanding of the factors that influence body weight, thereby reducing stigmatizing attitudes (17, 32, 38). Dietitians who interact regularly with a range of clients and patients of diverse body types, and who are committed to patient-centered care, will develop more inclusive attitudes. This will help them to reduce the biases that are often present in society (17). Professional training in nutrition and dietetics could further benefit from incorporating modules on weight bias and its implications for healthcare, equipping practitioners with the skills needed to deliver stigma-free care.

In conclusion, this study highlights the need for critical thinking in public health and nutrition education. Future dietitians will need to adopt a balanced and evidence-based approach to nutrition in order to influence public attitudes towards diet and body image. The reduction of weight stigma and the promotion of body diversity are of great public health importance. encourage public campaigns that normalize different body shapes and sizes and highlight the harms of weight stigma can change societal prejudices and promote a more inclusive social environment.

This study has several strengths, including the use of validated and reliable measurement tools, as well as the inclusion of a diverse sample of students, clinical dietitians, and individuals from the general population, which provides group comparisons. It contributes to the literature by exploring biases across different levels of nutrition education. However, the cross-sectional design limits causal interpretations. Although correlation analyses were conducted, regression models were not included due to the weak strength of associations observed between variables, which limited the feasibility of building predictive models. Furthermore, the use of self-reported data and the sampling from a single geographic region may affect the generalizability of the results.

5. CONCLUSION

In conclusion, the study shows significant differences in orthorexic tendencies, fatphobia, and obesity prejudice among students, clinical dietitians and the general population. The results highlight the need for educational interventions to promote more balanced attitudes in nutrition education. Public health strategies should also aim to reduce weight stigma and support body acceptance. Further research is needed to guide effective approaches to reducing weight stigma.

Acknowledgements: We would like to express their gratitude to all participants for their valuable contributions to this study.

Funding: This study was supported by the Scientific and Technological Research Council of Turkey (TUBITAK 2209-Project Number: 1919B012325524). The authors declare that there is no conflict of interest any other than this.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Ankara University, Noninvasive Clinic Ethics Committee (Approval date: 06.05.2024; Number: 56786525-050.04.04/1356448)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: MB

Design of the study: MB

Acquisition of data for the study: MNİ, NM, GT

Analysis of data for the study: MB

Interpretation of data for the study: MB

Drafting the manuscript: MB

Revising it critically for important intellectual content: MB

Final approval of the version to be published: MB, MNİ, NM, GT

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Supplementary Table 1. Correlation Coefficients Among Age, BMI, Orthorexia Nervosa (ON), Fatphobia (FP), and Obesity Prejudice (OP) Scores by Group

Variables	Students (n=301)	Clinical Dietitians (n=227)	General Population (n=309)
Age – BMI	.224**	.273**	.456**
Age – ON	.053	-.173**	-.159**
Age – FP	-.191**	-.103	.008
Age – OP	.054	-.029	.087
BMI – ON	-.043	.099	-.064
BMI – FP	-.205**	.068	-.019
BMI – OP	.128*	.083	.102
ON – FP	-.013	.313**	-.103
ON – OP	.074	.382**	.075
FP – OP	.090	.216**	-.043

ON: Orthorexia Nervosa, FP: Fatphobia, OP: Obesity Prejudice, * $p < .05$, ** $p < .001$

Optimizing qPCR Annealing Temperatures for Cancer-Related lncRNAs

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Received: 04.12.2024

Accepted: 29.05.2025

ABSTRACT

Objective: To determine the optimal annealing temperatures to detect copy number variation and expression levels of specific cancer-associated long non-coding RNAs (lncRNAs), to improve the accuracy of clinical tests in precision medicine.

Methods: Gradient qPCR analysis was performed to identify the optimal annealing temperatures for the detection of lncRNAs. These lncRNAs were H19, CCAT1, HOTAIR, NEAT1, MALAT1, PVT1, GAS5, BANC1, UCA1, HULC, and MEG3.

Results: Optimal qPCR annealing temperatures for the detection of lncRNA expression and copy number variations were determined as follows: 62.4°C for PVT1 and BANC1; 60°C for H19, CCAT1-b, HOTAIR, NEAT1, MALAT1; 58°C for GAS5 and HULC; 56.7°C for CCAT1-a, UCA1; and 56°C for MEG3.

Conclusion: In this study, we determined optimal annealing temperatures for some lncRNAs, which is crucial for the precision and accuracy of qPCR used to identify lncRNA expression and copy number changes. These results confirm the optimization of lncRNA analysis by determining optimal annealing temperatures, which is essential for the precision and accuracy of qPCR.

Keywords: cancer, lncRNA, qPCR, annealing temperature

1. INTRODUCTION

Cancer, one of the serious diseases that threaten human health, is caused by a combination of genetic and non-genetic environmental factors. In most cases, it is also characterized by mutations occurring in the non-coding region of the genome, beyond the protein-coding regions, which make up less than 2% of the genome (1,2).

Advances in genome sequencing technologies have revealed that more than 80% of the genome produces different RNA molecules, in contrast to the less than 2% that is transcribed to messenger RNA (mRNA) for protein synthesis. This means that a large part of the human genome that is transcribed are called non-coding RNAs (ncRNAs). Long ncRNAs (lncRNAs) are non-protein-coding RNA molecules longer than 200 nucleotides that are transcribed by RNA polymerase II (Pol II) (3).

Genome and transcriptome analyses have highlighted the involvement of lncRNAs in numerous epigenetic regulations, including chromatin remodeling, DNA methylation, and histone modification (4). In addition, lncRNAs have crucial post-translation roles, controlling the function of proteins by silencing genes through the production of endogenous siRNA or microRNA binding. Some lncRNAs have oncogenic roles or tumor suppressor functions, while others play dual roles in tumor suppression and oncogenesis in cancer (5).

H19, a paternally imprinted lncRNA first isolated in the 1980s, exhibits both oncogenic and tumor-suppressive functions. As a tumor suppressor, it inhibits cell proliferation in some cancers such as colorectal cancer, hepatocellular carcinoma, and osteosarcoma. It also has an oncogenic role in breast cancer, ovarian cancer, gastric cancer, and other

How to cite this article: Yalçinkaya B, Eskin Z, Mammadova N. Optimizing qPCR Annealing Temperatures for Cancer-Related lncRNAs. Clin Exp Health Sci 2025; 15: 387-391. <https://doi.org/10.33808/clinexphealthsci.1596074>

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cancers by promoting survival, metastasis, and epithelial-mesenchymal transition (6,7).

Metastasis-associated lung adenocarcinoma transcript 1 (MALAT1) gene, one of the most studied lncRNAs, produces various splicing variants and full-length MALAT1. It can exhibit both oncogenic and tumor-suppressive functions in several cancer types. Similarly BANC1, NEAT1, MEG3, and PVT1 (8) (9).

HOTAIR, a trans-regulator lncRNA that has been identified in fibroblasts, shows oncogenic effects by regulating HoxD cluster genes. It has an important role in proliferation, metastasis, apoptosis, invasion, and drug resistance in various cancers like breast, lung, ovarian, and gastric cancers(10). Other lncRNAs with reported oncogenic effects include CCAT1, HULC, and UCA1 (9).

GAS5 (Growth Arrest-Specific5) serves as a tumor suppressor lncRNA which is frequently deactivated in various cancers, especially in breast cancer, hepatocellular carcinoma, and gastric cancer. GAS5 functions by suppressing proliferation, cell survival, metastasis, and therapy resistance. (11).

H19, CCAT1, HOTAIR, NEAT1, MALAT1, PVT1, GAS5, BANC1, UCA1, HULC, and MEG3 are the most commonly studied cancer-related lncRNAs. There are different primer sequences published for targeting these lncRNAs in the literature. However, limited publications shared both primer sequences and optimal annealing temperature information. Optimizing primer assay temperatures in qPCR is crucial for obtaining precise and reliable results.

In this study, we aimed to optimize the qPCR annealing temperature of the target-specific primers for these lncRNAs. The experimental design considered annealing temperatures identified from a comprehensive review of previous studies (Table 1).

2. METHODS

2.1. RNA Isolation and Reverse Transcription

5 mL of whole blood was collected from a healthy individual and aliquoted to 500 µL. Total RNA was extracted from the 500 µL whole blood sample using the QIAamp RNA Blood Mini Kit (Qiagen Cat. No. / ID: 52304) following the manufacturer's protocol. The concentration and purity of the extracted RNA were measured at 230 nm, 260 nm, and 280 nm using a NanoDrop Spectrophotometer (ND-1000, Thermo Fisher Scientific).

Total RNA was converted to cDNA using random hexamers with the SuperScript™ III First-Strand Synthesis System (Thermo Fisher Scientific, Waltham, MA, USA; Cat: 18080051) following the manufacturer's protocol.

2.2. Annealing Temperature Optimization

The annealing temperature optimization of BANC1, CCAT1-a, CCAT1-b, GAS5, H19, HOTAIR, HULC, MALAT1, MEG3, NEAT1, PVT1, and UCA1 was carried out with abm® Bright Green 2X qPCR Master Mix-No Dye (Cat. No. Master Mix-S; Lot No. 023.485.4746001, Canada) and the BIO-RAD® CFX96™ Touch Real-Time PCR Detection System. The gradient qPCR was performed as follows: initial denaturation at 95°C for 10 min, 50 cycles of 95°C for 15 seconds, and 30 seconds of annealing temperature adjusted between 56°C and 66°C.

The total reaction volume was 20 µL containing 5 µL of cDNA sample. Forward and reverse primers shown in Table 1 were synthesized and purified via HPLC (High-Performance Liquid Chromatography) by Oligomer (Turkey). Each primer was employed at a concentration of 500 nM in the reaction. Also RPPH1 F: 5'-GTCAGACTGGGCAGGAGATG-3' and R: 5'-TGGCCGTGAGTCTGTTC-3' was used as a reference gene. All temperatures were assessed in duplicate. Bio-Rad CFX Maestro 1.1. Software was used to analyze the qPCR results.

Table 1. Primer Sequences of lncRNAs

lncRNA	Forward Primer Sequences	Reverse Primer Sequences	References
BANC1	5'-ACAGGACTCCATGGCAAACG-3'	5'-ATGAAGAAAGCCTGGTGCACT-3'	(12)
CCAT1-a	5'-TTTATGCTTGAGCCTTGA-3'	5'-CTTGCTGAAATACTTGC-3'	(13)
CCAT1-b	5'-AGAAACACTATCACCTACGC-3'	5'-CTTAACAGGGCATTGCTAATCT-3'	(14)
GAS5	5'-CTTCTGGGCTCAAGTGATCCT-3'	5'-TTGTGCCATGAGACTCCATCAG-3'	(15)
H19	5'-ACTCAGGAATCGGCTCTGGAA-3'	5'-CTGCTGTTCCGATGGTGTCTT-3'	(16)
HOTAIR	5'-CAGGAGTGATTATGCAGTGGG-3'	5'-ACCCCTTCTGTGTCTACATGC-3'	(17)
HULC	5'-TCATGATGGAATTGGAGCCTT-3'	5'-CTCTTCCTGGCTTGCAGATTG-3'	(18)
MALAT1	5-AGGCGTTGTGCGTAGAGGA-3'	5'-GGATTTTACCAACCACTCGC-3'	(19)
MEG3	5'-ATCATCCGTCACCTCCTTGTCTTC-3'	5'-GTATGAGCATAGCAAAGGTCAGGGC-3'	(20)
NEAT1	5'-TGGCTAGCTCAGGGCTTCAG-3'	5'-TCTCCTTGCCAAGCTTCCTTC-3'	(21)
PVT1	5'-GGGGAATAACGCTGGTGGAA-3'	5'-CCCATTGACATCAAGCTGT-3'	(22)
UCA1	5'-ACGCTAACTGGCACCTTGT-3'	5'-TGGGGATTACTGGGGTAGGG-3'	(23)

3. RESULTS

This study aims to optimize the annealing temperature for primer assays that target specific cancer-related lncRNAs. The experimental design includes annealing temperatures defined in the review of the literature. For the gradient qPCR analysis, the annealing temperature was adjusted between 56°C and 66°C.

Following gradient qPCR analysis, optimum annealing temperatures were determined for various lncRNAs expressions. For analyzing the expression of PVT1 and BANC1, the optimal annealing temperature was determined as 62.4°C. For H19, CCAT1-b, HOTAIR, NEAT1, and MALAT1,

the annealing temperature was determined as 60°C, which revealed lower Cq level and gave a higher fluorescence signal compared to other temperatures tested. The negative control samples did not show any false positive findings.

The optimal annealing temperature for GAS5 and HULC expression was found to be 58°C among the temperatures analyzed. Similarly, the ideal annealing temperature for CCAT1-a, UCA1 expression analysis was determined as 56.7°C. Additionally, the optimal annealing temperature for MEG3 expression analysis was found to be 56°C (Table 2). For all assays, no false positive signals were observed in the negative control samples.

Table 2. Cq Values from Gradient qPCR for Determining Optimum Annealing Temperatures

Annealing Temperature °C	H19		MEG3		CCAT1-a		CCAT1-b		GAS5		HOTAIR	
	Cq	±	Cq	±	Cq	±	Cq	±	Cq	±	Cq	±
66	33.7	-	-	-	-	-	28.7	1.6	22.8	0.3	28.3	0.7
65.5	28.5	-	-	-	-	-	28.9	4.4	22.5	0.1	26.1	1.0
64.3	28.1	-	40.0	3.0	-	-	24.5	0.3	22.4	0.2	24.9	0.0
62.4	34.0	7.8	43.7	2.4	-	-	24.0	0.6	22.1	0.0	24.5	0.0
60	28.6	0.3	39.7	0.7	-	-	23.5	0.2	22.3	0.1	24.5	0.0
58	29.5	0.2	36.4	0.1	28.7	2.0	23.9	0.2	22.2	0.0	24.7	0.1
56.7	28.5	0.5	34.3	0.2	26.6	0.0	23.9	0.0	22.4	0.1	31.7	0.0
56	29.2	1.7	33.8	0.0	28.0	0.1	24.1	0.0	23.0	0.9	24.9	0.0
Annealing Temperature °C	NEAT1		UCA1		BANC1		MALAT1		PVT1		HULC	
	Cq	±	Cq	±	Cq	±	Cq	±	Cq	±	Cq	±
66	29.5	0.7	24.6	0.0	25.3	0.2	26.5	0.1	24.9	0.1	25.6	0.2
65.5	32.5	0.6	24.2	0.1	25.0	0.1	26.4	0.0	24.8	0.2	25.3	0.1
64.3	28.1	0.0	24.1	0.1	25.0	0.1	26.0	0.2	25.1	0.5	25.0	0.0
62.4	27.0	0.3	24.1	0.0	24.6	0.2	33.8	0.2	24.5	0.1	25.0	0.2
60	26.3	0.1	23.6	0.0	25.1	-	26.3	0.0	24.6	0.1	25.0	0.0
58	26.4	0.0	23.1	0.1	32.3	0.0	32.5	0.1	32.2	0.1	24.8	0.2
56.7	33.8	0.1	22.9	0.0	29.8	0.1	31.8	0.0	25.3	0.1	24.9	0.4
56	27.2	0.2	23.0	0.1	25.4	0.1	31.5	0.2	25.2	0.1	24.7	0.1

In this study, the annealing temperatures of primer assays were determined by using the TM calculator available at <https://www.thermofisher.com/>. The calculated TMs were compared with values obtained from gradient PCR. It was observed that the annealing temperature values of some lncRNAs were found to be 2°C higher than the calculated values with informatics tools (Table 3). This temperature difference might potentially affect the qPCR results (24). It requires accurate measurement of the expression level of lncRNAs to investigate their distinctive roles in carcinogenesis. It is required that the annealing temperature be optimized in qPCR experiments to quantify accurate and reliable lncRNA transcripts.

Table 3. Calculated TM and Optimum Annealing Temperatures

lncRNA	Optimum TM	Calculated TM	Differences
H19	60	61.9	-1.9
CCAT1-b	60	53.4	6.6
HOTAIR	60	59.9	0.1
NEAT1	60	60.6	-0.6
MALAT1	60	59.6	0.4
PVT1	62.4	59.3	3.1
GAS5	58	61.3	-3.3
BANCR	62.4	59.8	2.6
CCAT1-a	56.7	50.6	6.1
UCA1	56.7	58.2	-1.5
HULC	58	58.7	-0.7
MEG3	56	63.5	-7.5

4. DISCUSSION

While numerous primer assays have been developed to analyze lncRNA expression profiles in different cancers, experimental results tend to differ from predicted theories. The method most popularly employed to predict optimal annealing temperatures is computational prediction according to GC content, but optimal PCR efficiency is usually attained by optimizing variables including RNA secondary structures and minor primer design specifics (25).

In the literature, HOTAIR, ANRIL, CCAT1, H19, PVT-1, and MEG3 annealing temperatures were published as 55°C using different target-specific primer sequences (26). Another study for MALAT1 and UCA1 at 55°C, for HOTAIR and PVT1 at 57°C, and for CCAT1 at 60°C annealing temperature was published (27).

Moreover in the literature, for BANCR expression analysis 57°C (28), for HULC expression analysis 52°C (29), and for GAS5 expression analysis 62.5°C set as annealing temperature (30) have been reported.

Accurate determination of annealing temperatures for specific lncRNA targets is necessary to enhance the sensitivity and accuracy of assays in cancer research. We know that lower and non-optimized annealing temperatures could lead to non-target amplifications. Thus optimization of PCR conditions is essential for accurate analysis of gene

expression and copy number changes. Validated methods not only improve the reliability of PCR-based assay data but also enhance our understanding of the roles of the target genes in cancer biology and their potential as therapeutic targets.

In this study, we performed annealing temperature optimization for several cancer-related lncRNAs. Optimization of the annealing temperatures for lncRNAs has the importance for improving the accuracy of biomarker detection and for developing the most suitable personalized treatment strategies tailored to individual patients.

5. CONCLUSION

As a conclusion, long non-coding RNAs (lncRNAs) play a crucial role in regulating oncogenic processes in cancer due to their involvement in several epigenetic mechanisms. Their importance as biomarkers and therapeutic targets has led to a significant increase in lncRNA research exponentially over the last several years.

Accurate measurement of lncRNA expression by qPCR, which is considerably dependent on optimization of experimental conditions such as annealing temperature, is crucial for obtaining precise and reliable results.

Our findings establish a foundation for future studies, contributing to the growing body of knowledge and guiding additional research in the field of lncRNA-targeted studies.

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

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Istanbul University, Clinical Research Ethics Committee (Approval date: 07.10.2024 Number: 2935468)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: BY

Design of the study: BY

Acquisition of data for the study: BY, ZE

Analysis of data for the study: BY, ZE

Interpretation of data for the study: BY

Drafting the manuscript: BY, ZE

Revising it critically for important intellectual content: BY

Final approval of the version to be published: BY, ZE

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Evaluation of Root Canal Anatomy and Morphology of Lower First Premolar Teeth in a Turkish Subpopulation: Cone Beam Computed Tomography Study

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Received: December 16, 2024 **Accepted:** May 29, 2025

ABSTRACT

Objective: The aim of the present study is to evaluate the anatomy and morphology of mandibular first premolar teeth in a Turkish subpopulation, based on common classification using cone beam computed tomography.

Methods: Five hundred and five teeth that met in inclusion criteria included the study. Teeth classified according to the Vertucci Classification. All evaluations were made by two endodontists for each tooth. After recording demographic data, the root canal configuration of the teeth, number of roots, number of canals, direction and level of canal branching were recorded and evaluated. The results were statistically analysed using chi square.

Results: The most common morphology in both tooth group was Vertucci Type 1, while the second most common morphology was Vertucci Type 5. A significant difference was found between root number and gender ($p < .05$). Males were three times more likely to have two roots than females. No statistically significant difference was found between Vertucci classification and tooth location (right-left) and age group. Additionally, no statistically significant difference was found between tooth localization and canal number, root number, branching level and branching direction. ($p > .05$) According to the findings of the current study, a statistically significant difference was found between Vertucci classes and gender. ($p < .05$) However, no significant difference was shown between the number of roots and tooth location and age group. ($p > .05$)).

Conclusion: Having information about the morphology of premolar teeth with variable anatomical variations will prevent possible complications and increase success. CBCT is complementary to clinical applications in fully determining anatomical variations in three dimensions.

Keywords: anatomy, classification, Cone Beam Computed Tomography, morphology, premolar

1. INTRODUCTION

The success of root canal treatments depends on the thorough cleaning and three-dimensional obturation of the root canal system, which has a very complex structure. Being aware of the complex anatomy of the root canal system and possible anomalies is very useful during the preparation and filling of root canals (1). Ingle (2) reported that the most important cause of endodontic failures is incomplete canal instrumentation followed by incorrect canal filling. Anatomical variations that manifest themselves in different ways in each tooth group; It may appear as extra roots, extra canals, and canal branching that can be seen in different localizations. Endodontic treatment is challenging, especially in mandibular first premolars, due to the existence of many variations and limited access to the second canal (3,4). Slowey (5) stated

that mandibular premolar teeth are the most difficult teeth to treat endodontically due to differences in canal anatomy. Variations in root canal morphology may lead to endodontic flare ups and failures. Clinically, visual methods and hand sensitivity are used to determine root canal anatomy. Although radiological evaluations are performed before and after treatment, the therapeutic and diagnostic value of cone beam computed tomography is difficult (6). Also although conventional radiographs provide general information to clinician, there are situations where they may be insufficient. Extra roots, extra canals, branches in the root canal anatomy, internal and external root resorptions may not be detected on routine radiographs can be factors that make endodontic treatments more complex. These factors are very important

How to cite this article: Sağlam H, Başeski EG. Evaluation of Root Canal Anatomy and Morphology of Lower First Premolar Teeth in a Turkish Subpopulation: Cone Beam Computed Tomography Study. Clin Exp Health Sci 2025; 15: 392-398. <https://doi.org/10.33808/clinexphealthsci.1602573>

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and must be fully understood by the clinician before starting root canal treatment to ensure a successful intervention (7). In such cases, cone beam computed tomography is useful for a more accurate diagnosis and subsequent successful treatment.

Mandibular first premolar teeth are generally single-rooted and single-canal teeth known in the Turkish population. However, today, variations of these teeth have become more common, especially in the younger generation. Age and gender (8,9) as well as research design, canal identification methods, and ethnic differences all contribute to such differences (10). A study on the Saudi population published in 2019 (11) found that mandibular premolars exhibited one root in 96.4% of first premolars and 95.6% of second premolars. Similarly, many studies have reported that single-rooted lower premolars constitute 98% of the Thai population (12), 100% of the Spanish population (13), and 85.7 – 94.8% of the Iranian population (14). Various classifications have been made to classify the anatomical and morphological structures of teeth. The Vertucci classification (15-18), widely used in anatomy studies, uses eight types of root canal configurations and is based on the examination of transparent samples. The aim of the present study is to evaluate the morphology and anatomy of lower first premolar teeth in a Turkish subpopulation, based on common classification using cone beam computed tomography.

2. METHODS

Ethics committee approval for the present study was obtained from Clinical Research Ethics Committee (Annex 1). In the present study CBCT images obtained as part of the patients' diagnosis and treatment planning were retrospectively examined. No informed consent was required for this type of study based on institutional review board.

All images were taken using Galileos Machine (Sirona Dental Systems, Bensheim, Germany)

with image capture parameters set at 90 Kv and 6.0 mA, and an exposure time of 2.3 s. The voxel size of the images was 0.3 mm and the field of view (FOV) was 15 cm. The inclusion criteria were as follows:

- Patients between the ages of 18-65,
- Teeth with complete root formation,
- Lower first premolar teeth,
- Fully erupted teeth,
- Each patient had to have at least one (or two) mandibular first premolar,

The exclusion criteria were as follows:

- Teeth with periapical lesions,
- Teeth with root resorption,
- Previously endodontically treated teeth,

-Teeth with incomplete root development and open apex

All scans were evaluated separately by two endodontists to ensure objectivity and no data was recorded until a consensus was reached. In case of discrepancies between the two researchers, the image was randomly re-evaluated by both researchers on three different days. A majority vote resolved disagreements. For each image, the classification that achieved the majority was accepted as the answer. To assess inter-examiner reliability of the researchers, 15% of the radiographs randomly assigned by the investigators were randomly reviewed each day for 10 days. Results were analyzed using Wilcoxon matched pairs signed-rank test showed no statistically significant differences. After recording the demographic data of the patients, the mandibular first premolar teeth of each patient in both quadrants were examined by tomography. For each tooth, its presence in the mouth, tooth number, number of roots and canal morphology were recorded according to the Vertucci Classification. The data were confirmed by examining each tooth separately in coronal, axial and sagittal sections. Classifications of anatomical and morphological findings were made as follows:

2.1. Number of roots

The number of roots was determined as follows:

Single-rooted tooth: A tooth with a single distinct root.

Double-rooted tooth: A tooth with roots separated by bifurcation (regardless of whether the root is partially or completely separated).

Triple-rooted tooth: A tooth with three separate roots (regardless of whether the root is partially or completely separated).

2.2. Root bifurcation

According to sagittal and coronal section images, each root was examined in three sections.

- Coronal third: From the cemento-enamel junction to 1/3 of the root length (CT)
- Middle third: From 1/3 to 2/3 of the root length (MT)
- Apical third: From 2/3 of the root length to the radiographic apex. (AT)

2.3. Root Canal Morphology

2.3.1. Root canal configuration

Root canal configurations were classified according to the Vertucci classification. The configuration classification and coding made according to this classification are as follows:

- Type I (1): V1
- Type II (2-1): V2
- Type III (1-2-1): V3

- Type IV (2): V4
- Type V (1-2): V5
- 2 Roots 2 Canals: V6
- 3 Roots 3 Canals: V7

2.3.2. Canal branching level

The branching levels of the root canals were also evaluated as “coronal third” (CT), “middle third” (MT) and “apical third” (AT). If there was no branching in the canal, it was recorded as “no branching” (N).

2.3.3. Canal branching direction

When there is branching in the root canals, if the branching canal is buccal, it is evaluated as “buccal” (B), if it is lingual, it is evaluated as “lingual” (L), if there is central and equal branching, it is evaluated as “central” (C). If there is no branching in the canal, it is recorded as “no branching” (N).

2.4. Statistical analysis

The results were statistically analyzed using SPSS 20.0 (SPSS, Inc., Chicago, IL, USA). Power analysis was performed to determine a sufficient number of samples and a minimum sample population of 500 was found to be sufficient at a significance level of .05 at a 95% power scale. Data were analyzed using Fisher's Exact and Chi-square tests.

3. RESULTS

308 patients were evaluated for the study. 51 of these patients were excluded from the study because of not having the teeth to be examined. 257 patients (131 female, 126 male), 505 teeth were examined. Of these, 254 were lower left first premolars (MLFP), 251 were lower right first premolars (MRFP). Of the 254 MRPLs, 1 had 3 roots, 33 had 2 roots, and 220 had 1 root. Of the lower right first premolars, 39 had 2 roots, and 212 had a single root. Information and percentage distributions regarding gender, tooth position and root number of the evaluated patients are shown in Table 1. Some of CBCT images are shown in Figure 1, Figure 2, and Figure 3.

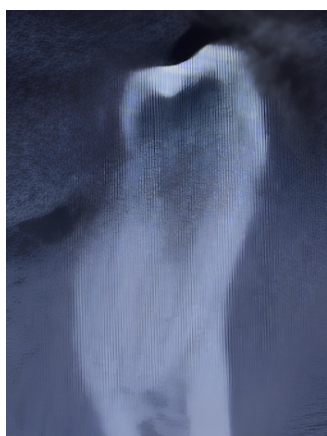


Figure 1. The canal divided into two at the middle third level of the root.

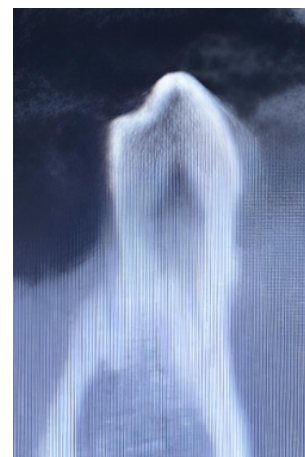


Figure 2. Double-rooted tooth.



Figure 3. Vertucci type V.

Table 1. Frequency distribution of root number (percentage of teeth) in mandibular first premolars (MFP) according to gender and tooth position

	MFP	One root (%)	Two root (%)	Three root (%)	Total (%)
Gender	Female	237 (%92.57)	19 (%7.03)	1 (%0.4)	257
	Male	195 (%78.62)	53 (%21.38)	0 (%0)	248
	Total	432 (%85.54)	72 (%14.25)	1 (%0.19)	505
Tooth Position	Right	212 (%84.8)	39 (%15.2)	0 (%0)	251
	Left	220 (%86.61)	33 (%12.99)	1 (%0.4)	254
	Total	432 (%85.71)	72 (%14.09)	1 (%0.2)	505

According to the findings of the study, the most common morphology in both tooth groups was Vertucci Type 1. The second most common morphology was Vertucci Type 5. Vertucci distribution according to tooth localization, gender and age group is shown in Table 2. The distribution of canal number, root number, branching level and branching direction according to tooth localization is shown in Table 3.

Table 2. Vertucci distribution according to tooth localization, gender and age group

	Group	Vertucci Type														P'
		V1		V2		V3		V4		V5		V6		V7		
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	
Tooth localization	Right (44)	153	60.95	3	1.19	3	1.19	5	1.99	48	19.12	39	15.53	0	0	.07
	Left (34)	145	5.08	1	0.39	4	1.57	0	0	70	27.55	33	12.99	1	0.39	
Gender	Male	132	53.22	2	0.80	3	1.20	2	0.8	56	22.58	53	21.37	0	0	.01
	Female	166	64.59	2	0.77	4	1.55	3	1.16	62	24.12	19	7.39	1	0.38	
Age group	18-35	194	59.32	2	0.61	4	1.22	2	0.61	74	22.62	50	15.29	1	0.30	.19
	36-50	54	54.54	1	1.01	0	0	2	2.02	25	25.25	17	17.17	0	0	
	51-65	50	63.29	1	1.26	3	3.78	1	1.26	19	24.05	5	6.32	0	0	

* significance level<.05, V1:Vertucci Type I, V2:Vertucci Type II, V3:Vertucci Type III, V4:Vertucci Type IV, V5:Vertucci Type V, V6: 2 Roots 2 Canals, V7:3 Roots 3 Canals

Table 3. Distribution of canal number, root number, branching level and direction according to tooth localization

	Group	Tooth localization				<i>p</i> *
		Right		Left		
		n	%	n	%	
Canal number	One Canal	152	51.18	145	48.82	.47
	Two Canal	99	47.80	108	52.20	
	Three Canal	0	0	1	100	
Root number	1	212	49.07	220	50.92	.45
	2	39	54.16	33	45.84	
	3	0	0	1	100	
Branching level	CT	15	62.50	9	37.50	.41
	MT	52	46.85	59	53.15	
	AT	32	44.44	40	55.56	
	N	151	51.01	145	48.99	
Branching direction	B	3	30	7	70	.22
	L	15	37.50	25	62.50	
	C	80	51.61	75	48.39	
	N	152	51.18	145	48.82	

* significance level<.05, CT: coronal third, MT:Middle third, AT:Apical third, N:No branching, B:Buccal, L:Lingual, C:Central,

4. DISCUSSION

The present study provides a detailed report on the root canal anatomy and morphology of mandibular first premolars in a Turkish subpopulation. Images obtained from tomography sections were used to examine root canal anatomy and morphology. Studies have reported that variations in root canal anatomy are frequently observed (19). For successful root canal treatment, it is necessary to have sufficient knowledge about the morphology and anatomy of the relevant tooth (17). Causes of failure in root canal treatment are inadequate disinfection, untreated

canals, and insufficient obturation. When all canals have been found, irrigated, shaped and obturated, the treatment can be considered as successful. Having knowledge about the number of roots and canals commonly seen in the relevant tooth will increase the success of the treatment. Therefore, accurate radiographic and clinical evaluation is essential for the success of root canal treatment (11). Clinical evaluation is integrated with diagnostic imaging. Two-dimensional imaging techniques always may not be sufficient for accurate diagnosis. In cases where two-dimensional imaging is not sufficient, three-dimensional imaging techniques should be used. CBCT is a three-dimensional imaging technique used to evaluate teeth before and after treatment. CBCT images are important for diagnosis and treatment as well as for future treatment plans (20). CBCT has some advantages over other conventional methods. One of them is that it provides a three-dimensional image of the region of interest. In addition, conditions such as broken instruments in the canal, existing perforations and their locations, and overfillings can be accurately diagnosed with CBCT. Additionally, CBCT provides images of interested region in a smaller area with less radiation, and the image quality is also better. Traumatic injuries, inadequate information obtained from clinical examination and periapical radiographs, determination of the extent and boundaries of resorption in the presence of resorption, imaging of suspected extra canals, three-dimensional evaluation of the neighborhoods to anatomical landmarks, determination of the depth and location of the fracture line in root fractures can be listed as endodontic indications for the use of CBCT. The findings obtained with CBCT can guide us in the clinical applications of endodontic treatments. Variations, extra roots, and canals that cannot be determined in two-dimensional imaging can be clearly visualized with CBCT. Thus, treatment failures that may occur due to incomplete treatment of canals that cannot be found can be prevented. In resorptions with unclear boundaries, the spread of existing pathology in lesions can be determined with CBCT and the necessary treatment plan can be made

more accurately. Different techniques have been developed for the evaluation of root canal morphology. CBCT is a highly reliable clinical tool that has recently been used for this purpose. While CBCT is considered reliable and reproducible, lower image resolution compared to micro-CT may hinder its capacity to detect more complex anatomical structures (21). However, in one study (22), micro-CT and CBCT were used simultaneously in mandibular premolars and a consistency of 85.2% was determined between the results when the Vertucci classification was considered. In addition, another study (23) showed that the CBCT method is as reliable as the clear tooth method, which is considered the gold standard in this regard. The current study is a retrospective study based on image analysis, and since it was not performed on extracted teeth, the clearing method was not used in the evaluation. For these reasons, CBCT, which provides a high reliability rate, was used as the evaluation method in the current study.

There are various classifications regarding root canal anatomy. Vertucci classification is the most valid of these, and it classifies the anatomy of the root canals into eight groups (24). This classification was used in the current study. According to the findings of the current study, 59% of the patients examined had Vertucci Type I configuration. The second most common configuration was Vertucci Type V. Similarly, in a study examining the morphology of lower premolar teeth in the Spanish population in 2014 (25), the most common configuration was Vertucci Type I, while the second most common configuration was Vertucci Type V. Similarly, in a retrospective CBCT study in the Saudi population (11), the most common root canal configuration in mandibular first premolars was Type I. The second most common configuration was Type II. In another study conducted in a selected German population (26), morphology varied to varying degrees, with the most common morphology being Type V (55.7%) and the second most common morphology being Type I (21.9%). Considering these results, it can be said that the two most common morphologies in mandibular first premolars in different populations are Type I and Type V.

Considering the findings of the current study, no statistically significant relationship was found between Vertucci classification and tooth localization (right-left) and age group ($p>.05$). In a study conducted in another Turkish population in 2014 (8), it was similarly stated that root canal configurations did not show any significant difference between the right and left sides ($p>.05$). Although not specific to the mandibular first premolar tooth, some studies (27,28) have mentioned that there are differences in the root canal system structure between different age groups in permanent teeth. Additionally, no statistically significant relationship was found between tooth localization and canal number, root number, branching level and branching direction. ($p>.05$)

The relationship between gender and root structure has been discussed in some studies on dental anatomy (8,29-31). In these studies, according to the results obtained from Spanish (29), Nepalese (30) and Turkish (8) populations, no

statistically significant difference was shown in the number of roots in male and female teeth. However, according to the findings of the current study, a statistically significant relationship was found between the number of roots and gender. ($p<.05$) Accordingly, the number of double-rooted MFs in males was approximately three times higher than in females. According to a study (32), the X chromosome contains genes related to root canal structure. This may explain the effect of gender on root number. A systematic review (34) also reported that single-rooted premolars were more common in females and double-rooted premolars were more common in males. These findings are consistent with the current study. In addition, according to the findings of the current study, a statistically significant relationship was found between Vertucci classes and gender. ($p<.05$) However, no significant difference was shown between the number of roots and tooth localization, and age group. ($p>.05$)

It is necessary to consider the existence of some limitations in the present study. As the current study is a retrospective study, data may not have been recorded consistently or accurately as they were not designed to be a part of the present study. Since the study was based on existing records, control over the study design may be limited. Existing records may have been recorded with different equipment and procedures, which may cause inconsistencies. The quality of images may vary depending on how the image was initially obtained. It may also be more prone to bias because it relies on historical data that may be incomplete or inaccurate. Vertucci classification in the present study defines the main root canal configuration, but this classification ignores the accessory canals, apical deltas and isthmuses, which are important for the completion of treatment.

Although CBCT is a suitable imaging technique for clinical use and provides detailed information, there may be artifacts such as scattering, motion artifacts, and noise that can reduce image quality (35,36).

5. CONCLUSION

Clinicians should have extensive knowledge about the variations that can be seen in root canal morphology in premolar teeth. In cases where clinical and conventional methods are not sufficient, the use of CBCT will positively affect the success and prognosis of the treatment. While the most common morphology in the population is Vertucci Type 1, the frequency of two roots in mandibular first premolars in males is 3 times higher than in females.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Biruni University, Ethics Committee (Approval date: 22.12.2023; Number: 2023/85-15)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: HS

Design of the study: HS

Acquisition of data for the study: HS, EGB

Analysis of data for the study: HS

Interpretation of data for the study: HS

Drafting the manuscript: HS, EGB

Revising it critically for important intellectual content: HS

Final approval of the version to be published: HS

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Impact of Education and Text Messages on Cardiovascular Disease Risk Factors Awareness Knowledge and Quality of Life

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Received: December 18, 2024 **Accepted:** June 02, 2025

ABSTRACT

Objective: This study was conducted to evaluate the effect of health education based on the health belief model and text messages on knowledge, awareness and quality of life regarding cardiovascular disease risk factors in firefighters.

Methods: The research data were collected by the researcher between December 2023 and May 2024 at two different fire stations on the European side of İstanbul. The intervention group received a 3-session Health Belief Model-based health education on prevention of cardiovascular disease risk factors. Following the health education, a total of 39 reminder text messages were sent via WhatsApp three or four times a week for 12 weeks to increase self-efficacy and health motivation. Data were collected using the Introductory Information Form, Cardiovascular Disease Risk Awareness Rating Scale, Cardiovascular Disease Risk Factor Knowledge Level Scale and EQ-5D-5L Quality of Life Scale.

Results: In the post-test, the mean scores of the intervention group on the Cardiovascular Disease Risk Awareness Rating Scale and Cardiovascular Disease Risk Factors Knowledge Level Scale were significantly higher than those of the control group ($p < 0.05$).

Conclusions: Health Belief Model-based cardiovascular disease risk factor prevention education and text messages increased firefighters' awareness, knowledge and quality of life in cardiovascular disease risk factor prevention.

Keywords: Cardiovascular Disease, Health Belief Model, Health Education, Firefighter, Occupational Health Nursing.

1. INTRODUCTION

Cardiovascular diseases (CVDs) are the most common, fatal and non-communicable diseases in Turkey as well as in the world (1). The World Heart Federation states that CVDs caused 20.5 million deaths in 2021; approximately one in three deaths worldwide is related to this issue (2).

The prevalence of CVD is predicted to increase with the aging of populations and prolonged life expectancy (3). Although it is known that cardiovascular function decreases with age and age is an important factor in CVD, there are many risk factors that can be controlled to prevent these diseases (4). WHO reports that CVDs can be averted by controlling behavioral risk factors (5). According to the latest data from the Turkish Statistical Institute (TUIK), CVD is the primary cause of death among adults in Turkey (6). The primary goal in interventions to reduce the incidence and mortality rates of CVDs is to create lifestyle changes for risk factors. The lack of information about CVD risk factors hinders the prevention

and treatment of these diseases and affects individuals' awareness of risk factors and lifestyle (7). When the studies on CVD prevention and promotion of lifestyle changes are examined in the literature, it is seen that programs to inform the target audience are generally implemented (8, 9, 10). Many studies have shown that the Health Belief Model (HBM) can be used as an acceptable model to predict protective behaviors against various diseases (11, 12). Considering that adults constitute a significant portion of Turkey's population (13), efforts to increase knowledge and raise awareness about CVD risks should be carried out in every environment where individuals can be reached. Workplaces are one of these environments (14). Firefighting is a demanding profession in which firefighters face life-threatening situations and endure enormous physical pressure (15). Existing research has revealed that firefighters have high exposure to CVD risk factors (16,17). Extensive scientific literature shows that firefighters have one of the highest percentages (45%) of

How to cite this article: Kartoğlu Z, Kolaç N. Impact of Education and Text Messages on Cardiovascular Disease Risk Factors Awareness Knowledge and Quality of Life. Clin Exp Health Sci 2025; 15: 399-408. <https://doi.org/10.33808/clinexphealthsci.1603898>

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deaths owing to unexpected cardiac death and the majority are associated with underlying CVD risk factors, while many firefighters often exhibit multiple risk factors associated with CVD or poor overall cardiovascular health, which affects their occupational performance (17, 18, 19, 20). A study has demonstrated that on-duty CVD incidents in the fire service do not occur randomly and occur much more frequently during strenuous tasks (21).

On-duty cardiovascular occurrences have been reported to occur predominantly in firefighters who are predisposed to CVD and have traditional risk factors for CVD (15).

All these findings suggest the consistent and strict application of preventive measures with proven benefits to firefighters (17, 22).

Due to the detrimental association between CVD risk factors, poor physical fitness, and firefighter line-of-duty mortality, health professionals need to establish health promotion programs to reduce CVD risk and improve firefighter physical fitness (21). It has been reported that workplace wellness programs are effective in reducing modifiable CVD risk factors in healthy individuals and people with CVD (23). It is important to create health education programs for firefighters, who are at elevated risk for CVD, and to establish conditions that promote health in the workplace to prevent risk factors and encourage healthy lifestyle behaviors. In the literature, it is stated that firefighters' knowledge of CVD is low despite their high CVD risk, but with a short and simple educational intervention, firefighters' awareness of these risk factors can be increased in the short term (24, 25). However, these studies are not sufficient and there is no interventional study on CVD risk factors for firefighters in Turkey. The aim of this study was to analyze the effect of HBM-based training program and text messages on information level, awareness and quality of life concerning CVD risk factors in firefighters.

2. METHODS

2.1. Ethical Considerations

Ethics Committee Permission was obtained from the clinical research ethics committee of the medical faculty of a state university (14.07.2023; Protocol No: 09.2023.931), and institutional permission was obtained from the authorized institution to which the fire departments are affiliated (28.11.2023; BK No: 4298). Scale use permissions were obtained by the scale authors. Written informed consent was obtained from all participants.

2.2. Study Design And Sample Selection

The universe of the study consisted of firefighters working in fire stations located in two different districts on the European side of Istanbul province in Turkey (N = 160). The sample size was determined by power analysis performed on the G-Power 3.1 program. Power analysis was applied at 5% significance level, two-way, based on 80% power requirement. As a result

of the analysis, the minimum sample size required for each group in the study was calculated as 67 people. Considering the risk of data loss, the sample size was increased by approximately 10% and was determined as 148 people in total, with at least 74 people in each group. As a result, the study sample consisted of a total of 160 firefighters, 84 in the intervention group and 76 in the control group. The study data were collected by the researcher between December 2023 and May 2024 using a questionnaire method. In order to prevent interactions between groups and to ensure randomization, stations were determined as intervention and control groups by drawing lots. During the study, 3 participants in the intervention group and 2 participants in the control group were excluded due to CVD. After the pre-tests were applied, 2 participants in the intervention group were excluded from the study because they could not attend the training, and 1 participant in the control group left the study voluntarily (Figure 1).

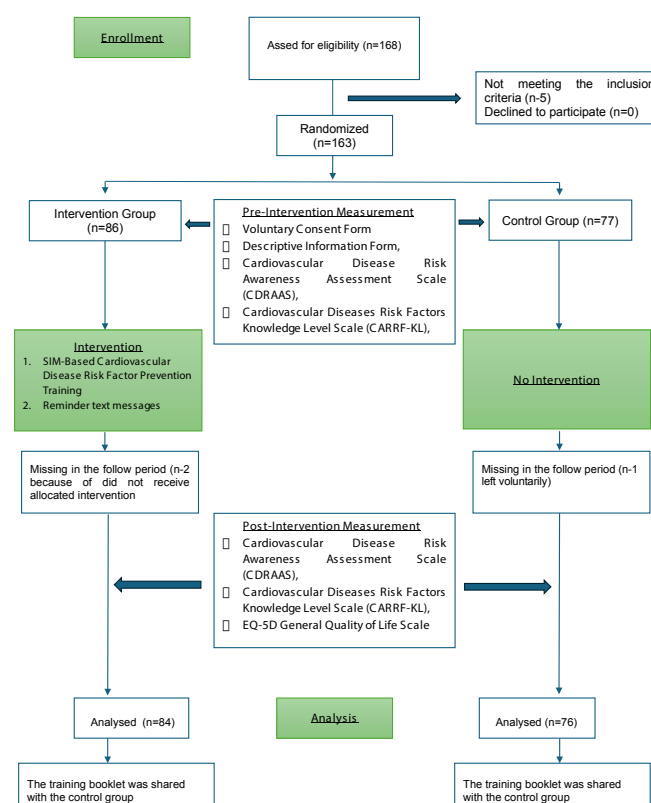


Figure 1. Consort Flow Diagram

Sample selection criteria

- Not having any cardiovascular disease
- To be working in the institution where the research is carried out
- Not having any a disease or disability that would prevent working
- Not having any training in preventing cardiovascular disease.

2.3. Data Collection Procedure And Tools

The pre-test of the study was conducted between December 4-15, 2023 and the post-test between April 30-May 5, 2024. Health education was given on February 1-6, 2024 and the post-test was administered 12 weeks after the education. During the 3-month follow-up period after the training, text messages were sent by phone.

2.3.1. Descriptive Form

It was prepared by the researcher in line with the literature to determine the sociodemographic characteristics of firefighters (22, 26). The form includes 24 questions about the characteristics of firefighters such as age, education level, marital status, smoking status, regular exercise and salt consumption.

2.3.2. Cardiovascular Disease Risk Awareness Assessment Scale (CDRAAS)

The scale was adapted into Turkish by Birgül Vural Doğru et al. in 2021. The scale consists of three sub-dimensions: perceived heart attack/stroke risk, perceived benefits and intentions to change, and healthy eating intentions. The Cronbach's alpha value of the scale was $\alpha=0.80$ (43) whereas it was found to be $\alpha=0.66$ in this study. The scale, which consists of 22 items in total, is a 4-point Likert scale and is scored between 1 (strongly disagree) and 4 (strongly agree). Increased scale and subscale scores indicate increased awareness of CVDs (27).

2.3.3. The Cardiovascular Disease Risk Factors Knowledge Level (CARRF-KL) Scale

CARRF-KL is a 28-item scale measuring the level of knowledge about cardiovascular disease risk factors. While the first four items in the scale are related to the characteristics of CVDs, preventability and age factor, 15 items question risk factors and nine items question the outcome of change in risk behaviors. Each correct answer is evaluated as 1 point. Scores that can be obtained from the scale are between 0 and 28. The higher the score, the higher the level of knowledge (28). The Cronbach's alpha value of the scale was $\alpha=0.76$ (28), whereas it was found to be $\alpha=0.82$ in this study.

2.3.4. EuroQoL Quality of Life Scale (EQ-5D-5L)

It is a quality of life scale that measures how individuals perceive and evaluate their own health status. The scale consists of two parts: EQ-5D index and EQ-5D VAS. EQ-5D index: It consists of 5 dimensions: movement, pain, general activities, self-care, anxiety/depression. The answers to each dimension have 5 options: no problem, mild problem, moderate problem, severe problem and extreme problem. EQ-5D VAS: It is a visual analog scale in which individuals give values between 0 and 100 about their current health status

and mark it on a thermometer-like scale. An increase in the scale score indicates a positive perception of health.

2.4. Data Analysis

Statistical Package for Social Sciences (SPSS) v27 statistical program and Microsoft Excel 2016 program were used for data analysis. The frequencies (f) and percentages (%) of the responses to the descriptive information form were determined. Chi-Square analysis was applied to determine whether the intervention and control groups were homogeneous. The internal consistency levels of the data were checked by examining the Cronbach's Alpha values to test whether they were reliable and the skewness and kurtosis values to test whether they were normally distributed. Dependent group t test was used for intra-group mean score comparisons and independent group t test was used for inter-group mean score comparisons. As significance level, $p \leq .05$ and $p \leq .01$, 95% and 99% confidence intervals were used.

2.5. Interventions

2.5.1. Health Education

One of the fire stations in Istanbul constituted our intervention group. In line with the literature review, "HBM-Based CVD Prevention Training" was created in order to increase the level of knowledge of firefighters regarding CVD risk factors, improve their awareness and positively affect their quality of life. This training was given in 3 different sessions by meeting face-to-face with firefighters in the training hall of fire stations. Each session lasted 40 minutes. Answers were given to the questions asked at the end of the session. **The training was created under the following main headings in line with the Health Belief Model:**

Perceived Responsiveness: Messages about the individual's perceived risk of developing CVD.

Perceived Seriousness: It includes messages that identify the individual's perceived threat, including harmful consequences based on the risk of CVD occurrence.

Benefit Perception: Messages about the individual's perceived benefits of eating well, exercising and quitting smoking to prevent CVD.

Perceived Barriers: Messages about the individual's perceived barriers to eating well, exercising and quitting smoking to prevent CVD.

Perceived Self-Efficacy: Messages that include the degree of confidence that the individual perceives about doing behaviors to prevent CVDs.

Health Motivation/Activators: Messages that identify different degrees of willingness to engage in CVD-preventive behaviors to prevent CVD from occurring.

2.5.2. Text Messages

After the HBM-based health education, 39 text messages were sent via WhatsApp application 3-4 times a week for 3 months to increase the effectiveness of the education and the motivation of firefighters in CVD prevention. The messages were created in line with the literature (29, 30, 31) by taking the suggestions of 10 academicians who are experts in their field. A pilot study was conducted before the text messages were sent. According to expert opinions, the Content Validity Index (CVI) value of the messages was found to be above 0.80 (CVI>0.80). Example of Short Messages:

- Losing excess weight is important in reducing cardiovascular mortality and morbidity.
- Refined foods (canned foods, acidic drinks, white sugar, etc.) and saturated fats increase the risk of cardiovascular diseases.
- Smoking causes deterioration of the vascular structure.

3. RESULTS

3.1. Participant Characteristics

Firefighters in the intervention and control groups had average ages of 36.61 ± 7.87 and 38.25 ± 8.09 years, respectively. Male firefighters constituted 98.8% of the intervention group and 92.1% of the control group. The mean weights of the intervention and control groups were 84.99 ± 12.05 and 83.09 ± 11.26 kilograms, respectively, and the mean heights of the intervention and control groups were 176.69 ± 5.88 and 175.88 ± 5.78 centimeters, respectively. There was no meaningful difference ($p > .05$) between the two groups concerning the independent variables of the study (age, gender, education, marital status, smoking and alcohol use, daily vegetable and fruit consumption, etc.) (Table 1). The pre-intervention mean scores for the intervention and control group firefighters on the CDRAAS and its sub-dimensions, CARRF-KL and EQ-5D-5L Quality of Life Scale, revealed no statistically meaningful difference ($p > .05$).

Table 1. Comparison of individual characteristics according to firefighters

Variable	Group	Control Group (n=76)		Intervention group (n=84)		Chi-squared	
		f	%	f	%	χ^2	p
Age	23-34	25	32.9	38	45.2	2.77	.250
	35-44	39	51.3	37	44.0		
	45-55	12	15.8	9	10.7		
	Mean $\pm$ SD/Min.-Max.	38.25 $\pm$ 8.09	25-55	36.61 $\pm$ 7.87	23-55		
Gender	Woman	6	7.9	1	1.2		.054*
	Male	70	92.1	83	98.8		
Marital Status	Married	56	73.7	62	73.8	0.00	.986
	Single	20	26.3	22	26.2		
Education Level	High school	18	23.7	22	26.2	0.83	.661
	Universty	54	71.1	55	65.5		
	Master / PhD	4	5.3	7	8.3		
Weight (kg)	58-75 kg	21	27.6	20	23.8	1.72	.424
	76-95 kg	49	64.5	52	61.9		
	96 kg and above	6	7.9	12	14.3		
	Mean $\pm$ SD / Min.-Max.	83.09 $\pm$ 11.26	58-110	84.99 $\pm$ 12.05	62-130		
Height (cm)	162-174 cm	32	42.1	31	36.9	1.36	.506
	175-184 cm	35	46.1	46	54.8		
	185-193 cm	9	11.8	7	8.3		
	Mean $\pm$ SD / Min.-Max.	175.88 $\pm$ 5.78	162-193	176.69 $\pm$ 5.88	165-190		
Body Mass Index	Normal	17	22.4	21	25.0	1.45	.484
	Overweight	49	64.5	47	56.0		
	Obese	10	13.2	16	19.0		
Working time	0-5 years	21	27.6	27	32.1	1.06	.590
	5-10 years	5	6.6	8	9.5		
	11 Years and above	50	65.8	49	58.3		
Daily Computer Usage Time	0-3 Hours	73	96.1	74	88.1	3.38	.066
	4-7 Hours	3	3.9	10	11.9		
Blood Pressure	Hypotension	3	3.9	3	3.6	3.85	.278
	Normal	48	63.2	41	48.8		
	Prehypertension	23	30.3	38	45.2		
	Hypertension	2	2.6	2	2.4		
Family history of CVD	Yes	21	27.6	20	23.8	0.31	.580
	Hayır	55	72.4	64	76.2		

Smoking	Yes	41	53.9	47	56.0	0.41	.815
	No	31	40.8	31	36.9		
	Drop	4	5.3	6	7.1		
Alcohol	Yes	5	6.6	10	11.9	1.33	.248
	No	71	93.4	74	88.1		
Exercising Regularly	Yes	42	55.3	38	45.2	1.60	.205
	No	34	44.7	46	54.8		
Chronic Illness	No	76	100.0	84	100.0	-	
Regular Medication Use	Yes	2	2.6	5	6.0		.447*
	No	74	97.4	79	94.0		
Salt Consumption	Unsalted	2	2.6	6	7.1	1.78	.411
	Low Salt	61	80.3	63	75.0		
	Salty	13	17.1	15	17.9		
Daily Fruit Consumption	Yes	55	72.4	50	59.5	2.92	.088
	No	21	27.6	34	40.5		
Daily Vegetable Consumption	Yes	56	73.7	51	60.7	3.03	.082
	No	20	26.3	33	39.3		
Low-Fat Diet	Yes	50	65.8	44	52.4	2.96	.085
	No	26	34.2	40	47.6		
Oil Preference	Vegetable Oil	38	50.0	44	52.4	0.30	.862
	Butter	18	23.7	21	25.0		
	Olive oil	20	26.3	19	22.6		
Cooking Method	Baking	25	32.9	24	28.6	1.07	.785
	Boiled	17	22.4	16	19.0		
	Grill	3	3.9	5	6.0		
	Frying in Oil	31	40.8	39	46.4		
Source of health news	Doctor / Nurse	10	13.2	14	16.7	2.72	.436
	TV News	33	43.4	30	35.7		
	Other	23	30.3	22	26.2		
	Unfollow	10	13.2	18	21.4		

χ^2 : Chi-Square test value. *Fisher correction.

3.2. CDRAAS, CARRF-KL VE EQ-5D-5L Quality of Life Scale

According to the independent sample t-test results, no substantial difference was observed between the pre-test scores of the intervention and control groups on the CDRAAS total ($t=1.65$; $p=.102$) and Perceived Heart Attack/Stroke Risk ($t=0.53$; $p=.594$), Healthy Eating Intentions ($t=0.32$; $p=.323$), Perceived Benefits and Intentions to Change ($t=1.85$; $p=.066$) sub-dimensions (Table 2). No substantial difference was observed between the CARRF-KL ($t=1.79$; $p=.075$), EQ-5D-5L Index ($t=1.06$; $p=.290$) and EQ-5D-5L VAS ($t=1.51$; $p=.133$) pre-test scores of the intervention and control groups (Table 2). There was no meaningful difference between the pre-test and post-test mean scores of the control group in the CDRAAS total ($t=-0.48$; $p=0.628$) and Perceived Heart Attack/Stroke Risk ($t=-0.22$; $p=.823$), Healthy Eating Intentions ($t=-1.72$; $p=.090$), Perceived Benefits and Intentions to Change ($t=0.75$; $p=.457$) sub-dimensions (Table 3). There was no meaningful difference between the mean CARRF-KL pre-test and post-test scores of the control group ($t=1.83$; $p=.072$) (Table 3). There was no meaningful difference between the pre-test and post-test mean scores of the EQ-5D-5L Quality of Life Scale of the control group ($t=-0.84$; $p=.405$) (Table 3). According to the independent sample t-test results, a

meaningful difference was found between the CARRF-KL post-test mean scores of the intervention and control groups ($t=-5.60$; $p=.000$) (Table 4). The outcomes of the independent sample t-test revealed that a meaningful difference was found between the CDRAAS total ($t=-4.72$; $p=.000$) and Perceived Heart Attack/Stroke Risk sub-dimension post-test scores ($t=-2.49$; $p=.014$) of the intervention and control groups (Table 4). However, no meaningful difference was found between the mean scores of CDRAAS Healthy Eating Intentions ($t=-1.84$; $p=.068$), Perceived Benefits and Intentions to Change ($t=-1.62$; $p=.107$) sub-dimensions (Table 4). According to the results of the independent samples t-test performed to examine the comparison of the mean quality of life scores between the groups, no meaningful difference was found between the EQ-5D-5L index ($t=-0.06$; $p=.950$) and EQ-5D-5L VAS ($t=-1.36$; $p=.177$) post-test mean scores of the intervention and control groups (Table 4). A meaningful difference was found between the pre-test and post-test mean scores of the intervention group on CDRAAS total ($t=-8.50$; $p=.000$) and Perceived Heart Attack/Stroke Risk ($t=-4.15$; $p=.000$), Healthy Eating Intentions ($t=-5.56$; $p=.000$), Perceived Benefits and Intentions to Change ($t=-3.82$; $p=.000$) sub-dimensions (Table 5). A meaningful difference was found between the mean CARRF-KL pre-test

and post-test scores of the intervention group ($t=-9.74$ 13.643, $p=.000$) (Table 5). A meaningful difference was found between the pre-test and post-test mean scores of EQ-5D-5L Index ($t=-2.69$; $p=.009$) and EQ-5D VAS ($t=-4.56$; $p=.000$) of the intervention group (Table 5).

Table 2. Comparison of pre-intervention CDRAAS, CARRF-KL, EQ-5D Quality of Life Scale mean scores according to intervention and control groups

Scale / Sub-Scale	Group	n	Mean	SD	t	p
CDRAAS	Control Group	76	42.17	5.04	1.65	.102
	Intervention Group	84	40.76	5.71		
Perceived Risk of Heart Attack/Stroke	Control Group	76	17.88	2.98	0.53	.594
	Intervention Group	84	17.61	3.47		
Healthy Eating Intentions	Control Group	76	12.26	2.74	0.32	.323
	Intervention Group	84	11.82	2.88		
Perceived Benefits and Intentions to Change	Control Group	76	6.37	1.24	1.85	.066
	Intervention Group	84	5.96	1.49		
Knowledge	Control Group	76	5.43	1.78	0.23	.819
	Intervention Group	84	5.37	1.81		
CARRF-KL	Control Group	76	17.42	4.54	1.79	.075
	Intervention Group	84	16.12	4.63		
EQ5D5L Index	Control Group	76	0.97	0.06	1.06	.290
	Intervention Group	84	0.96	0.07		
EQ5D5L VAS	Control Group	76	87.29	10.99	1.51	.133
	Intervention Group	84	84.46	12.51		

*Independent groups t-test was applied.

Table 3. Comparison of the mean scores of the control group's pre-test CDRAAS, CARRF-KL, EQ-5D Quality of Life Scale with the post-test mean scores

Scale / Sub-Scale	Test	n	Mean	SD	t	p
CDRAAS	Pre-Test	76	42.17	5.04	0.48	.628
	Post-Test	76	42.38	6.08		
Perceived Risk of Heart Attack/Stroke	Pre-Test	76	17.88	2.98	0.22	.823
	Post-Test	76	17.95	3.35		
Healthy Eating Intentions	Pre-Test	76	12.36	2.82	1.72	.090
	Post-Test	76	12.64	2.83		
Perceived Benefits and Intentions to Change	Pre-Test	76	6.37	1.24	0.75	.457
	Post-Test	76	6.29	1.38		
Knowledge	Pre-Test	76	5.43	1.78	0.22	.827
	Post-Test	76	5.46	1.84		
CARRF-KL	Pre-Test	76	17.42	4.54	1.83	.072
	Post-Test	76	16.67	5.33		
EQ5D5L Index	Pre-Test	76	0.97	0.06	0.84	.405
	Post-Test	76	0.97	0.05		
EQ5D5L VAS	Pre-Test	76	87.29	10.99	0.43	.672
	Post-Test	76	86.84	11.70		

*Dependent (Paired) groups t-test was applied.

Table 4. Comparison of post-intervention CDRAAS, CARRF-KL, EQ-5D Quality of Life Scale mean scores according to intervention and control groups

Scale / Sub-Scale	Group	n	Mean	SD	t	p
CDRAAS	Control Group	76	42.38	6.08	4.72	.000
	Intervention Group	84	46.68	5.44		
Perceived Risk of Heart Attack/Stroke	Control Group	76	17.95	3.35	2.49	.014
	Intervention Group	84	19.23	3.14		
Healthy Eating Intentions	Control Group	76	12.64	2.83	1.84	.068
	Intervention Group	84	13.44	2.65		
Perceived Benefits and Intentions to Change	Control Group	76	6.29	1.38	1.62	.107
	Intervention Group	84	6.61	1.09		
Knowledge	Control Group	76	5.46	1.84	6.37	.000
	Intervention Group	84	7.11	1.36		
CARRF-KL	Control Group	76	16.67	5.33	5.60	.000
	Intervention Group	84	20.39	2.40		
EQ5D5L Index	Control Group	76	0.97	0.05	0.06	.950
	Intervention Group	84	0.97	0.05		
EQ5D5L VAS	Control Group	76	86.84	11.70	1.36	.177
	Intervention Group	84	89.11	9.07		

*Independent groups t-test was applied.

Table 5. Comparison of the mean scores of the intervention group's pre-test CDRAAS, CARRF-KL, EQ-5D Quality of Life Scale with the post-test mean scores

Scale / Sub-Scale	Test	n	Mean	SD	t	p
CDRAAS	Pre-Test	84	40.76	5.71	-8.50	.000
	Post-Test	84	46.68	5.44		
Perceived Risk of Heart Attack/Stroke	Pre-Test	84	17.61	3.47	-4.15	.000
	Post-Test	84	19.23	3.14		
Healthy Eating Intentions	Pre-Test	84	11.82	2.88	-5.56	.000
	Post-Test	84	13.44	2.65		
Perceived Benefits and Intentions to Change	Pre-Test	84	5.96	1.49	-3.82	.000
	Post-Test	84	6.61	1.09		
Knowledge	Pre-Test	84	5.37	1.81	-10.26	.000
	Post-Test	84	7.11	1.36		
CARRF-KL	Pre-Test	84	16.12	4.63	-9.74	.000
	Post-Test	84	20.39	2.40		
EQ5D5L Index	Pre-Test	84	0.96	0.07	-2.69	.009
	Post-Test	84	0.97	0.05		
EQ-5D5L VAS	Pre-Test	84	84.46	12.51	-4.56	.000
	Post-Test	84	89.11	9.07		

*Dependent (Paired) groups t-test was applied.

4. DISCUSSION

This original study provides important evidence on the effect of HBM-based planned health education program and subsequent text messages sent to firefighters via WhatsApp on knowledge, awareness and quality of life of firefighters in

the prevention of CVD risk factors. As far as we are aware, there is no interventional study on the effect of education on CVD risk factor knowledge, awareness levels and quality of life of firefighters in Turkey; our study is the first to address this field.

According to the results of this study, the HBM-based health education and brief messages program in the prevention of CVD risk factors was effective in increasing awareness, knowledge and quality of life concerning CVD risk factors. While there was no notable disparity between the quality of life scores of the control and intervention groups after the intervention, there was a notable disparity between the pre-test and post-test mean scores of the intervention group. It is thought that this may be due to the fact that the quality of life scores of the control and intervention groups were close to each other before the intervention. Similarly, many a variety of studeies have revealed that HBM-based health education programs are effective in improving health knowledge, awareness of CVD diseases and quality of life (32, 33, 34). After the HBM-based intervention, it was revealed that there was a statistically noteworthy increase in the CDRAAS and perceptions of heart attack/stroke risk, healthy eating intentions, perceived benefits and intentions to change and knowledge sub-dimensions of the firefighters in the intervention group. Similarly, it was revealed that the post-test scores of the CARRF-KL and EQ-5D-5L Quality of Life Scale of the firefighters who took part in the intervention scheme were considerably higher than the pre-test scores.

HBM emphasizes that increasing individuals' perceived health risks plays a critical role in changing health behaviors (35, 36). Increased awareness and perceived risk, especially for serious health events such as heart attack and stroke, may lead individuals to make more informed decisions regarding cardiovascular health. Studies emphasize that educational programs can make significant changes in individuals' perception of health risks and that these changes can improve health outcomes in the long term (37). In one study, it was emphasized that individuals' perception of the seriousness of health threats may increase their motivation to change their behavior (38). In this study, HBM-based intervention was found to increase risk perception in firefighters. The outcomes of the study are consistent with similar studies in the literature (11, 39).

There is abundant evidence in the literature that education and constant reminders are crucial in the improvement and maintenance of healthy eating habits (40, 41, 42, 43). As seen in this study, training and text message interventions for firefighters were effective in increasing their healthy eating intentions.

HBM emphasizes that perceived benefits are an important source of motivation for individuals to adopt healthy behaviors (35, 36). The findings of the study reveal that individuals started to see the benefits of CVD risk factor avoidance behaviors more clearly after the intervention and tended to participate in change processes more willingly and decisively. Participants had a clearer understanding of

the benefits of CVD preventive behaviors such as healthy nutrition, regular physical activity, quitting smoking and stress avoidance, and accepted these behaviors as necessary for a healthy life.

The elevate in the CARRF-KL post-test score of the intervention group reveals that the education and text message intervention led to a significant improvement in CVD risk factor knowledge. This study's findings support the conclusions of other research in the field that interventions such as education and reminder text messages are effective in increasing the knowledge level of CVD risk factors in individuals (24, 25, 44, 45, 46). Many studies have included multiple interventions similar to this study and mostly applied educational interventions to develop behavior change (47, 48). In this study, a planned health education and informative and motivational text messages were used to promote behavior change.

In order to develop healthy lifestyle behaviors and to be protected from risk factors, information should be obtained. Having information about the possible negative consequences of diseases is considerable importance, especially in the establismet of healthy lifestyle behaviors (36). Some studies have indicated that healthy lifestyle behaviors increase with increasing knowledge of risk factors for CVD (10, 26, 46, 49). Increased comprehension and awareness of CVD risk factors may lead individuals to feel more competent to take steps to reduce these risks. This study shows that workplace health education and motivational text messages played an important role in increasing knowledge of CVD risk factors among firefighters. The intervention program resulted in a significant increase in knowledge among firefighters, demonstrating the feasibility and effectiveness of such programs in the workplace, particularly for critical-risk occupational groups.

In the post-test, the overall health status of the firefighters was positively affected according to the EQ-5D-5L. Firefighters already reported their overall quality of life as good before the intervention. After the intervention, the perceived improvement in their quality of life increased minimally. This is a valuable finding in that regular and planned interventions can significantly affect quality of life and improve health. Taking these results into account, interventions can be tailored to effectively address the specific needs of firefighters and ultimately can aim to effectively improve the quality of life of firefighters. Considering the high exposure of firefighters to CVD risk factors, it is important to take measures to prevent CVD and improve cardiovascular health in firefighters in order to reduce or prevent these diseases and the problems they will bring with them. It is thought that nurses are in a strong position in this regard and have important roles in health protection and promotion. Occupational health nurses can motivate firefighters to take measures to inform them about the seriousness of CVDs and encourage better lifestyle behaviors. The outcomes of the study clearly show the impact of HBM-based training and text messages by improving firefighters' quality of life, knowledge and awareness. It is

believed that such programs can elevate the awareness and comprehension level of employees at workplaces about CVD, improve their quality of life, improve their general health status and create healthier environments at workplaces.

The data for this study were collected through self-reporting. The findings are particular to the specific fire brigade group involved in the research and cannot be extrapolated to other fire brigade units.

5. CONCLUSIONS

The results showed that HBM-based CVD risk factor prevention training and text messages increased awareness and knowledge of CVD risk factors in firefighters and positively affected their quality of life. According to the results obtained from the study, we recommend that studies should be conducted to elevate awareness and knowledge levels to prevent CVDs in firefighters who are at great risk for CVDs, occupational health nurses should plan HBM-based health education and reminder interventions in workplaces, and models that improve quality of life and promote behavioral change in firefighters should be transformed into effective programs. The study can serve as an example for the planning and implementation of health protection and promotion programs in workplaces.

Acknowledgements: We would like to thank Marmara University for providing access to academic databases, Niyazi Kartoğlu for inspiring this study and all the firefighters who participated in the study.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Marmara University, Noninvasive Clinic Ethics Committee (Approval date: 14.07.2023; Number: 09.2023.931)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: ZK

Design of the study: ZK, NK

Acquisition of data for the study: ZK, NK

Analysis of data for the study: ZK, NK

Interpretation of data for the study: ZK, NK

Drafting the manuscript: ZK, NK

Revising it critically for important intellectual content: NK

Final approval of the version to be published: ZK, NK

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Clinical Evaluation of Complications for Single Visit Class III and Class V Restorations at the First Recall Appointment

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Received: January 8, 2025

Accepted: March 7, 2025

ABSTRACT

Objective: Clinical evaluation of senior students' Class III and Class V restorations at the first recall (control) appointment, regarding revised FDI criteria.

Methods: Seventy-six anterior Class III and V restorations were assessed. A nano-ceramic, simplyshade composite (NeoSpectra-ST, Dentsply) was used. Restorative procedures were checked and approved by an experienced (3 years) restorative dentistry instructor. The first recall (control) appointment was scheduled 1 week after the restorations and a restorative instructor re-evaluated the restorations based on the biological, functional, and esthetic aspects of revised FDI criteria.

Results: Significantly greater scores were observed for Esthetic criteria compared to Functional and Biological criteria ($p < .001$). Six failures were detected for form and contour, two for surface luster and texture, two for marginal staining, and two for color match. Only for the form and contour criteria, Class V restorations obtained significantly higher scores than Class III ($p = .033$).

Conclusion: Although anterior composite restorations were approved by an experienced instructor, various irreversible complications were observed at the first recall. Following the restorative procedure, a control appointment shortly is considered mandatory. The highest risk for failure was detected for Esthetic criteria. Class III restorations are considered more prone to failures compared to Class V.

Keywords: Resin composite, recall, complication, class III, class V.

1. INTRODUCTION

The longevity of single-visit direct composite restorations can be influenced by tooth-related factors, restorative material-related factors, operator-related factors, and patient-related factors. The tooth-related factors concern the occlusal/proximal contacts, cavity size, tooth position, deep margins, and endodontic treatment (1). The restorative material-related factors concern the selection of resin-based materials and photo-polymerization which may simplify the restorative procedure and improve the quality of the restoration (1, 2). Moreover, as the resin-based restorative materials may positively or negatively influence the level of success, it is advantageous for the operator to experience also some alternative materials previously for a proper selection depending on the case and for performing effectively during the restorative process (2). The level of clinical experience of the operator as well as the facilities of the clinical environment play a very important role during the restorative procedure in

planning the restorative treatment correctly, performing the restorative procedure properly, and avoiding or overcoming possible restoration-related complications clinically (1, 3, 4). Besides, the patient-related factors are usually beyond the operator's control which may affect the outcome significantly (2, 5). Individual choices and demands, caries risk and diet, socioeconomic status, periodontal health, oral hygiene level, brushing pattern, parafunctional habits, and smoking habits are some of the many patient-related factors accordingly (1, 6). The operator usually tries to minimize these risk factors by increasing the awareness and thereby the motivation of the patient.

Previous short-term and mid-term clinical trials reported that indication, restorative material selection, field isolation, surface polishing, frequent recalls, and operator's experience are required to succeed in direct anterior composite restorations (2, 6-8). Therefore, the assessment of success

How to cite this article: Doğu Kaya B, Korkut B, Kızıl Öztürk E, Alkan E, Yılmaz Atalı P. Clinical Evaluation of Complications for Single Visit Class III and Class V Restorations at the First Recall Appointment. Clin Exp Health Sci 2025; 15: 409-420. <https://doi.org/10.33808/clinexphealthsci.1615250>

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for dental restorations should be a stepwise decision-making process accordingly and is usually evaluated by specific clinical criteria such as United States Public Health Service (USPHS) criteria, Ryge criteria, and Fédération Dentaire Internationale (FDI) criteria (1-3). Especially the modified USPHS criteria were previously used in many clinical studies even though it's limitations regarding the definitive scoring (3, 5). However, FDI criteria were first published in 2007 and updated in 2010 to overcome the problem by providing more accurate, descriptive, and standardized evaluation criteria for the researchers compared to the predecessor USPHS (6, 8-10). The FDI criteria classified the restorations according to 3 main headings: functional, biological, and esthetic properties, including sub-groups in each one. Also, the evaluation scores (1 to 5 as very good, good, satisfactory, unsatisfactory, and poor respectively) are more detailed for the clinical assessments, which may provide enhanced judgment quality (6, 8, 10). The scores of 1, 2, and 3 indicate that the restoration is clinically sufficient/acceptable, while 4 and 5 indicate that it is clinically insufficient/inacceptable (5, 6, 10). Recently, in 2023 the FDI criteria were updated again for a better understanding and handling through a more standardized evaluation (10). It includes a revised set of criteria in different categories which can be selected independently and used as a modular diagnostic system.

Every single-visit direct composite restoration must be checked by the operator through one of the criteria above to approve the finalization. It is always better to combine clinical examination with radiographic findings when necessary (2). Generally, this approval is done immediately after the restoration. However, is it always possible to check all the FDI criteria immediately after the restoration clinically? Shade matching may be affected by the dehydration process during the restorative procedure depending on the chair time. As a result, assessing the shade matching, especially for the anterior composite restorations immediately after, may lead the operator to misjudge. Moreover, the status of surrounding gingival health is a very good indicator to assess the contour of the emergence profile while it may be affected by patients' oral hygiene level. However, it may also not be accurate to assess the gingival health immediately after the restoration as it usually has acute inflammation due to the field isolation during the restorative procedures, depending on the cavity size and location (2). In addition, bleeding may block the quality of visual inspection immediately after as well. Therefore, it may not be always possible to fill all the checklist in the FDI criteria of success immediately after the restoration (2).

This clinical prospective study aimed to investigate the potential complications for the immediately approved Class III and Class V restorations at the first recall (one-week) appointment through the revised FDI criteria. It also aimed to investigate the clinical reversibility of the observed complications. The null (H_0) hypotheses of the study are (a) no difference in overall success between immediately after and one-week controls, (b) no difference in failure rates among FDI's biological, functional, and esthetic criteria at

one-week control, (c) no difference in success rates for Class III and Class V restorations.

2. METHODS

This clinical study was approved by a local ethical committee (protocol number: 09.2023.888).

2.1. Participants and Inclusion Criteria

The study included patients who applied to a university clinic requiring class III and class V restorations in anterior teeth. Senior students treated the patients under the control of an experienced restorative dentistry instructor with at least 3 years of clinical experience.

Healthy patients between 18-55 years of age, who had a complete initial periodontal treatment and had caries, abrasion, abfraction, and/or erosion lesions in the anterior teeth were included in the study. Systemic diseases, mental disabilities, severe periodontal diseases, former root canal treatment or indication, teeth that may require indirect or direct pulp capping, former restorations in anterior teeth, primary dentition, Class IV cavities, teeth with mobility, and cracked/fractured teeth were considered the exclusion criteria.

A minimum of 64 teeth were required for the study for a power of 80% (1- β) and a confidence interval of 95% (1- α), with an effect size of $w=0.352$ and a significance level of 0.05 (G*Power V.3.1.9.6, Germany) (11). Therefore, the present study was conducted with 32 patients who treated 26 senior students (graduate degree/5th class) with the same level of clinical experience, and a total of 76 restorations (44 Class III, 32 Class V) were evaluated. All the Class III restorations were performed due to caries and the restorations involved the buccal surface of the tooth. Seventeen Class V restorations were performed due to caries, while fifteen were due to abrasion/erosion. None of the Class III and Class V restorations were larger than 1/3 of the mesio-distal and servico-insical size of the tooth.

2.2. Restorative Procedure

An experienced restorative dentistry instructor who is responsible for the university clinic for the day approved the indications for Class III and Class V restorations for the students through clinical and radiographic examinations.

Before the preparation for caries removal, the composite shade was selected visually by using the Button technique in the very first 3 minutes of the appointment to avoid dehydration. The carious lesion was removed minimally-invasively without rubber-dam isolation using a diamond bur (at 20000 rpm with water-cooling) and a carbide bur (at 8000 rpm without water-cooling) for infected enamel and dentin tissues, respectively (Horico, Germany). Regarding the cavity margins, approximately 45° of beveling was performed on vestibular sharp enamel edges. The unsupported enamel tissues were also removed for preservation. Then, a 25% aluminum chloride-impregnated retraction cord (Cerkamed,

Poland) was used for isolating the tooth margins. For Class III cavities, a transparent strip (Tor Vm, Russia) was placed and fixed with a wooden wedge (Tor Vm), whereas the free-hand layering technique was used for the Class V cavities. Then the cavity was roughened with 37% phosphoric acid (President Dental, Germany) with the total-etch technique (30 seconds on enamel and 15 seconds on dentin). A universal adhesive agent (Prime & Bond Universal, Dentsply, USA) was applied to the cavity surfaces according to the manufacturer's instructions. A led curing unit with irradiation of 1000 mW/cm² (OLED Plus, Woodpecker, China) was used for photopolymerization. A nano-ceramic paste-type, simplyshade resin composite (Neo Spectra ST, Dentsply) was used for the restorations in 2 mm of incremental layering (Table 1).

Each composite load was polymerized with the curing unit. The occlusal contacts were checked not only statically but also dynamically at a sitting position using an 80 µm grit articulating paper (Hanel, Germany). The identified primary contacts were selectively reduced with a yellow-banded flame-shaped diamond bur. Medium and fine grits of composite polishing discs (Finishing Discs, BISCO, USA) were

used for the finishing procedure of embrasures. Interdental polishing was performed by medium, fine, and superfine paper strips (Tor Vm, Russia). Restoration surface polishing was performed by yellow and white polishing rubbers (Kenda, Liechtenstein).

The final preparation, adhesive agent application, composite layering, occlusion check, and finishing/polishing steps for all the restorations were checked, accordingly corrected by the student if needed, and then approved by an experienced restorative dentistry instructor who is in charge of the day at the clinic. The interdental surface of the Class III restorations was also evaluated through bitewing radiographs. The patients left the clinic only when the restorative dentistry instructor approved the final restoration. Patients were instructed to avoid coloring foods and beverages such as cigarettes, coffee, red wine, etc., especially for the first 24 hours, and to maintain good oral hygiene (by brushing and flossing). A control appointment was scheduled as the first recall one week after the restorative procedure for evaluating the quality of the previously approved restorations (2).

Table 1. Materials and their content were used in this study.

Material (Manufacturer)	Content	Instruction for use
Etching Gel (President, Germany)	37 % orthophosphoric acid	Total-etch is applied by waiting for 30 seconds on the enamel and 15 seconds on the dentin.
Neo Spectra ST (Dentsply Sirona, USA)	Nano ceramic restorative material, barium aluminum borosilicate glass fillers, 57% (by volume) / 76% (by weight) filler ratio, 1.1-1.5 µm filler size range	It is polymerized in layers with a maximum depth of 2 mm and condensed into the cavity using the incremental layering technique.
Prime & Bond Universal Adhesive (Dentsply Sirona, USA)	UDMA, PENTA, R5-62—1 resin, bisphenol-A dimethacrylate, butylate, silicon dioxide, acetone	The adhesive is applied for 20 seconds. Dry for 5 seconds and polymerize for 10 seconds.

Abbreviations, UDMA: urethane dimethacrylate, PENTA: Dipentaerythritol penta-acrylate monophosphate

2.3. Evaluation Protocol

A pilot study was conducted previously including 20 restorations that were different from those included in this study. Two restorative dentistry specialist instructors with the same level of experience (3 years of specialty education in restorative dentistry) evaluated and scored the restorations. According to the correlation results, an 80% high positive correlation between the two observers was obtained, therefore the present study included one of these restorative instructors for the scoring at the first recall appointment. The evaluations were performed visually for all the Class III and Class V restorations by the single observer at a one-week control appointment, based on the revised biological, functional, and esthetic aspects of the FDI criteria (2023) (Table 2a-c) (10). The evaluations were undergone in both dry and wet conditions in accordance with the revised FDI. No magnification was used for the visual scoring.

The observer evaluated 74 restorations (42 Class III and 32 Class V) in total according to the revised FDI criteria and then scored. The results were recorded per tooth. By the criteria,

1-3 scores were considered acceptable scores which are considered reversible complications. Whereas 4 and 5 scores were considered unacceptable scores (failures) which are considered irreversible complications. Also, the score 3 was evaluated individually in this study, to evaluate the potential risk of failure for the restorations with this score shortly.

2.4. Statistical Analysis

Data were analyzed using IBM SPSS V23 software. Normality was investigated using Kolmogorov-Smirnov Test. Fisher's Exact Test and Pearson Chi-Square Test were used to evaluate the acceptability rates for the criteria. Multiple comparisons were done with the Z Test with Bonferroni Correction. Friedman Test was used to compare the scores which were not normally distributed and multiple comparisons were done with the Dunn Test. The results were presented as frequency (percent), average $\pm$ standard deviation, and medium (minimum–maximum). The deemed significance was set at $p < .05$.

Table 2a. Evaluation of biological aspects (Domain B) according to revised FDI.

DOMAIN B	B1: Caries at restoration margins (CAR)	B2: Dental hard tissue defects at restoration margin	B3: Postoperative hypersensitivity & Pulp status
1. Clinically very good restoration (sufficient/ acceptable)	B1.1 No caries / demineralization at the restoration margin detectable after air drying.	B2.1 Intact dental hard tissue without crack lines and fractures at the restoration margin.	B3.1 No postoperative hypersensitivity or pain on chewing and/or cold/warm food items reported by the patient. Normal (short) reaction to sensitivity test on cold.
2. Clinically good restoration (sufficient/acceptable)	B1.2 First visible signs of a non-cavitated caries lesion at the restoration margin detectable after air drying.	B2.2 Minor vertical/horizontal hairline crack lines in enamel at the restoration margin.	B3.2 Patient reports minor postoperative hypersensitivity or minor pain on chewing and/or cold/warm food items reported by the patient for a limited period of time (<1 week). Normal (short) reaction to sensitivity test on cold.
3. Clinically satisfactory restoration (sufficient/ acceptable)	B1.3 Established, non-cavitated caries lesion or microcavity at the restoration margin detectable without air drying.	B2.3 Distinct enamel chipping or enamel fracture at the restoration margin. If necessary, deficiencies can be corrected by refurbishment.	B3.3 Patient reports distinct postoperative hypersensitivity or distinct pain on chewing and/or cold/warm food items reported by the patient for a prolonged period of time (>1 week). Normal (short) or more intense reaction to sensitivity test on cold.
4. Clinically unsatisfactory restoration (insufficient/ unacceptable)	B1.4 Localized dentin cavity (width >250 µm, depth >2 mm) at the restoration margin. Repair is possible.	B2.4 Severe marginal (enamel) fracture, partially fractured cusp or ridge at the restoration margin. Repair is possible.	B3.4 Patient reports severe/persistent, postoperative hypersensitivity or persistent pain on chewing and/or cold/warm food items reported by the patient for a prolonged period of time (>1month) AND/OR intense reaction to sensitivity test on cold. Both symptoms indicate an irreversible pulpitis. Endodontic treatment requires access cavity only.
5. Clinically poor restoration (insufficient/unacceptable)	B1.5 Extensive dentin cavity at the restoration margin. Repair not possible/ reasonable.	B2.5 Cusp or tooth fracture, e.g. involving enamel, dentin and cementum possible with mobile fragments/ pain when biting OR cracked tooth syndrome related to restoration. Repair not possible/reasonable.	B3.5 Irreversible pulpitis, nonvital tooth, pulp necrosis with or without periapical periodontitis after restoration placement. Endodontic treatment requires replacement of the restoration.

Table 2b. Evaluation of functional aspects (Domain F) according to revised FDI.

DOMAIN F	F1: Fracture of material & Retention	F2: Marginal adaptation	F3: Proximal contact point	F4: Form & Contour	F5: Occlusion & Wear
1. Clinically very good restoration (sufficient/ acceptable)	F1.1 Restoration is completely present without deficiencies detectable after air drying: No crack, chipping/delamination or Material bulk fracture.	F2.1 Ideal marginal adaptation of the restoration at the dental hard tissue after air drying. No marginal gap detectable by gentle probing.	F3.1 Ideal contact point: 25 µm metal blade can pass through proximal contact and no inflammation of the gingiva/ periodontium due to the proximal restoration. No food impaction.	F4.1 Outline, contour, convexity, embrasure and/or marginal ridges are restored ideally in comparison to the individual, age-related and functional anatomy. No marginal step detectable by gentle probing	F5.1 Ideal individual and age-related static and dynamic occlusion with multiple antagonistic contact points. No premature contacts, non-/ hyper-occlusion and/or balancing interferences.
2. Clinically good restoration (sufficient/acceptable)	F1.2 Restoration is completely present with minor deficiencies detectable after air drying, e.g. insignificant material chipping or one hairline crack.	F2.2 Slight deficiencies of marginal adaptation after air drying: Minor, superficial marginal gap(s) or ditching.	F3.2 Slightly weak contact point: 50 µm metal blade can pass through proximal contact and no inflammation of the gingiva/periodontium due to the proximal restoration. No food impaction.	F4.2 Minor deviations in outline, contour, convexity, embrasure and/or marginal ridges in comparison to the individual, age-related and functional anatomy AND/OR minor marginal steps, overhangs detectable by gentle probing.	F5.2 Minor deviations in individual and age-related static and dynamic occlusion with at least one antagonistic contact point per tooth. No premature contacts, non-/hyperocclusion and/or balancing interferences.

3. Clinically satisfactory restoration. (sufficient/acceptable)	F1.3 Restoration is present with deficiencies detectable without air drying, e.g. hairline cracks or distinct material loss (chipping). Material loss can mainly be corrected by refurbishment if needed.	F2.3 Distinct deficiencies of marginal adaptation without air drying: marginal gap(s) or ditching (width <250 µm and/or depth <2 mm).	F3.3 Oversized contact point or excessive material: 25 µm metal blade cannot pass through proximal contact and inflammation of the gingiva/periodontium due to the proximal restoration. Refurbishment is possible. OR severely weak contact point: 100 µm metal blade can pass through proximal contact but no inflammation of gingiva or discomfort.	F4.3 Outline, contour, convexity, embrasure and/or marginal ridges are distinctly misshaped, but clinically acceptable AND/OR distinct negative/positive steps, overhangs. Refurbishment (removal of overhangs/steps) to some extent is possible.	F5.3 Hyper-occlusion, premature contacts and/or balancing interferences which can be eliminated by refurbishment.
4. Clinically unsatisfactory restoration (insufficient/inacceptable)	F1.4 Localized but severe deficiencies regarding fracture and retention, e.g. chipping/delamination which cannot be refurbished, bulk fracture or partially loose/lost restoration. Repair is possible. A lost, indirect restoration which can be recemented/reluted is considered here.	F2.4 Localized but severe deficiencies of marginal adaptation: width ≥250 µm and/or depth ≥2 mm marginal gap(s). Partially loose/lost restoration. Repair is possible.	F3.4 Severely weak contact point: 100 µm metal blade can pass through proximal contact or unintended interlocked contact point. Inflammation of the gingiva/periodontium due to the proximal restoration and/or food impaction. Repair is possible.	F4.4 Outline, contour, convexity, embrasure and/or marginal ridges are in parts severely undersized in comparison to the individual, age-related and functional anatomy AND/OR prominently negative marginal steps. Repair is possible.	F5.4 Localized, flat occlusal structure with severe non-occlusion AND/OR severely worn restoration. Repair is possible.
5. Clinically poor restoration (insufficient/inacceptable)	F1.5 Generalized severe deficiencies, e.g. extensive delamination, multiple bulk fractures or (nearly) completely loose/lost restoration. Repair not possible/reasonable.	F2.5 Generalized and severely compromised marginal adaptation: width ≥250 µm and/or depth ≥2 mm. Complete loose/lost restoration. Repair not possible/reasonable.	F3.5 Severely weak contact point: 100 µm metal blade can easily pass through proximal contact or unintended interlocked contact point (impossible to pass). Inflammation of the gingiva/periodontium due to the proximal restoration and/or food impaction. Repair not possible/reasonable.	F4.5 Outline, contour, convexity, embrasure and/or marginal ridges are generally and severely under – or oversized in comparison to the individual, age-related and functional anatomy. Repair not possible/reasonable.	F5.5 Generalized, severe non-occlusion AND/OR extensively worn restoration. Repair not possible/reasonable.

Table 2c. Evaluation of esthetic aspects (Domain A) according to revised FDI.

DOMAIN A	A1: Surface luster & surface texture	A2: Marginal staining	A3: Color match
1. Clinically very good restoration (sufficient/ acceptable)	A1.1 Surface luster and surface texture comparable to dental hard tissue/adjacent teeth after air drying. A1.2 Slightly dull surface luster and/or surface texture with minor deviations, e.g. isolated/small marks, pores and/or voids detectable compared to dental hard tissue/adjacent teeth after air drying.	A2.1 No marginal staining detectable after air drying. A2.2 Minor marginal staining detectable after air drying.	A3.1 No deviation in shade, translucency/opacity between restoration and neighbouring dental hard tissue/adjacent teeth. A3.2 Minor deviation in shade, translucency/opacity between restoration and neighbouring dental hard tissue/adjacent teeth detectable.
3. Clinically satisfactory restoration (sufficient/acceptable)	A1.3 Dull surface luster and/or surface texture with distinct deviations, e.g. marks, pores and/or voids detectable compared to dental hard tissue/adjacent teeth detectable without air drying. Refurbishment is possible.	A2.3 Distinct marginal staining detectable without air drying but not displeasing. Refurbishment is possible.	A3.3 Distinct deviation in shade, translucency/opacity between restoration and neighbouring dental hard tissue/adjacent teeth detectable – but not displeasing.
4. Clinically unsatisfactory restoration (insufficient/inacceptable)	A1.4 Localized, displeasing dull surface luster and/or rough surface texture with substantial deviations/multiple pores/voids detectable compared to dental hard tissue/adjacent teeth which can be repaired.	A2.4 Localized, displeasing deep marginal staining. Marginal staining can be removed/improved by repair.	A3.4 Localized, displeasing deviation in shade, translucency/opacity between restoration and neighbouring dental hard tissue/adjacent teeth which can be improved by repair.
5. Clinically poor restoration (insufficient/inacceptable)	A1.5 Generalized, displeasing dull surface luster and/or rough surface texture with substantial deviations/multiple pores/voids compared to dental hard tissue/adjacent teeth. Repair not possible/reasonable.	A2.5 Generalized, displeasing deep marginal staining. Repair not possible/reasonable.	B3.5 Generalized, displeasing deviation in shade, translucency/opacity between restoration and neighbouring dental hard tissue/adjacent teeth. Repair not possible/reasonable.

3. RESULTS

35.1% of the participants were male and 64.9 % were female. 18.9 % of the restorations were on tooth #22, followed by 13.5 % and 12.2 % for teeth #11 and #21, respectively.

Significant differences were observed among the main criteria of FDI. Significantly greater scores were observed for the Esthetic criteria compared to the Functional criteria, and it was followed by the Biological criteria ($p < .001$; Table 3).

Table 3. Comparisons for the main criteria.

	Average $\pm$ S.dev	Median (min. – max.)	Test Statistics	p*
Biological	1.11 $\pm$ 0.19	1 (1 – 1.67) ^c	60.65	< .001
Functional	1.31 $\pm$ 0.33	1.2 (1 – 2.4) ^b		
Esthetic	1.46 $\pm$ 0.44	1.4 (1 – 3.48) ^a		

*Friedman Test; a-c: No difference between the main criteria with the same letter, S. dev: Standard deviation, min.-max.: minimum-maximum.

Twelve unacceptable scores out of 74 restorations were obtained, and all were observed in Class III restorations (Table 4). Six unacceptable scores were detected for form and contour criteria (Fig. 1), two were detected for surface luster and surface text criteria (Fig. 2), two were detected for marginal staining criteria, and two were detected for color match criteria (Fig. 3). However, regarding the acceptability rates, a significant difference was observed only for form and contour criteria between the Class III (85.7 %) and Class V (100 %) restorations ($p = .033$; Table 4).

Score 3 was observed 27 times in total and 26 scores were for Class III restorations while only 1 score was for Class V restorations (Table 5). Score 3 was observed 4 times for postoperative hypersensitivity and pulpal status criteria, 2 times for proximal contact point criteria, 10 times for form and contour criteria, 6 times for surface luster and surface texture criteria, 2 times for marginal staining criteria, and 3 times for color match criteria. However, significant differences were only observed for form and contour criteria ($p = .036$) and surface luster and surface texture criteria ($p = .033$).

Table 4. Comparison of restoration types regarding the criteria and acceptable and unacceptable scores.

	Restoration Type		Test Statistics	p*
	Class III	Class V		
Caries in restoration margin				
Acceptable	42 (100)	32 (100)	---	---
Inacceptable	0 (0)	0 (0)		
Dental hard tissue defects at restoration margin				
Acceptable	42 (100)	32 (100)	---	---
Inacceptable	0 (0)	0 (0)		
Postoperative hypersensitivity and pulp status				
Acceptable	42 (100)	32 (100)	---	---
Inacceptable	0 (0)	0 (0)		
Fracture of material and retention				
Acceptable	42 (100)	32 (100)	---	---
Inacceptable	0 (0)	0 (0)		
Marginal adaptation				
Acceptable	42 (100)	32 (100)	---	---
Inacceptable	0 (0)	0 (0)		
Proximal contact point				
Acceptable	41 (100)	32 (100)	---	---
Inacceptable	0 (0)	0 (0)		
Form and contour				
Acceptable	36 (85.7)	32 (100)	---	.033
Inacceptable	6 (14.3)	0 (0)		
Occlusion and wear				
Acceptable	42 (100)	32 (100)	---	---
Inacceptable	0 (0)	0 (0)		
Surface luster and surface texture				
Acceptable	40 (95.2)	32 (100)	---	.502
Inacceptable	2 (4.8)	0 (0)		
Marginal staining				
Acceptable	40 (95.2)	32 (100)	---	.502
Inacceptable	2 (4.8)	0 (0)		
Color match				
Acceptable	40 (95.2)	32 (100)	---	.502
Inacceptable	2 (4.8)	0 (0)		

*Fisher's Exact Test; Scores of 1,2, and 3 are acceptable; 4 and 5 are unacceptable according to FDI criteria.

Table 5. Comparison of restoration types regarding the criteria and score 3.

	Restoration Type		Restoration Type	p*
	Class III	Class V		
Caries in restoration margin				
Score 3	0 (0)	0 (0)	---	---
Other	42 (100)	32 (100)		
Dental hard tissue defects at restoration margin				
Score 3	0 (0)	0 (0)	---	---
Other	42 (100)	32 (100)		
Postoperative hypersensitivity and pulp status				
Score 3	4 (9.5)	0 (0)	---	.129
Other	38 (90.5)	32 (100)		
Fracture of material and retention				
Score 3	0 (0)	0 (0)	---	---
Other	42 (100)	32 (100)		
Marginal adaptation				
Score 3	0 (0)	0 (0)	---	---
Other	42 (100)	32 (100)		
Proximal contact point				
Score 3	2 (4.9)	0 (0)	---	.501
Other	39 (95.1)	32 (100)		
Form and contour				
Score 3	9 (21.4)	1 (3.1)	---	.036
Other	33 (78.6)	31 (96.9)		
Occlusion and wear				
Score 3	0 (0)	0 (0)	---	---
Other	42 (100)	32 (100)		
Surface luster and surface texture				
Score 3	6 (14.3)	0 (0)	---	.033
Other	36 (85.7)	32 (100)		
Marginal staining				
Score 3	2 (4.8)	0 (0)	---	.502
Other	40 (95.2)	32 (100)		
Color match				
Score 3	3 (7.1)	0 (0)	---	.254
Other	39 (92.9)	32 (100)		

*Fisher's Exact Test.

**Figure 1.** The mesial class III restorations scored 4 according to the form and contour criteria (lower left central and lateral)**Figure 2.** The mesial class III restoration scored 4 according to the surface luster and surface structure criteria (left upper lateral).



Figure 3. The mesial class III restoration scored 4 according to the color match criteria (right upper lateral).

4. DISCUSSION

All the hypotheses of the study were rejected. Even though all the evaluated restorations were approved by a restorative dentistry instructor, some of the restorations were considered inacceptable due to several irreversible complications at the first control appointment just one week after the restorative procedure. The inacceptable scores differed among the restoration types.

Direct resin composite restorations offer several advantages including durability, permanence, esthetics, ease of application, and a good imitation of dental tissues (12, 13). In addition, they are preferred because of their low cost, immediate aesthetic results, and shorter fabrication time since they do not require laboratory procedures (14). To ensure a high-quality composite restoration, restorative procedures play an important role besides the selected composite material. Korkut, mentioned the esthetic success and longevity of a direct anterior restoration depend on the indication and treatment planning, composite and instrument selection, shade selection, isolation, adhesion, layering procedure, finishing and polishing, and frequent recalls (2). Color mismatch, plaque retention, marginal discoloration, marginal chipping, secondary caries, gingival inflammation, and fracture of restoration were presented as the possible reasons for failure (15, 16). In this study, the most frequent reasons for failure were observed in the form and contour criteria and it was followed by the color match (Table 4) in the first recall due to several factors such as external/internal discoloration and improper composite/shade selection, layering strategy, or finishing/polishing procedures (2, 6, 7).

It is essential to use objective, reliable, repeatable, and outcome-related criteria for the clinical evaluation of the anterior composite restorations (2). Previously, several evaluation systems were used accordingly (9, 17). Recently, in 2023, Hickel et al. published the revised FDI criteria with improved clinical understanding and handling (10). The criteria are based on the evaluation of biological, esthetic, and functional parameters which can be selected or adjusted

according to the needs of the clinician. Although the United States Public Health Service (USPHS) criteria are the most frequently used method in previous clinical research for evaluating the clinical success of the restorations, the sensitivity in revealing the changes of the restoration is lower than the FDI criteria (6-8). Previous studies mentioned FDI assessments as more sensitive than even the modified USPHS criteria regarding the small changes in clinical outcomes (18) and the marginal discoloration and compatibility (19). Therefore, the latest revision of the FDI criteria was selected in the present study to evaluate the restorations, clinically. Additionally, Mesinger et al., stated that the clinicians may have some difficulties in the assessments with the revised FDI criteria due to significant differences in categories and tooth types. He suggested observer training and calibration to ensure a reliable assessment (20). In accordance with that statement in the present study, the restorations were carried out by two different restorative dentistry specialist instructors with the same level of clinical experience (at least 3 years) under the same conditions, to minimize the operator-related variability.

Twelve inacceptable scores out of 74 restorations were observed at the first control appointment in this study. Therefore, the first hypothesis of the study was rejected. A systematic review in 2021 by Shah et al., and a recent one in 2023 by Demarco et al., reported that the primary reasons for failure in anterior restorations are related to the restoration fractures and esthetic appearance (21). The mid-term clinical reports of Korkut and Türkmen, and Korkut et al. mentioned that the unacceptable esthetic and anatomical form is the most common reason for the failure of the anterior composite restorations clinically (4, 6, 8). Consistent with that, the failure rate in this very short-term clinical follow-up study for the Esthetic criteria was significantly higher compared to the Functional and Biological criteria ($p < 0.001$; Table 3), and the failures were mostly observed for the form and contour criteria with 6 inacceptable scores (Table 4). Thus, the second hypothesis of the study was rejected. According to our results, a control appointment shortly after the restorative procedure is needed to check the form and contour.

On the other hand, Freitas et al. evaluated direct anterior restorations in recent clinical research according to the FDI criteria and stated that the most frequent complication was related to the color which was followed by anatomical form, and fracture of restoration (22). Liu et al. and Demarco et al. mentioned that the type of organic matrix and inorganic filler particle sizes and quantity influence the surface structure and mechanical and optical properties of resin composites (4, 23). In the present study, a simplyshade nano-ceramic composite with an inorganic filler size of 1.1-1.5 μm (76% in weight) was used for all the restorations. Only two inacceptable scores were observed in color match criteria with no significant difference ($p \geq 0.05$) at the control appointment (Table 4). This might be related to the high color adjustment potential of the selected simplyshade composite which also minimizes the shade selection mistakes (24, 25). The selection of the composite shade always in the first 3

minutes and the incremental layering under the control of an experienced instructor to avoid dehydration, may also be the reason for this result, even though the restorations were performed by the senior students (26, 27). Therefore, it can be interpreted that, depending on the experience of the clinician and the color adjustment potential of the resin composite, a higher failure rate in shade matching may be expected at the control appointment. Moreover, the level of polymerization as well as the rehydration affects the level of color match, especially for partial direct restorations (7, 28). Accordingly, the color adjustment cannot be evaluated immediately after the restorative procedure, precisely and an additional appointment is mandatory in this regard (2, 28). There is evidence that color training for the clinician may also have a positive effect on restoration shade matching in clinical practice (29).

All the unacceptable scores were observed for the Class III restorations in this study, while no failures were observed for the Class V restorations at the first control (Table 4). Therefore, the third hypothesis of the study was rejected. Regarding the comparisons between the restoration types, a greater risk for failure was mentioned previously for the larger restorations with less surrounding dental tissue (2, 6, 7). At the university student clinics, Class III restoration cases of the senior dentistry students usually have cavities lacking one or two marginal enamel wall loss, compared to Class V. Class III restorations also present additional challenges, including the need to mask the cavity line, management of contact points, and achieve color harmony. This might be the reason for the observed significant difference between class III and V restoration types in the form and contour criteria in the present study ($p=0.033$; Table 4). Also, the absence of rubber-dam isolation might be another reason for the higher unacceptable scores of Class V restorations (30). In this clinical study, rubber dam isolation was not utilized, as this is a standard procedure in the student's clinic. Although the two restoration types were considered statistically similar for all the criteria other than form and contour, Class III restorations also obtained unacceptable scores for surface luster and surface texture, marginal staining, and color match. It is important to remember that Class III and Class V restorations have different regional requirements in terms of contouring and polishing, supporting the previous report of Vargas et al. (28). As a result, Class III restorations might be considered riskier in terms of possible failures at the first control, and it might be advantageous for clinicians to be aware of that.

This study also assessed the score 3, to evaluate the potential failure risk for the restorations in the future. Accordingly, score 3 was observed in some restorations for postoperative hypersensitivity and pulp status, proximal contact point, form and contour, surface luster and surface texture, marginal staining, and color match criteria. Class III restorations were significantly less acceptable than the Class V restorations regarding form and contour criteria ($p=0.036$) and for surface luster and surface texture criteria ($p=0.033$) (Table 5). However, the clinical situation of some criteria such as fractures, external discoloration, or wear could not

be identified due to the very short period of evaluation. The possibility of encountering failures in such criteria gets higher in long-term evaluations (3, 21, 29, 31).

No remaining caries were detected at the margin of the restorations in the present study. Other than the control of the restorative dentistry instructor during the restorative process, the intensive preclinical training in the 1st and 2nd grades and then the clinical experience since the 3rd grade probably played an important role in the obtained 83.8% overall success rate of the students at one week control. This education strategy is very intensive and relatively different compared to many other European countries. Accordingly, Velayo et al., showed that preclinical performance was positively associated with clinical success (32).

This study is limited by the fact that although there was an 80% high positive correlation, the evaluations of the two instructors may have differed, and the students may have exhibited individual differences in education and skills, despite being at the same level of education. The findings of this very short-term clinical follow-up study revealed the importance of the control appointment shortly after the direct restorative procedure of anterior teeth, clinically. There is a lack of evidence in the literature regarding this. Whereas the restoration types were limited in this study, and it might be better to expand the anterior restoration types and the posterior restorations with an increased number, for further studies. Additionally, patient-related risks should be considered when evaluating composite restorations, clinically (33-35).

5. CONCLUSION

Even though the single-visit anterior composite restorations were approved by an experienced restorative dentistry instructor, various irreversible complications were observed at the first recall appointment. Following the restorative procedure, the arrangement of a control appointment shortly is considered mandatory to re-evaluate the restoration and thereby avoid possible complications. The highest risk for failure was detected for the Esthetic criteria and followed by Functional and Biological criteria, respectively. Class III restorations are considered more prone to form and contour failures compared to Class V restorations.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Marmara University Faculty of Medicine Clinical Research Ethics Committee (Approval date: July 14, 2024; Number: 09.2023.888). Consent was obtained from the patients during the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: BK

Design of the study: BK, BDK

Acquisition of data for the study: BDK, EKÖ, EA

Analysis of data for the study: BK, BDK, PYA

Interpretation of data for the study: BK, BDK, PYA

Drafting the manuscript: BDK, EKÖ, EA

Revising it critically for important intellectual content: BK, PYA

Final approval of the version to be published: BDK, BK, EKÖ, EA, PYA

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Evaluation of Accuracy of Intraoral Scanner with Different Inlay Preparation Geometry

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Received: January 19, 2025

Accepted: April 24, 2025

ABSTRACT

Objective: This in vitro study aimed to assess the accuracy of an intraoral scanner in inlay preparations with different geometry.

Methods: The upper second premolar tooth-shaped models were designed and prepared using a 3D printer (Phrozen Mega 8K, Phrozen, Taiwan). Three distinct inlay preparation configurations were utilized, including buccal and palatal wall divergence at 6°, 8°, and 10°. The reference 3D images were acquired through scanning of each model with varying inlay preparation using an extraoral scanner (E1, 3Shape, Denmark). Thirty 3D images (samples) were obtained from each of the three models (n = 10) using an intraoral scanner (Trios 3, 3Shape, Denmark). The samples and reference images were saved in Standard Tessellation Language (STL) and imported into software (Geomagic Control X 2022, 3D Systems Inc., USA). Discrepancies between the reference image and the samples were recorded as root mean square (RMS) and standard deviation (SD). Kruskal Wallis and Mann Whitney U tests, and interquartile range (IQR) were used for statistical analysis with THE significance level $p < .05$.

Results: The RMS was highest at 6°, both of which were statistically significant from the other degrees ($p < .001$). Highest SD values were obtained in 10° samples ($p < .001$). To evaluate the infer precision with IQR, RMS values were smallest at 10° and SD values smallest at 6°.

Conclusion: The divergence angle of the preparation in the inlay cavities can potentially affect the accuracy of the intraoral scanner.

Keywords: accuracy, divergence angle, inlay, intraoral scanner, precision, trueness.

1. INTRODUCTION

In recent years, intraoral scanners (IOS) have become an integral component of contemporary dental practice. Despite their numerous advantages over conventional methods, many studies have investigated their limitations, as well as the factors affecting scanning accuracy. It is critical to assess the accuracy of IOS to enhance the longevity of indirect restorations. Achieving optimal marginal fit and cement spacing is paramount to prevent microleakage at the restoration's edges, as this can facilitate caries formation and compromise the integrity of the margins (1).

A variety of factors have been shown to affect trueness and precision of IOS. Such factors include lighting conditions (2), operator influence (3), scanning pattern (4), scanning distance (5), scanning area size (6), scanner technology and design (7), and the anatomy of the scanned jaw (8) and tooth position (9). In addition to these factors, many tooth-related factors have been shown to affect scanning

accuracy as well. Some of these factors comprise the depth (10), angle (11, 12), and configuration of the preparation (13), as well as the amount of loss in the tooth substance (14, 15).

The assessment of the accuracy of IOS has been addressed by the International Organization for Standardization (ISO), which has established a set of terms and methodologies for this purpose. The term “trueness” is defined as the deviation from the ratios of the reference object, while “precision” is defined as the measurement obtained when the process is repeated continuously. Ideally, an IOS should exhibit both high precision, characterized by a more predictable measurement when the process is repeated continuously, and high trueness, characterized by minimal deviation from the reference object proportions (16). Many research has been dedicated to the evaluation of IOS accuracy. These studies were utilized extraoral scanners,

How to cite this article: Kaya Doğu B, Özden YE, Kayahan Özkurt Z, Atalı Yılmaz P. Evaluation of Accuracy of Intraoral Scanner with Different Inlay Preparation Geometry. Clin Exp Health Sci 2025; 15: 421-426. <https://doi.org/10.33808/clinexphealthsci.1623198>

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which utilize a fixed and unique scanning method to obtain a reference three-dimensional model (17, 18). With precision assessments, although there are studies that evaluate different methodologies (19), one of the most common is the definition of the average absolute distances measured between all scanned specimens and the reference model in terms of the interquartile range (20-22).

Although there are studies that examine various preparation designs and cavity depths in teeth from different locations (9, 10, 23-25), there is a notable absence of studies evaluating the divergence angle (11, 12). To the best present knowledge, there are no studies that have evaluated the accuracy of IOSs in relation to the divergence angle in inlay preparations. Therefore, the objective of this in vitro study was to assess the accuracy of an intraoral scanner in inlay preparations with three distinct buccal and palatal wall angles. The null hypothesis posited that “altering the divergence angle in the inlay cavity does not impact the scanner’s accuracy”.

2. METHODS

2.1. Production of tooth-shaped model

A total of three different inlay preparation configurations were utilized in the present study. The upper second premolar tooth-shaped models were designed using digital software (ZBrush 2023, Maxon, Germany) and prepared using a 3D printer (Phrozen Mega 8K, Phrozen, Taiwan) to obtain standardized preparations and eliminate the potential for arbitrary preparation (26). The preparation of the cavities was designed with rounded internal line angles, an occlusal isthmus width of 2.5 millimeters (mm), and a contact opening of 0.5 mm on the mesial region with the adjacent tooth. All cavity edges in the mesial area were completed with a 90° cavosurface. An intact margin of 2.5 mm was maintained at the distal region of the model, while an intact structure of 3 mm was preserved at the buccal and lingual cusp areas (Figure 1). The cavity depth was 5 mm with a non-proximal box configuration. The configurations of inlay preparation are outlined as such: the production of buccal and palatal wall divergence at 6°, 8°, and 10° in three distinct models (Figure 2).

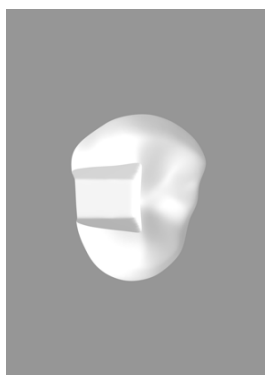


Figure 1. Three-dimensional inlay preparation design.

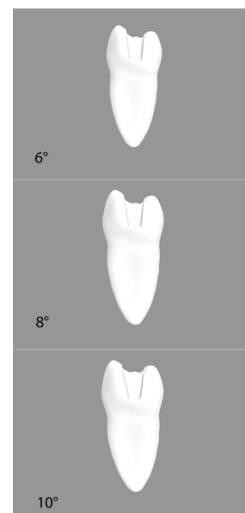


Figure 2. Inlay preparation design with buccal and palatal wall divergence at 6°, 8°, and 10°.

2.2. Scanning Procedure

A total of 30 three-dimensional (3D) images were obtained from each of the three models ($n = 10$) using a Trios 3 (3Shape, Denmark) intraoral scanner. Given the findings of prior studies indicating the Trios 3 scanner’s superior accuracy under room light conditions (20), it was imperative that all scans be conducted under identical illumination (room light at approximately 4100 K), in accordance with the scanning direction as outlined by the manufacturer’s guidelines. The 3D images (samples) were saved in STL (standard triangle language) format. The intraoral scanners’ own illumination was employed during the scanning process, in accordance with the manufacturer’s instructions. To acquire the reference sample, each model with different inlay preparation was scanned once using an extraoral scanner (E1, 3Shape, Denmark).

2.3. Evaluation of trueness and precision

Samples were imported into Geomagic Control X 2022 software (3D Systems Inc., USA) to assess the trueness. The reference 3D image and each scanned sample were overlapped, and it was utilized to calculate the “best-fit alignment” tool’s analysis of the 3D differences. Discrepancies between the reference image and the samples were recorded as root mean square, or RMS, and standard deviation, or SD. The outer surfaces of the tooth were considered as the reference for alignment, and the RMS values at 150 points selected from the inner surface of restoration area were calculated (Figure 3). Measurement points were randomly selected from the walls and floor of the preparation. The RMS data is calculated by the program based on the following formula:

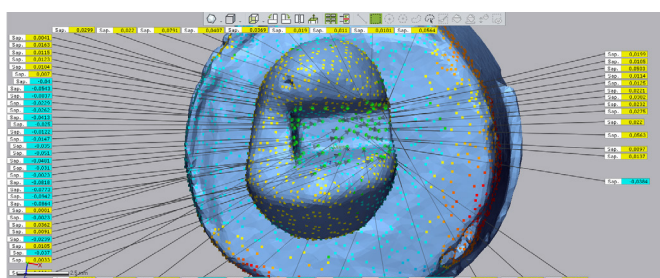


Figure 3. Calculation of RMS values at 150 points selected from the inner surface of the restoration area.

$$RMS = \frac{1}{\sqrt{n}} \cdot \sqrt{\sum_{i=1}^n (X_{1,i} - X_{2,i})^2}$$

$X_{1,i}$ denotes the measurement point of i for the reference models, $X_{2,i}$ denotes the measurement point of i for the test models, and n denotes the total number of points measured in each analysis. The root mean square (RMS) value is a measure of the absolute distance between the point clouds of the reference and test models. Therefore, an RMS value close to zero indicates a high degree of 3D accuracy. To assess the precision, it was defined in terms of the interquartile range of the average absolute distances measured between all scanned samples and the reference model (20, 22).

2.4. Statistical Analysis

The present study employed IBM SPSS version 29 to facilitate the analysis of the collected data. The root mean square (RMS) and standard deviation (SD) values were presented as median, first to third percentiles, and interquartile range (IQR). The disparities in RMS distributions across different angles were subjected to analysis using the Kruskal-Wallis test, followed by pairwise comparisons with the Mann-Whitney U test, which was adjusted with the Bonferroni correction. A Type I error rate of 5% was designated as statistically significant for all analyses.

3. RESULTS

The distribution of RMS and SD values calculated from samples with different angles is presented in Table 1. For asses the trueness, the RMS was highest at 6°, both of which were statistically significant from the other degrees ($p < .001$) (Figure 4). Highest SD values were obtained in 10° samples ($p < .001$). To evaluate the infer precision with IQR, RMS values were smallest at 10° and SD values smallest at 6°.

Table 1. The distribution of RMS and SD values according to divergence angle.

Angle	RMS	SD
10°	0.067 (0.065 – 0.069) ^a	0.054 (0.053 – 0.058) ^a
8°	0.046 (0.044 – 0.053) ^b	0.042 (0.039 – 0.043) ^b
6°	0.083 (0.078 – 0.088) ^c	0.041 (0.040 – 0.042) ^b
p^*	<.001	<.001
Angle	IQR	IQR
10°	0.004	0.005
8°	0.009	0.004
6°	0.010	0.002

*Kruskal Wallis Test, median (1st – 3rd Percentiles), RMS: root mean square, SD: standard deviation, a,b,c There is no statistically significant difference between groups with the same letter, IQR: interquartile range.

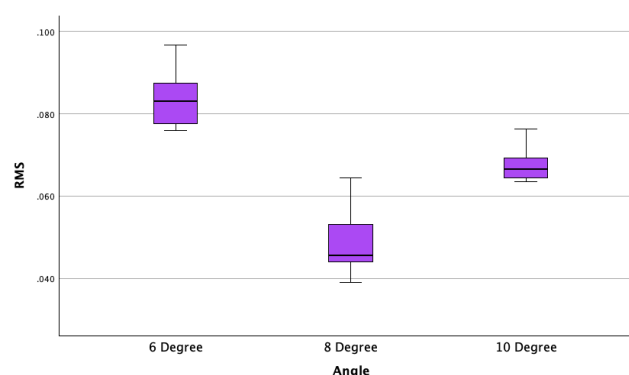


Figure 4. The distribution of RMS according to angle.

4. DISCUSSION

The findings of the present in vitro study demonstrated that inlay preparations exhibiting divergent angles affected the accuracy of the intraoral scanner. Consequently, the null hypothesis; “altering the divergence angle in the inlay cavity does not impact the scanner’s accuracy” was rejected. Numerous studies have examined the trueness and precision of intraoral scanners and the factors that affect their accuracy (20, 21). In order to produce an ideal indirect restoration, it is essential that the 3D image of the preparation transferred to the design stage is accurate, and that the device possesses high trueness (27). Additionally, scanners are expected to demonstrate high levels of repeatability, which is synonymous with high precision, to ensure the consistency of their performance in accordance with established standards (28). A multitude of factors have been identified as contributors to the accuracy of intraoral scans, including technological aspects, the configuration of the scanner tip, and the resolution of the device (29, 30).

In addition to these factors, the accuracy of the scan can be influenced by clinician-related variables and the configuration of the tooth preparation (12, 15, 23). The objective of this in vitro study was to evaluate the accuracy of an intraoral scanner with confocal microscopy technology

in inlay preparations with varying wall angles. Despite the existence of studies that examine various preparation designs or indirect preparations with different amounts of tooth loss and cavity depths (9, 10, 15, 24, 31, 32), there is a lack of studies that evaluate the divergence angle (11, 12). Upon evaluation of the angle-dependent trueness data in this study, it was determined that the preparation at a 6° exhibited the most significant deviation from the reference image with respect to the RMS value. On the other hand, according to SD data, the highest deviation was found in the 10° configuration. This discrepancy can be attributed to the fact that the terms root mean square (RMS) and standard deviation (SD) express differences depending on the calculation process and program.

According to the manufacturer, RMS is a measure of the magnitude of all deviation values, whereas the SD is the standard deviation of all gap distance values. Given that both parameters are evaluated in this study, it can be concluded that 8° for trueness is optimally suitable for both RMS and SD. This is supported by the finding that 6° in RMS and 10° in SD showed the maximum deviation. The results of precision analysis with interquartile range (IQR) data indicated that, consistent with trueness, RMS values exhibited greater deviation at 6° of preparation, while SD values demonstrated the most significant deviation at 10°. Considering the obtained results, it can be concluded that the trueness and precision, the accuracy of the scanner at varying angles, exhibited significant variation. Although Attia et al. utilized a preparation with cavity depths different from those in this study, they found higher trueness in the inlay preparation for the same intraoral scanner with a 12° angle compared to a 6° (32), similar to this study. Likewise, Ashraf et al. found that 6° had a higher deviation from the reference than 12° for RMS values in trueness assessments with Trios 3 in intracoronary inlay preparations (12). In this study, the angles of 6, 8, and 10° were included, in contrast to the 6 and 12° included in the other two studies. However, consistent with previous studies, the highest deviation in root mean square (RMS) values for trueness was found at 6°, while the lowest deviation was found at 8°. One potential explanation for this finding is that, in the present study, a non-proximal box-shaped and 5 mm deep intracoronary preparation design was utilized. Although the preparation angles cannot be adjusted with precision by the clinician under clinical conditions, the effect of the preparation angle on the accuracy of the scanner was observed in this study. It is imperative to note that in recent years, the accuracy of CAD/CAM restorations has become a significant area of concern, as it plays a pivotal role in determining the clinical success of these restorations (33).

Given the acknowledged variability in outcomes associated with the utilization of intraoral scanners (34), due consideration must be given to the design of the cavity and its limitations when evaluating the results. Furthermore, limitations of this study include the use of a single technology intraoral scanner. The Trios 3 intraoral scanner (3Shape, Copenhagen, Denmark) provides ultrafast colored imaging

based on confocal microscopy principles with a scanning depth of 17 mm. It captures single pictures, which are stitched together into a three-dimensional network (35). Research has indicated that more recent iterations or advanced technologies tend to demonstrate enhanced accuracy. As demonstrated in previous studies, the accuracy and precision of different intraoral scanners can be influenced by various parameters (12, 23, 36). Furthermore, it is important to acknowledge the inherent limitations of the extraoral scanners utilized in this study, from which the reference file was obtained (37). In further studies, it would be beneficial to examine various preparation configurations by incorporating different intraoral scanners or varying divergence angles.

5. CONCLUSION

Preparations for inlay restorations involving different divergence angles demonstrated that the accuracy of the intraoral scanner varied for both deviation parameters. A similar pattern was observed with precision, which was also influenced by the angles.

Acknowledgements: The authors would like to thank Dr. Mustafa Enes Özden for his valuable support in the analysis and interpretation of the data.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: Not applicable.

Author Contributions:

Research idea: BDK and YEO.

Design of the study: BDK, YEO, ZOK, PYA

Acquisition of data for the study: BDK, YEO.

Analysis of data for the study: BDK, YEO.

Interpretation of data for the study: BDK, YEO, ZOK, PYA

Drafting the manuscript: BDK, YEO.

Revising it critically for important intellectual content: ZOK, PYA.

Final approval of the version to be published: BDK, YEO, ZOK, PYA

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Mandibular Radiomorphometric Analysis in Patients with Different Stages of Periodontitis

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Received: February 09, 2025

Accepted: June 20, 2025

ABSTRACT

Objective: This study aims to evaluate a possible change in the mandibular trabecular structure of patients diagnosed with different stages of periodontitis and to compare them with gingivitis and periodontally healthy individuals.

Methods: The periodontal diagnosis of 180 patients (90 females and 90 males) was made based on the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions. The patients were divided into six groups: periodontally healthy (n=30), gingivitis (n=30), Stage I (n=30), Stage II (n=30), Stage III (n=30), and Stage IV (n=30) periodontitis. Seven regions of interest (ROIs) were determined for fractal analysis (FA) on panoramic radiographs. Fractal dimension (FD) and mandibular cortical width (MCW) were evaluated.

Results: The mean age of the study population was 30.64±7.48 years. No statistically significant difference was observed among the groups in terms of FD. There was a statistically significant difference in gender distribution only for the MCW value (p<.05), and this value was found to be higher in male participants (23.87±4.59 mm vs. 22.50±3.75 mm). Although significant correlations were found between FD values of different regions (anterior FD, premolar FD, molar FD, angulus FD, and total FD), FD was not significantly correlated with age.

Conclusion: The results of this study suggest that FA calculated from panoramic radiographic images of periodontally healthy patients, gingivitis and different stages of periodontitis shows comparable results and indicates no superiority.

Keywords: Bone, fractals, mandible, panoramic radiography, periodontitis

1. INTRODUCTION

Periodontitis is a chronic, multifactorial disease in which attachment loss occurs as a result of a host-mediated inflammatory reaction in response to bacterial biofilm (1,2). The prevalence of periodontitis was reported to be more than 60% between 2011 and 2020 (3). For this highly prevalent disease, addressing and eliminating risk factors such as smoking, early periodontal treatment, and plaque control have been clearly emphasized (4). However, the detailed periodontal assessment is needed to tailor the treatment procedure. Therefore, both clinical and radiological evaluations are employed (2). The clinical evaluations include parameters which determine disease severity, such as the degree of gingival inflammation, probing pocket depth (PPD), and the presence of bleeding on probing (BOP). Radiographic evaluations serve as a valuable auxiliary tool in periodontal diagnosis and provide an insight into the extent of alveolar bone loss. Although radiographs have several limitations (*i.e.*, two-dimensional image acquisition and low resolution), they are widely used in clinical assessment (5). Furthermore, in the

2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions, determination of the extent of radiographic bone loss was presented as an important factor after assessment of interdental attachment loss while determining disease severity (1). However, the limitations of radiographs have led to the recommendation of the fractal analysis (FA) method for the diagnosis and monitoring of trabecular changes developing in the alveolar bone associated with periodontitis (6).

Fractal analysis is a mathematical method which describes irregular and complex structures such as bone tissue, and its numerical result is evaluated as fractal dimension (FD) (7,8). In other words, FA identifies and analyzes complex shapes and structural patterns, while FD is a quantitative measure of this image complexity (9).

Several studies have used FA for the evaluation of trabecular bone changes in radiographs of individuals with periodontally healthy, gingivitis or periodontitis (6,10-18). Mishra et al.

How to cite this article: Altındal D, Kaya S. Mandibular Radiomorphometric Analysis in Patients with Different Stages of Periodontitis. Clin Exp Health Sci 2025; 15: 427-433. <https://doi.org/10.33808/clinexphealthsci.1636403>

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(12) compared the periodontally healthy group with the periodontitis group and reported that FD could be used as a quantitative method to detect cancellous bone changes in different-stages of periodontitis. Yarkac et al. (13) presented their evaluations without including Stage IV periodontitis patients and they reported that trabecular bone had different FD values in periodontal disease status. Korkmaz et al. (18) included periodontally healthy and Stage III/IV periodontitis individuals in their study and reported that FD values of periodontitis individuals were significantly lower compared to the periodontally healthy. Soltani et al. (16) observed that FD values were significantly different between the bone of individuals with moderate and severe periodontitis and healthy group. However, Eser and Saribas (14) reported that there was no significant difference in mean FD values between individuals with gingivitis and periodontitis. To the best of our knowledge, there is only one study available to classify periodontitis into four different stages according to the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions and to use FA to measure trabecular changes in this patient population (12).

In the present study, we hypothesized that there would be no change in the mandibular trabecular structure of patients with periodontitis and healthy individuals. We, therefore, aimed to use the FA method and evaluate a possible change in the mandibular trabecular structure of patients diagnosed with Stage I, II, III, and IV periodontitis and to compare them with gingivitis patients and periodontally healthy individuals.

2. METHODS

2.1. Study Design and Study Population

This study was conducted at Van Yüzüncü Yıl University, Faculty of Dentistry, Departments of Periodontology and Oral and Maxillofacial Radiology. Prior to study, a written informed consent was obtained from each patient. The study protocol was approved by the Non-Interventional Clinical Research Ethics Committee at the University of Van Yüzüncü Yıl (No: 2024/03-12, Date: 08/03/2024). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Inclusion criteria were as follows: age ≥ 18 years, having no missing teeth in the mandible, and having periodontal disease or health status determined as a result of clinical and radiological evaluations. Exclusion criteria were as follows: presence of any systemic disease affecting the bone structure and/or use of systemic medications; presence of cysts and tumors affecting the bone structure in the head and neck region; history of radiotherapy and/or chemotherapy; radiographs with poor image quality, movement and/or metal artifacts; presence of pathology in the mandible (cysts, tumors, enostoses, idiopathic osteosclerosis, condensing osteoid, periapical lesions); presence of crowns, bridges, or implants; severe malocclusion. Finally, a total of 180 participants who met the inclusion criteria were recruited. The patients were divided into six groups: periodontally

healthy (n=30), gingivitis (n=30), Stage I (n=30), Stage II (n=30), Stage III (n=30), and Stage IV (n=30) periodontitis.

2.2. Periodontal Evaluation

Periodontal diagnosis for each patient was determined according to the 2017 World Workshop on the Classification of Periodontal and Peri-implant Diseases and Conditions. The clinical periodontal parameters (clinical attachment loss (CAL), PPD, BOP (19)) were recorded by a single clinician using a Williams periodontal probe (Hu-Friedy, Chicago, IL, USA). Measurements were taken from six surfaces (mesiobuccal, midbuccal, distobuccal, mesiolingual/palatal, midlingual/palatal, distolingual/palatal) of each tooth, except for the third molars. Additionally, panoramic radiographs (ORTHOPHOS XG, Sirona Group, USA) were obtained from each patient to assess bone loss. Accordingly, the patients were divided into six groups: periodontally healthy, gingivitis, Stage I periodontitis, Stage II periodontitis, Stage III periodontitis, and Stage IV periodontitis. The patients who did not develop CAL and radiographic bone destruction were included in the periodontally healthy, if the BOP score was $<10\%$ (20), and in the gingivitis group if the BOP score was $\geq 10\%$. Periodontitis assessment was made according to the severity and complexity of the disease (1,21). The patients who had CAL value of 1 to 2 mm were grouped as Stage I periodontitis; CAL value of 3 to 4 mm was grouped as Stage II periodontitis; and CAL value of ≥ 5 mm was grouped as Stage III and IV periodontitis. Stage III and IV periodontitis were separated according to complexity factors (1). Individuals with generalized periodontitis were included in all periodontitis groups. Accordingly, the number of affected teeth was $\geq 30\%$, excluding third molars.

2.3. Radiographic Evaluation

The exposure parameters of the device used for radiographic evaluation were determined as 60 kV, 3 mA, and 14.1 s exposure time (ORTHOPHOS XG, Sirona, USA). The images were converted to Digital Imaging and Communications in Medicine (DICOM) format and Image J software (National Institutes of Health, Bethesda, MD, USA) was used for image analysis. Radiological analyses were performed by a single oral and maxillofacial radiologist. The data on the stage of periodontitis and the periodontal status of other patients were presented blindly to the radiologist. In case of a long radiological examination, the radiologist performed the data analysis on a 23-inch computer in the dark room where the radiographic data was reported and for a maximum of three hours per day to eliminate the loss of gray scale sensitivity. Intra-examiner agreement of the radiologist's measurements was assessed by repeating 20% of the randomly selected data. The reliability analysis demonstrated good intra-examiner agreement for FA of seven regions of interest (ROIs) (intraclass correlation coefficient [ICC]=0.853) and excellent intra-examiner reliability for the mandibular cortical width (MCW) (ICC=0.932).

2.4. Fractal Analysis

The current study was based on the studies of Kato et al. (22) and seven ROIs were determined for FA. Using the rectangle tool of Image J, 40×40 pixel squares were manually created in the right angulus, right molar and right premolar, left angulus, left molar and left premolar and anterior regions. Furthermore, ROIs were determined by drawing bilaterally from the mental foramen region to the third molar region on the cortical bone using the Polygon tool (Figure 1).

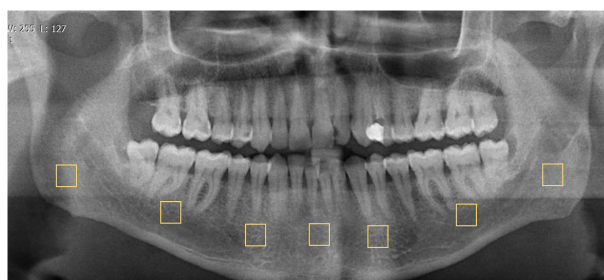


Figure 1. Selected regions of interest for fractal analysis.

The stages of FA were performed using the Image J software according to the protocol of White and Rudolph). Each ROI was multiplied after cropping. The multiplied image was blurred using a Gaussian filter (sigma, 35) to eliminate large-scale brightness changes. The blurred image was subtracted from the original image. Then, 128 gray values were added to distinguish between trabecular bone and bone marrow spaces. Binarization was performed to obtain an image in binary color (black and white) format. The noise was removed by erosion and the outlines of the structures were expanded and sharpened. After the inversion process, the black areas represented the trabecular bone and the white areas represented the marrow spaces. Finally, skeletonization was performed. The FA was performed by counting the boxes of 2 to 64 pixels in the skeletonized image using the fractal box counting plugin of Image J (Figure 2). The FD calculated using the software in the ROIs in the angulus, molar, premolar and anterior regions on the right and left sides was recorded by averaging on the right and left sides.

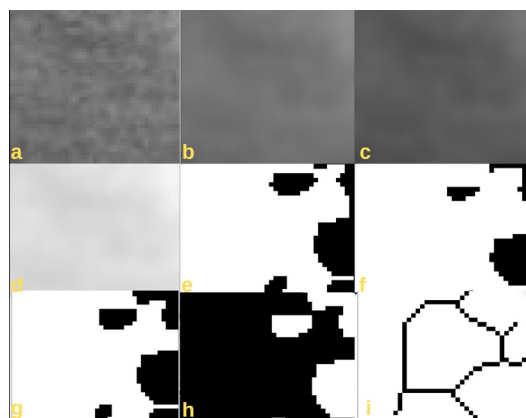


Figure 2. Stages of fractal analysis. Duplicated image after cropping (a). Blurred image using a Gaussian filter (sigma, 35) (b). Subtraction process from the original image (c). Addition of 128 Gy values (d). Binarization (e), erosion (f), dilatation (g), inversion (h), skeletonization (i).

2.5. Mandibular Cortical Width

The cortical bone surrounding the mental foramen region was measured. This procedure was applied to both sides of the jaw. Next, two parallel lines were drawn through the upper and lower borders of the cortex. Then, a third line was drawn perpendicular to these two lines and through the center of the mental foramen. The length between the other two lines of the third line was recorded as MCW. The averages of the right and left side measurements were recorded (Figure 3).



The primary outcome of the study was to compare FA values among the groups. The secondary outcome was to compare MCW among the groups.

2.6. Statistical Analysis

In the study, FA was considered to primary outcome. According to previous study (13); the standard deviation (s) for the fractal analysis ranged from 0.06 to 0.15. Thus, 0.11 was considered to compute sample size. Effect size (d) was assumed to be 0.04, and Z value of 1.96 was used for the 0.05 type I error rate. The sample size was found 29.05 (about 30) by using the equation for sample size calculation ($n = Z^2 s^2 / d^2$). Descriptive statistics for the continuous variables were presented as mean, standard deviation, minimum and maximum values while count and percentages for categorical variables. One-way ANOVA was performed for the comparison of group means. Duncan multiple comparison test was also used to identify different groups. In addition, the Pearson correlation coefficients were computed to the determine linear relationship. Statistical significance level was considered as 5% and SPSS (ver: 21) statistical program was used for all statistical computations.

3. RESULTS

Of a total of 180 participants included in the study, 90 were females and 90 were males with a mean age of 30.64 ± 7.48 years (Table 1). While the mean age of female was 29.73 ± 7.38 years, the mean age of male was calculated as 31.54 ± 7.52 years. In terms of age, a statistically significant difference was found among the groups ($p < .05$). Accordingly, individuals with Stage I periodontitis, gingivitis and periodontally healthy had a lower mean age.

Table 1. Descriptive statistics and comparison results for age

		N	Mean	Std. Dev.	p
Age	Female	90	29.73	7.380	.105 [#]
	Male	90	31.54	7.525	
	Total	180	30.64	7.488	
	Stage I	30	28.10 ^b	5.950	.001 ^{##}
	Stage II	30	35.83 ^a	7.751	
	Stage III	30	33.43 ^a	8.148	
	Stage IV	30	32.90 ^a	7.073	
	Gingivitis	30	26.50 ^b	4.241	
	Periodontally Healthy	30	27.07 ^b	6.108	

N: number of sample size, Std. Dev: Standard deviation.

(Independent Samples t-test); ## (One-Way ANOVA).

a, b: Different lower case represent statistically significant difference among the age groups

p < .05

When the evaluation between gender was examined, the FD of each region evaluated, mean of total FD and MCW values are shown in Table 2. Accordingly, a statistically significant difference was observed only for the MCW value (p<.05), and this value was found to be higher in male (23.87±4.59 mm) than in female (22.50±3.75 mm).

Table 2. Descriptive statistics and comparison results for the values of fractal dimension and mandibular cortical width among genders

		N	Mean	Std. Dev.	Min	Max	p #
Anterior FD	Female	90	0.992	0.277	0.10	1.27	.078
	Male	90	1.057	0.205	0.10	1.27	
	Total	180	1.024	0.245	0.10	1.27	
Premolar FD	Female	90	1.071	0.111	0.56	1.26	.200
	Male	90	1.095	0.138	0.24	1.23	
	Total	180	1.083	0.125	0.24	1.26	
Molar FD	Female	90	1.024	0.132	0.10	1.27	.356
	Male	90	1.041	0.114	0.49	1.21	
	Total	180	1.033	0.123	0.10	1.27	
Angulus FD	Female	90	1.016	0.150	0.53	1.24	.098
	Male	90	0.963	0.266	0.10	1.26	
	Total	180	0.989	0.217	0.10	1.26	
Total FD	Female	90	1.031	0.093	0.53	1.14	.717
	Male	90	1.036	0.113	0.31	1.20	
	Total	180	1.034	0.103	0.31	1.20	
MCW	Female	90	22.509	3.750	15.41	36.10	.030
	Male	90	23.873	4.592	13.75	37.13	
	Total	180	23.191	4.236	13.75	37.13	

FD: Fractal dimension, MCW: Mandibular cortical width, N: number of sample size, Std. Dev: Standard deviation.

p < .05 (Independent Samples t-test).

In the intergroup evaluations, no statistically significant difference was observed among the groups in terms of all the parameters examined (Table 3). The correlation evaluation of FD for each region, total FD and MCW values are presented in Table 4. Accordingly, anterior FD had a significant positive correlation with molar, premolar and total FD, while angular FD had a significant positive correlation with MCW and total FD. In addition, molar FD had a significant positive correlation with premolar and total FD, while MCW had a significant positive correlation with angular FD and mean FD. On the

other hand, no significant correlation was found between age and other parameters.

Table 3. Descriptive statistics and comparison results for the values of fractal dimension and mandibular cortical width among the groups

		N	Mean	Std. Dev.	Min	Max	p# #
Anterior FD	Stage I	30	1.057	0.198	0.11	1.21	.111
	Stage II	30	1.091	0.089	0.88	1.24	
	Stage III	30	0.913	0.390	0.10	1.27	
	Stage IV	30	1.027	0.205	0.10	1.23	
	Gingivitis	30	1.033	0.207	0.10	1.25	
	Periodontally Healthy	30	1.025	0.263	0.10	1.27	
	Total	180	1.024	0.245	0.10	1.27	
Premolar FD	Stage I	30	1.074	0.140	0.56	1.21	.937
	Stage II	30	1.093	0.076	0.97	1.23	
	Stage III	30	1.091	0.133	0.66	1.23	
	Stage IV	30	1.075	0.145	0.57	1.21	
	Gingivitis	30	1.098	0.062	0.99	1.23	
	Periodontally Healthy	30	1.070	0.169	0.24	1.26	
	Total	180	1.083	0.125	0.24	1.26	
Molar FD	Stage I	30	1.045	0.084	0.77	1.17	.703
	Stage II	30	1.011	0.125	0.52	1.18	
	Stage III	30	1.012	0.182	0.10	1.18	
	Stage IV	30	1.051	0.081	0.81	1.17	
	Gingivitis	30	1.043	0.135	0.49	1.24	
	Periodontally Healthy	30	1.033	0.107	0.67	1.27	
	Total	180	1.033	0.123	0.10	1.27	
Angulus FD	Stage I	30	0.989	0.225	0.10	1.21	.994
	Stage II	30	1.010	0.223	0.10	1.24	
	Stage III	30	0.993	0.231	0.10	1.26	
	Stage IV	30	0.989	0.208	0.10	1.21	
	Gingivitis	30	0.983	0.202	0.53	1.25	
	Periodontally Healthy	30	0.973	0.230	0.10	1.19	
	Total	180	0.989	0.217	0.10	1.26	
Total FD	Stage I	30	1.039	0.081	0.81	1.13	.877
	Stage II	30	1.045	0.073	0.85	1.16	
	Stage III	30	1.015	0.124	0.53	1.15	
	Stage IV	30	1.037	0.084	0.79	1.13	
	Gingivitis	30	1.040	0.089	0.79	1.20	
	Periodontally Healthy	30	1.025	0.150	0.31	1.14	
	Total	180	1.034	0.103	0.31	1.20	
MCW	Stage I	30	23.926	3.451	17.98	30.36	.488
	Stage II	30	23.994	4.714	15.85	37.13	
	Stage III	30	22.307	3.366	15.87	29.18	
	Stage IV	30	22.571	4.120	15.51	31.31	
	Gingivitis	30	23.577	5.274	13.75	36.10	
	Periodontally Healthy	30	22.772	4.213	15.41	32.62	
	Total	180	23.191	4.236	13.75	37.13	

FD: Fractal dimension, MCW: Mandibular cortical width, N: number of sample size, Std. Dev: Standard deviation

#p < .05 (One-Way ANOVA).

Table 4. Pearson correlation coefficients among age, fractal dimension and mandibular cortical width

	Age	Anterior FD	Angulus FD	Molar FD	Premolar FD	MCW	Total FD
Age	1						
Anterior FD	-0.078	1					
Angulus FD	0.045	0.115	1				
Molar FD	0.004	0.233**	-0.005	1			
Premolar FD	0.044	0.274**	0.145	0.265**	1		
MCW	0.107	-0.040	-0.151*	-0.077	-0.100	1	
Total FD	0.018	0.583**	0.689**	0.509**	0.618**	-0.165*	1

FD: Fractal dimension, MCW: Mandibular cortical width

* $p < .05$; ** $p < .01$ (Pearson correlation analysis).

4. DISCUSSION

In the present study, we compared the radiomorphometric parameters of the mandible in patients diagnosed with gingivitis and periodontitis with those of periodontally healthy individuals. Therefore, changes in the mandibular microstructure in different stages of periodontitis were investigated. In this study, no statistically significant difference was found in terms of FD values among the groups.

Periodontitis is an advanced gingival disease which causes alveolar bone loss and destruction through host immune and inflammatory response-dependent mechanisms (24). Advanced bone loss can result in tooth loss and a complex treatment procedure. Therefore, radiographs which provide information about bone loss can be critical importance in the evaluation of the diagnosis and prognosis of the disease. Recently, the FA method has been used in radiographs for detailed analysis of these evaluations (10-14,16,18). While using this method, mandibular premolar, molar, canine and antegonial regions were preferred (10,13,16,18). In the current study, the ROIs determined in the mandibular premolar and molar regions were calculated. Additionally, ROIs of the angular and anterior regions were also evaluated. Similar to the previous study (10), in the present study, image processing was also performed as reported by White and Rudolph (23).

In their study, Sener et al. (6) reported that FA could provide quantitative values in periodontally healthy patients and those with moderate periodontitis and, in addition, changes in the trabecular bone could be detected with this method. The authors also found a significant difference between the groups and reported that FD values were higher in the healthy group. Aktuna Belgin and Serindere (10) obtained periapical radiographs from mandibular first molars of 35 periodontally healthy and 35 patients with periodontitis and reported that the calculated FD values were significantly higher in the group of periodontally healthy. Yarkaç et al. (13) used digital panoramic radiographs, periodontitis patients were evaluated as Stages I, II, and III, and they reported similar results to the previous study in terms of FD mean values. In another study, Soltani et al. (16) reported that FD values, except for distal

ROIs, were significantly different in cases of moderate and severe periodontitis compared to healthy periodontal bone. However, the same researchers reported that FD values did not represent a statistically significant difference between the periodontally healthy group and the mild periodontitis group. In a study evaluating periodontitis in four stages, Mishra et al. (12) showed that FD values decreased significantly in advanced stages where the severity of the disease increased. However, Korkmaz et al. (18) included periodontally healthy individuals (control group) and individuals with only Stage III/IV periodontitis in their study and reported that FD values of individuals with periodontitis were significantly lower than those of the control group. In the current study, no significant differences were observed among the groups. Of note, the differences between the results of the reported studies and current study may have been affected by the discrepancies in the jaw regions or inconsistencies in the selection of ROI (25). Although the effect of ROI location on FD calculation is controversial, different areas have been selected as ROIs (12, 17). The image preprocessing and selection of ROI may affect the results until a consensus is reached (9).

Eser and Saribas (14) reported no significant difference between the groups in the mean FD values calculated from panoramic radiographs obtained from 64 individuals with gingivitis and 64 individuals with periodontitis. In the current study, periodontally healthy patients, individuals with gingivitis and periodontitis were compared and, similarly, no statistically significant difference was observed among the groups. Thus, this study reports similar results to Eser and Saribas (14) in terms of comparing gingivitis and periodontitis groups.

Furthermore, Kayaalti-Yüksek et al. (11) evaluated systemically healthy patients and patients with diabetes mellitus with periodontitis using FA. Five groups were formed consisting of patients with diabetes mellitus with moderate and severe periodontitis, systemically healthy individuals with moderate and severe periodontitis, and systemically healthy individuals with gingivitis. The authors found no significant difference in bone trabeculation in the periodontitis groups. These findings are consistent with our study results, as we found

no significant difference in the periodontitis groups in the current study.

Lang et al. (26) evaluated the trabecular structure of peri-implant diseases using the FA method with periapical radiographs and reported that there was no significant difference in FD measurements in the case of peri-implant health, peri-implant mucositis and peri-implantitis. Considering the similarities in the clinical and radiological nature of periodontitis and peri-implantitis, the lack of a significant difference in trabecular integrity changes is similar to the current study.

Moreover, Aktuna Belgin and Serindere (10), Updike and Nowzari (17), and Yarkac et al. (13) reported no significant difference in FD values of jaw bones according to gender. However, Yarkac et al. (13) found a negative correlation between age and FD values. Korkmaz et al. (18) found no significant correlation between age and FD. In the present study, we observed no statistically significant difference in FD values between genders. In addition, we found no significant correlation between age and FD.

In this study, similar to the previous study (27), it was concluded that the effect of FA was limited. Nonetheless, there are some limitations to this study. The mean age of the periodontitis groups (Stage II, III and IV) was found to be higher than the healthy and gingivitis groups. There is another study (10) in the literature with this limitation, and it is thought that the lower mean age in healthy individuals may have affected the findings of the current study. Other limitations include the small number of samples, the use of only panoramic images, and the lack of use of other radiographic diagnostic images and technologies with higher resolution.

5. CONCLUSION

In conclusion, our study results suggest that FA calculated from panoramic radiographic images of periodontally healthy patients, gingivitis and different stages of periodontitis shows comparable results and indicates no superiority. In addition, FA does not offer an advantage in terms of diagnostic potential in different regions of the jaws in current study. Based on these findings, it should be kept in mind that clinical periodontal parameters are crucial in disease diagnosis. Therefore, in detailing the use of FD in periodontal disease diagnosis, different designed, large-scale studies using different radiographic images are warranted.

Acknowledgment: The authors of this study would like to thank Prof. Dr. Siddık Keskin for statistical analysis at the Faculty of Medicine, Department of Biostatistics, Van Yüzüncü Yıl University.

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Van Yüzüncü Yıl University, Noninvasive Clinic Ethics Committee (Approval date: 08/03/2024; Number: 2024/03-12)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: DA, SK

Design of the study: DA, SK

Acquisition of data for the study: DA, SK

Analysis of data for the study: DA, SK

Interpretation of data for the study: DA, SK

Drafting the manuscript: DA

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Final approval of the version to be published: DA, SK

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Therapeutic Potential of Irisin in Ovarian Torsion-Detorsion: Mitigating Oxidative Stress and Inflammatory Response

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Received: February 10, 2025

Accepted: June 23, 2025

ABSTRACT

Objective: Ovarian torsion (OT) is a critical gynecological emergency marked by partial or complete rotation of the ovary around its ligamentous supports, resulting in impaired blood flow and potential ischemic injury or necrosis if not treated promptly. This study explores the potential of irisin in mitigating ischemia-reperfusion (I/R) injury following ovarian torsion-detorsion (T/D), with a focus on oxidative stress and inflammatory mediators.

Methods: Twenty-four female Sprague-Dawley rats were allocated into three groups: Sham, T/D, and irisin 10 µg/kg. Oxidative stress markers—total oxidant status (TOS), oxidative stress index (OSI), malondialdehyde (MDA), and myeloperoxidase (MPO)—were measured to assess tissue damage. Antioxidant parameters, including superoxide dismutase (SOD) activity and total antioxidant status (TAS) were evaluated. Serum levels of tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β) were analyzed to assess systemic inflammation and irisin's modulatory role.

Results: The T/D group showed elevated MPO and MDA levels relative to the sham group ($p < .05$), alongside significant reductions in SOD activity and TAS levels ($p < .05$). Irisin administration reversed these imbalances, decreasing MPO and MDA levels and enhancing SOD and TAS levels ($p < .05$ vs. T/D group). TNF-α and IL-1β levels, which were significantly elevated in the T/D group, were reduced by irisin treatment ($p < .05$ vs. T/D group), indicating its anti-inflammatory efficacy.

Conclusion: The findings support the potential of irisin as a therapeutic agent for mitigating oxidative stress and inflammation in ovarian I/R injury. Irisin may offer clinical benefits in preserving ovarian function during conditions related to T/D.

Keywords: Ovarian torsion-detorsion, ischemia-reperfusion injury, irisin, oxidative stress, inflammatory response

1. INTRODUCTION

Ovarian torsion (OT) refers to the rotation of an ovary around its pedicle, typically occurring during gynecological events (1). This rotation can disrupt normal ovarian blood flow, leading to vascular compromise and potentially severe clinical outcomes (2). Although OT is relatively uncommon, it predominantly affects women of reproductive age and can have serious implications. Notably, 15% of OT cases occur during adolescence (3). This condition is often associated with underlying ovarian masses or cysts. Despite its rarity, OT accounts for approximately 3% of all gynecological emergencies (4, 5).

Detorsion procedures are employed to restore blood flow and preserve ovarian viability (6). However, the reperfusion that follows detorsion induces an overproduction of reactive oxygen species (ROS) and promotes lipid peroxidation (7). These processes can damage follicles and contribute to the development of atretic bodies within the ovarian tissue. Prompt diagnosis and treatment are crucial for distinguishing OT from other conditions and protecting reproductive function (8). Recent investigations aim to mitigate the damage caused by T/D, with a particular focus on minimizing cell damage resulting from reperfusion injury following ischemia (9-11).

How to cite this article: Güler CM, Bircan B, Eraslan E, Akdemir Ekinci NF, Yazıcı Ş, Erdoğan Güzel D, Öztürk D, Polat E, Tanyeli A. Therapeutic Potential of Irisin in Ovarian Torsion-Detorsion: Mitigating Oxidative Stress and Inflammatory Response. Clin Exp Health Sci 2025; 15: 434-439. <https://doi.org/10.33808/clinexphealthsci.1636484>

Irisin is a myokine secreted primarily by adipose tissue in response to physical activity, and it exerts numerous biological effects, especially in muscle metabolism. It enhances metabolic rate, increases energy expenditure, and facilitates fat oxidation (12). There is growing scientific interest in irisin's anti-inflammatory, anti-apoptotic, and antioxidative properties, which are implicated in the pathogenesis of various diseases, including liver disorders, myocardial infarction, pulmonary injury, renal diseases, cancer, and atherosclerosis (13, 14).

Given the established protective effects of irisin in ischemic models, we hypothesize that exogenous irisin administration could attenuate oxidative stress and inflammation in ovarian I/R injury, thereby preserving ovarian structural integrity. This study aims to assess the therapeutic potential of irisin in a rat model of ovarian T/D by evaluating its impact on oxidative stress markers (malondialdehyde [MDA], oxidative stress index [OSI], total oxidant status [TOS], and myeloperoxidase [MPO]), antioxidant defense mechanisms (superoxide dismutase [SOD] and total antioxidant status [TAS]), and proinflammatory cytokines (interleukin-1 beta [IL-1 β] and tumor necrosis factor-alpha [TNF- α]). These findings aim to provide new insights into the clinical applicability of irisin for preventing ovarian injury in gynecological settings.

2. METHODS

2.1. Ethical Approval

This study was approved by the Animal Experiments Local Ethics Committee of Atatürk University (Approval Date: 30.06.2017; Protocol No: 5). All procedures adhered to the ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines to ensure ethical conduct, transparency, and reproducibility.

2.2. Chemicals

A 10% povidone-iodine solution (Batticon, Adeka) was used for disinfection. Anesthesia was achieved using a combination of ketamine (Ketalar®, Pfizer, Istanbul) and xylazine hydrochloride (Rompun®, Bayer, Istanbul). Irisin (CAS 1465928-51-1, purity $\geq 95.0\%$) was obtained from Sigma-Aldrich (St. Louis, MO, USA).

2.3. Animals

Female Wistar albino rats (12–16 weeks old, 200–250 g) were sourced from the Atatürk University Laboratory Animals Research and Application Center. Rats were housed under standard conditions with a 12-hour light/dark cycle, controlled temperature, and relative humidity ($55 \pm 5\%$). Standard pellet feed and water were provided *ad libitum*. Animals were fasted overnight before procedures, with water available throughout.

2.4. Experimental Groups

The experimental animals were prepared for the experimental process. They were supine positioned. The abdominal areas

were shaved and disinfected with 10% povidone-iodine. For anesthesia, intraperitoneal (i.p.) ketamine (100 mg/kg) and xylazine (15 mg/kg) were preferred based on previous research (15). A total of 24 female Wistar albino rats (12–16 weeks old, 200–250 g) were randomized into three experimental groups (n=8 per group):

Group I (sham): Underwent laparotomy (1–2 cm incision) without any ovarian manipulation.

Group II (T/D): The T/D model is represented in Figure 1, based on a previous study (16). Following laparotomy, bilateral ovarian torsion was induced by rotating the ovaries 360° in a clockwise direction and securing them with atraumatic microvascular clamps for three hours. Following the torsion phase, the clamps were carefully removed, allowing blood circulation to resume for another three hours before the surgical site was closed.

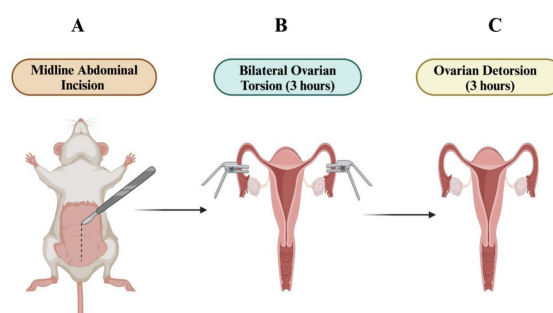


Figure 1. Schematic representation of the ovarian torsion/detorsion (T/D) experimental model. A) Midline abdominal incision (1–2 cm) for surgical access. B) Induction of bilateral ovarian torsion via 360° clockwise rotation, stabilized with atraumatic vascular clamps for a 3-hour ischemic phase. C) Initiation of the reperfusion phase by clamp removal, restoring blood circulation during detorsion (Created in <https://BioRender.com>).

Group III (Irisin 10 $\mu\text{g/kg}$): Underwent the same procedure as Group II, with the addition of intravenous irisin (10 $\mu\text{g/kg}$) administered via tail vein 30 minutes before detorsion. The irisin dose was selected based on prior research (17).

Following a 3-hour detorsion period, rats were humanely euthanized via intraperitoneal (i.p.) ketamine (100 mg/kg) and xylazine (15 mg/kg) administration to induce deep anesthesia, followed by cervical dislocation to ensure death.

2.5. Biochemistry Methods

For biochemical analyses, 100 mg of ovarian tissue was homogenized in 2 mL of 10% phosphate-buffered saline (PBS) using a homogenizer (IKA, Staufen, Germany) at 10,000 rpm for 5 minutes while kept on ice. The homogenate was centrifuged at $3,000 \times g$ for 30 minutes at 4°C and utilized for biochemical assays. The analyses included measurements of MDA, MPO, SOD, TAS, and TOS. Additionally, proinflammatory cytokines, like TNF- α and IL-1 β , were quantified using a rat-specific ELISA kit (Elabscience, Wuhan, China).

MDA levels were determined following a modified thiobarbituric acid (TBA) assay, initially described by Ohkawa et al. (1979) (18). In this assay, tetramethoxypropane was used as an external standard, and the concentration of lipid peroxidation products was expressed in MDA nanomoles. The reaction between TBA and MDA was measured spectrophotometrically (PowerWave™ XS Biotek). The assay involved incubating the sample with butylated hydroxytoluene (BHT) in methanol and adding phosphoric acid and TBA reagents. The mixture was heated for 60 minutes at 95°C. Following the cooling, the sample was centrifuged for 3 minutes at 10,000×g.

MPO activity was assessed using the method outlined by Bradley et al. (19). This method quantifies the oxidation of o-dianisidine in the presence of hydrogen peroxide (H₂O₂), forming a yellow-orange complex. After centrifuging the tissue suspension at 40,000×g for 15 minutes, the supernatant was analyzed with a spectrophotometer (PowerWave XS Biotek).

SOD activity was determined using a method adapted from Sun et al. (20). This technique assesses the inhibitory effect of SOD on nitro blue tetrazolium (NBT). The optical density was recorded using a spectrophotometer (PowerWave XS Biotek).

Total protein concentrations in the tissue homogenates were determined using the Bradford protein assay (Bio-Rad, USA), with bovine serum albumin (BSA) as the standard. All biochemical parameters (MDA, MPO, SOD, and cytokines) were normalized to the protein content and expressed as units per milligram of protein.

TAS and TOS levels were determined using commercial kits (Rel Assay Diagnostics, Gaziantep, Turkey), where TAS was expressed in terms of Trolox equivalents (mmol Trolox Eq/L) and TOS in hydrogen peroxide equivalents (μmol H₂O₂ Eq/L). The oxidative stress index (OSI) was calculated as the ratio of TOS to TAS, following normalization to the same unit (Arbitrary unit) (21).

2.6. Statistics

All data are represented as mean±standard error of the mean (SEM). Statistical analyses were completed using SPSS version 16.0 (SPSS Inc. and Lead Tech. Inc., Chicago, IL). Before analysis, the normality of the data was evaluated to determine the appropriate statistical methods. Group comparisons were conducted using the Kruskal-Wallis test for nonparametric data. In cases where significant differences were observed, the Mann-Whitney U test was employed to pinpoint the specific groups responsible for the variation. A p-value of ≤ .05 was the threshold for statistical significance.

3. RESULTS

3.1. Assessment of Oxidative Stress and Antioxidant Markers

Biochemical analyses revealed notable differences in oxidative stress parameters among the experimental groups (Figure 2). The T/D group exhibited significantly elevated MPO activity and

MDA levels compared to the sham group (p<.05). Conversely, irisin administration (10 μg/kg) significantly reduced both MPO activity and MDA levels relative to the T/D group (p<.05), indicating a protective effect against oxidative stress.

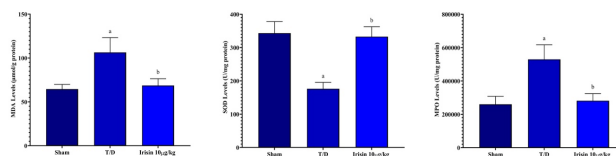


Figure 2. Effects of irisin on oxidative stress markers. Superoxide dismutase (SOD) activity, malondialdehyde (MDA) levels, and myeloperoxidase (MPO) activity across experimental groups. Data represent mean±SEM. ^ap<.05 vs. sham group, ^bp<.05 vs. D/T group (one-way ANOVA with Tukey's post-hoc test). Irisin (10 μg/kg) administration significantly reduced MDA and MPO levels while restoring SOD activity, demonstrating its antioxidant efficacy in mitigating oxidative damage.

In contrast, SOD activity, an essential antioxidant enzyme, was significantly decreased in the T/D group compared to the sham group (p < .05). Irisin treatment effectively restored SOD activity to levels comparable to those of the sham group (p < .05 vs. T/D), underscoring its antioxidative efficacy.

3.2. Ovarian Tissue Oxidative Status

The T/D group demonstrated a significant reduction in TAS compared to the sham group (p<.05), reflecting diminished antioxidant capacity. Treatment with irisin resulted in a statistically significant increase in TAS (p<.05 vs. T/D), suggesting enhanced antioxidant defense.

Conversely, TOS and OSI values were significantly elevated in the T/D group (p<.05 vs. sham), indicating increased oxidative stress. Irisin administration normalized these values, significantly reducing both TOS and OSI compared to the T/D group (p < .05), further highlighting its role in reestablishing redox balance (Figure 3).

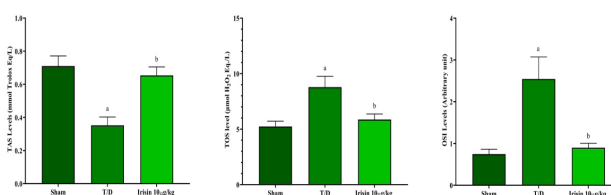


Figure 3. Modulation of systemic oxidative stress indices by irisin. Total antioxidant status (TAS), oxidative stress index (OSI), and total oxidant status (TOS) in sham, D/T, and irisin-treated groups. Values are expressed as mean±SEM. ^ap<.05 vs. sham group, ^bp<.05 vs. D/T group (one-way ANOVA with Tukey's post-hoc test). Irisin (10 μg/kg) treatment normalized TAS, TOS, and OSI levels, counteracting the oxidative imbalance induced in the D/T group.

3.3. Proinflammatory Cytokine Modulation

Serum concentrations of TNF-α and IL-1β were significantly higher in the T/D group compared to the sham group (p<.05), confirming the presence of a robust inflammatory

response following reperfusion injury. Irisin administration significantly reduced the levels of both cytokines ($p < .05$ vs. T/D), demonstrating its anti-inflammatory potential in this model (Figure 4).

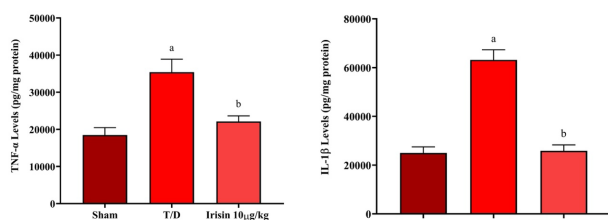


Figure 4. Irisin attenuates proinflammatory cytokine Levels. Concentrations of tumor necrosis factor-alpha (TNF- α) and interleukin-1 β (IL-1 β) in serum samples from sham, D/T, and irisin-treated groups. Data are presented as mean $\pm$ SEM. ^a $p < .05$ vs. sham group, ^b $p < .05$ vs. D/T group (one-way ANOVA with Tukey's post-hoc test). Irisin (10 μ g/kg) notably attenuated the elevation of IL-1 β and TNF- α , highlighting its anti-inflammatory role in the experimental model.

4. DISCUSSION

Ovarian torsion represents a significant threat to female fertility due to the risk of ischemia and subsequent tissue necrosis if not managed promptly (22). Although detorsion is a commonly employed intervention to restore perfusion, it is paradoxically associated with reperfusion injury mediated by excessive ROS generation (23, 24). ROS overproduction leads to lipid peroxidation by converting metabolic by-products into free radicals in ischemic tissues (25). Increased MDA concentrations during I/R injury are recognized as biomarkers of lipid peroxidation, reflecting oxidative damage to cellular membranes (26). MPO, a substance secreted by neutrophils and macrophages, is crucial in oxidative stress-related tissue damage by generating hydroxyl radicals (27). Our research supports the accuracy of these findings by demonstrating a substantial rise in MDA and MPO levels, which suggests the presence of I/R injury due to ovarian T/D, consistent with prior studies on ovarian I/R injury.

Oxidative stress triggers endogenous defense mechanisms, such as SOD, which neutralizes superoxide radicals, and non-enzymatic antioxidants like glutathione GSH, a critical cellular reductant. These antioxidant systems act synergistically to mitigate oxidative damage and restore redox homeostasis at the cellular level (28). Although cells have their defense mechanisms, in the case of ischemia, this balance is disrupted by oxidative stress (29). The imbalance between oxidants and antioxidants intensifies tissue damage during I/R injury. Thus, identifying pharmacological agents with potent antioxidant and anti-inflammatory properties is crucial for mitigating ovarian damage and improving the management of I/R injury (30). Our research

reveals a significant decline in SOD activity in the T/D group, consistent with the existing literature.

I/R injury is associated with elevated levels of pro-inflammatory cytokines, notably IL-1 β and TNF- α . Elevated levels of these cytokines have been observed in ovarian tissues subjected to I/R injury, contributing to tissue damage (31). Our findings also supported high proinflammatory cytokine levels (IL-1 β and TNF- α) in the T/D group, indicating inflammatory response during I/R injury.

Irisin has attracted attention because of its protective effects against I/R injury. Research indicates that irisin mitigates myocardial I/R injury by preserving mitochondrial function and reducing oxidative stress. Specifically, it enhances the activity of SOD 2, thereby decreasing ROS production and subsequent cellular damage (32). Additionally, irisin has been shown to activate the AMP-activated protein kinase (AMPK) pathway, leading to enhanced mitochondrial biogenesis and function, which are crucial in maintaining cellular energy homeostasis during ischemia-reperfusion (I/R) events (33). Beyond its mitochondrial protective roles, irisin exerts anti-inflammatory effects by modulating gut microbiota composition and enhancing intestinal barrier integrity, thereby reducing systemic inflammation associated with myocardial I/R injury (34). In another study, I/R-related ROS production and proinflammatory parameters (IL-1 β , IL-6, etc.) can be diminished by irisin (35).

The collective data from our study reinforce the hypothesis that irisin exerts both antioxidative and anti-inflammatory effects, thereby conferring tissue protection in ovarian T/D injury. These effects may be mediated through multiple mechanisms, including modulation of ROS production, preservation of antioxidant enzyme activity, and suppression of proinflammatory cytokine release.

Future studies should explore the molecular pathways underpinning these protective effects, such as irisin's interaction with the AMPK and SOD2 pathways, and evaluate its translational potential in clinical gynecology.

5. CONCLUSION

Ovarian torsion remains a gynecological emergency requiring swift intervention to prevent irreversible damage. This study provides experimental evidence that irisin effectively attenuates oxidative stress and inflammation associated with T/D-induced I/R injury. The observed reductions in oxidative biomarkers and pro-inflammatory cytokines, along with the restoration of antioxidant capacity, underscore the therapeutic promise of irisin. Further investigations are warranted to elucidate its molecular mechanisms and assess its clinical applicability in preserving ovarian function.

Acknowledgements: We would like to thank Marmara University for providing access to academic databases.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Atatürk University Animal Experiments Local Ethics Committee (Approval date: 30.06.2017; Number: 5).

Peer-review: Externally peer-reviewed.

Author Contributions: (Initials only)

Research idea: MCG, BB, EE, AT

Design of the study: MCG, BB, EE, FNEA, ŞY, DGE, DÖ, EP, AT

Acquisition of data for the study: EE, EP

Analysis of data for the study: EE, EP

Interpretation of data for the study: EE, MCG

Drafting the manuscript: MCG, BB, EE, ŞY, AT

Revising it critically for important intellectual content: MCG, EE, ŞY, AT

Final approval of the version to be published: MCG, BB, EE, FNEA, ŞY, DGE, DÖ, EP, AT

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Spiritual Care Needs and Perceived Social Support in Women Undergoing Hysterectomy: A Correlational Study

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Received: February 16, 2025

Accepted: May 25, 2025

ABSTRACT

Objective: Hysterectomy is one of the most common surgical procedures in gynecology worldwide. It is directly related to a woman's fertility, and removal of the uterus could have irreparable psychological, physiological, and sexual consequences. This study aims to determine the relationship between spiritual care needs and perceived social support in women who underwent hysterectomy surgery.

Methods: The study utilized a cross-sectional and correlational design and included a total of 272 women who underwent hysterectomy in the surgical clinic of a hospital located in western Turkey. Data were collected through the Personal Information Form, the Spiritual Care Needs Inventory (SCNI), and the Multidimensional Scale of Perceived Social Support (MSPSS).

Results: Women's SCNI total mean score was found 62.01, MSPSS total mean score was found 70.72. Among MSPSS and SCNI sub-scales, a negative correlation was detected between MSPSS and the "caring and respect" sub-scale of SCNI ($p < .05$). The linear regression analysis showed that spiritual support needs sub-scales of "meaning and hope" ($\beta = .221, p < .01$) and "caring and respect" ($\beta = -.271, p < .001$) were found to be related factors affecting the perceived social support of women who underwent hysterectomy. The caring and respect sub-scale decreased with the increase in the women's perceived social support.

Conclusion: In conclusion, evaluation and reinforcement of the spiritual support needs and perceived social support of women who underwent hysterectomy are recommended as the foundation of holistic care.

Keywords: Spiritual care needs, social support, hysterectomy, women

1. INTRODUCTION

Hysterectomy surgery, which includes the removal of the uterus, cervix, and sometimes the ovaries and fallopian tubes, is now one of the most frequently administered pelvic surgical procedures and is a common operation among women. Reproductive organs are important for women's sexual image, so hysterectomy could affect women's psychological state, personal interactions, and especially marital adjustment and sexual functions (1-3). As the uterus is seen as a symbol of reproduction by many women, its loss could carry different meanings. Therefore, hysterectomy surgery may cause experience of negative emotions such as loss of sexual functions, fertility ability, and the role of womanhood; deterioration of the relationship with the spouse; experience of menopausal symptoms; and thoughts about losing physical strength (4-6). Hence, meeting spiritual needs and providing social support is very important for

women to adapt to the physical and psychological changes they experience after surgery (1,7,8).

Spirituality is one of the fundamental characteristics of human beings. Spiritual care is not only a part of the art of nursing but also a very important component of holistic care. Spiritual care is very important for the individual's general health and well-being (9). Determination of spiritual needs, which is seen as the first step of holistic care, and provision of nursing care to meet these needs are reported to be important elements of health care services that support the individual's personal integrity and interpersonal relationships (10-12). Studies show that spiritual care can reduce anxiety and fears, and its effectiveness is closely linked to the presence of strong social support systems (13).

How to cite this article: Başgöl Ş, Karadağ Arlı S, Çiftçi Karan E. Spiritual Care Needs and Perceived Social Support in Women Undergoing Hysterectomy: A Correlational Study. Clin Exp Health Sci 2025; 15: 440-446. <https://doi.org/10.33808/clinexphealthsci.1640738>

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Perceived social support is generally defined as the perception that a person is cared for by others and has a reliable social network that she can turn to in times of need. At the same time, perceived social support is closely linked to spirituality and overall well-being. Women who feel socially supported are more likely to experience a sense of belonging and emotional security, which can enhance their spiritual well-being and coping mechanisms (7,14, 15). Research suggests that individuals with strong social support systems often report higher levels of spiritual well-being, highlighting the interplay between these factors (15,16).

The literature reported that determining patients' spiritual needs and meeting them and increasing their social support increase their compliance to treatment and quality of life in the treatment process and reduce their psychosocial problems (16, 17). Although women's spiritual and social support needs are considered to increase during the hysterectomy surgery process, the literature does not include an adequate number of studies on this issue. Therefore, this study aims to investigate the relationship between spiritual care needs and perceived social support in women who underwent hysterectomy surgery and thus contribute to the literature.

1.1. Research Questions

What are the perceived levels of spiritual care needs and perceived social support in women who underwent hysterectomy surgery?

What is the relationship between spiritual care needs and perceived social support in women who have undergone hysterectomy?

2. METHODS

2.1. Study design and participants

This study used a descriptive and correlational design. It was conducted in the surgical clinic of a hospital located in western Turkey. The reason for choosing this hospital is that women with various socio-demographic characteristics from the surrounding provinces seek treatment here, and annually an average of 950-1000 hysterectomy operations are administered. The target population of the study consisted of women who were hospitalized in the surgical clinic of the hospital between the 1st of August, 2022, and the 31st of January, 2023 and underwent hysterectomy surgery. The minimum sample size was calculated as 217 women according to the sampling formula with a known population (5% deviation, 95% confidence level). The sample of the study consisted of 272 women who were hospitalized in the surgical clinic, underwent hysterectomy surgery on the dates when the study was conducted, and met the research criteria. The inclusion criteria were being aged 18 years and older, being hospitalized in the surgical ward and having undergone hysterectomy surgery on the dates when the study was conducted, being able to speak and write Turkish, having no communication problems, and agreeing

to participate in the study. Exclusion criteria for this study included women who were unable to communicate, had a diagnosed psychiatric disorder, were taking psychiatric medication, did not fully complete the data collection forms., and wished to withdraw from the study. Additionally, women who underwent hysterectomy for malignant conditions, and those who underwent emergency obstetric hysterectomy (e.g., due to uterine atony) were excluded.

2.2. Data collection and measurements

Data were collected between the 1st of August, 2022 and the 31st of January, 2023 by meeting the participants face-to-face. Data collection was performed by meeting the women in the surgical clinic room where they were hospitalized. Filling in each form took around 15 minutes. Before data were collected, each woman participating in the study was given information about the purpose and method of the study. The participants were assured that the data obtained would be used only within the scope of the study; their names would not be included in the questionnaires; and participation was on a voluntary basis. Data were collected through the Personal Information Form, the Spiritual Care Needs Inventory (SCNI), and the Multidimensional Scale of Perceived Social Support (MSPSS).

2.3. The Personal Information Form

The Personal Information Form, which was prepared by the researchers in line with the literature, consists of a total of 18 questions that aimed to determine the participants' socio-demographic characteristics (age, education level, employment status, etc.), their spiritual support needs, and the factors that may affect their perceived social support (12, 15, 18).

2.4. Spiritual Care Needs Inventory (SCNI)

The Turkish validity and reliability of the scale, which was developed by Wu et al. (2016), was conducted by İsmailoğlu et al. (2019). The scale consists of 21 items and provides information about patients' spiritual care needs (18, 19). The items in the scale include patients' potential spiritual care needs. Respondents are asked to rate each spiritual care needs item on a 5-point Likert scale.

The items are responded on a scale from 1 to 5 as 1 = "Not at all necessary", 2 = "Not necessary", 3 = "Does not matter", 4 = "Necessary", and 5 = "Absolutely necessary". Higher total mean scores indicate patients' more spiritual care needs. The scale consists of two components: "meaning and hope" (13 items (questions:1-12, 14) and "caring and respect" (8 items (questions: 13, 15-21). The minimum score for the meaning and hope component is 13, and the maximum score is 65; for the caring and respect component, the minimum score is 8, and the maximum score is 40. The lowest possible total score on the scale is 21, and the highest possible total score is 105. An increase in the total score average indicates that

the patient has greater spiritual care needs. Cronbach's alpha internal consistency coefficient of the scale was reported as 0.93 (19). In this study, Cronbach's alpha internal consistency coefficient was found to be 0.94.

2.5. Multidimensional Scale of Perceived Social Support (MSPSS)

The Turkish validity and reliability of the scale developed by Zimet et al. (1988) were conducted by Eker et al. (2001). The scale, which was developed to measure the level of perceived social support, measures the adequacy of perceived social support from three different sources such as family, friends, and a significant other (20, 21). The 12-item scale consists of three sub-scales including family, friends, and a significant other. The items consist of the family (items 3,4,8 and 11), friends (items 6,7,9, and 12), and a significant other (items 1,2,5 and 10). Each item is rated on a seven-point Likert scale. While the sub-scale scores range from 4 to 28, the total score ranges from 12 to 84. The sub-scale score was obtained by summing the scores of four items in each sub-scale, and the total score of the scale was obtained by summing all sub-scale scores. Higher scores indicate a high level of perceived social support. Cronbach's alpha internal consistency coefficient of the scale was reported as 0.89 (21). In this study, Cronbach's alpha internal consistency coefficient was found to be 0.87.

2.6. Statistical analysis

The data obtained from the study were analyzed using SPSS 23.0 program (IBM SPSS Statistics for Windows, Version 23.0). Skewness and Kurtosis values (-1.50 and +1.50) were used to test the normality assumption. Numbers, percentages, arithmetic means, and standard deviations (SD) were used for descriptive statistics. Since the data were normally distributed, independent samples t-tests from parametric tests were performed. Mean differences were calculated by one-way analysis of variance (ANOVA) to test the significance of the difference among the three means. The relationship between two continuous variables was analyzed by Pearson correlation analysis. Analysis of variance (further analysis Bonferroni test) was used in multiple groups that were found significant according to independent variables. Multiple linear regression analysis was performed to analyze the factors affecting perceived social support. All other significant variables were included in the regression analysis. The level of significance was taken as $p < .05$ in statistical analyses. To assess multicollinearity, variance inflation factor (VIF) values were examined, and all were found to be below 5, indicating no significant multicollinearity issues. Additionally, the Durbin-Watson statistic was 1.758, suggesting no serious autocorrelation problem.

3. RESULTS

The average age of women who underwent hysterectomy was 53.06 years (SD 8.62) and 87.9% of them were married. The

average number of children was 2.88 (SD 1.49); 51.1% of the participants were not employed; 59.9% were primary school graduates and 60.7% had middle income (moderate). Besides, while 84.2% of the women lived in a nuclear family and 66.5% lived in a city, 54.4% went through menopause and 52.9% had no chronic diseases (Table 1). Results also showed that 96.7% of the women reportedly had a constant companion in the hospital and that their children (51.5%), husbands (20.6%), mothers/sisters (20.5%), and neighbors/friends (2.9%) supported them the most after hysterectomy surgery.

Spiritual support needs were found to be higher in women who had medium income (moderate) than women who had low income and in women who lived in the village than in women who lived in the district ($p < .05$). The perceived social support was found to be higher in working women than in non-working women, in those living in nuclear families than in those living in extended families, and in women who reported an impact on their sexual life after hysterectomy compared to those who did not ($p < .05$) (Table 1).

Participating women's SCNI mean score was found 62.01 (SD 17.45), and the "meaning and hope" and "caring and respect" sub-scale mean scores were found 35.27 (SD 1.09) and 26.73 (SD 8.37), respectively. The MSPSS mean score was found 70.72 (SD 11.74), and the sub-scale mean scores were 23.18 (SD 5.09) for the friends sub-scale, 25.27 (SD 3.08) for the family sub-scale, and 22.88 (SD 5.64) for the significant other sub-scale (Table 2).

Table 3 presents the correlation coefficients between the perceived social support and spiritual care needs of women who underwent hysterectomy surgery and age, number of children, spiritual support needs, and sub-scale total scores. A weak and negative correlation was found between the MSPSS and "caring and respect" (SCNI sub-scale) ($p < .05$). No relationship was found between MSPSS and SCNI total score, "meaning and hope" (SCNI sub-scale), age, and number of children ($p > .05$) (Table 3).

Table 4 demonstrates a multiple linear regression analysis of the risk factors that may affect the perceived social support of women who underwent hysterectomy surgery. The variables that were found to be significant as a result of the MSPSS total score statistics were included in the multiple linear regression analysis. The multiple linear regression model established to examine the independent variables affecting the perceived social support scale score of women who underwent hysterectomy surgery was found to be statistically significant ($F = 5.177$; $p = 0.000$). Hence, spiritual support needs sub-scales of "meaning and hope" ($\beta = .221$, $p = .004$) and "caring and respect" ($\beta = -.271$, $p = .000$) were found to be related factors affecting the social support perceived by women who underwent hysterectomy surgery. The perceived social support score of women whose sexual life was affected after hysterectomy surgery was found to be 3.347 units lower compared to those whose sexual life was not affected ($\beta = -.127$, $p = .034$). Family type and women's employment status were found to have no statistically significant effects on the Perceived Social Support Scale score ($p > .050$) (Table 4).

Table 1. SCNI and MSPSS scale score comparisons according to the participants' descriptive characteristics (n=272)

Characteristics			SCNI		MSPSS	
	<i>n</i>	(%)	<i>Mean (SD)</i>	<i>Test p value</i>	<i>Mean (SD)</i>	<i>Test p value</i>
Marital status						
Married	239	87.9	62.04 (17.44)	t= .069	71.00 (11.37)	t= 1.044
Single	33	12.1	61.81 (17.81)	p= .876	68.72 (14.20)	p= .139
Education level						
Primary school	163	59.9	63.31 (18.62)	F= 1,378	70.07 (12.40)	F= .639
High school	101	37.1	60.40 (15.08)	p= .254	71.76 (10.52)	p= .529
University and above	8	2.9	55.87 (19.88)		70.87 (13.09)	
Income level						
Low ^a	92	33.8	58.14 (14.30)	F= 3.996 p= .019 <i>b>a</i>	70.43 (9.73)	F= .096 p= .909
Moderate ^b	165	60.7	64.38 (18.63)		70.96 (12.62)	
Good ^c	15	5.5	59.73 (18.16)		69.93 (13.63)	
Employment status						
Working	133	48.9	58.54 (16.43)	t= 3.259	71.23 (11.04)	t= − .695
Not working	139	51.1	65.33 (17.82)	p= .055	70.24 (12.40)	p= .039
Family type						
Nuclear family	229	84.2	60.95 (17.31)	t= − 2.336	71.58 (11.14)	t= 2.415
Extended family	43	15.8	67.67 (17.32)	p= .770	66.18 (13.82)	p= .031
Lived place						
Province ^a	181	66.5	62.40 (17.60)	F= 3.245	71.18 (12.03)	F= .802
County ^b	72	26.5	58.91 (16.79)	p= .040	70.38 (10.57)	p= .450
Village ^c	19	7.0	70.05 (16.42)	c>b	67.68 (13.29)	
Smoking						
Yes	49	18.0	60.10 (15.98)	t= − .847	69.59 (11.76)	t= − .747
No	223	82.0	62.43 (17.77)	p= .056	70.97 (11.75)	p= .825
Alcohol consumption						
Yes	8	2.9	62.50(20.90)	t= .080	74.87 (11.39)	t= 1.014
No	264	97.1	62.00 (17.39)	p= .887	70.60 (11.75)	p= .970
Menopausal status						
Yes	148	54.4	59.70 (17.27)	t= − 2.407	70.87 (11.88)	t= .220
No	124	45.6	64.77 (17.34)	p= .632	70.55 (11.62)	p= .987
Having a chronic illness						
Yes	128	47.1	62.14 (17.49)	t= .112	71.39 (11.53)	t= .887
No	144	52.9	61.90 (17.48)	p= .885	70.13 (11.93)	p= .462
Presence of a constant companion at the hospital						
Yes	263	96.7	61.70 (17.48)	t= − 1.575	70.93 (11.68)	t= 1.549
No	9	3.3	71.00 (14.78)	p= .402	64.77 (12.75)	p= .876
Impact on sexual life after hysterectomy surgery						
Yes	74	27.2	59.90 (17.91)	t= − 1.219	73.77(10.00)	t= 2.883
No	198	72.8	62.80(17.26)	p= .854	69.59 (12.16)	p= .004
Age (years) mean±SD	53.06	±8.62				
Child number, mean±SD	2.88	±1.49				

SD: Standard Deviation; SCNI: Spiritual Care Needs Inventory; MSPSS: Multidimensional Scale of Perceived Social Support; t: independent samples t-test; F: One-way analysis of variance; Difference Between Groups: Bonferroni test; p=Significance Level.

Bold values: $p < .05$ is a statistically significant value

Table 2. SCNI and MSPSS scores of women who underwent hysterectomy (n = 272)

Scale and Sub-scales	Mean ± SD	Min-Max
SCNI	62.01±17.45	23-105
Meaning and hope	35.27±1.09	13-65
Caring and respect	26.73±8.37	9-40
MSPSS	70.72±11.74	31-84
Friends	23.18±5.09	6 – 28
Family	25.27±3.08	10-28
Significant other	22.88±5.64	4-28

SCNI: Spiritual Care Needs Inventory; MSPSS: Multidimensional Scale of Perceived Social Support; SD: Standard Deviation

Table 3. Relationship between Perceived Social Support and Spiritual Care needs of women who underwent hysterectomy, sub-scales, age, and the number of children (n=272)

Variables	Multidimensional Scale of Perceived Social Support	
	r	p
Spiritual Care Needs Inventory	-.058	.343
Meaning and hope	.035	.564
Caring and respect	-.166	.006
Age	.031	.613
Number of children	-.017	.780

r: Pearson correlation test; bold value: $p < .05$ is a statistically significant value

Table 4. Multilinear regression analysis according to the factors affecting the Perceived Social Support of women who underwent hysterectomy

Variables	Multidimensional Scale of Perceived Social Support				
	β_0 (%95 CI)	Std. Error	Beta	t	p value
Constant	75.140	2.835	-	26.503	.000
Meaning and hope	.236	.081	.221	2.937	.004
Caring and respect	-.380	.107	-.271	-3.567	.000
Working status Working	.524	.811	.038	.645	.519
Family type Nuclear family	-2.528	1.562	-.097	-1.618	.107
Impact on sexual life after hysterectomy surgery Yes	-3.347	1.566	-.127	-2.137	.034

β_0 = Unstandardized beta coefficient; Beta= Standardized coefficient; $F=5.177$; $p < .001$; $R^2=0.089$; Adjusted $R^2 = 0.072$, Durbin Watson=1.758

4. DISCUSSION

Hysterectomy is one of the most common surgical procedures in gynecology worldwide. It is directly related to a woman's fertility, and removal of the uterus could have irreparable psychological, physiological, and sexual consequences

(1,3,22). Women who underwent hysterectomy have been reported to experience physical discomfort and negative emotions and have strong mental resilience and self-adjustment skills to cope with negative emotions. Support and assistance to be provided by family, friends, and healthcare professionals is very important, particularly in the early postoperative period. The understanding and help of her husband are undoubtedly the most important of all the support needed by a female patient. Meanwhile, identifying and eliminating prejudices against women who have undergone a hysterectomy in countries and regions with different cultural beliefs are considered to reduce the spiritual burden and social pressure on women (2,5,23). The women in this study were found to have an above-average level of spiritual care needs and a high level of perceived social support. The spiritual needs of women living in the village were found to be higher, which is considered to have resulted from the inadequate educational and sociocultural characteristics of individuals living in the village.

Studies have reported on women's need for education about bodily changes and expectations after hysterectomy as well as the importance of social support from family, friends, and other women (24-26). This study determined a relationship between the effects on sexual life after hysterectomy surgery and perceived social support, which is in line with the literature. Regression analysis results in our study also showed that the perceived social support score of women whose sexual life was affected after hysterectomy surgery was lower than those whose sexual life was not affected. A study reported a decrease in marital adjustment and sexual function following hysterectomy. Therefore, specialized treatment and family counseling interventions are reported to be necessary to improve sexual performance and marital adjustment in women who underwent hysterectomy (27,28). After hysterectomy, women may experience sexual dysfunction and psychological challenges, which can increase their need for social support. However, when adequate support is not provided, their perception of social support may be negatively impacted. Furthermore, societal expectations may also influence this perception, as women may experience feelings of loneliness and social exclusion after the surgery (15,16). Therefore, our findings suggest that the perception of social support after hysterectomy may be influenced by the emotional and psychological challenges women face, such as sexual dysfunction and feelings of isolation, which can alter their social support needs and perceptions

Social support could come from family members, such as parents or siblings, friends, or health professionals. Therefore, knowing the availability of others to lend a helping hand in times of need is considered to be an important social resource. Surgical patients who have inadequate social support networks have been reported to be at greater risk for poor surgical outcomes (29,30). Since social support is one of the important factors affecting women's lives, the focus should be on building and strengthening the patient support network when working with female patients who are

in the process of hysterectomy surgery (7,30,31). Our study highlights the importance of spiritual care needs in women undergoing hysterectomy. This study found that “caring and respect”, one of the sub-scales of spiritual care needs, decreased with the increase in the perceived social support. This may result from the decrease in the spiritual needs of women who had more social support. This result may also be associated with strong family ties in Turkish society. This study showed that their children and husbands provided the greatest support to women after hysterectomy surgery. Our study reinforces the idea that a holistic approach, integrating spiritual care and social support, is essential in improving the psychological and emotional outcomes for women post-hysterectomy.

The topic and the sample size of the study constitute the strength of the study, which is considered to contribute to the literature. The limitation of the study is that the data were collected from a single hospital in a region. Therefore, the study results cannot be generalized.

5. CONCLUSION

Women's spiritual care needs and perceived social support should be considered and evaluated while they are provided with patient-centered care and holistic care during the hysterectomy surgery process. In this regard, women should be provided with quality healthcare services. Trainings should be planned to meet the spiritual and social support needs of women in the hysterectomy process. It is recommended to establish protocols prepared in line with evidence-based care for the monitoring and care of women who underwent hysterectomy.

Acknowledgements: Authors would like to thank all the participants for being a part of this study.

Funding: The author(s) received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Ondokuz Mayıs University, Noninvasive Clinic Ethics Committee (Approval date: 27.05.2022.; Number: 2022-509)

Peer-review: Externally peer-reviewed.

Author Contributions:

Research idea: ŞB, ŞKA

Design of the study: ŞB, ŞKA

Acquisition of data for the study: EÇK

Analysis of data for the study: ŞB

Interpretation of data for the study: ŞB, ŞKA, EÇK

Drafting the manuscript: ŞB, ŞKA, EÇK

Revising it critically for important intellectual content: ŞB, ŞKA, EÇK

Final approval of the version to be published: ŞB, ŞKA, EÇK

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A Natural Hope for Salivary Gland Health: Histological Evaluation of Cinnamic Acid in Diabetic Rats

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Received: April 15, 2025

Accepted: June 23, 2025

ABSTRACT

Objective: The aim of this study was to investigate the possible potential of cinnamic acid in preserving the structure and function of the parotid gland in diabetic rats.

Methods: The rats (n=32) were equally divided into four groups: Control (only physiological serum), Cinnamic acid (cinnamic acid 50 mg/kg/day), Streptozotocin-induced diabetes (experimentally-induced diabetes by intraperitoneal injection of streptozotocin 65 mg/kg), and Diabetes + cinnamic acid (cinnamic acid after diabetes induction). After the rats were sacrificed, tissue samples were obtained and processed for paraffin embedding. To visualize the histological structure, Hematoxylin&Eosin, Masson's Trichrome, and Periodic Acid-Schiff histochemical stains were applied, and images were captured.

Results: While normal serous acini, canal structures and normal connective tissue were observed in the control and cinnamic acid groups, deformation and atrophy were observed in some acinar cells in the diabetic group. In the treatment group, improvement in the shape of acinar cells and regular arrangement of parietal cells in glandular canals were noted compared to the diabetic group. The intense vacuolization observed in acinar cells in the diabetic group decreased in the treatment group. Periodic Acid-Schiff – positive reaction was determined in the basement membranes of acinar cells and parietal cells in glandular canals in all groups. No visible difference was obtained between the groups.

Conclusion: Diabetes affects the parotid gland, and cinnamic acid has been shown to prove a healing effect on deformed areas. Our study will guide further research in this area.

Keywords: Type 1 diabetes, cinnamic acid, parotid gland, histology

1. INTRODUCTION

Diabetes Mellitus (DM) is a common metabolic disease that occurs when the pancreas cannot produce insulin, called type 1 diabetes, or when body cells cannot use this insulin, called type 2 diabetes (1). Type 1 Diabetes is an autoimmune disease that occurs when the beta cells in the pancreas are destroyed by T cells, causing a disorder in their insulin production functions and the formation of autoantibodies at a rate of 70-90% (2). According to the World Health Organization's Diabetes Atlas, while the number of individuals with diabetes in the world is 537 million as of 2021, it is predicted that this number will increase by approximately 20% in 2030 to 643 million and by 46% (compared to 2021) to 783 million in 2045 (3). Type 1 diabetes is a disease characterized by chronic hyperglycemia, which often leads to diabetic complications

and affects systems such as the cardiovascular system, nervous system, or organs such as the kidneys, eyes, and salivary glands. The increasing complications and severity of diabetes have caused serious morbidity and mortality, and have also affected the cost of healthcare (4-6).

Salivary glands play a major role in maintaining oral health. The saliva they secrete as exocrine glands contains mostly molecules such as water, mucus proteins, proteoglycans, salivary amylase, proline-rich proteins and salivary agglutinin. They have the ability to help with important functions such as moisturizing the epithelium, facilitating chewing, tasting, swallowing and speaking. They also promote mineralization with bicarbonate ions, which prevent tooth enamel from decalcifying thanks to their buffering systems (7).

How to cite this article: Kılınç D, Türk S, Özyurt BG, Öztıp M. A Natural Hope for Salivary Gland Health: Histological Evaluation of Cinnamic Acid in Diabetic Rats. Clin Exp Health Sci 2025; 15: 447-452. <https://doi.org/10.33808/clinexphealthsci.1676505>

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Recent studies have revealed a significant link between salivary gland disorders and DM. Saliva composition is affected by the metabolic, neurological, immunological, hormonal and nutritional conditions of the individual. Both the oral, dental and digestive functions of saliva depend primarily on the precise composition of organic substances in the secretory product. Accordingly, any change in the composition of saliva can lead to significant deterioration in salivary functions and trigger long-term complications in both the oral mucosa and the body system (6,8-11).

Cinnamic acid (CA)(3-phenylprop-2-enoic acid) is an organic acid that is commonly found in plants. Cinnamic acid also has antifungal, antimicrobial, antioxidant, antimutogenic, anticancer and anti-inflammatory effects (12-14). Cinnamic acid and its derivatives have been reported to have significant antidiabetic effects such as improving insulin secretion, accelerating glycolysis in the liver, increasing adiponectin secretion, increasing glucose uptake, improving pancreatic β -cell function, and reducing diabetes-induced protein glycation, and preventing diabetes complications (15-17).

Thus, it is revealed that cinnamic acid exhibits anti-diabetic effects by improving glucose tolerance and insulin secretion (18). These effects disrupt the balance of the body's defense system and trigger oxidative stress. In addition, dehydration and inadequate blood glucose control caused by diabetic effects negatively affect the function of the salivary glands and weaken their resistance to infections. This can lead to infections triggered by the microflora in the mouth and cause inflammation and cellular damage in the salivary glands (2).

As is the case with numerous pharmaceutical treatments, experiencing side effects in Type 1 diabetes is unavoidable. Therefore, medicinal plants and polyphenolic compounds obtained from them, which have been widely used in traditional medicine for centuries, have recently been used in the treatment and prevention of various metabolic diseases. No study has been found showing the effects of cinnamic acid on histopathological changes in salivary glands of diabetic rats. This study aimed to investigate the possible protective effects of cinnamic acid against changes in the histological structure of the parotid gland caused by streptozotocin (STZ) in a diabetic rat model.

2. METHODS

2.1. Experimental Animals and Ethical Declaration

The Local Ethics Committee approved this study for Animal Experiments of Burdur Mehmet Akif Ersoy University Presidency with decision number 1.288. 32 male Wistar albino rats weighing 200-280 grams and aged 8-12 weeks obtained from Burdur Mehmet Akif Ersoy University Experimental Animals Production and Experimental Research Center were used. The animals were placed in plastic cages with stainless steel grid tops and kept under a 12-h light/dark cycle with controlled temperature ($23 \pm 2^\circ\text{C}$) and humidity (50%). The animals were fed with standard laboratory feed and were

allowed access to food and drinking water ad libitum. Blood sugar levels of animals were measured using the Accu-Check Performa Nano glucose meter (Roche, Germany) before the commencement of the study (13).

2.2. Experimental Design

Four groups were formed as control group (C) (n:8), streptozotocin-induced diabetes group (STZ-DM) (n:8), diabetes+cinnamic acid group (STZ-DM+CA) (n:8) and cinnamic acid (CA) (n:8) group. The CA group included animals that received an oral administration of 50 mg/kg CA in saline for 28 days after diabetes was induced. To induce type 1 diabetes in rats, 65 mg/kg dose of streptozotocin (19) freshly prepared in sodium citrate buffer (0.1 M, pH 4.5) (19) was administered intraperitoneally. After 72 h of diabetes induction, rats with fasted blood glucose level above 200 mg/dL were considered as diabetic. Following diabetic induction, only per os physiological serum was given to the control and diabetes groups for 28 days; 50 mg/kg dose of cinnamic acid prepared in DMSO was given orally to the cinnamic acid group and STZ-DM+CA group via gavage (13). In order to monitor whether the animals remained diabetic, weekly fasted blood glucose levels of animals (without feeding for 6 hours) were measured using the Accu-Chek Performa Nano glucose meter (Roche, Germany) throughout the study. At the end of this period, euthanasia was performed by cervical dislocation after anesthesia with ketamine/xylazine (90/10 mg/kg; Alfasan/Bayer) (20). The salivary gland material was then fixed in Bouin's solution and dehydrated in alcohol series of increasing concentrations. The samples were then passed through methyl benzoate and benzene series and embedded in paraffin.

2.3. Tissue Preparation for Histochemical Staining

Sections were taken, deparaffinized with xylol, and rehydrated in decreasing concentrations of alcohol (96%, 80%, 70%, 60%, 50% and then distilled water). The prepared preparations were stained with Hematoxylin and Eosin (H&E) for routine histological examination, Masson Trichrome (MT) for collagen fibers, and Periodic Acid Schiff (PAS) to show the polysaccharide concentration in the acinus and duct cells of the parotid gland (21). Then, the preparations were taken into distilled water and dehydrated, xylene and the samples were gradually rehydrated, and the slides closed with entellan. Figures were obtained using a light microscope (Zeiss, Germany) and photographed using DP72 digital camera (Olympus, Tokyo, Japan).

3. RESULTS

The examinations performed on tissue sections stained with H&E, MT, and PAS staining results of parotid gland were showed in Figure 1.

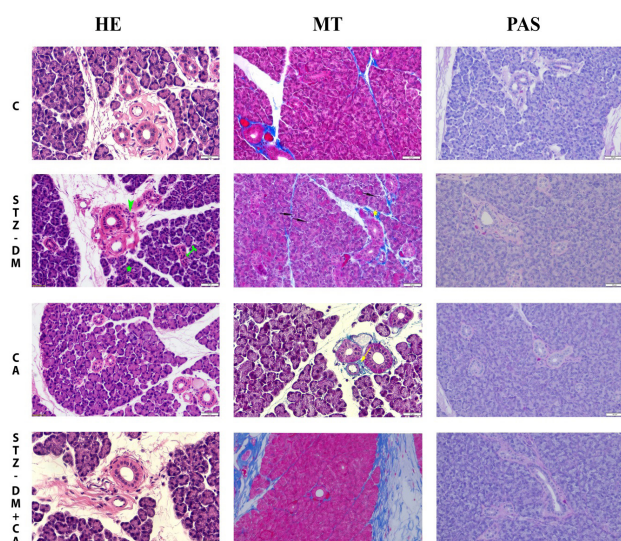


Figure 1. Microscopic image of the parotid gland for all groups, green star; degenerative acinar cells, green arrowhead; inflammatory cell infiltration into the connective tissue, green arrow; degenerative striated duct, H&E staining. Yellow asterisk; collagen fibers surrounding ducts and blood vessels, black arrows; acinar cells containing lipid droplets, yellow arrow; decreased collagen fibers surrounding ducts and blood vessels, MT staining. PAS-positive reaction in the basement membranes of acinar cells in the glandular ducts and in parietal cells, PAS staining. Scale bar: 50 μ m.

3.1. H&E staining results

Normal serous acinus structures, duct structures, and normal connective tissue structures were observed in the parotid gland of control and CA groups. The lumen of the gland ducts was also clearly visible in the parotid parenchyma, which consisted of neatly packed pure serous acini. The intralobular ducts exhibited normal histological features, including intercalated ducts and poorly defined lobules of serous acini, lined by pyramidal basophilic cells and characterized by round nuclei, separated by thin septa. The striated ducts were easily recognized as they were lined by simple columnar cells with round nuclei and basal striations.

STZ-DM group showed a widening of the interlobular space, some acini were confluent and fused, while others were shrunk and atrophic. In addition, most acini showed darkly stained nuclei of varying size and shape. Some ducts were dilated and surrounded by inflammatory cell infiltration and fibrous tissue. The ducts showed structural changes; some showed disruption and disorganization of their epithelial lining, and some showed retention of secretions. The duct cells showed darkly stained nuclei flattened with cytoplasmic vacuolation.

STZ-DM+CA group, acinar cells showed improvement in their shape, prominent lumen in gland ducts and regular parietal cells were detected compared to the STZ-DM group

3.2. Masson's Trichrome results

Normal connective tissue was observed around intralobular ducts and blood vessels in the control group. In addition, a regular structure in acinar cells and regular arrangement of parietal cells in glandular ducts and their lumen were observed.

Masson's trichrome-stained slides of the parotid gland of the diabetic rat showed the presence of collagen fibers, especially surrounding the ducts and blood vessels. Vacuolization of acinar cells, glandular ducts with irregular parietal cells, and dilated glandular lumen were determined in the parotid gland.

Collagen deposition between lobules in parotid gland decreased significantly in the CA group compared to control and STZ groups. Whereas collagen decreased significantly in the STZ + CA group compared to STZ group (Figure 1)

The number of lipid droplet cells in the parotid gland was significantly reduced in the STZ-DM+CA group compared to the STZ-DM group.

3.3. PAS results

Samples from all groups were examined in the parotid gland and a positive reaction was determined in the basement membranes of acinar cells and parietal cells in glandular ducts. No visible difference was determined between the groups.

Mast cells with dark purple-stained granules were determined in the connective tissue between the lobes, especially around the vessels.

4. DISCUSSION

Salivary glands have an important role in maintaining oral health as they are exocrine glands that secrete saliva, an enriched medium consisting fundamentally of water, mucus proteins, proteoglycans, salivary amylase, proline-rich proteins and salivary agglutinin. They have important functions such as epithelial hydration, ease of chewing, taste, swallowing and speech. They also have a buffering effect with bicarbonate ions that prevent enamel decalcification and promote remineralization (22).

DM is a multifactorial disease triggered by a combination of epigenetic, genetic, and environmental factors. Increased life expectancy and unhealthy lifestyle habits, such as sedentary lifestyle and consumption of foods rich in saturated fats and added sugars, are risk factors for the development of obesity and associated comorbidities such as metabolic syndrome, also called insulin resistance syndrome (8,23).

DM progresses silently in the early stages (24,25), but in the long term, it damages many vital organs such as the kidneys, blood vessels, heart, and bones (2,26). The high prevalence of DM, its fatal complications, and the incomplete pathogenesis

of DM necessitate the use of preclinical models to better understand the disease.

Diabetes leads to changes in the oral cavity (23,27). Most of these changes are directly related to the reduction in salivary flow and changes in salivary composition, and abnormalities in collagen metabolism in the mucosa and the formation of glycated end products that negatively affect collagen stability and vascular integrity. Several studies have reported a negative impact on periodontal health (28). In one study, the decrease in PAS reaction in acinus and ductal cells in the diabetic group (29) was explained by the decrease in polysaccharide concentration in the acinus (10). However, Nicolau et al. (30) observed that enhanced glycogen synthase activity and decreased glycogen phosphorylase activity resulted in glycogen buildup in the salivary glands of diabetic rats. In this study, no significant difference was detected between the groups in terms of PAS-positive reaction in the basement membranes of acinar cells and gland parietal cells.

Cinnamic acid and its derivatives are reported to have important antidiabetic effects such as improving insulin secretion, accelerating glycolysis in the liver, increasing adiponectin secretion, increasing glucose uptake, improving pancreatic β -cell function and reducing diabetes-induced protein glycation, and prevent diabetes complications (15,17,31). The study showed that cinnamic acid improved memory by reducing oxidative stress and cholinergic dysfunction in the brain of diabetic mice (32). In cell culture and animal experiments, it has been reported that cinnamic acid derivatives have stimulating effects on insulin secretion, depending on the dose (33). These effects disrupt the balance of the body's defense system and trigger oxidative stress. In addition, dehydration and inadequate blood glucose control caused by diabetic effects negatively affect the function of the salivary glands and weaken their resistance to infections. This can lead to infections triggered by the microflora in the mouth and cause inflammation and cellular damage in the salivary glands (2).

Studies have reported that various damages such as cellular hypertrophy, atrophy, hyperplasia, and DNA damage occur with the development of diabetes in the major salivary glands (6,34). In studies conducted by Hasegawa et al. (35), it was stated that the parotid gland was damaged and its functions were impaired in animals with experimental diabetes and that this could be due to oral infections developing due to decreased salivary secretion. In addition, it has been stated that various secretory irregularities occur in the salivary glands of diabetic and menopausal rats, and that these irregularities may lead to damage in the acinus epithelium and trigger the migration of inflammatory cells with an increase in the protein ratio in the secretory composition and the accumulation of unsaturated fat droplets (36). In this study, morphological and structural abnormalities were observed, especially in the parotid gland of STZ-DM rats. In parallel with this study, Morsy et al. (6) reported that abundant collagen fibers were seen in the parotid gland of a diabetic rat, especially around the ducts and blood vessels.

Anderson et al. (37) suggested that there were numerous lipid droplets, especially in the serous acini of the large salivary glands of diabetic rats, and that this could be due to excessive uptake into the cell to be used as an energy source or to decreased synthesis in secretory granules and plasma membrane material. Vacuolation was detected in parotid acinar cells in short-term DM, young and aging rats (8). In this study, the number of lipid droplet cells in the parotid gland was significantly reduced in the STZ-DM+CA group compared to the STZ-DM group.

Researchers who examined the effect of ascorbic acid on rats with a diabetes model reported that the STZ group showed normal glandular architecture with irregular acini, cytoplasmic vacuolization in glandular cells with apoptotic nuclei, thickened connective tissue septa with leukocyte infiltration, and congested vessels (10). Another study supported this with similar findings by (9,38), who reported severe acinar cell deformation and atrophy with reduced secretory granules, vacuolization, and leukocyte infiltration in the salivary glands of diabetic rats. In our study, it was determined that cinnamic acid improved the shape of acinar cells and had prominent lumens and regular parietal cells in the gland ducts in the salivary glands of diabetic rats compared to the DM group. The parotid glands showed a very similar picture to the control group in that the majority of acini and ducts had normal histological appearance.

One study showed that oral administration of CA could reduce body weight, FBG, and blood pressure in DIO mice and improve lipid profile (14). Moreover, CA derivatives have synergistic interactions with oral hypoglycemic drugs such as thiazolidinedione and metformin, which are useful in the treatment of diabetes (39), therefore, CA may offer preventive and therapeutic benefits in combating obesity and vascular dysfunction in diabetes.

5. CONCLUSION

Various mechanisms have been proposed by researchers to explain the effect of cinnamic acid and its derivatives on the management and prevention of diabetes and its complications. Although their potential benefits have been demonstrated in vitro and preclinical studies, there is insufficient clinical evidence to prove these beneficial effects. Therefore, more epidemiological studies are needed to evaluate the role of cinnamic acid on diabetes and its complications.

Acknowledgments: The authors thank TUBITAK for their support through the 2209-A University Students Research Projects Support Program 2023 (Project No: 1919B012319139).

Funding: The present work was supported by the fund of TUBITAK through the 2209-A University Students Research Projects Support Program 2023 (Project no: 1919B012319139).

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have no conflicts of interest to declare.

Ethics: Ethics committee approval was obtained from Burdur Mehmet Akif Ersoy University Local Ethics Committee (Date: 24.04.2024, Number: 1288)

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Design of the study: ST, DK, GBÖ

Acquisition of data for the study: ST, DK

Analysis of data for the study: ST, DK

Interpretation of data for the study: ST, DK

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Final approval of the version to be published: ST, DK, GBÖ, MÖ

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Impact of Nutrition Education on Dietary Inflammatory Index and Anthropometric Measurements in Individuals Who Regularly Engage in Exercise

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Received: April 15, 2025

Accepted: May 21, 2025

ABSTRACT

Objective: This study aims to evaluate the effects of nutrition education on Dietary Inflammatory Index (DII) and anthropometric measurements in individuals who engage in regular exercise.

Methods: This study, involving individuals who engaged in regular exercise, was conducted at a sports center between September and November 2024. In this study, one hundred participants received nutrition education, pre-test anthropometric measurements were made on the same day, and 24-hour food consumption records were taken. Post-test anthropometric measurements were taken 30 days after the initial measurement, 24-hour food consumption records were collected, and food consumption was evaluated using Bebis software, while DII was calculated.

Results: One month after nutrition education, it was shown that the levels of Vitamin A ($U=908$; $p<.05$) and Vitamin E ($t=2.503$; $p<.05$) intake in males had increased significantly compared to females. Statistically significant decreases were observed in the hip circumference ($p=.030$), triceps ($p=.008$), suprailiac ($p=.010$), chest ($p=.013$), and femur ($p<.001$) skinfold thickness measurements when comparing pre – and post-training values. There was no statistically significant difference between the pretest and posttest total DII scores of the participants ($p>.05$).

Conclusions: The findings indicate a positive impact of nutrition education on anthropometric measurements; however, no significant effect was observed regarding DII scores.

Keywords: dietary inflammatory index; anthropometry; nutrition education; exercise

1. INTRODUCTION

In the general population, regular exercise is widely recognized for its positive impacts on physical fitness, including increased aerobic capacity and muscle strength. These benefits are crucial for maintaining a physically active lifestyle and for overall health. To assess the role of regular exercise in managing overweight or obesity in adults, examining its impacts on physical fitness within this specific group is essential. In general, physical fitness (per kilogram of body weight) is lower in individuals with high BMI or obesity than in those of normal weight (1).

Nutrition is defined as a conscious behavior aimed at maintaining and improving health and enhancing the quality of life by consuming the necessary nutrients in adequate amounts and at appropriate times. As stated in the current

literature, adequate and balanced nutrition is among the protective factors that play a role in reducing health problems caused by nutrition (2).

Nutrition-related health issues are highly prevalent among both children and adults. Nutrition serves as a significant risk factor that notably influences people's health and is changeable. Indeed, dietary patterns, including food choices, consumption occasions, and habitual behaviors, have been demonstrated to exert a pivotal influence on the determination of individuals' health status (3). A state of energy imbalance, characterized by an excess of energy intake relative to expenditure, can lead to adverse health consequences, including overweight and obesity. It is imperative to maintain a balance between energy

How to cite this article: Zelka FZ, Aytulu T. Impact of Nutrition Education on Dietary Inflammatory Index and Anthropometric Measurements in Individuals Who Regularly Engage in Exercise. Clin Exp Health Sci 2025; 15: 453-460. <https://doi.org/10.33808/clinexphealthsci.1676934>

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expenditure and intake to ensure optimal health and well-being. Consequently, diet quality is a pivotal factor in maintaining a healthy body mass index (BMI). A healthy diet consists of consuming a variety of foods on a daily basis, including plant-based options (i.e., fruits and vegetables), grains, proteins, dairy, and fats. Additionally, following a healthy diet includes: a. selecting foods and beverages in portions that contribute to achieving and sustaining a healthy weight, b. consuming five or more servings of various vegetables and fruits each day, c. favoring whole grains over refined grains, and d. reducing the intake of red meat and processed meat products (4).

The benefits of nutrition and physical activity are often examined separately. However, it is becoming increasingly evident that strategies integrating nutrition and physical activity may yield more substantial and favorable health outcomes compared to approaches that focus on just one of these aspects. This dual approach may also contribute to immune system strengthening (5). Research by Sánchez-Díaz et al (6) suggests that implementing nutritional education for athletes participating in team sports can effectively improve their eating habits, anthropometry, and nutritional knowledge.

The Dietary Inflammatory Index (DII) was first developed by Cavicchia et al (7), demonstrating a negative correlation between DII and C-reactive protein (CRP). In adults, it is particularly associated with CRP, Interleukin-6 (IL-6), and tumor necrosis factor alpha (TNF- α) (8). The DII is a tool that is used to further examine the processes through which various dietary components contribute to inflammation. The method under discussion is predicated on a total of 45 food parameters, encompassing a range of compounds, nutrients, and food items that have been identified in the extant literature as having either anti – or pro-inflammatory properties. A notable advantage of DII is that, in contrast to the analysis of individual dietary compounds, it examines dietary patterns, thereby elucidating the intricate interplay among nutrients and compounds present within foods and diets. A substantial body of observational research has examined the association between DII and the risk of developing chronic diseases (9). A study found that people with a low DII score who were active had a 39% reduced risk of all-cause mortality when compared to those with a higher DII score who were sedentary. DII and physical activity were each found to be associated with mortality; specifically, DII was positively linked and physical activity was inversely linked to the risk of all-cause mortality (10).

This study aimed to examine the impacts of nutrition education on anthropometric measurements and the DII in individuals engaging in regular exercise.

2. METHODS

2.1. Research Group and Ethics Approval

In our study, a total of 100 individuals aged between 18 and 45 who engage in exercise regularly at a sports center in Istanbul were included. Regular exercise was defined as engaging in a minimum of 150 to 300 minutes of moderate-intensity aerobic physical activity or a minimum of 75 to 150 minutes of high-intensity aerobic physical activity weekly, as recommended by the World Health Organization (WHO) (11). Ethics committee approval for the research was obtained from the Üsküdar University Noninvasive Clinic Research Ethics Committee (Approval date: 26.03.2024; Number:03). Prior to participation, informed consent was obtained from all subjects who had volunteered for this study in either written or oral form.

2.2. Sample Size

The G*Power 3.1.9.4 package program was utilized to calculate the sample size of the study. When the effect size was set at 0.5, the study's power was determined to be 0.95, and the Type I error level was set at 0.05, the minimum required sample size was determined to be 54 individuals. Considering the possibility of missing data and losses in the study and to make the results of the study more representative of the general population, we increased the sample size to 100.

2.3. Inclusion And Exclusion Criteria

Healthy individuals between the ages of 18-45 years and regularly engage in exercise according to WHO criteria (11) were included in the study. Individuals suffering from chronic diseases who adhered to a particular dietary regimen, along with pregnant women, were excluded from the study.

2.4. Research Design

Two different measurements were taken using anthropometric methods before and one month after nutrition education was provided to the participants who consented to be part of the study, and 24-hour food consumption records were collected simultaneously with these measurements. Based on this data, alterations in the anthropometric measurements of the subjects were examined, and DII values were computed from the food consumption records. The food consumption record form, which was prepared by the researcher, was completed by the subjects retrospectively for a 24-hour period. A thorough evaluation of the collected food consumption records was conducted using the Nutrition Information System (BeBis).

Table 1. Descriptive statistics of demographic, health and habit findings of individuals according to gender

	Male (n=49)		Female (n=51)		Total (n=100)	
	N	%	N	%	N	%
Age (years)	24.57	6.49	30.35	8.40	27.52	8.03
Marital Status						
Married	6	12.2	20	39.2	26	26.0
Single	43	87.8	31	60.8	74	74.0
Education Status						
High School	21	42.9	15	29.4	36	36.0
Bachelor's degree	24	49.0	31	60.8	55	55.0
Postgraduate	4	8.2	5	9.8	9	9.0
Profession						
Officer	1	2.0	3	5.9	4	4.0
Worker/Private Sector	19	38.8	17	33.3	36	36.0
Self-employment	4	8.2	4	7.8	8	8.0
Student	24	49.0	14	27.5	38	38.0
Housewife	0	0.0	9	17.6	9	9.0
Not working	1	2.0	4	7.8	5	5.0
Income Level						
My Income is Less than My Expenses	23	46.9	26	51.0	49	49.0
My Income Equals My Expenses	17	34.7	12	23.5	29	29.0
My Income Exceeds My Expenses	9	18.4	13	25.5	22	22.0
Nutritional Supplement Use						
Yes	5	10.2	13	25.5	18	18.0
No	44	89.8	38	74.5	82	82.0
Type of Dietary Supplement Used*						
Omega3	1	20.0	7	53.8	8	44.4
Vitamin D	2	40.0	6	46.2	8	44.4
Vitamin C	1	20.0	3	23.1	4	22.2
Multivitamin	1	20.0	2	15.4	3	16.7
Magnesium	3	60.0	1	7.7	4	22.2
Smoking Status	N	%	N	%	N	%
Yes	22	44.9	10	19.6	32	32.0
No.	27	55.1	41	80.4	68	68.0
Amount of Smoking (pcs/day) ()	14.00	5.00	8.80	4.89	12.38	5.47
Alcohol Use Status						
Yes	11	22.4	11	21.6	22	22.0
No	38	77.6	40	78.4	78	78.0
Amount of Alcohol Use (drinking cups/month) ()	2.36	1.21	2.64	1.36	2.50	1.26
Daily Water Consumption (ml/day) ()	2122.45	780.83	1815.69	624.94	1966.00	718.76
Duration of Physical Activity (hours/week) ()	7.77	3.64	5.98	2.81	6.85	3.35

*: Multiple responses have been provided.

2.5. Dietary Inflammatory Index (DII)

Calculations were made using BeBis using z-scores from each participant's daily food/nutrient intake. Z-scores were determined by calculating the difference between

an individual's daily intake and the standard global intake, and dividing this by the standard deviation of the nutrient or nutrients in question. Subsequently, these z-scores were converted into percentile scores. To obtain a distribution that is symmetric about the mean, each percentile score was multiplied by two and then added to one. The centralized percentile values obtained for nutrients and nutrients were then multiplied by the "customized complete inflammatory effect score" calculated by Shivappa et al. (8). The results were aggregated to calculate the dietary inflammatory index (DII) score, which indicates the inflammatory burden of people's daily diets. If a nutrient or nutrient had a proinflammatory effect on inflammation markers such as C-reactive protein, it was scored as (+1). If it had an anti-inflammatory effect, it was scored as (-1). If it had no effect, it was scored as (0). The utilization of this scoring method was intended to ascertain the inflammatory or anti-inflammatory potential of nutrients.

2.6. The Content of The Nutrition Education

Individuals received face-to-face nutrition education sessions lasting an average of 20 minutes. During these sessions, they were informed about the daily requirements of macro and micronutrients, water consumption, and physical activity. Additionally, the training covered how to organize nutrition in terms of carbohydrates, proteins, and fats to support physical activity, as well as the consumption of nutritional supplements.

2.7. Data Collection

The researchers measured a number of anthropometric variables, including body weight, height, hip and waist circumference, triceps skinfold thickness (ST), biceps ST, scapula ST, suprailiac ST, chest ST, abdomen ST, thigh ST, and upper middle arm circumference. Furthermore, a 24-hour dietary record was documented. The measurements were taken prior to the intervention and once more one month after the conclusion of the nutrition education program. The BMI was computed and subsequently classified in accordance with the criteria established by WHO (12).

2.8. Data Analysis

Descriptive statistics pertaining to categorical variables are expressed as frequency and percentage. The statistical test known as the "Shapiro-Wilk test" was employed to verify whether the numerical variables conformed to a normal distribution. The descriptive statistics of the numerical variables were presented as the mean $\pm$ standard deviation ($\bar{X} \pm SD$) for data that was normally distributed and as the median (min-max) for data that was non-normally distributed. The comparison of two independent groups with normal distribution was made with an Independent Sample t-test. The comparison of two dependent groups with normal distribution was made with the "Dependent Sample T Test," and the comparison of two dependent groups without normal distribution was made with the "Wilcoxon Signed

Table 2. Comparison of energy, macronutrients and micronutrients differences after nutrition education among individuals according to gender

	Male		Female			
		Median (min-max)		Median (min-max)	t-U	P
Energy (kcal)	97,72534,95	93,9 (-1467,8-1012,8)	-52,40387,20	26,4 (-825,9-1058,6)	t=1.612	.110
CHO (g)	15,4995,97	13,2 (-245,7-201,3)	-11,3073,19	-18,1 (-156,5-193,3)	t=1.573	.119
Protein (g)	-6,1730,80	-6,5 (-90,8-64,1)	-1,5825,99	-0,8 (-78,3-59,3)	t=-0.808	.421
Fat (g)	6,0626,88	3,2 (-55,7-78,6)	-0,8626,60	0,9 (-57,4-64,4)	t=1.295	.198
Saturated Fat (g)	4,0531,43	-1,8 (-22,3-201,2)	0,9123,17	-0,8 (-22,5-145,8)	U=1191	.687
Monounsaturated Fat (g)	5,3723,92	1,8 (-18,3-149,9)	2,1419,46	-0,8 (-25,2-102,2)	U=1180	.632
Polyunsaturated Fat (g)	2,8410,85	0,8 (-29,6-27,9)	0,559,79	-0,7 (-18,3-27,8)	U=1074	.226
Fiber (g)	6,6513,12	4 (-29,2-36,2)	4,2514,98	1,4 (-20,3-81,4)	U=1034	.137
Vitamin A (µg)	223,191697,92	192,6 (-8634,3-2252,7)	108,381002,74	98,9 (-1503,9-5538,8)	U=908	.019*
Vitamin D (µg)	-10,0065,35	-13,5 (-117,9-234,9)	-5,8963,32	-8,2 (-162,6-156,7)	U=1146	.475
Vitamin E (mg)	3,619,28	2,1 (-19-27,8)	-1,129,60	-1,4 (-34,1-18)	t=2.503	.014*
Vitamin K (µg)	77,47205,07	22,2 (-386,9-540,3)	48,65210,75	22 (-732,6-402,1)	U=1249	.997
Vitamin B1 Thiamine (mg)	0,070,73	0,1 (-3,5-1,5)	0,010,75	-0,04 (-2,1-2,6)	U=1080.5	.244
Vitamin B2 Riboflavin (mg)	-0,141,03	-0,1 (-4,8-3,2)	0,110,58	-0,01 (-0,8-2,8)	U=1099	.299
Niacin (mg)	-0,4112,14	0,4 (-30,8-48,2)	0,808,57	1 (-27,9-27,8)	U=1158	.528
Vitamin B6 (mg)	0,383,09	-0,03 (-8,3-16,2)	1,267,89	0,2 (-6,2-55,4)	U=1078.5	.238
Vitamin C (mg)	49.80±105.56	34.5 (-170.7-310.4)	41.06±66.87	37.7 (-90.4-208.8)	U=1248	.992
Sodium (mg)	-2630.80±15917.74	-265 (-61569.5-51563.6)	-2036.67±11144.03	-225.5 (-61490.4-10694.7)	U=1234	.915
Potassium (mg)	402.69±1133.77	371.7 (-1917.1-2795)	359.17±1455.00	223.3 (-1455.1-8190.2)	U=1136	.434
Calcium (mg)	60.72±574.86	48.5 (-976.8-2896)	84.28±307.34	47.3 (-448.6-1053.1)	U=1196	.712
Magnesium (mg)	67.99±162.56	35.8 (-220.4-747.1)	13.22±148.60	-4.2 (-343.6-586)	U=1010	.099
Iron (mg)	1.80±9.81	1.1 (-15.6-52.5)	4.39±36.76	-0.7 (-16.8-258.6)	U=1071	.218
Zinc (mg)	0.42±5.57	1.1 (-12-10.6)	-0.77±3.91	-0.9 (-8.9-9.6)	t=1.229	.223

t: Independent Sample T Test; U: Mann-Whitney U Test

*p<.05

Rank Test.” The relationships between numerical variables were analyzed using two distinct methods: Pearson’s Product-Moment Correlation Coefficient for normally distributed data and Spearman’s Rank Correlation Coefficient for non-normally distributed data. The following criteria were used in the interpretation of the correlation coefficient: The correlation was determined to be “very weak” if it was less than 0.2, “weak” if it fell between 0.2 and 0.4, “moderate” if it was between 0.4 and 0.6, “high” if it was between 0.6 and 0.8, and “very high” if it was greater than 0.8 (13). The statistical significance level was established as “p<.05, p<.01, p<.001” in all calculations and interpretations. Hypotheses were established bidirectionally. The statistical data analysis was performed using SPSS v27 (IBM Inc., Chicago, IL, USA).

3. RESULTS

Among the participants in the study, 49% were male and 51% were female. The mean age of males was 24.57 6.49 years, 87.8% were single, 49% had a bachelor’s degree, 49% were students, 46.9% had income less than expenses, 10.2% used nutritional supplements, and 44.9% were smokers. It was found that the mean amount of smoking was 14.00 5.00 pieces/day, 22.4% drank alcohol, the mean amount of alcohol consumption was 2.36 1.21 drinking cups/month, the mean amount of daily water consumption was 2122.45

780.83 ml/day, and the mean amount of physical activity was 7.77 3.64 hours/week (Table 1).

The mean age of the females who participated in the study was 30.35 8.40 years, 60.8% were single, 60.8% had a bachelor’s degree, 33.3% were workers or in private sector, 51% had an income less than their expenses, 25.5% used dietary supplements. It was found that 19.6% smoked cigarettes, the mean amount of cigarette smoked was 8.80 4.89 pieces /day, 21.6% drank alcohol, the mean amount of alcohol consumption was 2.64 1.36 drinking cups/month, the mean amount of daily water consumption was 1815.69 624.94 ml/day and the mean amount of physical activity was 5.98 2.81 hours/week (Table 1).

Statistically significant differences were observed between the genders of the individuals participating in the study in terms of the difference values of Vitamin A (µg) (U=908; p<.05) and Vitamin E (mg) (t=2.503; p<.05) one month after the nutrition education. Upon examining the results, it was found that the median difference values of Vitamin A (µg) were higher in males [192.6 (-8634.3-2252.7)] compared to females [98.9 (-1503.9-5538.8)], and the mean difference values of Vitamin E (mg) were higher in males (3.61±9.28) compared to females [0.1 (-120.2-15.4)] one month after the education (Table 2).

Table 3. Comparison of anthropometric measurement pre-test – post-test values of individuals

	Pre-Test		Post-Test		T-W	P
		Median (min-max)		Median (min-max)		
BMI	23.70 3.30	23.5 (16.5-32.4)	23.57 3.15	23.3 (16.5-31.8)	T=2.577	.011*
Waist Circumference	79.20 10.76	79 (60-105)	78.81 10.56	78.3 (60-105)	W=-4.260	<.001***
Hip Circumference	100.72 6.92	101 (88-119)	99.67 6.46	100 (87-117)	T=10.103	<.001***
Waist/Hip Ratio	0.79 0.08	0.8 (0.6-1)	0.79 0.08	0.8 (0.6-1)	T=-3.165	.002**
Triceps ST	20.46 6.66	20 (5-39)	20.35 6.53	20 (5-38)	T=3.002	.003**
Biceps ST	13.07 6.18	11.5 (5-35)	13.02 6.14	11.5 (5-35)	W=-2.121	.034*
Subscapular ST	19.04 7.25	18 (7-42)	18.97 7.22	18 (7-42)	W=-2.640	.008**
Suprailiac ST	21.62 9.00	22 (6-44)	21.50 8.90	22 (6-44)	W=-3.500	<.001***
Chest ST	20.98 7.6	20 (7-42)	20.87 7.50	20 (7-41)	T=3.591	<.001***
Abdominal ST	28.24 8.71	26.5 (12-52)	27.94 8.62	26 (12-51)	T=6.335	<.001***
Femur ST	32.25 10.35	30 (13-57)	31.85 10.04	30 (13-55)	W=-5.388	<.001***
Femur Circumference	52.52 5.26	52.3 (43-65)	51.74 5.27	51.8 (42-64)	T=12.482	<.001***
Upper Mid Arm Circumference	30.22 4.35	30 (21.5-42)	29.92 4.38	29.3 (21-42)	W=-5.136	<.001***

T: Dependent Sample T Test; W: Wilcoxon Signed Rank Test

*p<.05; **p<.01; ***p<.001

Abbreviations: BMI, Body Mass Index; ST, Skinfold Thickness

Statistically significant differences were observed between the pre-test and post-test measurements for waist circumference (p<.001), BMI (p<.05), hip circumference (p<.001), waist/hip ratio (p<.01), triceps ST (p<.01), subscapular ST (p<.01), suprailiac ST (p<.001), biceps ST (p<.05), chest ST (p<.001), abdominal ST (p<.001), femur ST (p<.001), femur circumference (p<.001), and upper mid-arm circumference (p<.001) among study participants. Upon examining the results, pre-test values for waist circumference, BMI, hip circumference, waist/hip ratio, triceps, biceps, subscapular, suprailiac, chest, abdominal, and femur ST, as well as femur circumference and upper mid-arm circumference, were statistically higher than the post-test values (Table 3).

The study revealed statistically significant strong negative correlations between the male participants' total DII difference scores and the difference values of "Fiber (g)", "Vitamin E (mg)", "Potassium (mg)", and "Magnesium (mg)" (p<.001). Additionally, there were statistically significant weak negative correlations between the total DII difference scores and the difference values of "Vitamin A (μg)",

Table 4. Correlation coefficients between total difference scores of DII and energy, macro and micronutrient difference values after nutrition education of individuals according to gender

	Male		Female	
	DII Total		DII Total	
	R-s	P	R-s	P
Energy (kcal)	R=-0.044	.765	R=-0.122	.394
CHO (g)	R=0.032	.829	R=0.106	.458
Protein (g)	R=0.073	.617	R=-0.373	.007**
Fat (g)	R=-0.169	.245	R=-0.168	.237
Saturated Fat (g)	S=0.158	.278	S=0.286	.042*
Monounsaturated Fat (g)	S=-0.150	.304	S=-0.120	.400
Polyunsaturated Fat (g)	R=-0.389	.006**	S=-0.472	<.001***
Fiber (g)	R=-0.603	<.001***	S=-0.619	<.001***
Vitamin A (μg)	S=-0.464	<.001***	S=-0.516	<.001***
Vitamin D (μg)	S=-0.136	.353	R=-0.036	.800
Vitamin E (mg)	R=-0.690	<.001***	R=-0.493	<.001***
Vitamin K (μg)	S=-0.334	.019*	S=-0.521	<.001***
Vitamin B1 (mg)	S=-0.422	.002**	S=-0.680	<.001***
Vitamin B2 (mg)	S=-0.101	.488	S=-0.239	.091
Niacin (mg)	S=-0.034	.818	S=-0.475	<.001***
Vitamin B6 (mg)	S=-0.417	.003**	S=-0.402	.003**
Vitamin C (mg)	S=-0.456	0.001**	R=-0.493	<.001***
Sodium (mg)	S=0.060	.683	S=-0.115	.422
Potassium (mg)	R=-0.632	<.001***	S=-0.653	<.001***
Calcium (mg)	S=-0.124	.394	S=-0.398	.004**
Magnesium (mg)	S=-0.627	<.001***	S=-0.666	<.001***
Iron (mg)	S=-0.365	.010*	S=-0.463	<.001***
Zinc (mg)	R=-0.240	.097	R=-0.425	.002**

r: Pearson Product Moment Correlation Coefficient; s: Spearman Rank Difference Correlation Coefficient

*p<.05; **p<.01; ***p<.001

"Vitamin B1 (mg)", "Vitamin B6 (mg)", "Vitamin C (mg)", "Polyunsaturated Fat (g)", "Vitamin K (μg)", and "Iron (mg)" (p<.05; p<.01) (Table 4).

Upon examination of the results, it was observed that as the total DII difference scores for males increased, the difference values decreased by 38.9% for "Polyunsaturated Fat (g)", 60.3% for "Fiber (g)", 46.4% for "Vitamin A (μg)", 69% for "Vitamin E (mg)", 33.4% for "Vitamin K (μg)", 42.2% for "Vitamin B1 (mg)", 41.7% for "Vitamin B6 (mg)", 45.6% for "Vitamin C (mg)", 43.2% for "Potassium (mg)", 62.7% for "Magnesium (mg)", 36.5% for "Iron (mg)", and 49.6% for "Copper (mg)". These findings indicate that as the total DII difference scores increase, the difference values for these nutrients decrease (Table 4).

Significantly strong negative correlations were identified between the total DII difference scores of the females in the study and their difference values of "Fiber (g)", "Vitamin B1 (mg)", "Potassium (mg)", and "Magnesium (mg)" (p<.001). Additionally, there were statistically significant moderate negative correlations between the total DII difference scores and the difference values of "Polyunsaturated Fat (g)", "Vitamin A (μg)", "Vitamin C (mg)", "Iron (mg)", "Zinc (mg)", and "Copper (mg)" (p<.01; p<.001), and weak negative correlations with "Protein (g)" and "Calcium (mg)" (p<.05).

Table 5. Comparison of DII pre-test-post-test and total DII difference scores of individuals

			Median (min-max)	t-T	p
DII Total Score – Pre-test		0.00 1.85	0.1 (-4.1-4.2)	T=0.000	1.000
DII Total Score – Post-test		0.00 1.65	-0.2 (-3.1-4.3)		
DII Total Score	Male	-0.32 1.97	-0.2 (-5-4.2)	t=-1.625	.107
	Female	0.31 1.91	0.2 (-3.2-5.1)		

T: Dependent Sample T Test; t: Independent Sample T Test

There was also a statistically significant weak positive correlation with the difference values of “Saturated Fat (g)” ($p < .05$). These findings indicate that as the total DII difference scores increase, the difference values for these nutrients decrease, but the difference values for saturated fat slightly increase (Table 4).

Table 6. Correlation coefficients between DII difference total scores and anthropometric measurement difference values of individuals according to gender

	DII Total Score					
	Male		Female		Total	
	r*	P	r*	P	r*	P
BMI	-0.199	.170	0.079	.582	-0.024	.811
Waist Circumference	0.005	.971	-0.029	.841	-0.004	.967
Hip Circumference	0.057	.698	-0.181	.203	-0.100	.324
Waist/Hip Ratio	-0.007	.964	0.097	.498	0.051	.616
Triceps ST	-0.031	.031	-0.053	.712	-0.069	.495
Biceps ST	0.245	.245	-0.015	.918	0.032	.751
Subcapular ST	-0.162	.162	-0.040	.778	-0.101	.317
Subrailac ST	0.007	.960	-0.156	.273	-0.125	.214
Chest ST	0.007	.960	-0.087	.543	-0.101	.320
Abdominal ST	-0.063	.667	-0.129	.367	-0.111	.271
Femur ST	-0.093	.524	-0.074	.604	-0.141	.162
Femur Circumference	0.053	.720	-0.124	.387	-0.045	.655
Upper Mid Arm Circumference	0.043	.770	0.064	.656	0.042	.676

*Spearman Rank Difference Correlation Coefficient

ST Skinfold Thickness

Upon examination of the results, it was noted that the total DII difference scores for females increased, the difference values decreased by 37.3% for “Protein (g)”, 47.2% for “Polyunsaturated Fat (g)”, 61.9% for “Fiber (g)”, 51.6% for “Vitamin A (μg)”, 49.3% for “Vitamin E (mg)”, 52.1% for “Vitamin K (μg)”, 68% for “Vitamin B1 (mg)”, 47.5% for “Niacin (mg)”, 40.2% for “Vitamin B6 (mg)”, 49.3% for “Vitamin C (mg)”, 65.3% for “Potassium (mg)”, 39.8% for “Calcium (mg)”,

66.6% for “Magnesium (mg)”, 46.3% for “Iron (mg)”, 42.5% for “Zinc (mg)”, and 50.8% for “Copper (mg)”, while the difference values of “Saturated Fat (g)” increased by 28.6% (Table 4).

The analysis revealed no statistically significant difference ($p > .05$) in the total DII scores between the pre-test and post-test for the study participants, nor in the total DII difference scores among study participants based on gender (Table 5).

The study revealed no significant correlation observed ($p > .05$) between the total DII difference scores and the anthropometric difference values of male and female participants (Table 6).

4. DISCUSSION

This study’s participants comprised a total of one hundred subjects, with 51 of these subjects being female and 49 male. The study aimed to examine the impacts of nutrition education on the DII and anthropometric values in individuals who engaging in regular exercise. Anthropometric measurements were obtained prior to the training and 30 days after, while DII values were calculated based on food consumption records.

In the systematic review by Sánchez-Díaz S et al. (6), it is emphasized that nutrition education interventions generally improve eating habits, with these improvements applicable to both male and female athletes. However, the study demonstrated that one month after nutrition education, the levels of Vitamin A and Vitamin E intake in males increased significantly compared to females. A comprehensive analysis assessing the efficacy of nutrition education interventions on dietary intake in young Black males (14–21 years old) revealed insufficient evidence regarding the effectiveness of these interventions among young Black males (14). The observed discrepancies across studies may be attributable to variations in age and educational levels. Debnath M et al. (15) conducted a study to examine the effects of an eight-week nutrition education program on the daily dietary intake of young males. This study found that nutrition education interventions significantly increased the macro and micronutrient intakes of young male athletes. Significant increases were observed in the daily intake of calories, protein, calcium, phosphorus, iron, zinc, and selenium. Additionally, substantial increases were documented in the intake of vitamins A, C, E and B12 (15).

One of the most significant findings of the study was the impact of nutrition education on anthropometric measurements. Specifically, a notable decrease in BMI, hip and waist circumference, waist-to-hip ratio, and skinfold thickness at the triceps, biceps, subscapular, subiliac, chest, abdominal, and femur sites was observed one month after the nutrition education intervention compared to pre-test values. Additionally, decreases in femur circumference and upper mid-arm circumference were noted. Furthermore, a study on professional football players highlighted the association between nutritional status, anthropometric measurements

and DII, demonstrating that enhanced nutritional status was linked with improved anthropometric outcomes and reduced DII scores (16). A study was conducted among adults in Northern Serbia to examine the impact of nutrition education interventions on metabolic syndrome indicators. This study observed a statistically significant decrease in BMI six months after the nutrition education intervention (17). The study results reflect the changes observed only one month after the nutrition education intervention. Despite the relatively short duration, we demonstrated significant reductions in various anthropometric measurements.

Another significant finding in the study was the relationship between DII levels and nutrients. The observed differences between men and women suggest that dietary habits and DII levels may affect each gender differently. For male subjects, an increase in total DII difference scores was associated with a decrease in the difference values for fiber, vitamin E, potassium, and magnesium. For female subjects, a similar trend was observed, with increasing total DII difference scores corresponding to a decline in nutrient difference values, with the exception of saturated fat, which exhibited a slight increase. A comparison of the eating habits and dietary preferences of women and men reveals that they may differ from each other. In some cases, women may prefer foods that contain more saturated fat, which could explain the positive correlation between DII scores and saturated fat consumption (18). These findings are in line with a study that examined the inflammatory effects of diet, which reported that groups receiving an anti-inflammatory diet had higher intakes of iron, magnesium, niacin, vitamin C, and riboflavin compared to groups receiving a pro-inflammatory diet (19). In accordance with the findings of a study that examined the inflammatory effects of diet, anti-inflammatory diet groups exhibited higher intakes of iron, vitamin C, magnesium, niacin, and riboflavin compared to pro-inflammatory diet groups among a sample of young women and men who regularly engaged in physical activity (20). Additionally, an umbrella review examining the link between the DII and several health outcomes found that adherence to a pro-inflammatory diet model was significantly positively associated with 71% of the health outcomes examined (9). In a study conducted on young, physically active men found that DII is a promising method for identifying the risk of inflammation. Participants adhering to diets with the most anti-inflammatory properties exhibited significantly higher consumption of protein, magnesium, iron, zinc, antioxidant vitamins, and B vitamins (21).

Our study has several limitations. It was designed as an experimental study, but a control group was not established. Nutrition education was provided only once, and while we compared the short-term results of the education, the long-term results were not examined. Additionally, the subject group was limited.

5. CONCLUSION

Our study demonstrated that nutrition education can enhance anthropometric measurements even one month after the intervention in individuals who regularly engage in exercise. However, a short-term evaluation is inadequate for measuring changes in DII scores. To evaluate the effectiveness of nutrition education in this area, prospective, longitudinal studies with larger sample sizes, more extended follow-up periods, and more frequent nutrition education sessions are necessary.

Acknowledgements: The authors would like to thank all participants. This study is derived from Fatmanur Zehra Zelka's master's thesis entitled "Evaluation of the Impact of Nutrition Education on Dietary Inflammatory Index and Anthropometric Measurements in Individuals Who Exercise Regularly".

Funding: The authors received no financial support for the research.

Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Committee Approval: This study was approved by Ethics Committee of Üsküdar University, Noninvasive Clinic Ethics Committee (Approval date: 26.03.2024; Number:03)

Peer-review: Externally peer-reviewed

Author Contributions:

Research idea: FZZ, TA

Design of the study: TA

Acquisition of data for the study: FZZ

Analysis of data for the study: FZZ

Interpretation of data for the study: TA

Drafting the manuscript: FZZ, TA

Revising it critically for important intellectual content: FZZ, TA

Final approval of the version to be published: FZZ, TA

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Short Examination Times and Potential Risks in Psychiatric Clinics: Example of Türkiye

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Received: January 07, 2024

Accepted: December 3, 2024

ABSTRACT

Dear Editor, the reason I am writing this letter is to address the risks that may arise for psychiatry regarding the short examination times in our country. Recently, the increase in the number of applications in psychiatry outpatient clinics and the decrease in the number of physicians have led to the pressure to examine many patients in a short time. First of all, psychiatrists have great difficulty making diagnoses due to this short time. In terms of patients who cannot receive adequate and effective treatment, the short examination period first harms the patients. Secondly, it may cause psychiatrists to make many wrong legal decisions. As a result, it is extremely important for the relevant authorities to review the examine periods in consultation with professional organizations due to possible risks.

Keywords: Psychiatric patient examination time, misdiagnosis, malpractice

Dear Editor, the reason I am writing this letter is to address the risks that may arise for psychiatry regarding the short examination times in our country. Recently, the increase in the number of applications in psychiatry outpatient clinics and the decrease in the number of physicians have led to the pressure to examine many patients in a short time. In literature, the general physical examination time for the patient has been recommended as 20 minutes (1). In correlation with the shortening of this time, it has been reported that the physician concerned is more likely to face malpractice lawsuits in the future (2). The ideal examination time for psychiatric patients is much longer than this. Although the initial psychiatric evaluation varies from patient to patient, it is known that it usually takes between 45 and 90 minutes (3). Currently, in public hospitals, the system gives an appointment every 10 minutes on average. When we include patients who are accepted without an appointment to avoid disruption of their treatment, the examination time per psychiatric patient is sometimes 5 minutes. The current situation brings many problems together. First of all,

psychiatrists have great difficulty making diagnoses due to this short time. While in complex cases it is necessary to deepen the history and ask open-ended questions, in order to avoid legal and conscientious responsibility, the first questions asked by the psychiatrist are closed-ended questions such as "Do you have suicidal thoughts? Do you have thoughts of harming someone else?". If the answer to these questions is yes, the physician can only spend time deepening the history of these patients. For this reason, patients who think that they are not listened enough because they are allocated less time leave the treatment before it starts. Or they seek healing by going from physician to physician. This situation also leads to a waste of public resources. In terms of patients who cannot receive adequate and effective treatment, the short examination period first harms the patients. Secondly, it may cause psychiatrists to make many wrong legal decisions. For example, physicians assigned as psychiatric experts are obliged to give an urgent answer about the file that the authorized persons in the courts have worked on for about a year. Due to overcrowding in hospitals, the time

How to cite this article: İmre O. Short Examination Times and Potential Risks in Psychiatric Clinics: Example of Türkiye. Clin Exp Health Sci 2025; 15: 461-462. <https://doi.org/10.33808/clinexphealthsci.1415961>

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allocated to forensic cases is short because the physician who deals with forensic cases in hospitals is also obliged to perform disability/disability health boards, probation outpatient clinics, and sometimes examinations without an appointment. It can be stated that the short duration of the interviews may also create a deficiency in scientific terms. Structured interviews are important in terms of providing data for epidemiological studies and multicentre studies (4). The necessity to complete the interviews in a short time may cause incomplete collection of data on individuals. For this reason, epidemiological studies and multicenter clinical research cannot be conducted in our country, thus causing a scientific loss.

In other countries, the examination time allocated per patient is longer than in Turkey. In a survey conducted in the USA, it was reported that doctors spend an average of 20 minutes per patient and see 20 patients a day (5). In Australia, the average time allotted for a first psychiatric interview is 45 minutes (6). As a solution, I recommend that, the number of doctors should be increased and the workload should be reduced. For this purpose, first of all, encouraging initiatives should be initiated to reverse the brain drain that has increased significantly in recent times.

As a result, due to the possible risks of short examination times, the relevant authorities should review the examination times in consultation with professional organizations.

Best Regards

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