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The Role of Mothers' Varied Parenting Styles in Childhood Obesity

ABSTRACT

Objective: The aim of this study is to evaluate the role of mothers' democratic, authoritarian, permissive, and overprotective parenting styles in childhood obesity and mothers' perception of their children's body weight.

Method: The research was cross-sectional in design, and a total of 94 children aged between two and six years were included, together with their mothers. Mothers were administered the Parental Attitude Scale, and children's Body Mass Index (BMI) was classified using age-gender-specific tables of the International Obesity Task Force (IOTF). The effect of mothers' parental attitudes on their children's BMI groups was evaluated. However, mothers matched their child's appearance to the appearance they thought corresponded to the age and gender-specific weight plot and mothers' weight perceptions were evaluated.

Results: The prevalence of overweight-obesity among children was found to be 19.2%. There wasn't statistically difference between democratic, authoritarian, overprotective and permissive parenting styles and BMI categories of children (p=0.819, p=0.878, p=0.319, p=0.494). The mothers of overweight-obese children perceived their children as significantly overweight compared to other children (p<0.001), they associated their overweight-obese children with the normal body weight imagery. Mothers of children with a normal body weight also selected thinner child images to represent their own child.

Conclusions: Mothers of children with normal body weight and overweight-obese BMI, perceived their children's body weight as thinner than it actually was. It's recommended that mothers' perceptions of their children's body weight be assessed in well-child clinics. In cases where these perceptions are inaccurate, mothers should be informed and provided with educational materials.

Keywords: Parenting Style, Pediatric Obesity, Weight Perception.

Çocukluk Çağı Obezitesinde Annelerin Farklı Ebeveyn Tutumlarının Rolü

ÖZET

Amaç: Bu çalışmanın amacı annelerin demokratik, otoriter, izin verici ve aşırı korumacı ebeveyn tutumlarının çocukluk çağı obezitesindeki rolünü ve annelerin çocuklarının kilo durumuna ilişkin algısını değerlendirmektir.

Yöntem: Araştırma kesitsel tipte olup, 2-6 yaş arası 94 çocuk anneleriyle birlikte çalışmaya dahil edildi. Annelere Ebeveyn Tutum Ölçeği uygulandı ve çocukların Beden Kitle İndeksi (BKİ), Uluslararası Obezite Çalışma Grubu'nun yaşa ve cinsiyete özel tabloları kullanılarak sınıflandırıldı. Annelerin ebeveyn tutumlarının, çocuklarının BKİ grupları üzerindeki etkisi değerlendirildi. Aynı zamanda anneler, çocuklarının görünümünü, yaşa ve cinsiyete özel ağırlık çiziminde, karşılık geldiğini düşündükleri görünümle eşleştirdi. Annelerin kilo algıları değerlendirildi.

Bulgular: Çocukların %19,2'si fazla kilolu-obez olarak sınıflandırıldı. Annelerin demokratik, otoriter, aşırı korumacı ve izin verici ebeveyn tutumları ile çocukların BKİ kategorileri arasında anlamlı fark bulunmadı (p=0,819, p=0,878, p=0,319, p=0,494). Fazla kilolu-obez çocukların anneleri, çocuklarını diğer çocuklara göre anlamlı derecede kilolu olarak algılamakla birlikte (p<0,001), fazla kilolu-obez çocuklarını normal kilo çizimi ilişkilendirdiler. Benzer durum, normal ağırlıktaki çocukların annelerinde de görülmüş olup çocuklarını olduklarından daha zayıf çocuk çizimleri ile eşleştirdiler.

Sonuç: Annelerin ebeveyn tutumlarının, çocuklarının BKİ kategorileri üzerinde etkisi olmadığı görüldü ancak normal ve fazla kilolu-obez çocukların annelerinin, çocuklarını olduğundan daha zayıf görme eğiliminde olduğu saptandı. Sağlam çocuk kliniklerinde annelerin kilo algıları değerlendirilmelidir, hatalı algılamaları durumunda anneler bilgilendirilmeli, konuyla ilgili eğitim broşürleri verilmelidir.

Anahtar Kelimeler: Ebeveyn Tutumu, Pediatrik Obezite, Kilo Algısı.

INTRODUCTION

The World Health Organization (WHO) defines overweight and obesity as "abnormal or excessive fat accumulation that presents a risk to health." The WHO also identifies childhood obesity as one of the most significant public health challenges of the 21st century, noting that worldwide obesity rates have nearly tripled since 1975. In 2022, 37 million children under the age of five were classified as overweight or obese, representing a significant increase from previous years. Previously regarded as a phenomenon exclusive to high-income countries, the prevalence of overweight and obesity is now on the rise in low- and middle-income countries. (1).

The likelihood of an obese child or adolescent becoming obese in adulthood is five times greater than that of a non-obese child or adolescent. A significant proportion of obese children (55%) remain obese in adolescence, with 70% of obese adolescents being obese by the age of 30 (2). Obese children are at an increased risk of developing cardiovascular diseases, diabetes, musculoskeletal diseases (osteoarthritis, degenerative joint) and certain types of cancer (endometrium, breast, colon) in adulthood (1).

There is a general consensus that environmental factors play a pivotal role in the development of obesity, given the alarming increase in childhood obesity that cannot be attributed solely to genetic predispositions (3). The intrauterine environment, nutritional status, physical activity, familial and psychosocial characteristics are the primary environmental factors that influence the risk of obesity (4). A significant proportion of children's dietary and physical activity behaviours are influenced by their families during the preschool period. The child's acquisition of positive or negative habits is largely influenced by their family (5).

The attitudes and behaviours adopted by parents result in differences in the way children are raised (6). Parents have been examined in different dimensions according to this attitude and behaviour. The democratic, authoritarian and permissive dimensions defined by Baumrind were used in determining parenting styles. Democratic parents expect mature behaviour from their children and require them to adhere to the established rules. They listen to their children in a caring and patient manner and take their children's views into consideration when making decisions. Permissive parents afford their children considerable freedom, exhibit occasional negligence, and are unable to control their children. There are no restrictions regarding television viewing or computer gaming, and there is no established eating or sleeping routine. Authoritarian parents suppress children's efforts to challenge authority. They engage in minimal exchange with their children and expect unconditional compliance with the rules they set, otherwise they impose penalties (7). Furthermore, an additional dimension was proposed, namely that of overprotection (8). This concept encompasses the notion of maternal overprotection, which can be defined as an excessive level of care and control exerted by mothers over their children, characterised by frequent contact and the prevention of social maturity.

It is aimed to assess the role of mothers' democratic, authoritarian, permissive and overprotective parenting styles on childhood obesity and mothers' perceptions of their children's weight status.

MATERIAL AND METHODS

Participants: The research is cross-sectional. The sample size was calculated using a confidence interval of 95%, an effect size of 0.40, and a power of 90% in the G-Power 3.1 program, resulting in a required sample size of 84. A total of 201 children were admitted to the well-child clinic between July and August 2016. Of these, 107 were excluded from the study due to the presence of one or more exclusion criteria, including the presence of a chronic disease, the use of drugs that may cause obesity or weight loss, and the presence of an adult other than the child's mother. The remaining 94 children and their mothers were included in the study.

Data Acquisition: BMI of the children was calculated. The children were classified according to the age and gender specific tables of the International Obesity Task Force (IOTF) as morbidly obese, obese, overweight, normal, grade 1 underweight, grade 2 underweight and grade 3 underweight. Morbidly obese, obese and overweight have been combined as "overweight-obese". Grade 1 underweight, grade 2 underweight and grade 3 underweight were combined as "low body weight". A total of three groups were evaluated, including those with normal body weight.

The questionnaire comprises a series of questions pertaining to socio-demographic characteristics, daily activities, and the existing literature on the subject, with a total of 38 questions in all (9, 10).

The Parental Attitude Scale (PAS) was developed by Karabulut as a means of determining the parenting attitudes that parents have demonstrated in raising their children aged 2-6 (11). The scale comprises four dimensions: democratic, authoritarian, overprotective, and authoritarian. The Cronbach alpha reliability coefficients for the dimensions are 0.83, 0.76, 0.75, and 0.74, respectively. The scale comprises 46 items, with 17, 11, 9 and 9 items, respectively, for each dimension. Mothers were invited to express their parenting attitudes on a 5-point Likert scale. The points awarded for each dimension were calculated individually, with one point being awarded for each

dimension. A high score on the scale indicates that the respondent is embracing the behaviour that the dimension represents.

The mothers were presented with image of children of 2-6 age and gender specific weight imagery (Figure 1) (12). They were asked to indicate which child they believed their own child most resembled. The images comprised seven pictures, ranging from the thinnest child to the fattest child, with four images representing a normal body weight child.

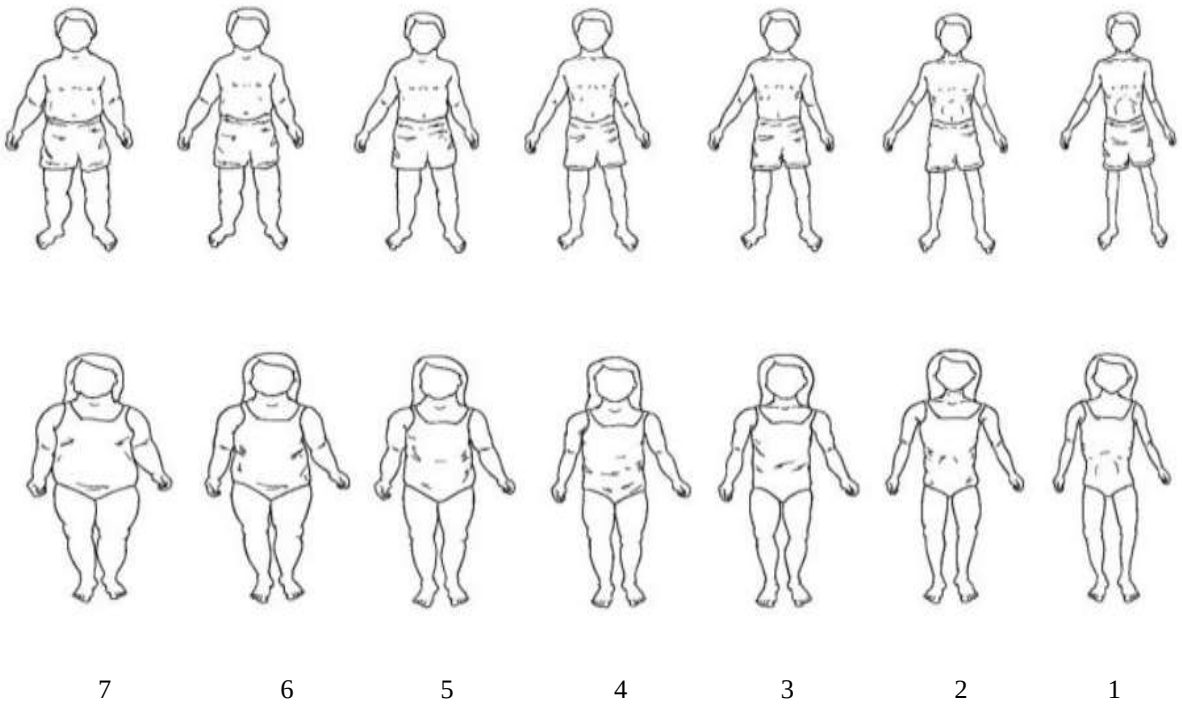

Figure 1. 2-6 age and gender specific weight imagery (© 2003 Scott Millard, medical illustrator). The first 3 numbers on the right are indicative of low body weight, the 4th number is within the normal body weight, and the numbers from 5 to 7 are indicative of overweight-obese.

A further comparison was made between the scores given by mothers of children with overweight-obese, normal body weight, and low body weight.

Written permission from medical illustrator Scott Millard was obtained for the utilisation of 2-6 age and gender specific weight imagery. Ethical approval for this study was granted by the X University Clinical Research Ethics Committee on 29/06/2016, with the protocol number 2016-72-29 / 06.

Statistical Analysis: The statistical analysis was conducted using the IBM SPSS Statistics for Windows, Version 24.0 (Armonk, NY: IBM Corp.) software.

The compatibility of numerical variables with a normal distribution was evaluated through the implementation of the Shapiro-Wilk test. Descriptive statistics were expressed as the arithmetic mean ± standard deviation (SD) and median (minimum-maximum) for numerical variables, and as numbers and percentages for categorical data. The Chi-square test was employed to analyse differences between groups in terms of categorical variables. In the case of numerical variables, one-way ANOVA of variance was utilised when parametric test assumptions were met, whereas Kruskal-Wallis variance analysis was employed when these assumptions were not satisfied. Dunn's test was used to compare the subgroups in pairs in the latter case, and a value of $p \leq 0.05$ was considered statistically significant.

RESULTS

Sociodemographic characteristics of the mothers were evaluated; the youngest mother was aged 21, while the oldest was 46 years old. The mean age was 31.35 ± 5.11 years. 1.1% (n=1) of the mothers were only literate, 29.8% (n=28) had completed primary school, 29.8% (n=28) had completed secondary school, 27.6% (n=26) had completed high school, and 11.7% (n=11) had graduated from an undergraduate program or above. All the mothers were married. The average income of the families was 742,3 ± 389,3 Turkish Dollars ($). The majority of families (75.5%, n=71) were of the nuclear type. The sociodemographic characteristics of the mothers participating in the study are provided in Table 1.

Table 1. Sociodemographic characteristics of mothers.

Sociodemographic characteristics		**n**	**Mean ± SD**	**Median (min-max)**
Age (years)		94	31.35 ±5.11	31 (21-46)
Family Income ($)		85	2277 ±1168	2000 (1000-6000)
Number of children		94	1.89±0,72	2 (1-4)
		n	**%**	
Educational status	Literate only	1	1.1	
	Primary school	28	29.8	
	Middle School	28	29.8	
	High school	26	27.6	
	License and above	11	11.7	
Occupation	Housewife	80	85.0	
	Officer	6	6.4	
	Employee	6	6.4	
	Other*	2	2.2	
Economic situation perception	Low	12	12.8	
	Middle	61	64.8	
	Good	20	21.3	
	Very good	1	1.1	
Family structure	Nuclear	71	75.5	
	Extended	23	24.5	

*Hairdresser, Coach

The age and gender distribution of children is analyzed; the youngest child was 24 months old, while the oldest was 71 months old, with an average age of 45.58 ± 12.92 months. Of the total number of children, 43.6% (n = 41) were female, while 56.4% (n = 53) were male. The mean birth weight of the children was 3107 ± 704.47 grams (Table 2).

A total of 24.5% (n=23) of the children were classified as having low body weight, 56.4% (n=53) were classified as having normal body weight, and 19.1% (n=18) were classified as overweight or obese. Of the children with low body weight, 13.0% (n=3) were underweight 3, 17.4% (n=4) were underweight 2, and 69.6% (n=16) were underweight 1. In the obese group, 66.7% (n=12) were overweight, 5.5% (n=1) were obese, and 27.8% (n=5) were morbidly obese.

Table 2. Sociodemographic characteristics of children.

Sociodemographic characteristics		**n**	**Mean ± SD**	**Median (min-max)**
Age (month)		94	45.58 ±12.92	44.5 (24-71)
Birth weight (gr)		91	3107 ±704.47	3230 (770-4600)
		n	**%**	
Gender	Girl	41	43.6	
	Boy	53	56.4	
Ever breastfed	Yes	88	93.6	
	No	6	6.4	

The mothers indicated that 26.6% (n=25) of their children use the computer for a minimum of two hours per day, 59.6% (n=56) watch television for a minimum of two hours, and 79.8% (n=75) engage in outdoor play for a minimum of two hours. The mean duration of computer/tablet usage was 1.08 ± 1.3 hours, television viewing was 2.07 ± 1.5 hours, and outdoor gaming was 3.04 ± 1.9 hours. The time spent using computers on a daily basis, the time spent watching television, and playing outside were not found to have a statistically significant impact on the weight of children (p=0.510, p=0.198, p=0.940).

Weight classification of children did not change with their age (p = 0.992).

The gender, family structure, and maternal educational status of children did not effect their weight (Table 3).

Table 3. The gender of children, family structure, educational status of mothers.

		Low body weight (n=23)		Normal body weight (n=53)		Overweight-obese (n=18)		p
		n	%	n	%	n	%	
Gender	Girl	10	24.4	20	48.8	11	26.8	0.225
	Boy	13	24.5	33	62.3	7	13.2	
Family structure	Nuclear type	20	28.2	37	52.1	14	19.7	0.271
	Extended type	3	13.0	16	69.6	4	17.4	
Educational status of mothers	Literate only and Primary school	8	27.6	19	65.5	2	6.9	0.151
	Middle School	8	28.6	13	46.4	7	25.0	
	High school	5	19.2	17	65.4	4	15.4	
	License and above	2	18.2	4	36.4	5	45.5	

The mean family income per month was 791± 371 721± 402 826± 385 dollars ($), and 2478±1157 $, respectively, for children with low, normal body weight, and overweight-obese. There was no statistically significant difference between family income and the weight of the children (p=0.438).

The effect of parenting styles on children's weight was evaluated. The findings revealed that the democratic, authoritarian, overprotective, and permissive dimensions did not effect children's weight (p = 0.819, p = 0.878, p = 0.319, p = 0.494) (Table 4).

Table 4. Effect of parental attitude dimension on children's weights.

	Low body weight (n=23) Median(min-max)	Normal body weight (n=53) Median(min-max)	Overweight-obese (n=18) Median(min-max)	p
Democratic	75(55-85)	73(57-85)	73(59-85)	0.819
Authoritarian	21(15-38)	21(14-42)	21,5(15-35)	0.878
Overprotective	37(33-45)	37(24-45)	33,5(21-45)	0.319
Permissive	21(12-32)	21(10-37)	20(12-35)	0.494

Mothers of low body weight, normal body weight and overweight-obese children marked the image that most closely resembled their children's appearance in the 2-6 age and gender specific child weight imagery (Figure 1). When the scores corresponding to the image they marked were compared, a significant difference was found (p<0.001). When the values in the body weight classification were compared pairwise, it was observed that the mothers of overweight-obese children gave significantly higher scores on the imagery than the other two groups (Table 5). The mean score of the overweight-obese group was 4.16, the mean score of the normal body weight group was 2.90, and the mean score of the low body weight group was 2.26. Although mothers of overweight-obese children perceived their children as significantly overweight compared to other children (p<0.001), they associated their overweight-obese children with normal body weight image number four. A similar pattern was observed in mothers of normal body weight children, who associated their children with image that were thinner than they were.

Table 5. The mothers' imagery scores according to children's BMI groups.

	Low body weight* (n=23)	Normal body weight* (n=53)	Overweight-obese* (n=18)	p	Post-hoc
Mean ± SD	2.26±1.17	2.90±1.21	4.16±1.65	<0.001	c>b** c>a***
Median (min-max)	2 (1-4)	3 (1-6)	5 (1-7)		

*: Low body weight: a, Normal body weight: b, Overweight-obese: c. **:< 0.05 ***:< 0.001

DISCUSSION

The prevalence of childhood obesity is rising globally, representing a significant public health concern (1). The 2021 report of the American Center for Disease Control and Prevention (CDC) indicates that the prevalence of obesity in children aged 2-5 is 12.7% (13). The latest features of the Turkey Nutrition and Health Survey reveal that the prevalence of overweight in children aged 0-5 in Turkey is 18%, with a prevalence of obesity of 9% (3). In various studies conducted in Turkey, the

prevalence of overweight or obesity during the preschool period has been reported to range from 8% to 26% (14, 15, 16, 17). The results of the research indicate that 12.8% of children aged 2-6 are overweight and 6.4% are obese. A total of 26.8% of girls and 13.2% of boys are classified as overweight or obese. This finding aligns with the results of numerous other studies that have demonstrated a higher prevalence of overweight and obesity in girls (16,17).

The effect of sociodemographic characteristics of mothers and children on children's body weights was evaluated; family income, mother's perception of economic status, mother's education level were not effective on children's weights. Similarly, Öztoprak Hacıoğlu and Edem reported that the mother's level of education, family income, and mother's perception of economic status did not affect the weights of children (9,10). Garipağaoğlu et al. also found no difference between maternal education level and obesity (18). In the United States, it has been reported that low income causes overweight and obesity, but it has also been reported that income has no effect on weight status (19, 20). There are studies reporting the effect of maternal education level on obesity with different results. In a study conducted in Germany among children aged 5-6 years, it was reported that the high level of education of mothers had a preventive effect on obesity in children (21). In a study conducted in China, it was reported that parents' high level of education had a preventive effect on obesity in children (22). In contrast to the studies conducted in Germany and China, in a study conducted in Turkey in children aged 6-12 years, the incidence of obesity was found to be higher in children of families with higher educational status and income (23). In some other studies conducted in Turkey, no significant difference was found between parental education level and obesity in children (9,10,18). These different results in the studies suggest that in addition to income and education level, cultural differences, attitudes towards nutrition and eating habits may also have an effect on children's weight. Another factor thought to affect children's weight status was television viewing time. The American Academy of Pediatrics recommends that children under the age of two should not watch television at all and children over the age of two should watch television for a maximum of two hours a day (24). In this study, no significant difference was found between television viewing time and weight status, but it was found that approximately 60% of the children watched television for at least two hours a day. The average television viewing time of children is more than two hours and is above the recommended time.

Parental attitudes may differ according to countries and cultures. In our study, in addition to democratic, authoritarian and permissive parental attitude dimensions, the "overprotective dimension", which is known to be common in Turkey, was also examined. Our study is important as it is the first study to include the overprotective dimension. When we evaluate the studies conducted in different countries, parental attitude was measured in four dimensions as democratic, authoritarian, permissive and "neglectful" dimension in the studies examining the effect of parental attitude on obesity in Australia and USA (USA Mexican origin parents) (5, 25). the study conducted in Mexicans, it was reported that obesity emerged three years later in children of permissive type parents (25). The study conducted in Australia, no significant difference was found between parental attitude and obesity (25). In this study, it was observed that parental attitude did not affect the weights of children. When mothers were asked to mark which image their children most resembled in the 2-6 age and gender specific child weight imagery, mothers of overweight-obese children marked the imagery with higher scores (heavier) than mothers of other children. This difference was found to be significant. However, both mothers of overweight-obese children and mothers of children with normal body weight matched their children with image of thinner children. This suggests that mothers tend to see their children as thinner than their actual weight. Many physicians encounter concerns from parents that their children are underweight, even though the weights of the children they monitor for growth are within normal limits. In one study, 36% of the parents labeled their children thinner than they were on the visualization, while 4% labeled them overweight (26). Although it is thought that this situation may differ between cultures, similar results are found in foreign studies (27, 28).

Limitations: The study was conducted in a single pediatric well-child clinic, and thus the results cannot be considered to represent the entire population. Participants were recruited from a pediatric well-child clinic during normal working hours. It is possible that working mothers may not have been able to apply to the university hospital, which is located far from the city centre, during working hours.

CONCLUSION

The parenting styles did not affect the BMI categories of the children. However, the mothers were likely to perceive their children's body weight as thinner than it actually was. Such perceptions may be more deleterious than protective in the context of the current global obesity epidemic. The affect of parenting style on children's weight can be researched in more than one center and during pediatric examinations in outpatient clinics, mothers' perception of their children's weight can be rapidly assessed with the use of age- and gender-specific imagery. In the event of a discrepancy between the actual weight of the children and the

perception of the mothers, the mothers should be informed and provided with educational materials on healthy nutrition.

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RESEARCH ARTICLE

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Predictive Factors of Peripheral Artery Disease in Homecare Patients

ABSTRACT

Objective: The aim of the present study was to investigate the predictive factors of peripheral arterial disease (PAD) in home care patients.

Method: This descriptive study was conducted in Istanbul with 285 homebound patients who applied for the first time to receive services from the Home Health Care Unit of a tertiary hospital between 01.07.2014 and 01.12.2014. The patients having known PAD diagnosis were excluded. Sociodemographic characteristics, home dependency duration, chronic diseases, medications used and smoking status were recorded. Then, deformities in the patients' toenails, peripheral hair loss, foot wounds were recorded, and the patients' functional status and skinfold thickness were evaluated peripheral arterial disease was evaluated by ankle–brachial index (ABI). An ABI below 0.9 was considered indicative of PAD. A chi-square test, Mann–Whitney U test and a logistic regression analysis were used in the statistical analysis.

Results: The mean age of the participants was 75.84±1.17 years (34% M; 65% F). Peripheral artery disease was detected in 16.8% (n=48) of the patients. Current or former smoking (β: 4.09), peripheral hair loss (β: 3.42), deformity of toenails (β: 3.02), and increased skinfold thickness (β: 1.124) were identified as predictors of PAD.

Conclusions: The findings of the present study suggest that home health care providers should inquire about the patient's smoking history, assess skinfold thickness, and examine the toes for hair loss and deformities, to predict PAD.

Keywords: Ankle-Brachial Index; Peripheral Artery Disease; Immobility; Cardiovascular Disease; Screening; Home Health Care.

Evde Bakım Hastalarında Periferik Arter Hastalığını Öngörücü Faktörler

ÖZET

Amaç: Çalışmanın amacı evde bakım hastalarında periferik arter hastalığı için (PAH) öngörücü faktörlerin araştırılmasıdır.

Yöntem: Tanımlayıcı tipte olan bu araştırma, İstanbul'da 01.07.2014-01.12.2014 tarihleri arasında üçüncü basamak bir hastanenin Evde Sağlık Birimine hizmet almak için ilk kez başvuran 285 hasta ile gerçekleştirilmiştir. Bilinen PAH tanısı olan hastalar çalışma dışı bırakılmıştır. Sosyodemografik özellikler, yatağa bağımlı kalma süresi, kronik hastalıklar, kullanılanı ilaçlar ve sigara içme durumu kaydedilmiştir. Daha sonra hastaların ayak tırnaklarında şekil bozukluğu, periferik kıl kaybı, ayak yaraları kaydedilmiş, hastaların fonksiyonel durumları ile deri kıvrım kalınlıkları değerlendirilmiştir. PAH ayak bileği-kol indeksi (ABI) ile değerlendirilmiş ve 0.9'un altı PAH olarak kabul edilmiştir. İstatistiksel analizde ki-kare testi, Mann-Whitney U testi ve lojistik regresyon analizi kullanılmıştır.

Bulgular: Katılımcıların yaş ortalaması 75,84±1,17 yıldır (%34 E; %65 K). Hastaların %16,8'inde (n=48) periferik arter hastalığı saptanmıştır. Halen veya geçmişte sigara kullanımı (β:4.09), periferik kıl kaybı (β:3.42), ayak tırnaklarında şekil bozukluğu (β:3.02) ve deri kıvrım kalınlığında artış (β:1.124), PAH varlığını öngören faktörler olarak belirlenmiştir.

Sonuç: Bu araştırmanın bulguları, evde bakım hizmeti sunanların PAH'ı öngörebilmek için hastaların sigara içme geçmişini sorgulaması, deri kıvrım kalınlığını değerlendirmesi ve kıllarda dökülme ve tırnak deformiteleri açısından ayak parmaklarını incelemesi gerektiğini göstermektedir.

Anahtar Kelimeler: Ayak Bileği-Kol İndeksi, Periferik Arter Hastalığı, İmmobilite, Kalp Ve Damar Hastalıkları, Evde Sağlık Hizmetleri.

INTRODUCTION

The elderly are the most rapidly growing segment of the population. The prevalence of chronic diseases due to increase in the elderly population has been increase. Chronic diseases limit an individual's daily activities by causing loss of some abilities, rendering patients with chronic diseases immobile, dependent, and bed/home bound. Immobility is a primary cause of peripheral arterial disease (PAD) and systemic atherosclerosis. Furthermore, immobility prevents the manifestation of symptoms of existing PAD, such as claudication, and leads to a delay in diagnosis (1). For this reason, evaluation of patients who are immobile and are served home health care for PAD is crucial to prevent occurrence of possible problems. However, there is no information in the literature regarding the screening for and the prevalence of PAD in patients who are served homecare. In population-based studies in our country, the prevalence of PAD was reported to be 19.76% in people over the age of 40 years and 17.6% in people over the age of 45 years (2, 3). The high prevalence of PAD and its association with ischemic and thromboembolic events and increased mortality increases the importance of its early diagnosis (4-7). In general, there is no screening that is recommended for PAD in healthy individuals without any risk factors; however, screening with ankle–brachial index (ABI) measurement is recommended for people at high risk for cardiovascular disease (8-10). In patients with a history or physical examination suggestive of PAD measurement of the ABI is indicated as a first-line non-invasive test for both screening and diagnosis of PAD (sensitivity: 68%-84%; specificity: 84% to 99%) (10). People who were served home health care may be at risk for developing PAD due to their immobility and concurrent chronic diseases.

The aim of the present study was to investigate the predictors of PAD in home care patients, therefore, to identify which findings that home health care providers encounter should lead them to suspect PAD.

MATERIAL AND METHODS

The population of this descriptive study includes patients who applied for the first time to receive services from the Home Health Care Unit of a tertiary hospital in Istanbul. No sample size was identified, and the study was designed to enrol all eligible patients among the patients applied for the first time to receive home health care between 01.07.2014 and 01.12.2014.

The inclusion criteria were voluntary participation in the study, absence of any known PAD, absence of physical and medical obstacles to ABI measurement, patients who are served homecare not for acute causes, such as postoperative homecare, and patients not receiving end-of-life care for a terminal illness. The exclusion criteria of the study were unwillingness to continue the study, failure to measure ABI, and an ABI>1.4 (these patients were excluded because an ABI above 1.4 suggested technical error or medial arterial calcinosis) (10).

The Home Health Care Unit had 578 registered patients in June 2014. During the study period, 308 patients applied to the Home Health Care Unit for the first time. All patients were contacted via phone to obtain verbal approval from the patient or their caregiver and to schedule a home visit appointment. After contacting via phone, as 45 patients died, 52 did not consent to participate in the study, 61 did not meet the inclusion criteria (48 patients under the age of 40, 7 patients with a known PAD, 6 patients in the terminal stage), 112 patients could not be reached because of a change in their address, phone number or a temporary change in residence. With the exclusion of 19 patients in whom ABI measurement could not be performed accurately due to peripheral edema and 4 patients with an ABI>1.4 at the time of home assessment, the final study included 285 patients.

Procedure: A questionnaire was administered to inquire about sociodemographic characteristics, duration of bedridden status, chronic diseases, medication, and smoking history. The data on the discharge summary explaining the reason for homecare dependency was recorded, if available. Next, a systemic examination was performed and any deformities of toenails, hair loss, and foot and bed sores were recorded; for obesity assessment, the skin fold thickness indicating subcutaneous fat tissue was measured; and the functional status of the patients was evaluated using the Barthel Index for Activities of Daily Living (ADL). The level of independence increases with high score of Barthel Index of ADL, and a maximum of 100 points can be obtained which represent complete independence. The scores of 0-20 indicate "total dependency", 21-60 "severe", 61-90 "moderate", 91-99 "slight" dependency (11). HbA1c values and lipid parameters of patients with diabetes or hyperlipidemia, evaluated in the last three months were recorded from the patient charts. Finally, the ABI was measured.

The ABI was measured by placing a sphygmomanometer on both arms and the lower part of the knee and using a vascular hand Doppler with an 8-MHz probe (Sonotrax B, Contec Medical Systems). For the measurement of ankle blood pressure, the Doppler probe was placed on the posterior border of the medial malleolus to detect the pulsations of the posterior tibial artery and between the first and second metatarsals to detect the pulsations of the dorsalis pedis artery. Arm pressure was measured from both arms using a vascular Doppler device. The ABI was calculated

by dividing the highest pressure measured in the posterior tibialis or dorsalis pedis arteries by the highest pressure in the right or left arm. The single measurement was considered the highest pressure value in people in whom only a single pressure measurement could be obtained. An ABI below 0.9 was considered in favor of PAD (10). All measurements were made by the same researcher.

The skinfold thickness measurement was made on the right arm, halfway between the acromion of the shoulder and the olecranon of the elbow. The midpoint was marked while the elbow was flexed at 90 degrees, and the skin and the underlying fat tissue 1 cm above this point were grasped between the two fingers and pulled away from the underlying muscle. The jaw of the caliper (Harpenden®, Baty International, UK), which is a special measuring instrument, was placed on the marked point perpendicular to the long axis of the arm. Two measurements were obtained in each patient and the average was recorded. In bedridden patients, the patient was placed on their side and the measurement was obtained by performing the above-mentioned procedures in order.

The wounds on the feet of the patients were evaluated as a "bed sore" when they were located in foot parts in contact with the bed, and as a "foot wound" due to poor circulation when they were on the fingertips. Since most of the patients were immobile and could not express themselves, complaints such as claudication related to PAD could not be evaluated. The drugs were classified according to the World Health Organization's International Anatomical Therapeutic and Chemical Classification system (ATC) (12).

Ethic: The study was approved by Local Ethics Committee of the School of Medicine in Marmara University (2014/1400123396). The participants and caregivers were informed about the study and their consent was obtained. Only voluntary people were included the study.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Analysis: Statistical analysis of the study was performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 16.0 package program for Windows. Descriptive statistics included frequency, percentage, mean, standard deviation, median, interquartile range, minimum and maximum values. In univariate analyses, a chi-square test was used to compare categorical variables, and a Mann–Whitney U test was used to compare continuous variables. Logistic regression analysis was used to idendify the predictors of PAD. A p value less than 0.05 was used as the level of statistical significance.

RESULTS

The study included 285 patients with a mean age of 75.84±1.17 years (min:42, max:100) (34% M; 65% F). Sociodemographic characteristics of the participants are presented in Table 1.

Table 1. Sociodemographic characteristics of the participants

		n	%
Sex	**Female**	186	65.3
	Male	99	34.7
Educational Status	**Illiterate**	182	63.9
	Literate	45	15.8
	Primary school	39	13.7
	Secondary school	12	4.2
	High school	5	1.8
	University	2	0.7
Marital status	**Widow**	176	61.8
	Married	96	33.7
	Single	10	3.5
	Divorced	3	1.1
Households	**Children**	184	64.6
	Spouse and at least one child	49	17.2
	Only spouse	37	13.0
	Alone	7	2.5
	Other*	10	2.8
Monthly income**	**<1,100**	98	34.4
	1,100–3,700	179	62.8
	>3,700	8	2.9

*Other: Relatives or caregivers.

**According to the study conducted by TÜRK-İŞ in June 2014, the hunger limit for a family of four is 1,158 liras and the poverty line is 3,772 liras.

Health-Related Data of Participants: The median duration of home dependency of the participants was 2 years (IQR:1.0–5.0). The most common diseases were hypertension (58.6%), cerebrovascular disease (CVD) (42.8%), diabetes mellitus (DM) (29.1%) (Table 2). The Barthel ADL index scores of the participants evaluating the functional status, skinfold thickness, HbA1c values of 56 patients (19.65%) and lipid parameters of 35 patients (12.28%) evaluated in the last three months are presented in Table 2. It was determined that 217 (76.1%) patients were never smokers, 61 (21.4%) were former smokers, and 7 (2.5%) were current smokers.

Table 2. Some parameters indicating health-related data of the participants

	n	**%**
Hypertension	167	58.6
Cerebrovascular disease	122	42.8
Diabetes mellitus	83	29.1
Dementia	70	24.6
Musculoskeletal system disease	40	14.0
Coronary artery disease	31	10.9
Heart failure	29	10.2
No any disease	9	3.2

	Median (25th–75th. Percentile)	**Minimum–Maximum**
Barthel ADL Index Score (n=285)	25.0 (0.0–50.0)	0–90
Skinfold thickness (cm) (n=285)	15.0 (11.0–20.0)	4–30
F (n=186)	22 (19–27)	8–37
M (n=99)	14 (10–18)	5–30
HbA1c (%) (n=56)	6.40 (5.80–6.98)	4.80–9.10
Total cholesterol (mg/dl) **(n=35)**	180.0 (146–212)	98–312
HDL (mg/dl) **(n=35)**	41.0 (33.0–48.0)	25–114
LDL (mg/dl) **(n=35)**	110.00 (89.75–140.25)	16–204
Triglyceride (mg/dl) **(n=35)**	130.0 (80.0–183.0)	51–355

HDL: high-density lipoproteins; LDL: low-density lipoproteins

The Associated Factors of Peripheral Artery Disease: Peripheral artery disease was detected in 16.8% (n=48) of the patients (ABI<0.9). It was determined that 91.6% of these patients had at least one risk factor for PAD other than age, and 62.5% had 2 or more risk factors. Half of them (n=24) were current or former smokers; it was found that 35 (73%) had HT, 20 (42%) had DM, 10 (21%) had CAD, and 6 (13%) had HL.

It was observed that only 27.8% (n=25) of the patients diagnosed with PAD used any anticoagulant or antiaggregant.

The prevalence of PAD was higher in males than in females; in smokers than in non-smokers; in patients with nail deformity and hair loss in the feet than in those without; in patients with obesity, HT, CAD, and diabetes than in those who did not have; and the skinfold thickness was found to be higher in patients with PAD than in those without PAD (p=0.006; p<0.001; p<0.001; p<0.001; p=0.027; p=0.015; p=0.036; p=0.004) (Tables 3 and 4). There was no association between PAD and CVD, HL, heart failure, renal failure and foot wound (Table 3). There was no association between the level of dependency calculated by the Barthel Index of ADL and PAD (Table 3).

Table 5 presents the results of logistic regression analysis, which was performed using a model (sex, smoking status, skinfold thickness, DM, HT, CAD, CVD, loss of peripheral hair, and deformity of the toenails) incorporating the factors that were found to be associated with PAD in univariate analysis and the presence of CVD that was found to have a strong relationship with PAD in the literature. Accordingly, "current smoking and former smoking" (β:4.09), loss of peripheral hair (β:3.42), deformity of toenails (β:3.02), and increased skinfold thickness (β:1.124) were identified as the factors predicting the presence of PAD (ABI<0.9), respective order (Table 5).

Table 3. Comparison between Presence of Peripheral Arterial Disease and categorical variables

	PAD (+) n (%)	PAD (-) n (%)	Total n (%)	p	x^2
Sex					
Female	23 (12.4%)	163 (87.6%)	186 (100%)	**0.006**	7.66
Male	25 (25.3%)	74 (74.7%)	99 (100%)		
Smoking status					
Current/former smoker	24 (35.3%)	44 (64.7%)	68 (100%)	**<0.001**	21.77
Never smoker	24 (11.1%)	193 (88.9%)	217 (100%)		
Diabetes Mellitus					
Present	20 (24.1%)	63 (75.9%)	83 (100%)	**0.036**	4.40
Absent	28 (13.9%)	174 (86.1%)	202 (100%)		
Hypertension					
Present	38 (20.9%)	144 (79.1%)	182 (100%)	**0.015**	5.86
Absent	10 (9.7%)	93 (90.3%)	103 (100%)		
Coronary Artery Disease					
Present	10 (32.3%)	21 (67.7%)	31 (100%)	**0.015**	5.90
Absent	38 (15.0%)	216 (85.0%)	54 (100%)		
Cerebrovascular Disease					
Present	25 (20.5%)	97 (79.5%)	122 (100%)	0.154	-
Absent	23 (14.1%)	140 (85.9%)	163 (100%)		
Hyperlipidemia					
Present	11 (23.4%)	36 (76.6%)	47 (100%)	0.422	-
Absent	37 (15.5%)	201 (84.5%)	238 (100%)		
Renal disease					
Present	3 (25.0%)	9 (75.0%)	12 (100%)	0.432	-
Absent	45 (16.5%)	228 (83.5%)	273 (100%)		
Heart Failure				0.117	-
Present	8 (27.6%)	21 (72.4%)	29 (100%)		
Absent	40 (15.6%)	216 (84.4%)	256 (100%)		
Foot wound					
Present	2 (20.0%)	8 (80%)	10 (100%)	0.678	-
Absent	46 (16.7%)	229 (83.3%)	275 (100%)		
Deformity of toenails					
Present	41 (25.2%)	122 (74.8%)	163 (100%)	**<0.001**	18.78
Absent	7 (5.7%)	115 (94.3%)	122 (100%)		
Loss of peripheral hair					
Present	38 (29.7%)	90 (70.3%)	128 (100%)	**<0.001**	27.37
Absent	10 (6.4%)	147 (93.6%)	157 (100%)		
Barthel Index of ADL*					
Total dependence	25 (18.5%)	110 (81.5%)	135 (100%)	0.109	-
Severe dependence	20 (19.4%)	83 (80.6%)	103 (100%)		
Moderate dependence	3 (6.4%)	44 (93.6%)	47 (100%)		

The percentages indicate the percentage of rows.

PAD: Peripheral Arterial Disease

*There were no any patients who were complete independent or slightly dependent.

Table 4. Comparison between Presence of Peripheral Arterial Disease and continuous variables

	PAD (+)	PAD (-)	
	Median (25th–75th. Percentile)	**Median (25th–75th. Percentile)**	**p**
Age *(year)*	74.0 (65.0–84.0)	80.0 (69.50–84.0)	0.24
Duration of home dependency *(year)*	3.0 (1.0–5.0)	2.0 (1.0–5.0)	0.33
Barthel ADL Index Score	17.5 (0.0–40.0)	25.0 (0.0–50.0)	0.292
Skinfold thickness *(cm)*	18.0 (11.0–25.0)	15.0 (11.0–18.0)	**0.004**

PAD: Peripheral Arterial Disease

Table 5. Factors predicting peripheral artery disease (Logistic regression analysis)

	B	S.E	Exp(B)	95% C.I. for Exp(B)	p value
Constant	-6.429	0.962	0.002		0.000
Smoking history *(Current/Former vs. Never smoked)*	1.410	0.487	4.095	1.578-10.627	**0.004**
Loss of peripheral hair *(Yes vs. No)*	1.228	0.498	3.415	1.288-9.058	**0.014**
Deformity of toenails *(Yes vs. No)*	1.105	0.545	3.02	1.037-8.784	**0.043**
Skinfold thickness *(cm)*	0.117	0.033	1.124	1.053–1.198	**<0.001**
Sex *(Female vs Male)*	-0.244	0.485	0.784	0.303-2.028	0.615
HT *(Yes vs. No)*	0.622	0.479	1.863	0.729-4.764	0.194
DM *(Yes vs. No)*	0.627	0.414	1.873	0.832-4.214	0.129
CAD *(Yes vs. No)*	0.379	0.523	1.461	0.524-4.077	0.468
CVD *(Yes vs. No)*	0.714	0.399	2.043	0.935-4.463	0.073

R^2=.228 (Cox ve Snell), .381(Nagelkerke), Modelχ2(9)=71.611

The model includes sex, smoking status, skinfold thickness, DM, HT, CAD, CVD, loss of peripheral hair, and deformity of the toenails. HT: Hypertension; DM: diabetes mellitus; CVD: cerebrovascular disease; CAD: coronary artery disease.

DISCUSSION

The aim of this study was to identify the which findings that home health care providers encounter should lead them to suspect PAD. Accordingly, smoking, loss of peripheral hair, toenail deformity, and increased skinfold thickness were the predictors of PAD in home care patients.

The prevalence of PAD has been reported between 5% and 19.76% in general population (2, 13, 14) but 12.2% and 40.0% in elderly patients (15-17). The difference of the present study from those is that it was not conducted in the general population, but with the patients who were served home health care due to immobility. In the present study, peripheral arterial disease was detected in 16.8% of home care patients, which is similar with the prevalence reported in those studies. In another study conducted with the patients over 60 years of age living in a nursing home in our country, the prevalence of PAD was found to be 5.9% (18). In the aforementioned study, the characteristics of the participants, such as age and frequency of chronic diseases, were similar to those in our study conducted with homebound patients; lower prevalence of PAD in their study compared to the present study can be explained by the fact that their patients received long-term care by full-time health professionals, and that the number of patients who were immobile were less in their study. The finding of high frequency of antiaggregant or anticoagulant use in the aforementioned study confirms that the individuals in their study had received high-performing health care services. In our study group, the participants have recently started receiving home health care. The fact that the frequency of using any antiaggregant or anticoagulant was quite low is an indication of that. In addition, it is obvious that our study group is more disadvantageous in terms of immobility, which is one of the most important risk factors for PAD.

While previous studies have reported a relationship between peripheral arterial disease and advanced age (2, 19), the present study found no relationship between increasing age and the prevalence of PAD. This difference may be related to the high mean age of individuals who need homecare (75.84±1.17 years) in our study. In general, the studies in the literature report higher prevalence of PAD in males than in females (2, 18, 20). Similarly, the present study found a higher prevalence of PAD in males than in females, but in the multivariate logistic regression analysis, the sex factor was eliminated, and smoking, which is known to be consumed more by males, was identified as the strongest factor predicting the presence of PAD, similar to that reported in the literature (21). Other studies investigating the risk factors of PAD have identified DM, CAD, HL, HT, smoking, and obesity as risk factors for PAD (5, 22-25). While DM, HT, and CAD appeared as factors associated with PAD in univariate analysis, DM, HT, CAD and HL were not identified as factors associated with PAD in regression model incorporating these factors. The use of different

models and the number of people participating in the study may have caused this difference.

The most important finding in the history of PAD is claudication, but because home care patients are immobile, this finding is absent or asymptomatic. Therefore, it is important to identify other findings when PAD is suspected. Physical examination findings in the guidelines include lower extremity pulse examination to detect vascular bruit, non-healing lower extremity wounds, lower extremity gangrene, and other suggestive lower extremity physical findings (e.g., elevated pallor/dependent rubor) (26-29). In addition, the sensitivity and specificity of nail deformities and peripheral hair loss for detecting PAD have been reported to be low. However, in our study, examination of the toes for hair loss and deformities with assessment of skinfold thickness came to the fore in predicting PAD in home care patients. The results of the present study suggest that home care providers should inquire about the patient's smoking history, assess skinfold thickness, and examine the toes for hair loss and deformity. In the presence of a history of smoking, increased skinfold and peripheral hair loss, and nail deformities in home care patients, it would be appropriate to measure the patient's ABI and perform the necessary interventions in accordance with guideline recommendations.

The strengths of this study are it is the first study to investigate the predictive factors of PAD in patients receiving homecare health services using ABI. The most remarkable limitation of this study is that measurement of ABI and clinical examination were made by the same researcher. Other limitations are the inability to reach all patients who were being followed up by the homecare health unit for various reasons, and the lack of generalizability of the findings due to the fact that the study was carried out only on patients from a single center. However, the present findings may add to increase the knowledge by paving the way for future studies or if the present data are included in a meta-analysis.

CONCLUSIONS

Considering that most of the patients who are homebound are at risk for PAD, the early diagnosis and management of PAD can reduce cardiovascular mortality of homebound patients. We can conclude that smoking status, peripheral hair loss, deformity of the toenails, and increased skinfold thickness should be evaluated by home care providers. If a suspicion, ABI measurement, a noninvasive and easy to perform can be performed. Therefore, healthcare professionals visiting homebound patients should be trained about signs of PAD and ABI measurement. In addition, our research findings suggest that the fight against smoking and obesity in homecare recipient should be an important part of the practice of homecare professionals.

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RESEARCH ARTICLE

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Sinonasal Anatomic Variations in Headache Etiology

ABSTRACT

Objective: Headache is a frequent clinical symptom with multiple etiologies. Our purpose is to investigate the correlation between variations in sinonasal anatomy and headaches.

Method: We retrospectively evaluated the paranasal computed tomography (CT) scans of patients with and without headaches. 118 patients presenting with headaches were included in the study group and 63 patients without headaches were included in the control group. Eight common anatomic variations were clarified and recorded in both groups regardless of whether unilateral or bilateral. Statistical analyses were performed with NCSS (Number Cruncher Statistical System) 2007 software. The results were evaluated at a significance level of $p<0.05$.

Results: Among the variations we investigated in our study agger nasi cells were observed as the most commenly encountered variation. Our study highlighted a statistically significant correlation between headaches and some anatomical variations. These variations including of Haller cell, septum-lateral nasal wall contact, and agger nasi cell.

Conclusions: Headaches have complex pathophysiological mechanisms and may be associated with sinonasal anatomic variations. The recognition of these variations will contribute to the management of the headache.

Keywords: Computed Tomography, Headache, Anatomical Variation.

Baş Ağrısı Etyolojisinde Sinonazal Anatomik Varyasyonlar

ÖZET

Amaç: Baş ağrısı çoklu etiyolojileri olan sık görülen bir klinik semptomdur. Amacımız sinonazal anatomideki varyasyonlar ile baş ağrısı arasındaki ilişkiyi araştırmaktır.

Yöntem: Baş ağrısı olan ve olmayan hastaların paranazal bilgisayarlı tomografi (BT) taramaları retrospektif olarak değerlendirildi. Baş ağrısı ile başvuran 118 hasta çalışma grubuna, baş ağrısı olmayan 63 hasta ise kontrol grubuna dahil edildi. Sekiz yaygın anatomik varyasyon, tek veya çift taraflı olmasına bakılmaksızın her iki grupta da var veya yok şeklinde değerlendirildi ve kaydedildi. İstatistiksel analizler NCSS (Number Cruncher Statistical System) 2007 yazılımı ile yapıldı. Sonuçlar $p<0.05$ anlamlılık düzeyinde değerlendirildi.

Bulgular: Çalışmamızda incelediğimiz varyasyonlar arasında agger nasi hücreleri en sık rastlanan varyasyon olarak gözlendi. Çalışmamız baş ağrısı ile bazı anatomik varyasyonlar arasında istatistiksel olarak anlamlı bir korelasyon olduğunu ortaya koymuştur. Bu varyasyonlar arasında Haller hücresi, septumun lateral burun duvarı ile teması ve agger nasi hücresi yer almaktadır.

Sonuç: Baş ağrıları karmaşık patofizyolojik mekanizmalara sahiptir ve sinonazal anatomik varyasyonlarla ilişkili olabilirler. Bu varyasyonların tanınması baş ağrısının yönetimine katkıda bulunacaktır.

Anahtar Kelimeler: Bilgisayarlı Tomografi, Baş Ağrısı, Anatomik Varyasyon.

INTRODUCTION

Headache is a common health issue arising from the interaction of various factors such as genetic traits, environmental influences, and anatomical variations. Headache encompasses various variable etiological factors, thus necessitating a multidisciplinary approach in research on its etiology. From the point of an otolaryngologist rhinogenic headaches are important. Rhinogenic headaches refer to the pain that originates from the nose. The most common causes of rhinogenic headaches are acute sinusitis, chronic sinusitis, and contact of septum to nasal wall (1). The terms "sinus headache" and "rhinogenic headache" are frequently mistakenly used in place of each other. The term "sinus headache" is a patient complaint rather than an accurate description of an underlying pathologic process (1). Rhinosinusitis develops when one or more paranasal sinuses become infected. The sinuses connect with the nasal passages through ostia, and blockage of the ostiomeatal complex leads to sinus problems in the maxillary, frontal, and ethmoid regions (2).

Embryologically all sinuses begin to develop in utero. Ethmoidal sinuses are the only sinuses that can be seen on imaging at birth. Ethmoid sınuses which are 2-4 cells at birth reach their size by the age of 12. Certain cells in the ethmoid bone have been assigned specific names due to their clinical significance. Ethmoid bulla, Agger nasi cells, Haller cells, and Onodi cells are cells that belong to ethmoid cells (3).

The maxillary sinus can be seen radiographically 5 months after birth. It enlarges first at the age of 3 and then between the ages of 7 and 12 years. It continues to grow until adulthood.

Frontal and sphenoidal sinuses are the last ones to complete their development in late teens and adulthood respectively (4).

Endonasal examination and CT contribute greatly to evaluating headache patients. With the use of CT scans, medical professionals may now see anatomical variations, major blockage locations, posterior sinuses, and the degree of pneumatization (5). Variations in the sinonasal region include concha bullosa, paradoxical curvature of the middle turbinate, septal deviation, frontal sinus aplasia, and some ethmoid cell variations (6). This study seeks to explore anatomical variations and their potential correlation with headaches.

MATERIAL AND METHODS

The paranasal sinus CT of 181 patients who admitted to Şehit Prof. Dr. İlhan Varank Training and Research Hospital between January 2019 and May 2022 were retrospectively analysed. A total of 118 patients who were suffering from headaches were included in the study group, and patients without headache constituted the control group. CT scans were performed with 5 mm sections and without contrast using a multidetector Canon TSX-035A CT Scanner. The study obtained ethical approval (2023/45) from the Ethics Committee of Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital. Patients with nasal polyps, sinusitis, and migraine are excluded from the study. Also patients under age 18 are not included. The coronal, axial, and sagittal sections of paranasal sinus CT were evaluated in terms of predetermined anatomical variations by two clinicians, and a radiologist. Anatomical variations noted included septal deviation, septum-lateral nasal wall contact , concha bullosa, Onodi cell, Agger nasi cell, Haller cell, paradoxical middle turbinate, and frontal sinus aplasia. Anatomical variations were recorded as present or absent regardless of whether they were unilateral or bilateral.

Statistical Analysis: Statistical analyses were performed with the NCSS (Number Cruncher Statistical System) 2007 program. The chi-square test was used for comparisons of qualitative data and OR (Odds Ratio) was used to determine risk. The results were analyzed at the significance level of $p<0.05$.

RESULTS

The study group included 78 females (66.1%) and 40 males (33.9%) with a mean age of 38,1 years and the control group included 33 females (52.4%) and 30 males (47.6%) with a mean age of 36,17 years. Regarding age and gender, there was no statistically significant difference between the two groups (p=0.303, p=0.071) (Table 1).

Table 1. Patient demographics

		StudyGroup	Control Group	p
Age		38±11.50	36.1±12.77	0.303
	Male	33.90%	47.6%	
Sex	**Female**	66.10%	52.3%	0.071

Nasal septal deviation was seen in 91 (77,1%) patients in the study group and in 41 (65%) patients in the control group. In comparison to the control group, the research group had 1.95 (1.02-3.74) times more contact points between the septum and lateral nasal wall. The difference was statistically significant (p=0,041).

Concha bullosa incidence was 48,3% in patients with headache, and 39,6 in patients with no headache.

Agger nasi cells were observed in 95,7% of the study group, and in 76,1 of the control group, respectively.

The Haller cell presence in the study group was found to be statistically higher than in the control group (p=0.018). The risk of Haller cell presence in the study group was two times higher than in the control group.

The presence of septum nasal wall contact (p=0.041), the Agger nasi cells (p=0.0001), and the Haller cells (p=0.018) were significantly more frequent in patients with headaches. When other anatomical variations were analyzed, no statistically significant difference was observed between the two groups (Table 2).

CT images showing anatomical variations of our patients are illustrated in figures 1-4.

Table 2. Frequency of anatomic variations

		Study Group		Control group		
		n	%	n	%	P value*
Nasal Septal Deviation	+	91	77,1	41	65,0	
	-	27	22,8	22	34,9	0,082
Contact between septum&concha	+	54	45,7	19	30,1	
	-	64	54,2	44	69,8	**0,041**
Concha bullosa	+	57	48,3	25	39,6	
	-	61	51,6	38	60,3	0,267
Onodicell	+	26	22,0	18	28,5	
	-	92	77,9	45	71,4	0,329
Agger nasi cell	+	113	95,7	48	76,1	
	-	5	4,2	15	23,8	**0,0001**
Haller cell	+	59	50,0	20	31,7	
	-	59	50,0	43	68,2	**0,018**
Paradoxical middle concha	+	20	16,9	5	7,9	
	-	98	83,0	58	92,0	0,094
Frontal sinusaplasia	+	8	6,7	8	12,7	
	-	110	93,2	55	87,3	0,181

The chi-square test was used; n: number of patients; *Significant at 0.05 level; + Present; - Absent

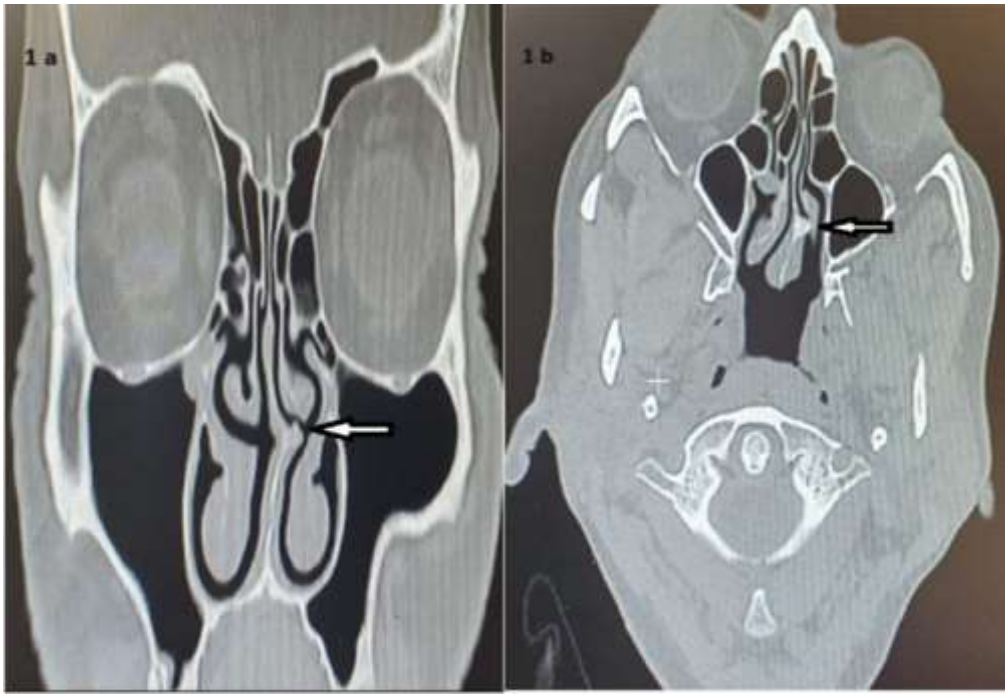

Figure 1 CT images showing nasal septal deviation. 1-a Coronal CT image showing:Leftward deviation of nasal septum (arrow). 1-b Axial CT image of the same patient showing:Leftward deviation of septum and contact of septum to lateral nasal wall (arrow).

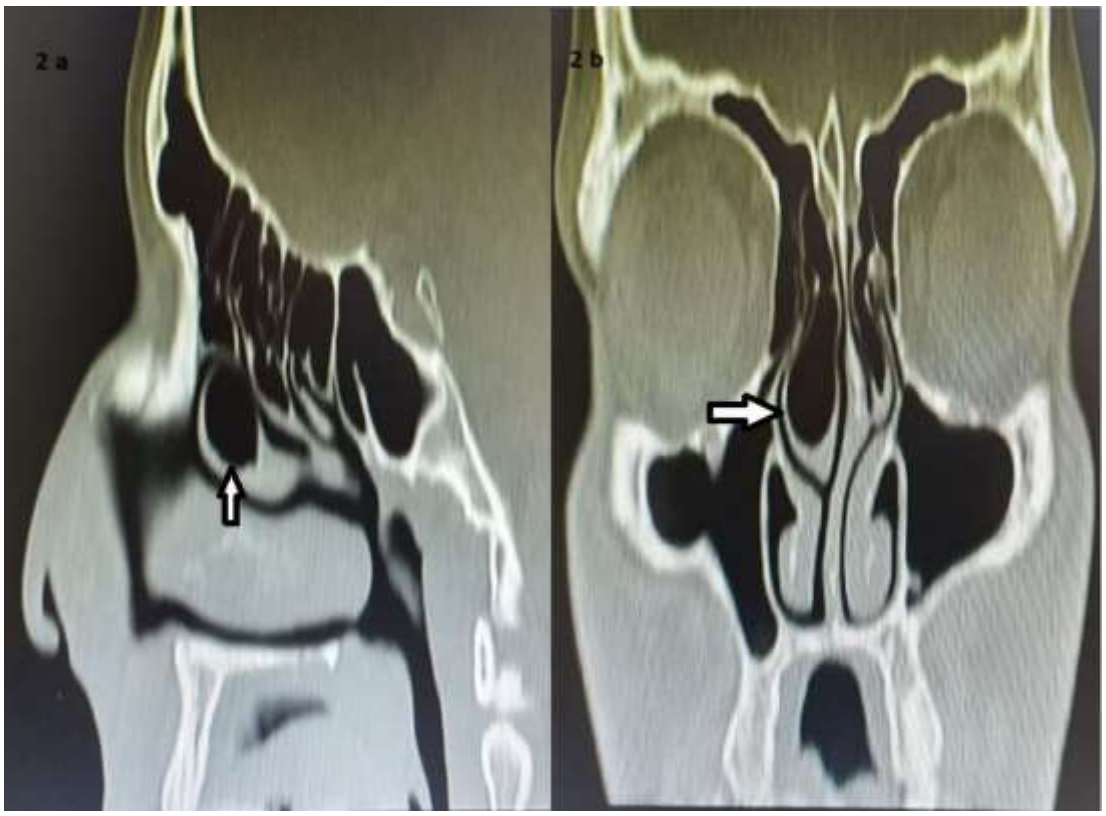

Figure 2. CT images showing concha bullosa cells. 2-a Saggital CT image showing concha bullosa (arrow). 2-b Coronal CT image of the same patient showing right concha bullosa cell (arrow)

Figure 3. CT images showing agger nasi cells. 3-a Saggital CT image of the showing agger nasi cell (arrow). 3-b Coronal CT image of the same patient showing bilateral agger nasi cells (arrows).

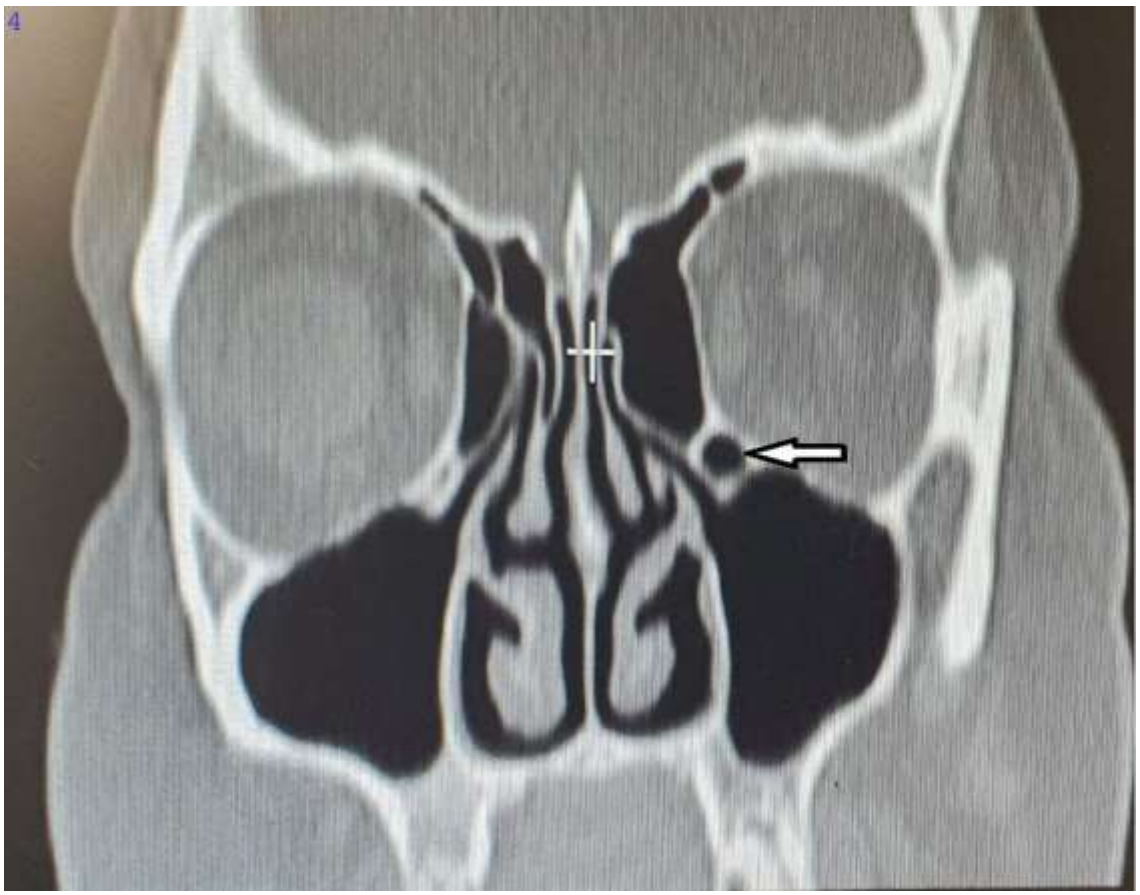

Figure 4. Coronal CT image of a patient showing left Haller cell (arrow)

DISCUSSION

There are limited number of studies that reveal the relationship between headache and anatomical variations. The current study is the first to suggest that agger nasi cells and Haller cells may be significant in headache etiology.

Septal Deviation and Septum-Lateral Nasal Wall Contact: Prior research has indicated a correlation between nasal septal deviation and rhinosinusitis (7,8). Also, the frequency of concha bullosa is found to be high in deviated nasal septum (8). The role of the deviated septum in the etiology of headaches has not been fully clarified. Septal deviation is found to be correlated with headaches in only a recent cohort study. Patients with septal deviation were found to have a higher risk of headache with a 1,37 adjusted hazard ratio and septoplasty was reported as the first-line treatment option (9).

The literature indicated a prevalence of septal deviation ranging from 40% to 96.9% (10). In 77,1% of patients with headaches and 65% of patients without headaches, the nasal septal deviation was discovered. Nevertheless, p=0.082 indicates that there was no statistically significant difference between the groups.

Stammberger and Wolf were the first ones who hypothesized contact point headaches. This suggests that when the septum comes into touch with the lateral nasal wall, substance P, a neurotransmitter, is released, which causes referred pain via unmyelinated C fibers (11). Surgical treatment of contact points resulted in symptom relief in most patients (12). Also, It has been shown that 85 percent of patients with headaches had pain relief after surgery (13). However, a systemic review including a wide range of studies concluded that most patients with contact points are asymptomatic and contact point has no effect on headaches (14). Also in another retrospective study, they found no correlation between mucosal contact points and headache (15). In the present study, contact of the septum to the lateral nasal wall is 1,95 times more frequent in the study group than it is in the control group ($p<0.041$). This result confirms the hypothesis of Stammberger and Wolf (11). The only deficiency of our study regarding this result may be that we evaluated the contact points according to CT and did not verify it with the endoscopic nasal examination.

Concha Bullosa: The presence of an air cell within the turbinate causes concha bullosa. The word "concha bullosa" is typically used to describe the middle turbinate's pneumatization. Concha bullosa of superior and inferior turbinates is rarely seen. It has three types 1- lamellar type involving vertical lamella 2-bulbous type involving the inferior part of concha 3-extensive type involving

both lamella and inferior part (16). The incidence varies between 14-53% (17).

Cantone E. et al investigated headache patients who had concha bullosa with mucosal contact points. They found improvement in headache symptom scores in patients after treatment for concha bullosa. The surgically treated group benefited more than the medically treated group (18). No correlation was found between concha bullosa and headache in this study. This result may be due to our inclusion criteria comprehending all types of concha bullosa, regardless of type, size, and contact point.

Paradoxical Middle Turbinate: Middle concha is generally laterally deviated, if it medially deviates it is called paradoxical middle concha. It is clinically important as it can narrow the osteomeatal complex and may cause rhinosinusitis (19). Its incidence varies between 3-26,1% (20). Incidence was 16,9% in patients with headache and 7,9% in patients with no headache. There are very few studies about paradoxical middle turbinate in headache etiology. Paradoxical middle turbinate deviation showed no association with headaches in our study.

Onodi Cell: The Onodi cell, which is located above the sphenoid sinus, is the most posterior ethmoid air cell. The presence of Onodi cells varies between 8-13%. There is no known direct correlation between headache and Onodi cells in the literature. In the current investigation, there was no association found between headache and Onodi cells.

Agger Nasi Cell: The most anterior ethmoid cell is the agger nasi cell. It is located anteriosuperior to the lateral nasal wall's middle turbinate insertion (11). In the literature, it shows a broad range of variability, from 2% to 100% (21). Ethnic differences may influence the incidence of variation.

In many studies, it has been reported that the agger nasi cell may expand posteriorly and narrow the frontal ostium and cause frontal sinusitis (22,23). In the study investigating the relationship between agger nasi cell size and frontal sinus ostium diameter, it was concluded that agger nasi cell size did not have a strong effect on frontal sinus ostium diameter (24). Comprehensive studies are needed to reveal the relationship between agger nasi cell and frontal sinusitis.

In the literature, the number of studies revealing the relationship between agger nasi cell and headache is limited. In a study comparing the anatomical variations of migraine patients with the control group, the incidence of agger nasi cells in the control group was higher than in the migraine group, so there was no correlation between migraine and agger nasi cell (20). In a recent study investigating anatomical variations that may cause rhinogenic headache; type 2, type 3 fronto ethmoidal cells and concha bullosa cell were found to be associated with headache. Agger nasi cell was not included in the anatomical variations evaluated (25). In the present study, the incidence of agger nasi was 76,1% in patients without symptoms and 95,7% in patients with a headache. There was a statistically significant correlation between agger nasi cells and headache and none of the patients had sinusitis. To our knowledge, this correlation is the first in the literature up to now. The possible mechanism may be due to limited unrecognized inflammatory mucosal diseases in the frontal recess or by completely a different physiopathology.

Haller Cell: Haller cells are ethmoidal cells that develop into the medial floor of the orbit. They mostly originate from anterior ethmoidal cells and rarely from posterior ethmoidal cells. They are of clinical importance as they can cause sinusitis by narrowing the infundibulum and ostium. Unlike other anatomical variations, it is difficult to diagnose Haller cells with endoscopic examination. The incidence rate of Haller cells varies between 2-51% in the literature (19). Haller cells were observed in 59(50%) of patients in the study group and 20(31,7%) of patients in the control group.

The presence of Haller cells was found to be statistically significantly higher in patients with headaches in the present study. The association of headache with Haller cells is poorly defined in the literature.

A previous study reported that Haller cell incidence was significantly high in migraine patients (20). Vanamaker also reported a case of a child with refractory headaches unresponsive to medical treatment. He had isolated opacification of Haller cell bilaterally and his headache dramatically improved after exenteration of Haller cell by bilateral functional endoscopic surgery (26). Haller cells may cause pressure on the infraorbital nerve, may cause sinusitis via the obstruction of the ostium, or may cause headache through contact with the infundibulum (27). Although the mechanism is not known Haller cell is the key anatomic variation in headache etiology with or without sinusitis. This study will guide future research exploring the significance of Haller cells in causing headaches.

Frontal Sinus Aplasia: Many people with frontal sinüs aplasia are asymptomatic. Frontal sinüs aplasia incidence has a wide range variety. This is explained by ethnic differences, gender, and environmental factors. Canadian Eskimos have unilateral frontal aplasia at 43%, while Germans have 3,4%. Females generally have higher incidences. Aydınoglu A. et al. found unilateral frontal cell aplasia in 3,8% of males, and in 5,9% of females in the Turkish population (28,29). Frontal sinüs aplasia incidence was 6,7% in the study and 12,7% in the control group. There was no association between frontal cell aplasia and headache.

There are limitations to our study. The first limitation is single ethnic subjects. Multi-ethnicity would provide less variable results. The study's second limitation is its single-center design, which could limit the generalizability of the findings to other settings.

CONCLUSION

These findings will contrubute to physicians in the evaluation and treatment of patients with headaches. Further comprehensive studies are needed to investigate the role of Haller cells and agger nasi cells in the etiology of headaches.

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RESEARCH ARTICLE

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A Phenomenological Qualitative Study: Family Physicians Experiences of Consulting Older Adults

ABSTRACT

Objective: Due to the aging population, older adult health became important. Family physicians play an important role in the health of older adults. This study aims to identify the challenges family physicians experience in counselling older adults.

Method: A qualitative, phenomenological methodology was used. Authors conducted three semi-structured focus group interviews with 22 family physicians. The recorded interviews were transcribed, and thematic analysis was applied.

Results: The mean age of the participants was 33.68 ± 8.37. The mean professional years of the participating physicians were 8.77±8.26 years. Seven of the participants were women and fifteen were men. Three themes emerged: (1) patient-related factors, (2) physician-related factors, and (3) physician remedies.

Conclusion: There are positive and negative aspects to consulting older adults. Understanding the difficulties experienced can facilitate the solution. Physicians stated that there was no geriatrics training both in their medical school undergraduate and postgraduate curriculum. They also stated that they found themselves inadequate in this regard and that creates anxiety. Effective communication is important both physically and emotionally during the interview. In fact, communication and active listening skills can be taught and postgraduate training in geriatrics can be organized.

Keywords: Older Adult, Qualitative Research, Comprehensive Approach.

Fenomenolojik Niteliksel Bir Çalışma: Aile Hekimlerinin Yaşlı Yetişkinlerle Görüşme Deneyimleri

ÖZET

Amaç: Yaşlanan nüfusa bağlı olarak yaşlı yetişkin sağlığı önem kazanmıştır. Aile hekimleri yaşlı sağlığında önemli rol üstlenmektedir. Bu çalışma, aile hekimlerinin yaşlı yetişkinlerle görüşme konusunda yaşadıkları zorlukları tanımlamayı amaçlamaktadır.

Yöntem: Niteliksel, fenomenolojik bir metodoloji kullanılmıştır. Yazarlar 22 aile hekimi ile yarı yapılandırılmış üç odak grup görüşmesi yapmıştır. Kaydedilen görüşmeler yazıya dökülmüş ve tematik analiz uygulanmıştır

Bulgular: Katılımcıların yaş ortalaması 33,68±8,37 yıldır. Katılımcı hekimlerin meslek yılı ortalaması 8,77±8,26yıldır. Katılımcıların yedisi kadın, onbeşi erkektir. Üç tema ortaya çıkmıştır: (1) hastaya bağlı faktörler, (2) hekime bağlı faktörler ve (3) hekimin çareleri.

Sonuç: Yaşlı yetişkenlerle görüşmede olumlu ya da olumsuz yönler bulunmaktadır. Yaşanan zorlukları anlamak çözümü kolaylaştırabilir. Hekimler tıp fakültesi lisans ve mezuniyet sonrası müfredatı içinde yaşlı sağlığı eğitiminin bulunmadığını belirttiler. Bu konuda kendilerini yetersiz bulduklarını ve bu durumun kaygı yarattığını da dile getirdiler. Etkili iletişim, görüşme sırasında hem fiziksel hem de duygusal olarak önemlidir. Aslında iletişim ve aktif dinleme becerileri öğretilebilir ve yaşlı sağlığı konusunda mezuniyet sonrası eğitim düzenlenebilir.

Anahtar Kelimeler: Yaşlı Yetişkin, Niteliksel Araştırma, Kapsamlı Yaklaşım.

INTRODUCTION

As life expectancy increases, health care of elderly becomes more important. Aging has its own characteristics, like childhood, and examination is different from other patient groups due to the physiological changes that occur (1). Older adults are often assumed to be debilitated or dependent. This is not true for every elderly person. Each elderly person's health care needs are shaped in line with the characteristics of their own health and life dynamics. That makes evaluating elderly people difficult for physicians (2). As the elderly population increases, health problems encountered, and health needs are changing. Preventive and therapeutic health services should be provided so that they can live independently. The quality of life becomes a priority. Quality of life and factors affecting quality become as important as living for a long time. Recently, healthy aging strategies have been developed (3). On the other hand, incidence of many diseases increases with age. Accepting that health will deteriorate with age may cause the diagnosis of diseases to be delayed (4). Disease symptoms of older patients may differ from younger patients. Disease may progress insidiously in older patient or may present with atypical symptoms other than what clinicians used to expect older patients are a vulnerable group whose general condition can change rapidly, and patients are also more susceptible to drug side effects and drug interactions. The drugs to be selected, drug doses and treatment targets are different in older patients than in younger patients. In addition, treatments in this age group should be planned individually, considering the performance, expected life expectancy and living conditions (5).

Since physicians often faced with chronic diseases that require continuous follow-up, patient and physician cooperation become even more important. When cooperation is ensured, treatment success and adherence to treatment increase. Comprehensive assessment of the geriatric population is important for prevention and improvement of quality of life. A biopsychosocial approach based on family medicine is particularly important for older adult care. Preventive medicine includes many practices, and the aim is to increase and protect the quality of life not only of the person himself, but also of those around older adult. Public health policies should include providing comprehensive health care, appropriate health care, social services for older adults, and continuing education on this subject for health professionals (6). The World Health Organization has projects aimed at basic education for primary health care providers about the health needs of older adult patients (7). The United Nations Decade on Healthy Aging (2021-2030) aims to reduce inequalities in health and improve the lives of older people (2). A comprehensive public health response must address this broad range of experiences and needs. Within the framework of search for solutions to the increasing medical and social needs of the older people, family physicians have important tasks and undertake an important role as the first contact in older adult's health care. Primary health care requires a wide variety of skills, reflecting the complexity and heterogeneity of ageing population. These skills are also fundamental components of the family medicine residency curriculum. Although there are times in these trainings when they experience visits of older adults, there is not a specific training program about older adult care. However, there are still some challenges about consulting older adults (8). This study aims to describe challenges of family physicians' when consulting older adults.

MATERIALS AND METHODS

Study Design: This is phenomenological qualitative research in which family physicians' experiences were analysed (9). Thematic content analysis was carried out in accordance with qualitative research methodology and analysis approaches (10). Consolidated Criteria for Reporting Qualitative Research guidelines were followed (11). The research was approved by the Non-invasive Clinical Research Ethics Committee (date no: 12.07.2019-e.43255). Each participant gave written and verbal consent before the interview.

Participants & Sampling Procedures: We used purposive sampling method. Twenty-two physicians (6 family medicine specialists, 8 family medicine residents in final year of education, 8 family medicine residents in second year of education) were involved in the study. Participants were invited to scheduled meeting and each focus group met once. The mean age was 33.68±8.37. The mean year in the profession of the participating physicians was 8.77±8.26. Table 1 shows some characteristics of the participants. First focus group consisted of 8 family medicine residents in final year of education. The mean year in the profession of the participating physicians was 7.0±3.81years. Second focus group consisted of 6 family medicine specialists. The mean year in the profession of the participating physicians was 19.0±8.89 years. The third and last one consisted of 8 family medicine residents in second year of education. The mean year in the profession of the participating physicians was 2.87±0.83 years.

Data Collection Procedures & Instrument: Data was collected between January 2020- March 2020. The focus-group interviews were conducted in a quiet environment with appropriate physical conditions for the focus group meeting in a round table arrangement. The primary author, trained in qualitative research methods, facilitated all interviews. During the focus group interviews, primary author conducted the meeting while the second one observed the participants,

Table 1. Characteristics of the participants

Acronym	Gender	Age	Years in occupation as Family Physician	Focus group
A1	Female	28	3	1
A2	Female	30	5	1
A3	Male	31	5	1
A4	Male	41	15	1
A5	Female	32	7	1
A6	Male	35	9	1
A7	Male	34	8	1
A8	Male	28	4	1
B1	Male	45	19	2
B2	Male	43	20	2
B3	Female	56	31	2
B4	Male	51	26	2
B5	Male	32	8	2
B6	Male	35	10	2
C1	Female	28	3	3
C2	Male	29	4	3
C3	Female	27	2	3
C4	Male	27	3	3
C5	Male	27	2	3
C6	Male	26	2	3
C7	Female	28	3	3
C8	Male	28	4	3

took notes and oversaw the audio recording. Data collection in the study was achieved through face-to-face semi-structured interviews conducted with the participating physicians, during which the researcher asked the respondents open-ended interview questions that were devised following a literature review (Table 2). During the interviews, the questions were asked to the participant in a clear and understandable way, and specific subjects were investigated deeper through additional questions if necessary. After all, the open-ended questions had been asked; the respondents were left to discuss. If there was no departure from the topic, no intervention was made, and the respondents were free to speak.

Table 2. Semi-structured questions in focus group interviews

1.	How does the interview process with the older patient happen?
2.	What do you feel in the older patient interview?
3.	How do you manage older patient interview?
4.	What might affect your approach to the older patient interview?
5.	What effects the older patient interview?
6.	Why does the patient choose you?

The first focus group interview was held with eight family medicine residents with experience with older adults who were in their final year of education, and lasted 44 min. The second focus group interview lasted for 42 min and was conducted with six family medicine specialists who were working actively with older adults. The third focus group interview lasted for 50 min and was conducted with eight family medicine residents in their second year of education who had limited experience with older adults during their residency training.

Analysis: All focus group interviews were recorded and transcribed verbatim on the same day using Microsoft Word. Three authors who were trained in qualitative research methods took part in analysis. Two coders, with different backgrounds in their academic disciplines, independently read the transcripts multiple times to internalize the topics. Next, coders independently coded and cross coded transcripts. During the theme creation process, meaning units were re-examined and evaluated, and the notes taken by the second author during the interviews allowed the data to be conceptualized more accurately. Coders met weekly to discuss their analyses and interpretations and created a list of themes in which similar codes were condensed. After a total of eight analysis meetings, the third author reviewed them all, and all coders discussed and reached consensus on themes and subthemes (12).

RESULTS

The main themes grouped as: (1) patient related factors, (2) physician related factors and (3) the physician's remedies (Table 3).

Patient Related Factors

Common Health Issues: Older adults may have comorbidities and multiple drug use. It is more difficult to manage patients who use multiple drugs and have problems related to old age, which is an issue that has been mentioned many times and is expressed as follows:

"They open a bag full of drugs and pour them onto your table which makes you more stressful."(A7)

Another common issue in older patients is mental problems. Memory problems are common although it does not always extent of disease. Physicians who participated in the study mentioned it as a challenge.

"Since Alzheimer's and memory loss is common in older patients, these always affect communication."(B6)

"You ask a question, s/he answers another question in her/his mind."(A4)

"They can really jump from branch to branch while talking."(C8)

It is also a challenge for physicians, older patients accept a symptom as a part of daily life and think it is normal for their age.

"*They do not consider the diseases for which they receive treatment and medications as a disease*."*(A4)*

As stated by one physician, "*If they have a new problem, they see it as a disease*" *(A4),* adding that they no longer consider their chronic diseases as a disease, and so a comprehensive inquiry should be made rather than focusing only on the main complaint.

Tablo 3. Examples of Categories and Themes

DATA	Categories	Themes
"*Since the older adults has more polypharmacy and many accompanying comorbid diseases, patient management is more difficult and more complex, and the process takes longer than younger patients*." *(B6)* *"They are confused about their medicine a lot; what time they will take it, what they will do… the treatment process, like, just like children." (B3)*	Common health issues	Patient related factors
"When an older patient comes (to my clinic), I need to take his/her arm and carry him/her to examination table. If the patient falls, a trauma comes out of nowhere." (A3) *"Instead of listening to his companion, we should listen to patients…. what is the real problem for the patient. Companion may explain his/her complaint, but we need listen to 'real' patient, especially if he has any other problems deeper." (A7)*	Physical obstacles	
"T*ime, they want to spend with me is much longer than young patients…The patient leaves when we are done about health care but older patients sometimes want to talk afterwards about politics, they want to chat about their daughter-in-law.*" (B1)	Social challenges	
"We did not take geriatrics class. Our education was not suitable for this, young doctors know better. It didn't exist in our time; I feel such an inadequacy. Indeed, it is difficult to manage older patient." (B4) *"Our appearance is very effective. 'Are you a doctor, my child? Are you still studying med?' etc."* (A2) *"They may argue that 'I know more than you, I have lived more, these have happened to me more, I have always solved them like this', and they may oppose something you have just presented. Because they have a dogma, they believed in them and you can't change it all at once."* (C4) *"Of course, older patient is a cause for fear and anxiety. Because the reason for the old patient's visit may be only one thing, but we know that many things can come out of it, investigating more, questioning more and fear of skipping something is a greater concern."* (A1) *"You wonder what will happen... they request from you to heal, but what you can do is limited, and it comes back to you as a psychological burden, you get sad..."* (B4)	Skills of physician	*Physician related factors*
"In general, there are two possibilities, they come for the purpose of prescribed drugs, or they have many very chronic diseases…the treatment of these diseases." (A6) *"We already have prejudices about it. I wonder if s/he will have too many complaints, does he have comorbidities, there are drug side effects, the frail elderly… And we need to think about them. We start with question marks when the old man/lady enters the room." (A2)* *"My anamnesis will take longer, I don't know if he will be able to tell me about his problem, or sometimes you see audio devices or something… Inevitably, as soon as the patient enters, they already appear." (A3)* *"You know, since most of them have such a chronic pain, as soon as the patient enters, I have a bias that there is no big problem." (A8)*	Prejudice due to common problems	
"*Maybe speaking a little louder and slower; using words that s/he can understand; or maybe using basic language*." (C5) *"Contact is critical indeed. Patting them on the back and holding their hand, or something similar, really boosts their confidence."* (B1) "*It may be an advantage to have someone who knows the situation and who can explain the situation better, as it allows us to communicate better with the patient during the examination.*"(C5) "*Knowing the patient also increases the number of applications of patients. S/He [the patient] says, 'My doctor knows me, s/he knows about my complaint as s/he has been following me for years', and so s/he feels s/he can trust the family physician more*." (A1).		The physician's remedies

"Their own body perceptions can be different."(B1)

"They have accepted the pain; their pain thresholds are very different."(A7)

Physical Obstacles: The vigour of the patient greatly affects the physician's physical examination. Physical insufficiency leads to anxiety about not being able to undergo the examination comfortably and can lead to time management problems for physicians:

"*The physical condition of the patient is critical. Will I be able to examine the patient the way I want? This affects my consultations a lot.*"*(A2)*

"When an older patient with walking difficulties comes... I just feel uncomfortable in terms of time management."(C8)

However; communication is another obstacle when assessing an older adult. Age-related disabilities are difficult to solve. In consultations, it is important that the patient and the physician understand each other as much as the physician's impressions of the patient. It is worth emphasizing the effects of both the patient's cognitive problems and hearing difficulties, which can cause communication barriers:

"*Communication problems makes me think. For example, will s/he be able to hear me and understand me sufficiently, or will s/he give an inappropriate reply to the question I ask?*"*(A5)*

"Sometimes they can express their complaints with very different words, the language they use can be outdated"(B1)

"His companion speaks. Patient really can't tell (about his/her own problem) properly. We understand patient's complaint after all, we don't have any other choice, frankly."(A8)

Social Challenges: It is not always easy to find companion for older adults "*One of the biggest problems in older adults is loneliness*" *(A6)* and it was emphasized that health care is not just about medical assistance, there is also a need of holistic approach that considers social aspects.

"… s/he is socially lonely, unable to buy his medication, maybe the medication I prescribed will be an additional burden for him…that is a big problem for her/him"(A5)

Another issue mentioned during the interviews was the mood of the patients. Physicians stated that changing patient emotions also affected their own practices, making interviewing difficult.

"Old people, maybe a little more, how can I say, touchy?"*(A3)*

"Not all older people are sweet, I mean, there are very sweet older people, but there are some who are so weirdly grumpy and targeted to quarrel."(B3)

"… they have lived 70-80 years, all those problems piled up, they carry on their back. You know, they don't travel around the world like these retirees in the west (countries), our people seem to be more worn out both physically and spiritually."(B4)

Physician Related Factors

Skills of Physician: Skills of the physician is another challenge mentioned in focus groups. physicians are trying to cope with many different problems at the same time in every older patient who enters the door. They know that they must think about many issues related to the patient, but they are not sure whether they can deal with them.

"We feel inadequate with polypharmacy and many chronic diseases in older patients."(B6)

"Also, it is very difficult to find the real reason, the real reason of urgency."(A8)

In addition, age or social differences between physician and patient can also cause a doubt in the patient about the competence of the physician. The physician who is aware of these doubts is affected.

"There are also those who enter (the room) to argue with the doctor. And some who come with prejudice so that doctors should understand what they mean by looking at their face..."(A2)

As a result of all these different reasons, our physicians stated that they experienced fear and anxiety or feelings of inadequacy while meeting with the patient. They explained that these feelings limited their abilities when examining them.

"When you see an elderly patient, you have the lottery surprise box, a surprise egg."(C4)

"S/He tells a lot of things. I have concerns about whether I will be able to analyze the important ones correctly."(A5)

"Since they have a lot of extra troubles, there is a concern whether I will be able to afford all these, on the one hand, there is the fear that I may miss something."(A2)

Physicians also mentioned confusing emotions that affect them when they meet an older patient. They stated that they had to cope with these feelings during their interviews and that they had to suppress them in order to act professionally.

"...I usually feel sad if s/he lives alone."(A6)

Prejudice due to Common Problems: Our physicians mentioned that they started to visualize some scenarios that are common in older patients as the patient enters the room. This can be explained by the phase in which the physician develops a theory about the patient, which exists in interview techniques, but the fact that it reaches the dimension of being biased may also affect the physician's right decision about the patient. It may affect the patient-centered approach.

"In general, there are two possibilities, they come for the purpose of prescribed drugs, or they have many very chronic diseases…the treatment of these diseases."(A6)

"He comes and says, 'My knee hurts, my child,' he wants medicine, he wants painkillers. That is why we may ignore the bigger problems in the very old patient."(A8)

The Physician's Remedies: Physicians consider actions such as raising their voice and speaking in turn during consultations with older adults as potential solutions to hearing problems, although it was also stated that examining patients at home could alleviate some of the physical barriers:

"*Maybe speaking a little louder and slower; using words that s/he can understand; or maybe using basic language*."(C5)

Most physicians noted that they feel they are closer to their older adults and said that being friendly makes conversation better, involving contact with the patient, the use of body language and using a sincere approach:

"*Sometimes holding their hand or patting their back, makes the patient happier. After conducting an examination, having contact with the patient while explaining the situation can motivate them*."(C4)

"… (when they come to my office) I treat them like one of my relative entering my office."(C8)

Improving the physical condition of family health care centre can also facilitate consultation. Participants stated that making the examination room and throughout the family health center suitable for elderly patients may ease of movement and increase comfort. There are mandatory regulations in our country to ensure this physical comfort. Participants stated that improving the physical conditions of the family health center could help the elderly overcome their physical disabilities, *"legal regulations such as 110 cm wide doors and ramps for the disabled"* (B6).

Communication is easier if older adult attends the consultation with a companion:

"*It may be an advantage to have someone who knows the situation and who can explain the situation better, as it allows us to communicate better with the patient during the examination.*"(C5)

The holistic approach and continuity of care associated with family medicine are the two principles that help family physicians most in overcoming the challenges they encounter.

It was stated that it was important among older adults to feel that their doctor is listening to them. As stated by one participant, *"… very important they feel like we are listening to them, as they may not feel this with another physician.*"(B1)

The appreciation of older adult patients when compared to that of other patient groups and the patient's ability to express himself/herself, create positive feelings in physicians. It was further stated that older adult patients tend to behave with more respect, and so the consultation process tended to be easier.

"*We might not be able to solve the problem completely, but if I can make him/her more comfortable, and they leave here satisfied, it is generally pleasing for me*."(A5)

DISCUSSION

Family physicians play an important role in the health care of the older adults (6). Physicians should support patients not only in case of illness but also in healthy aging. Primary care physicians require a wide range of skills to meet the needs of the aging population. Even though they contact with the elderly in training, there may be deficiencies in specific training regarding elderly care. However, there are still some challenges in counseling older adults (8). This study aims to identify the challenges family physicians experience when consulting older adults.

After analysis of this research data, three themes emerged: patient-related factors, physician-related factors, and physician remedies. From the physician's perspective, the problems in the elderly patient's ability to express their-selves during patient-physician consultation and examination are not clearly known. It is important to make this clear. It is inevitable that physicians need certain skills in consulting elderly patients in terms of diagnosing, preventing and maintaining health, and having good patient-physician relationship. It is also important that this is revealed by physicians; because it is a skill that can be improved. Obtaining this information will be a guide for this improvement. While physicians can find solutions to some of the problems in management of elderly patients, they cannot find solutions to others. Revealing not solved one's ease to think about solutions and find a way out.

As people age, they are more likely to experience several conditions (2). Changes due to nature of aging and common health issues of older patients can be challenging. Like literature, in our study, common health issues, comorbidities and polypharmacy were some reasons that made it difficult to interview the older patient (13). Studies have shown that multi-morbidity and polypharmacy increase with age, while the use of different medications causes problems in patients, which justifies the claims of the respondent physicians (14,15).

The challenges include communication barriers which is the basis of the patient-physician interview. Problems such as hearing problems, mental status changes, vigor of the patient also effect communication (2). Physicians mentioned that the presence of companion both facilitates and complicates consultation. It facilitates history taking and allows more information; helps physical movement, such as undressing during the examination; shortens the examination duration. Unfortunately, it may affect the depth of interview and avoiding private topics, but physicians stated brief talk is better due to workload.

Loneliness of the elderly has also been identified as an obstacle by physicians. Having someone at home to observe whether they are using the given treatment or suggested change correctly

makes it easier to assess compliance with the changes. There is also a strong relationship between loneliness, mood, and depression in older adults (16). A wide variety of interventions have been developed to combat loneliness and social isolation in the elderly (17). Not every person experience loneliness in the same way or to the same degree, and it is stated by our participants that ignoring the symptoms that exist as a part of old age is a challenge. Here, physicians should be alert to some issues that the patient himself may consider unimportant. In society, being old mostly contains negative statements. In fact, the definition of old age is stated as "showing the effects and features of increased age" (18). Thus, aging is considered as a process that should be avoided and undesirable. The society's view of aging, perception and prejudices may affect the services provided to older people. Health professionals need to address these ageist society attitudes, which can lead to discrimination, affect older people experience healthy aging (2). Not only the attitude of the physician to older patient, but also vice versa may be biased. The large age gap may cause the patient to treat the doctor as he treats his/her child. "I am wiser when I am older" also compels the physician. This cultural feature is very difficult to overcome. As mentioned before, while patients accept and ignore some symptoms as a part of aging, the physician may experience the same delusion. The prejudices of old age come into play and the evaluation of patient is affected on which physician may have overlooked another underlying problem. Participants are aware of these biases and that causes anxiety. However, they did not propose any solution to change.

Due to the nature of medicine, it is necessary to be solution oriented. In the focus group interviews, it was spontaneous to start talking about solutions. Physicians make some changes to enable patients more comfortably. Some practices to make older patient-friendly health center are also on their agenda. To make communication clear, speaking loudly and slowly was accepted as a solution to problems related to hearing. Slower speaking rate at a higher pitch and louder, repeating instructions and using basic words, and less grammatical complexity may help in communicating with the older adult patient (1). It is stated that if a good level of communication with the patient is not established, the patient will not trust the physician and as a result, the physician will be deprived of the patient's medical history (19). With sense of trust between the patient and the physician, a social safety net around these people can be contributed (20). A comprehensive approach when consulting older adults can have several benefits (6). Good communication can also support preventive health, diagnosis, treatment and decision-making. In this study, participants stated that they care about patients' emotions, and there is a scoping review in the literature that emphasize the importance of paying attention to patients' emotions when questioning their physical health and taking their stories (19). All participants approached their patients with similar goals but used different methods. Considering these data, the participants believed that consultation challenges are mostly attributable to patient-related or physician-related factors. In another study, difficulties encountered in the management of older adult patients were classified as those attributable to the patient, physician, and health system which was never mentioned in our research (21). Physicians mentioned that there is no geriatric training in their training that causes anxiety. However, training about communication and active listening skills was not mentioned as a solution which teachable and post-graduation education can be arranged about geriatrics.

The results of the research were discussed in detail. Revealing these findings may be a guide for family physicians to improve their skills in consulting elderly patients and take them to the next level because the patient-physician consultation is a learnable and fixable skill. Finding these and getting remedies from physicians, understanding what they experience and what deficiencies they feel about elderly patient consultation can help it. This study which explores family physicians' experiences of consulting older adults in primary care may provide valuable information for improving primary care. Family physicians who work in an aging society need to know more about characteristics of elderly patient population. Family physicians need to know their role in elderly care and basic competency requirements to develop evaluation strategies.

LIMITATIONS

This study has some limitations. First, the nature of qualitative study does not allow determining causality. Additionally, this study cannot represent larger population due to the non-probabilistic sampling method. Second, results may have been influenced by participants personal expressions, but since qualitative research is conducted with a sample appropriate to the research question, it aims to understand what participants experience on the issue. Further research may be planned to measure perceptions expressed by participants in our study.

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RESEARCH ARTICLE

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The Effect of COVID-19 Pandemics on the Quality of Life in Children of Type 1 Diabetes Mellitus and Their Families Using Insulin Infusion Pumps

ABSTRACT

Objective: This study aimed to assess the impact of the coronavirus disease (COVID-19) pandemic on the quality of life (QOL) of children with type 1 Diabetes Mellitus (T1DM) and their families, specifically focusing on the effects of insulin infusion pumps. We also aimed to identify changes in both children's and parents' QOL during the pandemic period.

Method: This study utilized the KINDL (KINDer Lebensqualitätsfragebogen: Children's QOL) questionnaire for the children, and the World Health Organization Quality of Life (WHOQOL)-BREF Turkish Version (TR) (WHO-QOL-BREF-TR) scale for their parents. Data were collected using Google Forms, with assessments performed before and during the pandemic.

Results: The study included 61 participants, 38 of whom were female (62.3%), with a mean age of 12.7±2.9 years and a mean diabetes duration of 6.4±2.5 years. Pre-pandemic KINDL scores for "emotional health" and "school" were significantly higher than those during the pandemic (p=0.022 and p=0.002, respectively). Surprisingly, HbA1c levels improved during the pandemic compared to the pre-pandemic values (p<0.001). There were strong correlations between children's and parents' QOL before and during the pandemic (p<0.001). Parents' physical health scores on the WHOQOL-BREF decreased significantly during the pandemic (p=0.012).

Conclusion: Improvement in HbA1c levels during the pandemic warrants further investigation. Additionally, the pandemic negatively affected the emotional well-being of children and the physical health of parents, highlighting the need for more support in these areas during times of crisis.

Keywords: COVID-19 Pandemic, Type 1 Diabetes Mellitus, Infusion Pumps, Quality of Life.

COVID-19 Pandemisinin Tip 1 Diyabetes Mellitus Tanılı Çocuklar ve Ailelerinin Yaşam Kalitesi Üzerindeki Etkisi: İnsülin İnfüzyon Pompası Kullanan Hastalar

ÖZET

Amaç: Bu çalışma, COVID-19 pandemisinin Tip 1 Diyabetes Mellitus (T1DM) tanılı çocuklar ve ailelerinin yaşam kalitesi (QOL) üzerindeki etkisini, özellikle insülin infüzyon pompalarının etkisine odaklanarak incelemeyi amaçlamaktadır. Ayrıca, pandemi süresince hem çocukların hem de ebeveynlerin QOL'undaki değişiklikler tespit edilmeye çalışılmıştır.

Yöntem: Çocuklar için KINDL (KINDer Lebensqualitätsfragebogen: Çocuk Yaşam Kalitesi Anketi) ve ebeveynler için Dünya Sağlık Örgütü Yaşam Kalitesi Ölçeği (WHOQOL)-BREF Türkçe Versiyonu (TR) (WHO-QOL-BREF-TR) kullanılmıştır. Veriler Google Forms üzerinden toplanmış, değerlendirmeler pandemi öncesi ve pandemi sırasında yapılmıştır.

Bulgular: Çalışmaya katılan 61 katılımcının 38'i (%62,3) kadındı ve katılımcıların yaş ortalaması 12,7±2,9 yıl, diyabet süresi ortalaması ise 6,4±2,5 yıldı. Pandemi öncesinde KINDL'nin "duygusal sağlık" ve "okul" alt boyutlarının puanları, pandemi süresindekilerden anlamlı derecede daha yüksekti (sırasıyla p=0,022 ve p=0,002). Şaşırtıcı bir şekilde, pandemi sırasında HbA1c seviyeleri pandemi öncesine göre iyileşmiştir (p<0,001). Pandemi öncesi ve sırasında çocukların ve ebeveynlerin QOL'ları arasında güçlü korelasyonlar bulunmuştur (p<0,001). Ebeveynlerin WHOQOL-BREF üzerindeki fiziksel sağlık puanları pandemi sırasında anlamlı şekilde düşmüştür (p=0,012).

Sonuç: Pandemi süresince HbA1c seviyelerindeki iyileşme dikkate değer olup, daha fazla araştırma gerektirmektedir. Ayrıca, pandemi çocukların duygusal sağlıklarını ve ebeveynlerin fiziksel sağlıklarını olumsuz etkilemiş, bu tür kriz dönemlerinde bu alanlarda daha fazla desteğin gerekliliğine işaret etmiştir.

Anahtar Kelimeler: COVID-19 Pandemisi, Tip 1 Diyabetes Mellitus, İnfüzyon Pompaları, Yaşam Kalitesi.

INTRODUCTION

Type 1 Diabetes Mellitus (T1DM) is an autoimmune condition that leads to destruction of insulin-producing beta cells in the pancreas. This condition predominantly affects children and adolescents and requires continuous insulin therapy for survival (1). Type 1 DM accounts for 5-10% of diabetes cases worldwide (2). In Turkey, the yearly incidence of type 1 DM under the age of twenty is 10.8/100.000, and its prevalence is around 75/100.000 (3). Approximately 3% of type 1 DM cases worldwide occur in Turkey. The prevalence among girls is higher than that among boys, and the disease is most commonly diagnosed between the ages of 0-4 and 10-14 years (3). Type 1 DM mostly follows an autoimmune process, preclinical autoimmunity with beta cell destruction, clinical onset, transient remission, emergence of clinical symptoms, and occurrence of complications (4). Quality of life (QOL) is affected by the clinical course of type 1 DM and worsens with increasing hemoglobin A1c (HbA1c) levels (5).

On January 30, 2020, the World Health Organization (WHO) defined the COVID-19 infection as an "international public health emergency." Due to the spread of the virus all over the world, the severe course of the disease, and the deaths, it was accepted as a pandemic on March 11, 2020 (6). With the declaration of the disease as a pandemic, many people have been isolated to prevent its spread. Since then, various countries have started to implement regional and national restrictions to prevent the spread of the disease, increasing the possibility of stress, anxiety, and a sense of helplessness, negatively affecting the QOL of patients (7).

DM impairs emotional, spiritual, physical, and social functioning in children and adolescents. Children diagnosed with DM show more psychosocial stress, low social activity, and high behavioral problems than healthy children (8). Additionally, the Coronavirus disease-19 (COVID-19) pandemic has caused psychological mood disorders in people with chronic diseases, such as type 1 DM, and affected their QOL (9).

While studies have explored the impact of the COVID-19 pandemic on adult populations with chronic diseases, limited research has focused on the pediatric T1DM population, especially in terms of psychological well-being and QOL during the pandemic. Additionally, little is known about how the use of insulin infusion pumps influences disease management.

We hypothesize that the COVID-19 pandemic has had a mixed effect on children with T1DM, potentially improving glycemic control due to increased parental involvement, while simultaneously worsening the emotional and social aspects of their QOL due to isolation and school closures. This study aimed to contribute to the limited body of research on the impact of the COVID-19 pandemic on the QOL of children with T1DM and their families. By examining both physical (HbA1c levels) and psychological (QOL scores) outcomes, this study provides insight into how these children and their caregivers have been affected by the pandemic, and highlights areas for future intervention and support.

MATERIALS AND METHODS

Study Design: This descriptive observational study aimed to assess the effects of the COVID-19 pandemic on the QOL of children with T1DM using insulin infusion pumps and their parents. The study was conducted between January 2020 and July 2020 in two phases: before and during the pandemic, allowing for a comparison of QOL metrics across these two periods. The pre-pandemic data were collected prior to the declaration of the COVID-19 pandemic, whereas the pandemic-phase data were collected after the onset of pandemic-related restrictions. This before-and-after study design enabled us to capture any significant changes in both physical and psychological health outcomes. Ethical approval (number 2020/117, dated June 15, 2020) was obtained from the Düzce University Faculty of Medicine's Clinical Research Ethics Committee. The reporting of the study was performed according to the STROBE guideline (10).

Patients with type 1 DM at follow-up were invited to participate in this study. The KINDL QOL Scale and World Health Organization QOL Scale were used to collect data. Sociocultural, sociodemographic, and therapeutic information about individuals was obtained from the hospital patient records. As specified in the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines (8), HbA1c levels were evaluated in three categories: good (HbA1c <7.5%), moderate (HbA1c 7.5-9%), and poor control (HbA1c> 9%). Of the invited participants, 76 responded to the lockdown. During the pandemic, these scales were uploaded to Google Drive. A group of 76 participants was created on WhatsApp, and the responsible physician informed the participants about the study and sent the study link to the phones of the patients or their parents via WhatsApp. Those who agreed to participate were included in the study. All the patients and their parents were asked to respond. The completed questionnaires were collected again using WhatsApp.

Sampling Method: The participants were selected using a non-probability convenience sampling method. The study population consisted of children aged 6–18 years who were diagnosed with T1DM and were being treated at the Pediatric Endocrine Department of Düzce University Hospital. The inclusion criteria were as follows.

1. The patient was diagnosed with T1DM by using an insulin infusion pump for at least one year.

2. No interruption in pump use exceeding one week.
3. Consent to participate: both the child and their parents or guardians.
4. The patients were aged between 6 and 18 years and received routine follow-up care.

The exclusion criteria included the presence of diabetic complications (e.g., nephropathy, retinopathy), psychiatric or chronic illnesses, or participation in similar studies. Based on these criteria, 61 children and their parents were included in the study, with data collected during two time points: pre-pandemic and during the pandemic.

Data Collection: Data collection involved two validated QOL instruments: the KINDL Children's Quality of Life Questionnaire for children (KINDer Lebensqualitätsfragebogen: Children QOL Questionnaire) scale and the World Health Organization Quality of Life (WHOQOL)-BREF Turkish Version (TR) (WHO-QOL-BREF-TR) scale for parents. Both questionnaires were adapted for online administration and were uploaded to Google Forms. Invitations to participate were sent via WhatsApp to parents and children who met the inclusion criteria. The participants were required to complete the questionnaire at two distinct time points: before the COVID-19 pandemic and once during the pandemic.

Insulin pump usage, diabetes management data, and HbA1c levels were extracted from hospital records. For each participant, HbA1c levels were evaluated before and during the pandemic. All responses were recorded electronically and subsequently analyzed for changes in QOL scores and glycemic control metrics, using HbA1c as the primary physical health indicator.

Variables: The KINDL scale was developed by Ravens-Sieberer and Bullinger in 1998 (11). It is a general-purpose QOL measurement tool specifically for young children and adolescents. KINDL has been translated into 14 languages. The questionnaire consists of 24 items and six dimensions. The scale consists of six dimensions: physical well-being, emotional well-being, self-esteem, family, friends, and school (school or kindergarten/nursery where daily activities are conducted). Each dimension consists of 4 items. While calculating the scores of the dimensions, the total QOL score, which consists of a combination of these six dimensions, was also obtained. KINDL can be used both clinically and non-clinically in healthy children and in children with chronic diseases. The KINDL QOL scale uses a five-point sequential response option ranked from 1 (never) to 5 (always). The score is calculated by summing the item responses for each dimension and converting them to a scale between 0 and 100. A high score indicates a good QOL.

The Turkish version of the World Health Organization QOL Scale (WHO QOL-BREF-TR) was evaluated using a five-point sequential response (1-5) option (12). In the evaluation of the scale, the arithmetic mean of the scores obtained from the sub-domains was calculated separately and multiplied by four to obtain the QOL score. As the subscale scores of the scale increased, QOL also increased.

Statistical Analyzes: The Statistical Package for Social Sciences program (SPSS for Windows, Version 25.0, Chicago, IL, USA) was used for statistical analysis. The survey data were collected using Google Drive and then uploaded to the SPSS software.

Results are presented as means and standard deviations or as median, minimum, and maximum values for numerical variables, while categorical data are presented as frequencies and percentages. The conformity of numerical variables to a normal distribution was evaluated using the Shapiro-Wilk test.

Statistical tests were performed based on parametric properties of the data. The independent samples t-test or Mann-Whitney U test was used to compare two independent groups, and the paired samples t-test or Wilcoxon Signed-Rank test was used to compare two dependent groups. Additionally, a marginal homogeneity test was used to compare the three categorical dependent groups. Pearson and Spearman correlation tests were used to determine the relationships between variables. A p-value of <0.05 was considered sufficient for statistical significance.

RESULTS

Of the participants, 38 (62.3%) were girls, 35 (57.4%) were adolescents aged 13-18, and 29 (47.5%) were attending secondary school. The mean age of the patients was 12.73±2.91 years, the mean diabetes duration was 6.37±2.54 years, and the mean pump usage time was 3.26±1.81 years (Table 1).

The mean age of the mothers was 38.3±5.7 years, and the mean age of the fathers was 41.0±5.4 years. Of the patients, 56 (91.8%) lived with their families, 44 (72.1%) did not work, and 50 (82.0%) lived with a nuclear family (Table 2).

All parents were alive. All fathers had a job. The pre-pandemic mean of the "Emotional health" and "School" sub-dimensions of the KINDL QOL scale was significantly higher than the mean of the pandemic period ($p=0.022$ and $p=0.002$, respectively) (Table 3).

When the Turkish version of the WHO QOL-BREF-TR findings of parents were evaluated between the two measurement points, a statistically significant difference was found only in the dimension of "physical health" ($p=0.012$) (Table 4).

Pre-pandemic HbA1c levels were significantly higher than HbA1c levels during the pandemic period ($p<0.001$) (Table 5). Positive and significant relationships were found between patients' general QOL scores, their caregivers' psychological and social relationships, and general scores in the pre-pandemic period. In addition, positive and significant relationships were found between the general QOL scores of patients during the pandemic and the general health, physical health, psychological, social relations, environment, and general scores of caregivers (Table 6).

Table 1. Descriptive characteristics of the patients

		n	**%**
Sex	Male	23	37.7
	Female	38	62.3
Age	6-7 year	3	4.9
	8-12 year	23	37.7
	13-18 year	35	57.4
Education	Preschool	1	1.6
	Primary	14	23.0
	Secondary	29	47.5
	College	17	27.9
$HbA1_C$ risk level (before pandemic) (%)	Poor	27	44.3
	Moderate	26	42.6
	Good	8	13.1
HbA1c Risk Level (during pandemic) (%)	Poor	8	13.1
	Moderate	33	54.1
	Good	20	32.8
	Mean ± SD	**Median (Min-Max)**	
Age (year)	12.73±2.91	13 (6-17)	
Diabetes duration (year)	6.37±2.54	6 (2-14)	
Pump usage (year)	3.26±1.81	3 (1-12)	
$HbA1_C$ (before pandemic) (%)	8.82±1.28	8.7 (6.30-13.30)	
HbA1c (during pandemic) (%)	7.92±1.11	7.9 (5.40-10.60)	

Poor HbA1C: Defined as HbA1C > 9%., **Moderate HbA1C**: Defined as HbA1C between 7.5% and 9%., **Good HbA1C**: Defined as HbA1C < 7.5%., **HbA1C**: Hemoglobin A1C, **SD**: Standard Deviation, **Min-Max**: Minimum and Maximum.

Table 2. Parental and Household Characteristics

		n	%
Parent relationship	Together	56	91.8
	Apart	5	8.2
Who does the patient live with?	Both	56	91.8
	With mother	1	1.6
	With father	1	1.6
	With mother-grandmother	1	1.6
	With mother-stepfather	1	1.6
	School pension	1	1.6
Mother's education status	Illiterate	1	1.6
	Primary school	22	36.1
	Secondary school	9	14.8
	High school	18	29.5
	College	3	4.9
	University	8	13.1
Father's education status	Primary school	18	29.5
	Secondary school	10	16.4
	High school	19	31.1
	College	2	3.3
	University	12	19.7
Mother's working status	Housewife	44	72.1
	Employed	17	27.9
Number of siblings	Single	5	8.2
	1	2	3.3
	2	34	55.7
	3 or more	20	32.7

Table 3. Comparison of the KINDL QOL scores of patients before and during the pandemic

		Before pandemic		During pandemic			
	n	**Mean**	**SD**	**Mean**	**SD**	**t/Z**	**p**
Physical well-being	61	68.85	17.95	69.02	20.66	-0.132	0.895[Z]
Emotional well-being	61	69.56	18.16	63.42	18.95	-2.288	**0.022[Z]**
Self-esteem	61	53.07	23.95	57.68	23.78	-1.469	0.142[Z]
Family	61	78.89	17.38	75.51	18.82	-1.653	0.098[Z]
Friends	61	75.51	18.23	75.71	19.70	-0.131	0.896[Z]
School	61	64.78	18.38	56.65	18.95	3.241	**0.002[t]**
General quality of life	61	68.45	11.43	66.47	11.65	1.499	0.139[t]
Disease	41	67.58	21.27	74.11	18.92	-1.776	0.076[Z]

[Z]: Wilcoxon Signed Rank test, [t]: Independent sample t-test, n: Number of participants, SD: Standard Deviation, KINDL (KINDer Lebensqualitätsfragebogen: Children Quality of Life Questionnaire)

Table 4. Comparison of Parents' WHO-QOL-BREF-TR Scores Before and During the Pandemic

		Before pandemic	During pandemic		
	N	**Mean**	**SD**	**Mean**	**SD**
Physical Health	61	68.55 ± 15.75	61.22 ± 16.89	2..53	0.012*
Psychological Health	61	65.84 ± 13.42	64.91 ± 14.02	0.64	0.524
Social Relationships	61	71.27 ± 14.33	69.98 ± 15.45	1.09	0.280
Environment	61	73.51 ± 13.48	72.03 ± 14.01	1.34	0.184
General Health	61	70.15 ± 12.67	68.74 ± 13.52	1.01	0.315

[Z]: Wilcoxon Signed Rank test, [t]: Independent sample t-test, n: Number of participants, SD: Standard Deviation, **WHOQOL-BREF-TR**: World Health Organization Quality of Life - Turkish Version

Table 5. Comparison of HbA1c levels regarding the pandemic

		Before pandemic		During pandemic		t	p
HbA1c (%)	Mean & SD	8.82	1.28	7.92	1.11	6.252	**<0.001**[t]
	Bad (n & %)	27	44.3	8	13.1		
HbA1c Status	Moderate (n & %)	26	42.6	33	54.1		**<0.001**[M]
	Good (n & %)	8	13.1	20	32.8		

[t]: Paired-samples T-test, [M]: Marginal homogeneity test
Poor HbA1C: Defined as HbA1C > 9%., **Moderate HbA1C**: Defined as HbA1C between 7.5% and 9%., **Good HbA1C**: Defined as HbA1C < 7.5%., **HbA1C**: Hemoglobin A1C

Table 6. Correlation between QOL questionnaire results of the patients and their parents

	General Health Status	**Physical Health**	**Psychological Health**	**Social Relationships**	**Environment**	**Overall Score**
Pre-Pandemic KINDL						
Physical Well-Being	0.230	0.115	0.269*	0.185	0.244	0.260*
Emotional Well-Being	0.352**	-0.105	0.230	0.214	0.153	0.230
Self-Esteem	-0.051	0.166	0.350**	0.137	0.013	0.174
Family	0.265*	-0.024	0.193	0.179	0.073	0.169
Friends	0.093	0.063	0.210	0.173	0.280*	0.186
School	0.116	-0.015	0.262*	0.307*	0.011	0.191
General Quality of Life	0.234	0.075	0.416**	0.332**	0.209	0.340**
Disease	0.106	-0.022	-0.084	-0.163	-0.010	-0.059
During Pandemic KINDL						
Physical Well-Being	0.287*	0.124	0.292*	-0.067	0.164	0.185
Emotional Well-Being	0.522**	0.275*	0.328**	0.381**	0.234	0.467**
Self-Esteem	0.121	0.137	0.347**	0.231	0.160	0.267*
Family	0.304*	0.377**	0.307*	0.215	0.157	0.339**
Friends	0.235	0.240	0.272*	0.244	0.315*	0.341**
School	0.194	0.051	0.057	0.045	-0.010	0.075
General Quality of Life	0.515**	0.293*	0.466**	0.334**	0.329**	0.462**
Disease	0.308*	0.209	0.216	0.175	0.217	0.274*

[1]: Pearson coefficients; [2]: Spearman coefficients; *p<0.05; **p<0.001
WHOQOL-BREF-TR: World Health Organization Quality of Life - Turkish Version., **KINDL**: Kinder Lebensqualität Fragebogen, a Quality-of-Life questionnaire for children., **Physical Health**: Refers to the overall physical well-being of Participants, **Psychological Health**: Measures emotional and psychological well-being, **Social Relationships**: Assesses the quality of relationships and social support. **Environment**: Measures satisfaction with one's surroundings, **Overall Score**: Represents a general score summarizing various aspects of quality of life.

DISCUSSION

This study assessed the impact of the COVID-19 pandemic on the QOL of children with T1DM and their parents with a specific focus on the use of insulin infusion pumps. This study contributes to the growing literature on the psychosocial and physiological effects of the pandemic in pediatric populations with chronic diseases. By examining both physical (HbA1c levels) and psychological outcomes (KINDL QOL scores), we provide insight into how the pandemic affected not only the glycemic control of children, but also their emotional well-being and school performance. Most notably, the study found a significant improvement in HbA1c levels during the pandemic alongside a decline in emotional and school-related QOL scores. These findings highlight the complex interaction between medical and psychological factors in managing T1DM during times of crisis and underscore the need for comprehensive care strategies that address both physical and mental health in pediatric populations.

In this study, the pre-pandemic means of the "Emotional health" and "School" sub-dimensions of the KINDL QOL scale were higher than the means during the pandemic period. When WHO QOL - BREF-TR findings of parents were evaluated, a significant difference was found only in the dimension of "physical health." Furthermore, pre-pandemic HbA1c levels were significantly higher than HbA1c levels during the pandemic period. In addition, positive and significant relationships were found between patients' general QOL scores, their caregivers' psychological and social relationships, and general scores in the pre-pandemic period. Finally, positive and significant relationships were found between the general QOL scores of the patients during the pandemic and the general health, physical health, psychological, social relations, environment, and general scores of the parents.

According to a study conducted in Turkey in 2006, 700 thousand children aged 0-19 years had chronic diseases (13). During the COVID-19 pandemic, those with chronic illnesses had to contend with the stress of both the disease and pandemic. A chronic disease is a situation in which the feeling of not being healthy is created. Even the idea of having a chronic illness is a source of unhappiness for children. Various psychopathologies are observed more frequently in children than in the general population (14). DM is a chronic disease that impairs the physical, emotional, and social functions of children and adolescents. Compared to healthy children, children with DM have higher psychosocial stress, lower social activity, and more behavioral disorders (15). In this study, the mean total QOL scores of children with type 1 DM were relatively lower than those reported in similar studies conducted in Turkey. In a study, the total QOL score of children with type 1 DM evaluated by KINDL was 73.9±9.1, while the total QOL score of children in the control group was 81.7±10.2 (16). In another study on the QOL of children with type 1 diabetes, the total QOL score was 77.7 (17). The general QOL score may have decreased because of the acute stress caused by the epidemic. In addition, although the questionnaires were administered face-to-face in previous studies, the fact that they were filled online in this study may have affected this result. We thought that we would encounter difficulties in the management and follow-up of the treatment of patients during the pandemic due to many factors, such as the anxiety of catching the disease, fear of dying or losing a loved one, feelings of isolation and loneliness at home, isolation from social areas such as school and friends, and staying away from physical activity. Surprisingly, there was a noteworthy improvement in HbA1c levels during the pandemic period compared to the pre-pandemic period. Supporting our results, there are publications stating that restrictions of the pandemic do not worsen HbA1c results (18,19). However, studies have also found higher HbA1c levels after quarantine (20). Arslanogu et al. (21) reported that 77.6% of 219 patients had decreased HbA1c levels (mean drop was approximately 9.71%) compared to the former test in the whole group in their study that evaluated HbA1c levels before and after the pandemic in patients with type 1 DM. Restrictive measures implemented because of the COVID-19 pandemic have led families to spend more time at home. This may have helped blood sugar monitoring to be performed better under parental control and to overcome difficulties in school snacks and nutrition. This close follow-up may have positively contributed to the success of treatment. In addition, the medical and psychological support provided by the diabetes team during all hours of the day may have contributed to this positive result. Chronic diseases negatively affect both parents and their children. Having a child with a chronic illness is stressful for parents (22,23). In addition, many problems, including the increasing financial expenses of families, tension caused by the treatment process, and decrease in social activities, contribute to this stress (24). Epidemics such as COVID-19 can cause psychological problems including family communication problems, outbursts of anger, anxiety disorders, depressive behaviors, sleep problems, and somatoform disorders (25–27). In this study, there was a decrease in the emotional health scores of the children during the pandemic. Many reasons may have contributed to this result, such as the fear of catching the disease, the illness of a family member, the worry of losing a loved one, the limitation of physical activity and psychological effects of home isolation, and the economic difficulties experienced by families. Schools were closed during the pandemic and

learning continued on the digital platform. School closure negatively affects students' mental health (28–30). In addition, the school discipline and authority disappeared. Furthermore, reliable internet connection and computer support, suitable physical conditions for homework and lessons, and access to necessary materials were not provided for many children. All of these factors may have led to a decrease in school scores during the pandemic. COVID-19 infection adversely affected QOL in the adult age group (31). The increase in the time spent at home, health concerns, increased stress-related eating disorders, decreased physical activity, and predominance of a sedentary lifestyle have adversely affected the emotional and physical health of people. Consistent with the literature, the physical health scores of parents decreased during the pandemic. In addition, the pandemic has changed people's daily routines and caused the interaction of children and parents to be experienced more intensely. Social restrictions during the pandemic caused children to spend almost all their time at home with their parents, and this situation created the potential for children to be directly affected by the attitudes and behaviors of their parents (32–34). The correlations found between the scores of adults and children in our study support those in the literature.

LIMITATIONS

Some limitations of the study are as follows: First, the research was conducted in a single center. Therefore, it is difficult to generalize our findings. Additionally, the study was conducted during the first few months of the pandemic. Further follow-up could reveal a higher burden, and thus, different results. Finally, all data were collected online, before and after the pandemic.

CONCLUSION

Children with Type 1 DM using insulin infusion pumps may need more support, especially in terms of emotional health and school success, in situations where social life is restricted, such as pandemics. It should be noted that the QOL of parents interacts with the QOL of their children, and thus, they should not neglect their physical health. More detailed studies are needed to clearly reveal the factors affecting the improvement of HbA1c levels during the pandemic.

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RESEARCH ARTICLE

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Can Nomophobia be a Contemporary and Novel Cluster of Symptoms of Adult Separation Anxiety Disorder?

ABSTRACT

Objective: The connection between adult separation anxiety disorder (ASAD) and nomophobia has been poorly investigated. The aim of this study is to evaluate whether there is a relationship between ASAD and nomophobia.

Method: The sample consisted of 68 university students diagnosed with ASAD and 77 university students without ASAD. All participants were evaluated by a structured clinical interview, Adult Separation Anxiety Questionnaire (ASA), Separation Anxiety Symptom Inventory (SASI), Nomophobia Questionnaire (NMP-Q), and Smartphone Addiction Scale-Short Version (SAS-SV).

Results: Participants with ASAD had longer daily phone usage times and had a higher frequency of checking the phone during the day and the rates of carrying a charger than controls. Compared to the control group, participants with ASAD had significantly higher ASA, SASI, NMP-Q, and SAS-SV scores and more severe nomophobia levels. The ASA scores were significantly positively correlated with SASI, NMP-Q, and SAS-SV. Regarding predictors of nomophobia, ASA, SASI, and SAS-SV scores had a positive and significant effect on nomophobia, and predicted nomophobia.

Conclusion: Our research adds to the body of knowledge on nomophobia by demonstrating that people with ASAD are susceptible to developing nomophobia. Clinicians should be aware of the association between ASAD and nomophobia, and nomophobia may be an important concept that should be considered in the therapy approach to patients with ASAD.

Keywords: Adult Separation Anxiety Disorder, Nomophobia, Separation Anxiety, Smartphone, Smartphone Addiction.

Nomofobi, Yetişkin Ayrılık Anksiyetesi Bozukluğunun Çağdaş Ve Yeni Bir Semptom Kümesi Olabilir Mi?

ÖZET

Amaç: Yetişkin ayrılma anksiyetesi bozukluğu (YAAB) ile nomofobi arasındaki bağlantı yeterince araştırılmamıştır. Bu çalışmanın amacı, YAAB ile nomofobi arasında bir ilişki olup olmadığını değerlendirmektir.

Yöntem: Örneklem, YAAB tanısı konmuş 68 üniversite öğrencisi ve YAAB olmayan 77 üniversite öğrencisinden oluşmaktadır. Tüm katılımcılar yapılandırılmış klinik görüşme, Yetişkin Ayrılık Anksiyetesi Anketi (YAAA), Ayrılık Anksiyetesi Belirti Envanteri (AABE), Nomofobi Anketi (NMP-Q) ve Akıllı Telefon Bağımlılığı Ölçeği-Kısa Versiyonu (ATBÖ-KF) ile değerlendirilmiştir.

Bulgular: YAAB olan katılımcıların günlük telefon kullanım süreleri daha uzundu ve gün içinde telefonlarını kontrol etme sıklıkları ve şarj aleti taşıma oranları kontrol grubuna göre daha yüksekti. Kontrol grubuyla karşılaştırıldığında, YAAB olan katılımcıların YAAA, AABE, NMP-Q ve ATBÖ-KF puanları anlamlı derecede yüksek ve nomofobi düzeyleri daha şiddetliydi. YAAA puanları AABE, NMP-Q ve ATBÖ-KF ile anlamlı derecede pozitif korelasyon göstermiştir. Nomofobinin öngörücüleri açısından YAAA, AABE ve S ATBÖ-KF skorları nomofobi üzerinde pozitif ve anlamlı bir etkiye sahipti ve nomofobiyi öngörüyordu.

Sonuç: Araştırmamız, YAAB olan kişilerin nomofobi geliştirmeye yatkın olduğunu göstererek nomofobi hakkındaki bilgi birikimine katkıda bulunmaktadır. Klinisyenler, YAAB ve nomofobi arasındaki ilişkinin farkında olmalıdır ve nomofobi, YAAB hastalarına terapi yaklaşımında dikkate alınması gereken önemli bir kavram olabilir.

Anahtar Kelimeler: Yetişkin Ayrılma Anksiyetesi Bozukluğu, Nomofobi, Ayrılma Anksiyetesi, Akıllı Telefon, Akıllı Telefon Bağımlılığı.

INTRODUCTION

Separation anxiety disorder is a state of overwhelming anxiety that arises in case of actual or anticipation of separation from specific attachment figures. It is reported that the main symptoms of separation anxiety can continue and/or appear in adulthood, and this is defined as adult separation anxiety disorder (ASAD) (1,2). ASAD may be triggered or initiated by leaving home, having a child, or having an emotional relationship (2).

When separated from their important attachment figures, individuals with ASAD worry excessively that they won't be able to reunite with them or that they will be hurt, and they feel the need to be constantly close to them (3-5). This excessive anxiety can lead to them feeling the need to constantly check and hear from the attachment figures (3-5), and in turn, they could feel compelled to keep in touch over the phone (6). Therefore, individuals with ASAD may be more inclined to use the mobile phone (MP) frequently and regularly and spend a lot of time on the MP, due to their desire to avoid disconnection and to be in constant contact with their attachment figures when they are separated. Further, under the influence of separation anxiety, the patterns of using MP that will enable individuals with ASAD to communicate with their attachment figures may include: frequently checking the MP for calls or messages, keeping it close while sleeping, and keeping the phone on throughout the day, carrying a charger, avoiding places where phone use is prohibited, worrying over thoughts such as losing the MP, being outside of the coverage area, running out of battery, and the right to call. Such MP usage patterns, which we assume may be likely to be seen in individuals with ASAD, are also symptoms of nomophobia (7-10). In addition to using their phones as a safety tool to lessen their symptoms, some ASAD sufferers might also excessively use phones with the motivation to relieve stress related to worries and real-life problems. In conclusion, it can be inferred that when separation occurs, the demands for individuals with ASAD to maintain closeness and communication with their attachment figures may result in problematic phone use and nomophobia symptoms, and, thus, we can anticipate the nomophobia levels of these individuals to be above the average. In this case, nomophobia may be a cluster of symptoms of ASAD as well as a compensatory mechanism in alleviating separation anxiety or one of the strategies for coping with separation anxiety.

Nomophobia (No Mobile Phone Phobia), which is not currently included in the current psychiatric classification system (1), refers to the anxiety and discomfort experienced when the MP cannot be accessed and/or communicated on the MP (7-9). According to the level of nomophobia, symptoms include spending a lot of time by using the MP frequently, owning one or more MPs, always carrying the charger with them, and avoiding places where mobile device use is not allowed as much as possible. Other characteristics of nomophobia are worrying intensely with thoughts such as losing the phone, not being nearby, not being connected to the internet, running out of battery and calling rights, checking the phone's screen for messages or calls, keeping the phone next to oneself while sleeping, and not turning it off all-day (7-9).

Despite growing interest in nomophobia, few studies on the psychological characteristics and determinants that can predict it have been conducted. Several studies have demonstrated that depression, stress and anxiety, loneliness, low self-esteem and self-efficacy, and impulsivity can predict nomophobia symptoms (11-15). Studies on the relationship between anxiety disorders and nomophobia mostly focused on panic disorder and agoraphobia, and it has been discovered that these individuals have high rates of phone abuse and nomophobia levels due to their desire to escape from anxiety (13,14). Although it is not directly related to nomophobia, a study of individuals with generalized anxiety disorder has found that those with comorbid ASAD called their families more frequently than those without comorbid ASAD (6). Some researchers have revealed that there is a link between adult attachment anxiety and smartphone addiction and that loneliness and depression mediate this relationship (12). However, there is currently very little research on the relationship between nomophobia and ASAD. We are aware of only one study in this field, and it demonstrated a positive and significant correlation between ASAD and nomophobia scores (10). Therefore, the relationship between ASAD and nomophobia is still poorly understood, and whether nomophobia is associated with ASAD remains a question. This study aims to examine the relationship between ASAD and nomophobia. It is hypothesized that individuals with ASAD will have higher levels of nomophobia compared to those without ASAD. Additionally, as the severity of separation anxiety symptoms increases, mobile phone usage is expected to increase as well. It is also suggested that ASAD may lead individuals to use their mobile phones as a way to cope with separation anxiety, which in turn could intensify nomophobia symptoms.

MATERIALS AND METHODS

Participants: This study included 68 university students diagnosed with ASAD (45 females [66.2%], mean age 21.65±1.29 years, range: 18-24 years) and 77 university students without ASAD (53 females [68.8%], mean age 21.39±1.07 years, range: 18-24 years), matched for age and sex with the ASAD group. Participants were recruited voluntarily from the general

university population. All participants underwent a psychiatric evaluation using the Structured Clinical Interview for DSM-5® Disorders-Clinician Version (SCID-5-CV) to determine diagnoses. The ASAD group was identified based on SCID-5-CV interviews. These interviews were conducted face-to-face by trained clinical psychologists, with the same interviewer conducting assessments for all participants to ensure consistency.

Inclusion and exclusion criteria were carefully established. Participants with any chronic medical condition, acute mania, psychosis, autism spectrum disorders, or alcohol and substance abuse were excluded from the study. The data collection process was carried out in a controlled laboratory setting. Before participation, all individuals were informed about the study procedures and potential consequences, and they provided written informed consent. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The ethics committee approval for this study was obtained from the Sivas Cumhuriyet University Faculty of Medicine Non-Interventional Ethics Committee (2021-11/29).

Data Collection Tools

Personal Information Form: This form was developed by the researchers based on literature knowledge. It is designed to collect participants' sociodemographic information and mobile phone usage patterns. The sociodemographic data include details such as age, sex, and family characteristics. Mobile phone usage patterns cover aspects such as daily usage time, purposes of use, and general usage behaviors.

Adult Separation Anxiety Questionnaire (ASA): It is a 27-item self-report scale that measures separation anxiety symptoms over age 18 (18). In this 4-point Likert questionnaire, items are evaluated between 0 (never felt) and 3 (very often felt). Turkish validity and reliability studies were performed by Diriöz et al., and the cutoff score is 25. The internal consistency reliability coefficient (Cronbach's alpha) for the ASA was found to be 0.93, indicating excellent internal consistency and high reliability. When examining the correlations of the items with the total score, it was observed that the correlation values for all items were above 0.20, which is an indicator of consistency. The item-total score correlations for all items, except item 17, ranged between 0.40 and 0.76. The test-retest reliability of the YAA scale was assessed by the correlation of total scores from the test and retest, and it was found to be r=0.93 (19).

Separation Anxiety Symptom Inventory (SASI): SASI measures childhood separation anxiety symptoms in adults, retrospectively, based on experiences prior to 18 years of age (20). It consists of 15 items that measure four-point Likert-type scales, and the items are rated from 0 (never) to 3 (very often). The validity and reliability of the Turkish version of the scale was conducted by Diriöz et al. and the cut-off point was calculated as 12 (19). The Cronbach's alpha value for the SASI was found to be 0.89. In the item analysis, the item-total score correlation method was used. It was determined that the item-total correlations ranged between 0.43 and 0.65. For test-retest reliability, the scale was administered a second time to 80 patients 7-21 days after the initial assessment. The average score from the first evaluation was 2.91 (SD=1.37), and the average score from the test-retest was 2.92 (SD=1.43). No significant difference was observed between the evaluations (t=-1.15, df=79, p=0.91).

Nomophobia Questionnaire (NMP-Q): It has 20 items, and the items are graded from 1 (strongly disagree) to 7 (strongly agree) and the total score varies between 20-140 points (8). Although NMP-Q includes four sub-dimensions (not being able to communicate; losing connectedness; not being able to access information; and giving up convenience), the total score was utilized in this study. The higher the score, the greater the severity of nomophobia. According to the total score, individuals are classified as follows: ≤ 20 points correspond to the absence of nomophobia, 21-59 points to mild nomophobia, 60-99 points to moderate nomophobia, and 100-140 points to severe nomophobia level. It was adapted into Turkish by Yildirim and colleagues. The reliability value of the scale (Cronbach's Alpha) was calculated to be 0.92, with subscale values of 0.90, 0.74, 0.94, and 0.91, respectively. In the adaptation study, Confirmatory Factor Analysis (CFA) was conducted to determine the structural validity of the scale, and the $\chi 2$ value was found to be 2.86. It was determined that the fit indices were within acceptable limits (9).

Smartphone Addiction Scale-Short Version (SAS-SV): SAS-SV is a 10-item scale that measures the risk of smartphone addiction and is evaluated with a six-point Likert scale (21). Items are scored from 1 (strongly disagree) to 6 (strongly agree), and the total score varies between 10-60 points. The higher the total score, the higher the risk for addiction. The scale has one factor and no subscales. The validity and reliability study of the Turkish version of the SAS-SV among university students was conducted by Noyan and colleagues. The internal consistency coefficient of the scale was found to be 0.91, and the reliability coefficient was 0.92 (22).

Statistical Analysis: All statistical analyses were performed with IBM SPSS Statistics version 23. The one-sample Kolmogorov-Smirnov test was used to determine whether the data had a normal distribution. The numerical and categorical data were shown as mean ± standard deviation (SD), number (n), and percentage (%) as appropriate. Comparisons of the groups were performed using the chi-square test for categorical variables, and the independent-samples t-test for continuous variables.

Correlations were evaluated using Pearson correlation analysis. To evaluate the predictor value of some main clinical variables (i.e., age, sex, and scores of ASA, SASI, and SAS-SV) on nomophobia, the linear regression models were performed. Statistical significance was considered as $p<0.05$.

RESULTS

Socio-Demographic and Familial Characteristics of Participants: The ASAD and control groups were similar in terms of age, gender, family structure, and family income level (all p-values>0.05). The sociodemographic characteristics of the participants are presented in Table 1.

Table 1. Socio-demographic and familial characteristics of participants.

	ASAD group (N=68)	**Control group (N=77)**	**p-value***
Age (mean-years±SD)	21.65±1.29	21.39±1.07	0.191
Sex (n,%)			0.733
Male	23 (33.8)	24 (31.2)	
Female	45 (66.2)	53 (68.8)	
Family type (n,%)			0.693
Nuclear	46 (67.6)	48 (62.3)	
Single-parent	12 (17.6)	18 (23.4)	
Extended	10 (14.8)	11 (14.3)	
Family income level (n, %)			0.950
Income more than expenses	12 (17.6)	15 (19.5)	
Income equal to the expenses	44 (64.8)	48 (62.3)	
Income less than the expenses	12 (17.6)	14 (18.2)	

Notes: *The chi-square test for categorical variables and the Independent-samples t-test for continuous variables were used to test group differences. **Bold font** indicates statistical significance: P < 0.05. *Abbreviations:* ASAD: Adult Separation Anxiety Disorder, SD: Standard Deviation.

Mobile Phone Usage Patterns of The Participants: The mobile phone usage characteristics of the participants are given in Table 2. Age at first phone use, number of years of phone use, checking the phone at night when going to bed and waking up, and turning off the phone at night were similar between the two groups (all p-values>0.05). However, the daily phone usage time of the participants in the ASAD group was significantly longer than the control group (4.54±1.65 hours vs. 3.32±1.51 hours, respectively, p<0.001). Again, a charger was carried by 67.6% (n=46) of participants in the ASAD group, compared to 45.5% (n=35) in the control group, and this difference was statistically significant (p=0.007). In addition, the frequency of checking phones during the day was significantly higher in the ASAD group compared to the control group (p<0.001).

Table 2. Mobile phone usage patterns of the participants

	ASAD group (N=68)	**Control group (N=77)**	**p-value***
Age of first mobile phone use (mean-years±SD)	14.71±1.42	14.91±1.51	0.407
Year of mobile phone use (mean-years±SD)	6.94±1.38	6.61±1.62	0.192
Daily mobile phone usage time (mean-hours±SD)	4.54±1.65	3.32±1.51	**<0.001**
Carrying a charger (n,%)	46 (67.6)	35 (45.5)	**0.007**
Checking the phone as soon as he/she wakes up (n,%)	54 (79.4)	56 (72.7)	0.348
Checking his/her phone before going to bed (n,%)	54 (79.4)	56 (72.7)	0.348
Turning off the mobile phone at night (n,%)	4 (5.9)	6 (7.8)	0.651
Frequency of checking phone during the day (n,%)			**<0.001**
Every 5-10 minutes	24 (35.3)	7 (9.1)	
Every 10-20 minutes	30 (44.1)	33 (42.9)	
Every 20 minutes or more	14 (20.6)	37 (48.1)	

Notes: *The chi-square test for categorical variables and the Independent-samples t-test for continuous variables were used to test group differences. **Bold font** indicates statistical significance: P < 0.05. *Abbreviations:* ASAD: Adult Separation Anxiety Disorder, SD: Standard Deviation.

Comparison of the Mean Scores ASA, SASI, SAS-SV, and NMP-Q and the Nomophobia Levels between the ASAD and Control Groups: As expected, the ASA mean scores of the participants in the ASAD group were significantly higher than the control group (p<0.001). Similarly, the mean scores of the SASI, which screened for childhood separation anxiety symptoms, and the SAS-SV mean scores were also significantly higher in the ASAD group compared to the control group (both p values<0.001). As for nomophobia, both the frequency of severe

nomophobia levels and the mean scores of NMP-Q were significantly higher in the ASAD group than in the control group (both p-values <0.001). Regarding the nomophobia levels, 20.6% (n=20.6) of the participants in the ASAD group exhibited mild, 26.5% (n=18) moderate, and 52.9% (n=36) severe nomophobia. On the other hand, of the participants in the control group, 53.2% (n=41) had mild, 26% (n=20) had moderate and 20.8% (n=16) had severe nomophobia. The mean scores of the scales used and nomophobia levels in both groups are shown in Table 3.

Table 3. Comparison of the mean scores ASA, SASI, SAS-SV, and NMP-Q and the nomophobia levels

	ASAD group (N=68) (mean±SD)	**Control group (N=77) (mean±SD)**	**p-value***
Adult Separation Anxiety Questionnaire (ASA) scores	40.12±10.18	15.01±4.59	**<0.001**
Separation Anxiety Symptom Inventory (SASI) scores	35.44±5.96	11.73±5.18	**<0.001**
Smartphone Addiction Scale-Short Version (SAS-SV)	40.71±13.81	30.09±12.27	**<0.001**
Nomophobia Questionnaire (NMP-Q) scores	106.53±33.48	56.18±33.75	**<0.001**
Degree of nomophobia (n,%)			**<0.001**
Mild nomophobia	14 (20.6)	41 (53.2)	
Moderate nomophobia	18 (26.5)	20 (26.0)	
Severe nomophobia	36 (52.9)	16 (20.8)	

Notes: *The chi-square test for categorical variables and the Independent-samples t-test for continuous variables were used to test group differences. **Bold font** indicates statistical significance: P < 0.05. *Abbreviations:* ASA: Adult Separation Anxiety Questionnaire, ASAD: Adult Separation Anxiety Disorder, NMP-Q: Nomophobia Questionnaire, SASI: Separation Anxiety Symptom Inventory, SAS-SV: Smartphone Addiction Scale-Short Version, SD: Standard Deviation.

Correlations between ASA and NMP-Q scores and SASI and SAS-SV Scores: Correlations between the scales used were analyzed separately in the ASAD group and control group and are presented in Table 4. The NMP-Q scores were significantly positively correlated with ASA, SASI, and SAS-SV in both the ASAD group and the control group (all p-values <0.001). Similarly, the ASA scores of both groups were significantly positively correlated with SASI, NMP-Q, and SAS-SV (all p-values <0.001). However, while the correlations between ASA scores and NMP-Q and SAS-SV scores were strong in the ASAD group, there was a moderate correlation in the control group.

Table 4. Correlations between ASA and NMP-Q scores and SASI and SAS-SV scores

Adult Separation Anxiety Disorder Group								
	ASA		**SASI**		**NMP-Q**		**SAS-SV**	
	p*	r*	p*	r*	p*	r*	p*	r*
NMP-Q scores	**<0.001**	0.883	**<0.001**	0.657	—	—	**<0.001**	0.941
ASA scores	—	—	**<0.001**	0.939	**<0.001**	0.883	**<0.001**	0.871
Control Group								
	ASA		**SASI**		**NMP-Q**		**SAS-SV**	
	p*	r*	p*	r*	p*	r*	p*	r*
NMP-Q scores	**<0.001**	0.621	**<0.001**	0.522	—	—	**<0.001**	0.917
ASA scores	—	—	**<0.001**	0.732	**<0.001**	0.621	**<0.001**	0.577

*Pearson correlation analysis. *Abbreviations:* ASA: Adult Separation Anxiety Questionnaire, NMP-Q: Nomophobia Questionnaire, SASI: Separation Anxiety Symptom Inventory, SAS-SV: Smartphone Addiction Scale-Short Version.

Predictors of Nomophobia in the Linear Regression Model: In the linear regression model we established, nomophobia was taken as the dependent variable, age, sex, ASA, SASI, and SAS-SV scores were taken as the independent variables, and it was determined that age and gender had no effect on nomophobia. On the other hand, ASA, SASI, and SAS-SV scores had a positive and significant effect on nomophobia, and predicted nomophobia (all p-values<0.001). In the model we established, 78.1% of nomophobia was determined by adult separation anxiety score (β=0.883, p<0.001), 63.5% by childhood separation anxiety score (β=0.797, p<0.001), and 88.8% by smartphone addiction (β=0.942, p<0.001). In other words, a 1-unit increase in the ASA score led to an increase of 0.781 units in the nomophobia score, a 1-unit increase in the SASI score led to an increase of 0.635 units in the nomophobia score, and a 1-unit increase in the SAS-SV score led to an increase of 0.888 units in the nomophobia score. Regression analysis results are presented in Table 5.

Table 5. Predictors of nomophobia in the linear regression model

Model		Unstandardized Coefficients		Standardized Coefficients	t	p	R^2
NMP-Q		B	Std. Error	Beta			
	Age	-4.782	3.140	-0.184	-1.523	0.133	0.034
	Sex	-11.838	8.523	-0.169	-1.389	0.170	0.028
	ASA	2.906	0.190	0.883	15.314	<**0.001**[*]	0.781
	SASI	4.477	0.418	0.797	10.721	<**0.001**[*]	0.635
	SAS-SV	2.283	0.100	0.942	22.876	<**0.001**[*]	0.888

[*]p<0.001

DISCUSSION

In this study, we examined whether there is a relationship between ASAD and nomophobia, and how ASAD affects nomophobia, and our results showed that ASAD has a positive significant effect on nomophobia. More specifically, we produced findings that ASAD diagnosis and childhood separation anxiety symptoms are predictors of nomophobia.

ASAD has high comorbidity rates with many psychiatric disorders in a wide spectrum (2,23). However, the link between ASAD and nomophobia has not been fully recognized. To our knowledge, there is only one study that specifically focuses on the relationship between separation anxiety and nomophobia, and researchers discovered a positive and significant correlation between adult separation anxiety scores and nomophobia scores (10). In addition, although it did not focus directly on separation anxiety disorder, another study examining the relationship between nomophobia and psychiatric symptoms also indicated that separation anxiety is positively related to nomophobia scores (15). Similarly, in our study, we determined that individuals with ASAD had higher nomophobia scale scores and more severe nomophobia compared to individuals in the control group and that high levels of adult and childhood separation anxiety symptoms predicted nomophobia. Our findings suggest that individuals with ASAD are at high risk for the development of nomophobia.

Some potential reasons could help explain why individuals with ASAD might acquire nomophobia. First, nomophobia symptoms may have arisen as a result of typical ASAD symptoms, in which case we can assume that ASAD may be a trigger or precursor of nomophobia or that nomophobia may be a new and modern cluster of symptoms or a complication of ASAD. As known, when an indispensable separation occurs, individuals with ASAD experience severe anxiety and feel vulnerable, which may lead them to constantly need to be close to their attachment objects and the urge to speak and communicate with them on the phone frequently (3-5,23). In this circumstance, an MP can be utilized as a protective shield to satisfy their communication, security, and closeness demands. Making more and more phone calls or texting can help someone with ASAD feel less alone and can also serve as a means of distraction from separation anxiety. Also, depending on the intense separation anxiety experienced, the following behavioral characteristics, which are also seen in nomophobia, may occur: keeping the phone on all the time, keeping the phone close even while sleeping, carrying the charger constantly, impulsively checking the phone's location and charging status, whether it is out of range, whether there are calls or messages, avoiding environments where the phone may be deprived or not allowed to be used. As a matter of fact, our findings that participants in the ASAD group use their phones for longer periods of time each day, have higher rates of carrying chargers, and check their phones more frequently throughout the day than the participants in the control group support this idea. Again, when these individuals are separated from their primary attachment figures, they may try to maintain intimacy with them through priceless virtual property such as digital photos, messages, and recordings which can lead to spending too much time with MP, which is also a symptom of nomophobia. Based on this possible speculation, it would be reasonable to infer that these individuals may exhibit higher levels of fear or discomfort and symptoms of nomophobia when they are deprived of access to their phones. Second, in addition to alleviating separation anxiety symptoms, some ASAD sufferers may more towards mobile activities such as videos, music, or online games that offer entertainment and relaxation on the phone to avoid anxiety, reduce stress from worries about the unpredictable future and real-life problems, or minimize their negative emotions, and so on they may then display excessive phone usage (14,24,25). Based on these possible explanations, it can be mentioned that as the severity of separation anxiety symptoms increases, the levels of nomophobia are likely to increase.

Both of the plausible reasons we offered above for why individuals with ASAD are more likely to develop nomophobia can also be explained by the compensatory internet use model. According to this model, the underlying motivations for turning to phone use and online activities are to move away from experienced anxiety, escape from present moments, get rid of loneliness, relieve certain negative feelings, and/or improve psychosocial well-being (25-27). In addition to this

model, the behavioral approach can also help to explain why individuals with ASAD are more likely to experience nomophobia. According to the behavioral approach, after engaging in a behavior, if a pleasant outcome is gained (positive reinforcement) or if an unpleasant situation is eliminated (negative reinforcement), the probability of performing that behavior by the individual increases (28,29). From this point of view, the tendency of individuals with ASAD to use phones more frequently, for whatever reason, may contribute to the development of nomophobia symptoms by making it easier for them to escape anxiety-inducing situations (negative reinforcement) and to receive a sense of pleasure (positive reinforcement).

Another argument regarding the relationship between ASAD and nomophobia might be the attachment theory, as the intersection point of the two, which may help to understand why individuals with ASAD experience more frequent and severe nomophobia symptoms. Both ASAD and nomophobia can be considered emotional and behavioral problems that arise as a result of the pathological attachment pattern (11,12,30-34). Previous studies have yielded strong correlations between insecure attachment styles, particularly anxious and ambivalent attachment styles, and separation anxiety disorder (30,33). Similarly, the possibility that attachment styles are one of the dispositional antecedents of nomophobia and problematic phone use was also underlined (11,31,32). A recent study has revealed that there is a relationship between nomophobia and attachment styles, and that anxious and avoidant attachment have positive direct and indirect significant effects on nomophobia (11). In conclusion, we can draw the conclusion that excessive MP use and nomophobia are manifestations of insecure attachment patterns, in individuals with ASAD.

Another reason for the association between ASAD and nomophobia could be that both may share some common clinical symptoms. Although we can evaluate nomophobia as a result of ASAD symptoms based on our findings, nomophobia may also be an expected consequence of increased cell phone use among young university students. That is, ASAD and nomophobia may be primary conditions that occur independently, but simultaneously, and may reinforce and mimic each other's symptoms. For example; the anxiety experienced when there is no mobile phone, constantly checking the phone, and never turning off the mobile phone seen in nomophobia can also be observed in individuals with ASAD who are separated from the people they are attached to and seek closeness to those people.

Another striking finding from our study was that nomophobia is impacted by childhood separation anxiety symptoms. This finding can be argued that childhood separation anxiety symptoms may persist or emerge as adult separation anxiety symptoms and may have an indirect effect on nomophobia through adult separation anxiety symptoms. Still, prospective longitudinal studies are warranted in order to draw firm conclusions about the relationship between childhood separation anxiety symptoms and nomophobia.

Our study findings may have two general implications in practice. First, assessing individuals with ASAD in terms of risk for nomophobia may help identify individuals who are at risk early and, if detected, prompt early treatment, thereby reducing the possibility of long-term complications and adverse course for ASAD. For example, a psychoeducation program and a specific approach to nomophobia can be developed for those at risk. Second, if reversed, might involve screening people with nomophobia symptoms for ASAD symptoms, which may offer an opportunity for a multifaceted approach to remedy nomophobia.

Despite its novelty, this study has several limitations. This study's findings are based on a sample of university-aged students, which limits generalizability to other age groups and broader populations. The relatively small sample size and cross-sectional design further restrict the ability to infer causal relationships and may affect the statistical power of the results. Additionally, potential biases in self-reported data and unaccounted sources of bias could influence the findings.

Future research should focus on specific age groups and clinical conditions to provide a more comprehensive understanding of the ASAD-nomophobia relationship. Studies should examine how these dynamics play out in various populations, including children, adolescents, and older adults, as well as in individuals with other comorbid psychiatric conditions. Additionally, the implications of these findings for clinical practice should be explored. Research should address how the identified relationship between ASAD and nomophobia can be integrated into clinical settings and how it might impact current treatment approaches. For example, developing targeted interventions that address both ASAD and nomophobia simultaneously could improve patient outcomes. Further studies should also evaluate how these findings could inform and enhance existing therapeutic strategies and psychoeducational programs.

CONCLUSIONS

This study is the first attempt in the literature to investigate the relationship between ASAD on nomophobia, and adds a fresh perspective to the interaction of modern technology and ASAD. Our findings broaden the body of knowledge on nomophobia by demonstrating that individuals with ASAD are at risk for nomophobia. Our findings suggest that ASAD may predispose to nomophobia

that individuals with ASAD also need help for nomophobia, and that clinicians should consider nomophobia symptoms when treating ASAD patients.

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RESEARCH ARTICLE

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Turkish Version of the Norwich Patellar Instability Score: Minimal Detectable Change among Patients with Traumatic Patellar Dislocation

ABSTRACT

Objective: This study aimed to calculate the minimal detectable change (MDC) in the Norwich Patellar Instability score (NPI) and validate the score for Turkish-speaking individuals with patellar instability.

Method: Sixty-four patients (mean age 21.87 ± 9.44 years) who had experienced at least one patellar dislocation during athletic activities participated in the study. The Turkish version of the NPI (NPI-T) was evaluated for reliability and internal consistency. The Minimal Detectable Change was calculated as an overall value for the participants. MDC was calculated based on the standard error of measurement (SEM) and the selected confidence level (ICC) for the study population. Pearson's correlations were examined to assess construct validity between the Kujala Patellofemoral Disorder score and the Lysholm Knee Score.

Results: The MDC for the NPI-T was 17.29, with a SEM of 6.24. The score demonstrated high internal consistency, with a Cronbach's alpha value of 0.85, indicating substantial reliability. The consistency of measurements was excellent, with an ICC2,1 of 0.95. Additionally, the NPI-T score exhibited a strong negative correlation with both the Kujala ($r = -0.85$, $p < 0.001$) and Lysholm ($r = -0.89$, $p < 0.001$) scores. A floor effect was observed, but no ceiling effect was present.

Conclusion: The study confirms that the NPI-T demonstrates strong psychometric properties, with high internal consistency and excellent reliability, as evidenced by its low MDC and SEM. The utility of the NPI-T as a reliable and valid tool for evaluating patellar instability in patients with patellar dislocation, providing valuable insights for clinicians.

Keywords: Patellofemoral Instability, Minimal Detectable Change, Reliability, Validity.

Norwich Patellar İnstabilite Skorunun Türkçe Versiyonu: Travmatik Patellar Dislokasyonu Olan Hastalarda Minimal Tespit Edilebilen Değişiklik

ÖZET

Amaç: Bu çalışmanın amacı, Norwich Patellar İnstabilite Skoru'nun (NPI) minimum tespit edilebilir değişikliğini (MDC) hesaplamak ve patellar instabilitesi olan Türkçe konuşan bireyler için skoru doğrulamaktır.

Yöntem: Çalışmaya, spor aktiviteleri sırasında en az bir patella çıkığı yaşayan 64 hasta (ortalama yaş 21,87 ± 9,44 yıl) katılmıştır. NPI'nin Türkçe versiyonu (NPI-T) güvenilirlik ve iç tutarlılık açısından değerlendirilmiştir. MDC, katılımcılar için genel bir değer olarak, çalışma popülasyonu için standart ölçüm hatasına (SEM) ve seçilen güven düzeyine (sınıf içi korelasyon katsayısı, ICC) dayalı olarak hesaplanmıştır. Kujala Patellofemoral Bozukluk Skoru ile Lysholm Diz Skoru arasındaki yapı geçerliliğini değerlendirmek için Pearson korelasyonları incelenmiştir.

Bulgular: NPI-T'nin MDC'si 17,29 ve SEM'i 6,24 olarak bulunmuştur. Skor, 0,85'lik Cronbach alfa değeriyle yüksek bir iç tutarlılık sergilemiş; bu da önemli bir güvenirliğe işaret etmektedir. Ölçümlerin tutarlılığı 0,95'lik ICC2,1 ile mükemmel seviyede bulunmuştur. Ek olarak, NPI-T puanı hem Kujala ($r = -0,85$, $p < 0,001$) hem de Lysholm ($r = -0,89$, $p < 0,001$) puanlarıyla güçlü bir negatif korelasyon göstermiştir. Zemin etkisi gözlenmiş ancak tavan etkisi mevcut olmamıştır.

Sonuç: Çalışma, NPI-T'nin düşük MDC ve SEM ile yüksek iç tutarlılık ve mükemmel güvenilirliğe sahip olduğunu doğrulamaktadır. NPI-T'nin patellar dislokasyonu olan hastalarda patellar instabiliteyi değerlendirmede güvenilir ve geçerli bir araç olarak kullanılması, klinisyenlere değerli bilgiler sunmaktadır.

Anahtar Kelimeler: Patellofemoral İnstabilite, Minimal Tespit Edilebilir Değişiklik, Güvenilirlik, Geçerlilik.

INTRODUCTION

Patellar instability presents significant challenges for individuals, impacting their performance and overall well-being. Accurately assessing the severity of patellar instability and comprehending its effects on the patients are crucial for effective management and rehabilitation. It is known that even after biomechanically successful treatment of patellar instability, patients experience fear during movements, which affects their function (1). Therefore, a comprehensive evaluation of patellar instability is very important. Patellar instability is a multifactorial issue that may develop depending on joint geometry, limb alignment, and contractile and non-contractile soft tissue quality (2). The incidence is higher among adolescent patients and the female gender, with a high-risk group aged 10-17 years (3, 4). Various factors contribute to the etiology of patellar instability, including acute traumatic events, anatomical pathologies such as trochlear dysplasia, muscle imbalances, hyperlaxity, and limb misalignments such as increased femoral anteversion, genu valgum, external tibial torsion, and an increased Q angle (2). Patients with patellar instability often experience complaints such as swelling, stiffness, and pain, in addition to a sense of instability in the knee (2).

Several knee-specific tools are available to assess pain intensity, function, and activity levels(5, 6). While the Kujala Patellofemoral Disorder Score, Lysholm Score, and Tegner Activity Score are commonly employed to evaluate patellofemoral instability, there has been no specific scale for assessing patellar instability (2, 7). These existing scales did not evaluate the particular sense of instability related to various activities. Until 2013, no disease-specific tools were designed to assess symptoms in patients with patellar instability. In response to this need, the Norwich Patellar Instability (NPI) score was developed in 2013, addressing the deficiency in the literature (8). The questions in the NPI score cover a wide range of activities, from daily tasks to athletic pursuits, and are designed to assess a broad spectrum of movement, including high energy efforts and both unidirectional and multidirectional movement patterns. Standardized patient-reported outcome measures are crucial for comprehensively assessing treatment efficacy and clinical responsiveness. The NPI Score exhibited good responsiveness to change, demonstrating a substantial effect size during the transitions from baseline to 12 months (E.S.: 0.43; 95% CI: 0.42 to 0.10) and from 12 to 36 months (E.S.: 0.67; 95% CI: 0.60 to 0.15) in individuals with recurrent patellar dislocation (9).

The absence of a disease-specific assessment tool for Turkish-speaking individuals with patellar instability presents challenges in evaluating patellofemoral instability and demonstrating the evidence-based effectiveness of treatments. In objective measurements based on quantitative data, calculating the Minimal Detectable Change (MDC) is important as it provides valuable information about the reliability and interpretability of measurements. MDC aids in distinguishing true changes from measurement error, and informs clinical decision-making and research design. MDC provides a threshold for determining whether changes in a measurement are clinically significant. If changes exceed the MDC, they are more likely to be meaningful and not simply due to chance or measurement error.

This current study aimed to calculate the MDC in the Norwich Patellar Instability score and validate the score for Turkish-speaking patients who had experienced at least one patellar dislocation during athletic activities We employed hypothesis testing to evaluate construct validity, adhering to the C.O.S.M.I.N. criteria regarding comparison with other outcome measurement instruments (18). We hypothesize that the adapted Turkish version of the Norwich Patellar Instability Score (NPI-T) will exhibit strong psychometric properties among Turkish-speaking patients who have experienced traumatic patellar dislocation. Specifically, we predict that the NPI-T will demonstrate high internal consistency and reliability, as evidenced by a low Minimal Detectable Change and Standard Error of Measurement.

MATERIALS AND METHODS

All procedures performed in studies involving human participants were by the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Ethics committee approval for the study was obtained from the Institutional Review Board affiliated with the authors, and written informed consent was obtained from all participants. This study was designed by C.O.S.M.I.N. standards, which define the methodological quality of studies assessing health-related research and scales' measurement properties (10). For the Turkish version of the Norwich Patellar Instability Score, permission was acquired from the original survey owner via email on 2017 (8). The translation and cultural adaptation of the questionnaire were conducted following the guidelines established by Beaton (11). The study was conducted in the Department of Orthopedics and Traumatology, Faculty of Medicine, Gazi University, with patients admitted to the hospital between April 2022 and December 2022. Questionnaires were administered to 64 patients who met the inclusion criteria and agreed to participate in the study during their initial visit, irrespective of their treatment history. To ensure the questionnaire's reliability, a test-retest was performed seven days after the initial

assessment, involving a random selection of 38 out of the 64 patients. The Minimal Detectable Change was calculated as an overall value for the participants. MDC was calculated based on the standard error of measurement and the selected confidence level. The convergent validity of the NPI-T questionnaire was assessed using the Kujala Patellofemoral Disorder Score and the Lysholm Knee Score.

Translation and Cultural Adaptation: The original NPI score underwent translation from English into Turkish following the translation and back-translation process outlined in the international guidelines by Beaton (11). Two independent bilingual translators translated the original NPI score into Turkish in the initial step. One of them was familiar with the questionnaire, while the other was unaware of the research. In the second step, the two translators assessed and discussed translation discrepancies after producing each "forward" translation version. A synthesis of the versions both translators agreed on was then developed (T12).

The third step involved two native English translators back-translating the T12 Turkish version into English, creating the RT1 and RT2 versions. In the fourth step, a multidisciplinary Coordinating Committee, including an orthopedic surgeon specializing in knee problems, two physiotherapists, a linguist, and translators, reviewed all versions (original, T1, T2, T12, RT1, and RT2) to generate the pre-final version of the NPI-Turkish. In the final stage, twenty patients were invited to complete the pre-final version of the NPI-Turkish. They were subsequently interviewed to identify any possible difficulties in understanding the questionnaire. Patients evaluated this pre-final version for relevance, comprehensiveness, clarity, brevity, cultural appropriateness, and usability. Subsequently, the pre-final version of the Turkish NPI score was designated as NPI-T and subjected to evaluation in terms of its reliability and validity.

Subjects: Sixty-four patients (42 females / 22 males, mean age 21.87 ± 9.44 years) had experienced at least one patellar dislocation included in the study. The inclusion criteria were: 1) at least 18 years old, 2) literate in Turkish, 3) patients who had experienced at least one lateral patellar dislocation during sports or athletic activities 4) exhibited patellar instability during physical examination or had patellar instability findings on M.R.I after the injury. Patients with other orthopedic problems that could lead to dysfunction in the patellofemoral and knee joints (such as ligament and meniscus injuries, osteochondral lesions, and osteoarthritis) and those who experienced patellar instability due to hypermobility were excluded from the study. The number of subjects participating in the study met the acceptable criteria outlined by C.O.S.M.I.N. (10).

Self-Report Measures: The Norwich Patellar Instability Score, developed by Smith et al., is a valid and reliable scale designed to understand the extent of patellar instability better and customize treatment plans accordingly (8). The NPI score consists of a 19-item self-report scale. These items cover both uniplanar (14 items) and multidirectional (5 items) daily living and sports activities, with 12 items related to low-energy activities and seven items for high-energy activities. A five-point Likert scale response ranging from "always" to "never" was used in the score to assess the feeling of instability during these activities. Each option has a point value between 0 and 25; the highest raw score obtained from the scale is 250. To get the final NPI score, the total score from each completed item is divided by the sum of the highest possible scores from the completed items and then multiplied by 100, thereby representing the score as a percentage. The total score is between 0 and 100, and a higher score indicates a more severe feeling of patellar instability (8).

The Kujala Patellofemoral Disorder Score was developed by Kujala et al. in 1993 (12). The score is a 13-item scale developed to evaluate the quality and level of patellofemoral complaints. The questions consist of 3, 4, or 5 items determining the severity of difficulty in activities and symptoms such as atrophy and pain. Each option in the scale carries a score ranging from 0 to 25, and the overall scale is rated between 0 and 100. Higher scores indicate more favorable outcomes. Higher scores indicate better results (12). The validity and reliability study of the Turkish version of the Kujala Patellofemoral Score was performed by Kuru et al., and the Turkish version of the questionnaire was found to be valid and reliable (13).

The Lysholm Knee Score was developed by Lysholm et al. in 1982 to facilitate the follow-up of surgical results in knee ligament injuries (14). The score includes eight items that evaluate symptoms of limping, using support, locking, instability, pain, swelling, climbing stairs, and squatting. It is scored from 0 to 100; a high score represents high functionality (14). The validity and reliability study of the Turkish version of the Lysholm Knee Score was performed by Çelik et al., and the Turkish version of the questionnaire was found valid and reliable (15).

Statistical Analysis: Windows-based S.P.S.S. (IBM SPSS Statistics, Version 23.0, Armonk, NY, U.S.A.) package program was used for statistical analysis. The conformity of the variables to the normal distribution was examined with the Kolmogorov-Smirnov test. Data were expressed as mean, standard deviation, frequency, and percentage. Test-retest and internal consistency analyses were applied to determine the reliability of the Norwich Patellar Instability Score. To assess the reproducibility, 38 patients were randomly chosen

to complete the NPI-T again seven days after their first visit without receiving any treatment. Internal consistency was evaluated using the intraclass correlation coefficient average measures and a one-way random effects model ($ICC_{2,1}$) analysis. Interpretation of $ICC_{2,1}$ was as follows: 1- 0.75 indicates excellent, 0.60–0.75 shows good, and 0.40–0.59 indicates fair reliability (16). Internal consistency reliability of the NPI-T score was determined by calculating Cronbach's alpha. The acceptable range for Cronbach's alpha values is 0.70 to 0.95 (17).

To determine the measurement error, we used the standard error of the measurement and minimal detectable change at 95% confidence interval levels as follows: SEM= SD*√(1-ICC), MDC_{95}=1.96*SEM*√2, respectively (18). The MDC was calculated as an overall value for the patient group. The MDC represents the slightest change in the group's measurements that can be considered accurate and not due to measurement error. The group-level MDC was based on the S.E.M. and the confidence level chosen for the study population.

The new questionnaire was compared to previously validated questionnaires with a similar context to assess construct validity. The NPI-T was tested against the Kujala Patellofemoral Disorder and Lysholm Knee scores. The correlation was calculated using the Pearson correlation coefficient. Correlation coefficients within the 1.0–0.81, 0.8–0.61, 0.6–0.41, 0.4–0.21, and 0.20-0.00 indicated excellent, very good, good, fair, and poor validity, respectively (19).

It was determined if floor or ceiling effects existed by calculating the percentage of NPI-T total scores concentrated at the bottom and top of the questionnaire range. More than 15% of floor or ceiling effects were significant (20).

RESULTS

The demographic and clinical characteristics of the patients are presented in Table 1. The translation and cultural adaptation process were completed following the abovementioned procedure, and no problems were reported.

Table 1. Description of the subjects

Variable	Value
Age (X±SD) (years)	21.87 ± 9.44
Body Mass Index (X±SD) (kg/m^2)	23.01 ± 2.31
Gender n (%)	
Female	42 (65.6)
Male	22 (34.4)
Operative procedure	
MPFL reconstruction	34 (53)
Conservative treatment	30 (47)
Number of episodes of dislocation (X±SD)	4.20 ± 6.51
Questionnaire scores (X±SD)	
NPI-T	33.14 ± 28.40
Kujala Score	69.34 ± 21.25
Lysholm Score	71.06 ± 22.27

NPI-T: Norwich Patellar Instability - Turkish version

The Turkish version of the NPI score and scoring sheet are in the appendix. The MDC and SEM of the NPI-T were 6.24 and 17.29, respectively. The test-retest analysis involved 38 participants who were assessed seven days apart. These participants did not undergo any interventions that might have induced changes in their symptoms or clinical status during this period. In the assessment of test-retest reliability, the initial NPI score for the patients had an average of 14.96 ± 11.68, while the subsequent score showed an average of 16.25 ± 18.26. Cronbach's α for the NPI-T was 0.85, indicating acceptable internal consistency. The ICC value was 0.95, indicating excellent reliability. Test-retest results, ICC scores, and Confidence Intervals (CI) are summarized in Table 2. A strong negative correlation was observed between the NPI-T and the Kujala Patellofemoral Disorder Score (r = -0.85; p < 0.001) and the Lysholm Knee Score (r = -0.89; p < 0.001) (Table 3). A floor effect was detected in the NPI-T, and there was no ceiling effect.

Table 2. Internal consistency, test-retest reliability, and minimal detectable change of the NPI-T

	Internal consistency (n=64)	**Test-retest reliability (n=38)**	**Measurement error**	
	Cronbach's α	**ICC (95% CI)**	**SEM**	**MDC_{95}**
NPI-T	0.85	0.95(0.90-0.74)	6.24	17.29

NPI-T: Norwich Patellar Instability -Turkish version, ICC: Intraclass Correlation Coefficient, SEM: Standard Error of Measurement, MDC_{95}: Minimal Detectable Change.

Table 3. Correlation values of NPI-T with other scores

	NPI-T (n=64)		
	Score (X±SD)	r	p
Kujala Patellofemoral Disorder Score	69.34 ± 21.25	-0.85	< 0.001*
Lysholm Knee Score	71.06 ± 22.27	-0.89	< 0.001*

*Statistical significant, NPI-T: Norwich Patellar Instability -Turkish version

DISCUSSION

This study support the use of the NPI-T as a reliable and valid tool for evaluating patellar instability in patients with traumatic patellar dislocation. The low MDC and SEM values indicate that the NPI-T has good sensitivity to detect true changes in patellar instability scores. The MDC for the NPI-T was found to be 17.29, with a SEM of 6.24. Any change in the NPI-T score greater than 17.29 can be considered a true change and not just due to measurement variability. This information is crucial for making informed decisions about treatment effectiveness and monitoring patient progress in patellar instability related sports injuries.

In a study evaluating knee-specific outcome measures in patient assessment after an acute patellar dislocation, reporting that only the Fulkerson and Lysholm scales could be used to distinguish between patients with and without patellar instability (5). In 2008, Smith et al. systematically reviewed knee outcome measures and emphasized their suitability for patellofemoral dysfunction and ligament injuries, highlighting the need for outcome measures specific to patellofemoral instability (21). The absence of a patellar instability-specific scoring system hindered demonstrating the evidence-based efficacy of patellofemoral instability treatment. The NPI score assesses the instability during sports and daily living activities, incorporating questions related to physically challenging and less demanding activities. It provides an objective scoring of perceived patellar instability (22). Disease-specific tools are crucial for demonstrating evidence-based results of evaluations and treatment efficacy rather than relying on general tools. The MDC helps clinicians interpret changes in scores. By comparing the magnitude of change to the MDC, it can determined whether the observed change is meaningful and not just a result of measurement error. Therefore, verifying the Turkish version of NPI's MDC and reliability was necessary. The Turkish version of the NPI score is the sole disease-specific tool for evaluating patellar instability for Turkish patients.

Examining the psychometric properties of the NPI score, Smith et al. reported that the minimally important clinical change and minimally clinically important difference should be determined for the NPI score, which is crucial for its interpretation, guiding future clinical trial sample size calculations, and strengthening the validity of the NPI score(9). MDC allows researchers and clinicians to quantify the amount of measurement error associated with a particular assessment tool. This understanding helps in interpreting changes observed in subsequent measurements. MDC provides a threshold for determining whether changes in a measurement are clinically significant. If changes exceed the MDC, they are more likely to be meaningful and not simply due to chance or measurement error. The MDC of 17.29 points and SEM of 6.24 points for the NPI-T indicate the level of change that can be considered beyond measurement error and the average amount of variability in the measurements, respectively. These values provide important information for clinicians and researchers when interpreting and evaluating the NPI-T scores in the context of patellar instability in sports injury.

Internal consistency refers to the interrelatedness of the items within a sample of the test. When Cronbach's alpha demonstrates high internal consistency, it suggests that the items in the scale are measuring the same underlying construct. The original English version of the NPI score has high internal consistency with a Cronbach's alpha of 0.93 (8). Similarly, Van Sambeek et al. reported a high level of internal consistency for the Dutch version of the NPI score (Cronbach's alpha=0.97) (23). Likewise, the Turkish version of the NPI score displayed significant internal consistency, with a Cronbach's alpha of 0.85, confirming the scale's reliability for assessing patellar instability. This high level of consistency among the items suggests that they reliably measure the same construct, thus strengthening the overall reliability of the scale in assessing patellar instability.

Reliability, a critical parameter in outcome measurements, pertains to the consistency of measurement. Test-retest reliability, which measures the consistency of results over time, is essential to medical field scales due to the diverse nature of the parameters being assessed (e.g., symptoms, disability) (16). This study, 38 patients were included in the test-retest reliability analysis, with a one-week interval between the two tests. While the original NPI score's test-retest reliability has not been established, the Turkish version of the NPI score demonstrated excellent test-retest reliability, as indicated by an ICC value of 0.95. It is worth noting that previous studies on the Dutch and Brazilian versions of the NPI score did not investigate the test-retest reliability of the scale (23, 24). Therefore, the current research contributes valuable insights by providing evidence of the test-retest reliability of the NPI score.

The Kujala Patellofemoral Disorder Score and Lysholm Knee Score are commonly used to assess knee joint symptoms and functional outcomes. These scales primarily focus on evaluating patellofemoral dysfunction, each featuring only one item dedicated to assessing patellofemoral instability (12, 14). The convergent validity of the original English NPI score was evaluated using the Kujala and Lysholm scores. The original English NPI score was moderately correlated with the Kujala Patellofemoral Disorder Score (rho = -0.66; $p < 0.01$) and Lysholm Knee Score (rho = -0.54; $p = 0.03$) (8). In this study, we used the same questionnaires for convergent

validity. The Turkish version of the NPI score exhibited a strong negative correlation with the Kujala and Lysholm scores (r = -0.85 and r = -0.89, respectively). This strong correlation confirms the convergent validity of the Turkish version of the NPI score. The Turkish version of the NPI score had a higher correlation coefficient with both questionnaires than the original version of the NPI score. There are some possible explanations for this difference. In our study, 53% of the participants (34 of 64 patients) underwent operative treatment, whereas 38% (39 of 102 patients) received operative treatment in the original study. However, for the assessment of convergent validity, the Kujala score was applied to 60 subjects, while the Lysholm score was administered to only 17 subjects in the original NPI score study. The authors did not specify how many patients who completed the Kujala and Lysholm scores had undergone surgical treatment. Additionally, the current study excluded patients with orthopedic disorders that could potentially result in patellofemoral and knee joint dysfunction, such as ligament and meniscus injuries. As a result, the participants in our study exhibited less patellofemoral dysfunction, leading to higher Kujala and Lysholm scores. In the original version of the NPI score study, the median Kujala score of the patients was 55.0, and the Lysholm score was 56.0, while, in our study, the median Kujala score was 71.50, and the Lysholm score was 75.0.

Factor analysis was not performed in other versions of the NPI score studies. The original NPI score study did not include an analysis of floor or ceiling effects (8). However, in a study involving the NPI score applied to individuals conservatively managed following their first-time patellar dislocation, T. Smith et al. reported that 13 out of 19 items exhibited a floor effect. In contrast, no ceiling effect was observed (25). The Dutch version of the NPI score found a floor effect but no ceiling effect (23). Similarly, a floor effect was detected in the present study, and no ceiling effect was evident. The presence of a floor effect in these studies, including the current study, indicates that the NPI score may have limited sensitivity in detecting lower levels of patellar instability. Clinically, the scale might not effectively differentiate between individuals with very mild symptoms and those with no symptoms at all. As a result, the NPI score may be more suitable for assessing moderate to severe patellar instability rather than mild cases. This information may be beneficial when interpreting the NPI score in cases of patellar instability with mild symptoms. Smith et al. performed a responsiveness analysis of the NPI, revealing that the score demonstrated sensitivity to changes from baseline to 12 months post-injury (8). However, in this study, responsiveness analysis, accuracy analysis, sensitivity, and specificity analysis for the Turkish NPI score were not performed.

The current study has several limitations. Firstly, we did not calculate a Minimum Important Clinical Change (MICC) for the NPI-T score. The determination of MICC is crucial for comprehending the clinical significance of changes in NPI scores and would have offered valuable insights into interpreting our findings. Additionally, the study did not include an analysis of the NPI-T score's responsiveness to changes in patients' conditions over time. Understanding how the score detects clinically meaningful changes and its sensitivity to interventions is essential for evaluating its utility in clinical practice. Moreover, the study did not explore the NPI-T score's responsiveness to various treatments for patellar instability, such as surgical and conservative approaches. These limitations prevent a comprehensive understanding of the magnitude of clinically meaningful changes observed in NPI-T scores.

CONCLUSION

The present study showed that the Turkish version of the NPI score is reliable and valid with a MDC of 17.29 points for assessing patient-perceived patellar instability during activities in patients who have experienced at least one patellar dislocation during sport.

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RESEARCH ARTICLE

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Evaluation of Lower Extremity Venous Doppler Ultrasonography Outcomes Before and After The COVID-19 Pandemic; A Retrospective Study

ABSTRACT

Objective: COVID-19 test positivity has been reported among asymptomatic individuals and asymptomatic people are also considered to be at risk for thromboembolic events. The aim of this study was to compare the results of patients who underwent lower extremity Doppler ultrasonography (DUS) with a preliminary diagnosis of deep vein thrombosis (DVT) before and after the pandemic, regardless of COVID-19 testing.

Method: Patients who underwent RDUS in the Department of Radiology during a total period of 35 months (01/08/2018 - 01/07/2021) were analyzed. A total of 599 patients underwent RDUS during the study period.

Results: More positive DVT findings were observed after the pandemic (n=43, 18.3%, p=0.005) (only two of these patients had a positive COVID-19 result). History of hospitalization in the last three months, D-dimer, Platelet (PLT) count, Mean platelet volume (MPV), White blood cell (WBC) count, neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio (NLR) values, comorbidity and antiaggregant use were not different (p>0.05).

Conclusion: Even individuals (especially elderly individuals) who have been exposed to the virus during the pandemic but who do not show symptoms are at risk of DVT.

Keywords: COVID-19, Deep Vein Thrombosis, Doppler Ultrasonography.

COVID-19 Pandemisi Öncesi ve Sonrası Alt Ekstremite Venöz Doppler Ultrasonografi Sonuçlarının Değerlendirilmesi; Retrospektif Bir Çalışma

ÖZET

Amaç: COVID-19 testi pozitifliği asemptomatik bireyler arasında bildirilmiştir ve asemptomatik kişilerin de tromboembolik olaylar için risk altında olduğu düşünülmektedir. Bu çalışmanın amacı, COVID-19 testinden bağımsız olarak, pandemi öncesi ve sonrasında derin ven trombozu (DVT) ön tanısıyla alt ekstremite Doppler ultrasonografisi (DUS) yapılan hastaların sonuçlarını karşılaştırmaktır.

Yöntem: Toplam 35 aylık süre boyunca (01/08/2018 - 01/07/2021) Radyoloji Bölümünde RDUS yapılan hastalar analiz edildi. Çalışma dönemi boyunca toplam 599 hastaya RDUS yapılmıştır.

Bulgular: Pandemi sonrasında daha fazla pozitif DVT bulgusu gözlenmiştir (n=43, %18,3, p=0,005) (bu hastaların yalnızca ikisinde pozitif COVID-19 sonucu vardı). Son üç ay içinde hastaneye yatış öyküsü, D-dimer, platelet (PLT), ortalama platelet hacmi (MPV), (lökosit sayısı) WBC, nötrofil sayısı, lenfosit sayısı, nötrofil/ lenfosit oranı (NLR) değerleri, komorbidite ve antiagregan kullanımı farklı değildi (p>0.05).

Sonuç: Pandemi sırasında virüse maruz kalan ancak semptom göstermeyen bireyler (özellikle yaşlı bireyler) bile DVT riski altındadır.

Anahtar Kelimeler: COVID-19, Derin Ven Trombozu, Doppler Ultrasonografi.

INTRODUCTION

The COVID-19 pandemic caused by a new type of coronavirus called SARS-CoV-2 has been effective all over the world since the first months of 2020 (1,2). The first case was seen in our country on 11/03/2020. Infected individuals may be asymptomatic or may have clinical presentations ranging in severity from upper respiratory tract disease such as fever, dry cough, fatigue, sore throat to lower respiratory tract infection that can progress to ARDS (3,4).

It is known that COVID-19 infection causes coagulation abnormalities and leads to thromboembolic events and this contributes to morbidity and mortality related to the disease (5). Polymerase chain reaction (PCR), which is the gold standard diagnostic method during the pandemic period, cannot be performed in every center and some patients may not apply to health institutions because they are asymptomatic (3). As up to 30% PCR positivity has been reported among asymptomatic individuals (6,7), asymptomatic patients are also considered to be at risk for thromboembolic events (8).

Based on this information, in this study, analyses were performed independently of the COVID-19 PCR test. The aim of this study was to compare the results of patients who underwent lower extremity Doppler ultrasound (DUS) with a prediagnosis of deep vein thrombosis (DVT) in our hospital before and after the pandemic.

MATERIALS AND METHODS

The study was planned retrospectively in the emergency department of a tertiary hospital. Ethics committee approval was obtained from local ethic committee (Decision no: 2022/147 Date: 03/20/2022).

Patients who underwent RDUS in the Department of Radiology during a total period of 35 months (01/08/2018 - 01/07/2021) were analyzed. A total of 599 (annual average of 205.4) patients underwent RDUS during the study period. The data of 12 of these patients could not be accessed and were excluded from the study.

Patients; RDUS result (positive or negative for DVT), age, gender, history of hospitalization in the last three months, Covid PCR test result (checked for post-pandemic patients), laboratory tests [D-dimer, Platelet (PLT) count, Mean platelet volume (MPV), White blood cell (WBC) count, neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio (NLR)], comorbid diseases, antiaggregant and anticoagulant use were questioned.

Patients' d-dimer values (<0.5, 0.5-1, >1), PLT counts (<50,000, 50,000-150,000, 150,000-450,000, >450,000), MPV values (<6, 6-9, 9-11 and >11), WBC values (<10, 000 and >10,000), lymphocyte counts (<1000, 1000-5000 and >5000), neutrophil counts (<1000, 1000-8000 and >8000) and NLR values (<5 and >5).

Statistical Analysis: Descriptive statistics were presented as number and percentage. Demographic data were presented as Mean, Standard Deviation (SD), Median, IQR. Pearson chi-square test and Fisher's exact test (when the expected number was less than five) were used for independent categorical variables. Bonferroni correction was used for subgroup analyses and $p<0.016$ was considered significant. Mc Nemar test was used for dependent categorical variables. Student-t test was used for numerical two-group variables with normal distribution. Mann Whitney U test was used for numerical two-group variables that did not show normal distribution. Statistical analyses were performed using SPSS software for Windows, version 23 (IBM, Chicago, IL, United States of America). $P < 0.05$ was considered significant.

RESULTS

A total of 587 patients were included in the study. Of these, 235 (40%) came after the pandemic, COVID-19 test results were obtained in a total of 70 (29.8%) patients, 9 (12.9%) of whom had positive COVID-19 test results. The majority of patients (52.9%) were male, the mean age was 61.19±18.55 years, and right lower extremity venous doppler was requested the most (29.7%).

The mean age was higher after the pandemic (63.60±17.222) (p=0.013). Gender distribution was not different between the two periods (p=0.273). More DVTs were observed after the pandemic (n=43, 18.3%, p=0.005) and only two of these patients had a positive COVID-19 PCR result. History of hospitalization in the last three months, D-dimer, PLT, MPV, WBC, neutrophil count, lymphocyte count, NLR values, comorbidity and antiaggregant use were not different (p>0.05). After the pandemic, it was determined that DUS was requested more frequently in patients who did not use anticoagulants (n=40, 17%, p=0.02) (Table 1).

DISCUSSION

DVT describes unstable and excessive clotting that occurs most commonly in the popliteal vein, femoral vein and pelvic iliac veins and grows towards the heart, which is the direction of blood flow (9). Risk factors include; Reduced blood flow (conditions that cause prolonged immobilization such as bed rest, general anesthesia, surgeries, stroke, long journeys), increased venous pressure (neoplasm, pregnancy, stenosis), direct injury to the vein (trauma, surgery, peripherally placed venous catheters, intravenous drug use), increased blood viscosity (polycythemia, thrombocytosis, dehydration), genetic defects that create a tendency to coagulation (protein C and S deficiency,

Table 1. Descriptive and comparative data before and after the pandemic

		Period				
		Pre-pandemic		Post-pandemic		
		n	%	n	%	p
Gender	Male	180	51.14	131	55.74	0.273
	Female	172	48.86	104	44.26	
DVT	Yes	36	10.3	43	18.3	**0.005**
	No	315	89.7	192	81.7	
Hospitalization in the last three months	Yes	47	13.4	20	8.5	0.069
	No	304	86.6	215	91.5	
D-dimer	<0.5	12	18.46	7	8.24	0.162
	0.5-1.0	11	16.92	14	16.47	
	>1.0	42	64.62	64	75.29	
PLT	<50	4	1.47	3	1.37	0.988
	50-150	30	10.99	22	10.05	
	150-450	219	80.22	178	81.28	
	>450	20	7.33	16	7.31	
MPV	<6	0	0.00	2	0.91	0.363
	6-9	200	73.26	157	71.36	
	9-11	64	23.44	56	25.45	
	>11	9	3.30	5	2.27	
WBC	<10000	138	50.55	123	56.68	0.177
	>10000	135	49.45	94	43.32	
Lymphocyte	<1000	67	24.81	56	25.93	0.751
	1000-5000	200	74.07	156	72.22	
	>5000	3	1.11	4	1.85	
Neutrophil	<1000	3	1.11	5	2.31	0.104
	1000-8000	151	55.93	137	63.43	
	>8000	116	42.96	74	34.26	
NLR	<5	143	52.96	126	58.33	0.237
	>5	127	47.04	90	41.67	
Comorbidity	Yes	272	77.3	171	72.8	0.214
	No	80	22.7	64	27.2	
Antiaggregant using	Yes	127	36.7	75	31.9	0.234
	No	219	63.3	160	68.1	
Anticoagulant using	Yes	87	25.1	40	17.0	**0.020**
	No	259	74.9	195	83.0	

*Bonferroni correction was made for subgroup analyses and p<0.016 was considered significant. DVT: deep vein thrombosis, PLT: Platelet, MPV: Mean platelet volume, WBC: White blood cell, NLR: neutrophil/lymphocyte ratio.

antithrombin III deficiency, factor V Leiden mutation), acquired causes predisposing to clotting (cancer, sepsis, myocardial infarction, heart failure, vasculitis, systemic lupus erythematosus and lupus anticoagulant, Inflammatory bowel disease, nephrotic syndrome, burns, oral estrogens, smoking, hypertension, diabetes, obesity, pregnancy, age over 60, surgery, intensive care hospitalization (9-11). Endothelial damage, hypercoagulability and venous blood stasis (Virchow's triad) play an important role in the pathophysiology of thrombosis (9,12). Damage to the vessel wall leads to pro-inflammatory (and prothrombotic) cytokine production, increase in available tissue factor, proliferation of adhesion molecules and increased platelet activation. These cytokines initiate interactions between leukocytes and endothelial cells that trigger inflammation. Activation of leukocytes and endothelial cells ultimately leads to the formation of adhesion molecules, which triggers a process that initiates clot formation (9,11,12).

In COVID-19 patients, one of the factors aggravating the disease is the overproduction of inflammatory mediators, defined as a cytokine storm (13,14). In COVID-19 patients, factors such as platelet hyperactivation, increased mean platelet volume, and increased release of P-selectin and E-selectin adhesion molecules on the surface of endothelial cells are thought to be involved in vascular occlusive events that increase in the course of the disease (14-16). Occlusive vascular events are thought to be both complications and aggravating factors, including the measures taken.

PCR test positivity in patients admitted to hospital with COVID-19 symptoms ranges from 0.005% to 39.7% (6,17,18). COVID-19 PCR test positivity in asymptomatic patients varies according to the prevalence of the disease in the community (1-30%) (7,19). Asymptomatic and symptomatic

individuals are also thought to have a higher risk for vascular phenomena (8). This suggests that vascular events such as DVT may increase in the community, although it is almost impossible to know the number of asymptomatic individuals.

In a meta-analysis of 63 studies including 104920 COVID-19 positive patients, the rate of deep vein thrombosis was found to be 20%, pulmonary embolism 8% and arterial thrombosis 5% (10). In this study, the prevalence of deep vein thrombosis was found to be high especially in elderly patients (P<0.05) (10). In another review, 42 studies were evaluated, the prevalence of DVT was found to be 0.43-60.87% in COVID-19 positive cases and it was pointed out that DVT was a factor worsening the COVID-19 clinic (11). Based on the available data, this study was planned with the idea that there are infected but asymptomatic individuals who have encountered the virus during the COVID-19 pandemic and that these individuals are at risk for DVT and will increase the incidence of DVT. In our study, more positive findings (18.3%) were observed in DUS results obtained after the pandemic. Only two of these patients (2/43) had positive COVID-19 PCR results. Exposure to the virus may have caused the increase in DVT positivity, which was 10.3% before the pandemic, as well as staying at home more and moving less as part of the precautions.

LIMITATIONS

The limitations of the study are that it was a single center, the number of patients was small, and there was insufficient information about the mobilization status of the patients. In addition, the fact that fewer patients underwent DUS in the post-pandemic period and the mean age was higher may suggest that patient selection was more sensitive.

CONCLUSION

After the COVID-19 pandemic, more DVT findings were observed in lower extremity DUS results evaluated independently of the PCR test. This result suggests that even individuals (especially elderly individuals) who have been exposed to the virus during the pandemic but who do not show symptoms are at risk of DVT.

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RESEARCH ARTICLE

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AB0 Blood Group Phenotypes and Rhesus Factor in The Pathogenesis of Gestational Diabetes Mellitus

ABSTRACT

Objective: Some AB0 blood group phenotypes can be considered as risk factors in the pathogenesis of both type II diabetes mellitus (DM) and type I DM. The aim of this study was to investigate whether some AB0 blood group phenotypes and Rhesus (Rh) factor are risk factors for the occurrence of the disease in pregnant women diagnosed with gestational diabetes mellitus (GDM).

Method: This study is a case-control study, and the data were analyzed retrospectively. Pregnant women who applied to a training and research hospital for one year and had a 75-gram oral glucose tolerance test (OGTT) were included in the study. According to the OGTT results, pregnant women diagnosed with GDM (case group) and healthy pregnant women (control group) were divided into two groups.

Results: In a one-year data scan, the prevalence of GDM was found to be 15.94%. The average age of pregnant women with GDM was found to be higher than healthy pregnant women ($p<0.001$). There was no significant difference between the percentage frequency distributions of AB0 blood group in pregnant women with GDM and healthy pregnant women ($p>0.05$). Rh factor positivity of both groups was not different ($p>0.05$).

Conclusion: In conclusion, no relationship was found between GDM pathogenesis, AB0 blood group phenotypes and Rh factor.

Keywords: AB0 Blood Group, Gestational Diabetes, Rh Factor.

Gestasyonel Diyabetes Mellitus Patogenezinde AB0 Kan Grubu Fenotipleri ve Rhesus Faktörü

ÖZET

Amaç: Bazı AB0 kan grubu fenotipleri hem tip II diabetes mellitus (DM) hem de tip I DM'nin patogenezinde risk faktörü olarak kabul edilebilir. Bu çalışmanın amacı, bazı AB0 kan grubu fenotiplerinin ve Rhesus (Rh) faktörünün, gestasyonel diabetes mellitus (GDM) tanısı almış gebe kadınlarda hastalığın ortaya çıkması için risk faktörü olup olmadığını araştırmaktır.

Yöntem: Bu çalışma bir vaka-kontrol çalışması olup veriler retrospektif olarak analiz edildi. Bir eğitim ve araştırma hastanesine bir yıl süreyle başvuran ve 75 gram oral glukoz tolerans testi (OGTT) yaptıran gebe kadınlar çalışmaya dahil edildi. OGTT sonuçlarına göre GDM tanısı almış gebe kadınlar (vaka grubu) ve sağlıklı gebe kadınlar (kontrol grubu) iki gruba ayrıldı.

Bulgular: Bir yıllık veri taramasında GDM prevalansı %15,94 olarak bulundu. GDM'li gebelerin yaş ortalaması sağlıklı gebelere göre daha yüksek bulundu ($p<0,001$). GDM'li gebeler ile sağlıklı gebelerde AB0 kan grubunun yüzdelik frekans dağılımları arasında anlamlı bir fark yoktu ($p>0,05$). Her iki grubun Rh faktörü pozitifliği farklı değildi ($p>0,05$).

Sonuç: Sonuç olarak GDM patogenezi ve AB0 kan grubu fenotipleri ile Rh faktörü arasında bir ilişki bulunamadı.

Anahtar Kelimeler: AB0 Kan Grubu, Gestasyonel Diyabet, Rh Faktörü.

INTRODUCTION

Gestational diabetes mellitus (GDM), defined as a transient form of diabetes caused by pancreatic beta cell dysfunction and insulin resistance during pregnancy, is recognized as one of the main challenges to improving child and maternal health. Approximately 9.0-25.0% of pregnancies worldwide are affected by acute, long-term and intergenerational health complications of this disease (1). The etiology of GDM, the most common metabolic disorder in pregnancy, is complex; environmental and genetic factors are involved in epidemiologic and mechanistic studies. Although short-term benefits of treatment with lifestyle and pharmacologic interventions have been proven, the long-term effect of intrauterine exposure to antidiabetic drugs on offspring remains unclear (2). The prevalence of GDM has continued to increase in recent years. It is expected to continue to increase in the coming years. The public health impact of GDM is increasing and may lead to the development of non-communicable chronic diseases in both mothers and their children in the long term. Early detection of high-risk women can help implement interventional and preventive measures to reduce adverse perinatal outcomes and the risk of GDM (3).

Antigenic determinants of the AB0 blood group, whose antigens were discovered more than a century ago, are known to be present not only on the erythrocyte membrane but also in other cells and tissues (gastrointestinal epithelial platelets, respiratory system cells and salivary glands). In the last decade, a large number of studies and systematic literature have been published on the association between a particular disease and blood group type. This shows the clinical importance of defining blood group typing not only for the selection of blood and its components for transplantation and transfusion, but also for the diagnosis of patients with different nosologies, determination of the risk group and treatment tactics (4). The best known and definitive blood group system is the AB0 group system. It is also the only system in which antibodies are continuously present in the blood serum. In studies on pregnant women, scientists have discovered the impact of blood type on the development of pre-eclampsia, the risk of preterm birth and even coronavirus disease-19 inflammation. Due to the heterospecificity of AB0, the influence of the mother's blood group also affects the birth weight of the newborn and the development of hemolytic disease in the newborn. Blood group has also been shown to influence the likelihood of developing certain diseases and complications in infancy (5).

In case of significant carbohydrate metabolism disorder, immunologic reaction (total IgE) indices have been reported to be lower in patients with blood group 0 and A compared to patients with other blood groups. On the other hand, it has been reported that immunologic reaction indices in patients with blood group B and type II diabetes increased two-fold compared to the upper limit of the standard (6). In a meta-analysis including 15 studies examining the relationship between blood group AB0 and type II diabetes, it was reported that individuals with blood group B were at higher risk for type II DM, whereas individuals with blood group 0 were at lower risk for the development of type II DM. In addition, due to the high risk of type II DM, it is recommended that people with B blood group should be closely monitored by their physicians (7). In a study involving 892 childhood cases in seven European research centers, blood group incompatibility (Rh factor and AB0) was found to be an important risk factor for type I DM. In addition, AB0 incompatibility was reported to be a more common and stronger risk factor than Rh incompatibility. It was also reported that the effect of AB0 blood group incompatibility on treatment was not related to this (8).

Although there are studies in the literature showing a relationship between type I and type II DM pathogenesis and AB0 blood group phenotypes, the results of studies examining the relationship between GDM pathogenesis, and AB0 blood group phenotypes are contradictory (9-12). The reason for the contradictory results may be that the studies were conducted in different populations. There is no study examining the relationship between GDM pathogenesis and AB0 blood group phenotypes in the region where this study was conducted. In this study, we aimed to investigate whether there is a relationship between the occurrence of the disease in pregnant women with GDM and AB0 blood group.

MATERIALS AND METHODS

Study Design: The study is a single-center case-control study and is a retrospective study. The study included 24–28-week pregnant women who underwent 75-gram oral glucose tolerance test (OGTT) between 01/01/2023 and 31/12/2023 in the Gynecology Outpatient Clinic of Samsun Training and Research Hospital. Pregnant women without blood group analysis were excluded from the group comparison. Pregnant women who underwent 50- or 100-gram oral glucose tolerance test were also excluded. Pregnant women with type I or type II diabetes were also excluded. The diagnosis of GDM was made according to the criteria including glucose concentration thresholds determined by the International Diabetes and Pregnancy Study Group (IADPSG) (13).

Data Collection and Analysis: Age and blood group information, fasting blood glucose, OGTT 1st hour and OGTT 2nd hour values of both healthy pregnant women and pregnant women diagnosed with GDM were retrospectively scanned from the hospital information management system.

Pregnant women diagnosed with GDM were included in the case group. Healthy pregnant women were included in the control group.

Statistical Analysis: Statistical Package for the Social Sciences (SPSS) version 22.0 for Windows was used for statistical analysis of variables. Continuous variables were defined as X±SD (mean±standard deviation). Categorical data were defined as percentage frequency. Continuous data of the groups were compared by Independent Sample T test. Categorical variables of the groups were compared with the chi-square test. A P value below 0.05 was considered significant.

RESULTS

OGTT was performed in 1468 pregnant women and 234 (15.94%) of these women were diagnosed with gestational diabetes. Blood group analysis was performed in 835 (56.88%) of the pregnant women who underwent OGTT. Descriptive data of these pregnant women aged between 18 and 45 years are presented in Table 1.

Table 1. Descriptive information of pregnant women

Parameter		**Pregnant n=835**
Age X±SD		28.62±5.51
Fasting blood glucose X±SD (mg/dL)		81.76±10.91
Oral glucose tolerance test 1-hour X±SD (mg/dL)		133.71±34.64
Oral glucose tolerance test 2-hour X±SD (mg/dL)		108.12±28.81
Pregnant women diagnosed with gestational diabetes n (%)		167 (20.00)
AB0 blood groups n (%)	A Rh (positive)	343 (41.08)
	A Rh (negative)	53 (06.35)
	B Rh (positive)	106 (12.69)
	B Rh (negative)	13 (01.56)
	AB Rh (positive)	46 (05.51)
	AB Rh (negative)	9 (01.08)
	0 Rh (positive)	231 (27.66)
	0 Rh (negative)	34 (04.07)

It was determined that 167 (20.00%) of the pregnant women who underwent blood group analysis with OGTT were diagnosed with gestational diabetes. The mean age of pregnant women with GDM was 30.46±5.82, while the mean age of healthy pregnant women was 28.16±5.34. The mean age of pregnant women with GDM was higher than that of healthy pregnant women ($p<0.001$). Table 2 shows the percentage frequency distribution of AB0 blood group in pregnant women with GDM and healthy pregnant women.

Table 2. AB0 blood group percentage frequency distribution of pregnant women with gestational diabetes and healthy pregnant women

AB0 blood group	**Healthy pregnant n=668**	**Pregnant women with gestational diabetes n=167**
A Rh (positive) n (%)	273 (40.87)	70 (41.92)
A Rh (negative) n (%)	42 (06.29)	11 (06.59)
B Rh (positive) n (%)	87 (13.02)	19 (11.38)
B Rh (negative) n (%)	8 (01.20)	5 (02.99)
AB Rh (positive) n (%)	38 (05.69)	8 (04.79)
AB Rh (negative) n (%)	8 (01.20)	1 (00.60)
0 Rh (positive) n (%)	182 (27.25)	49 (29.34)
0 Rh (negative) n (%)	30 (04.49)	4 (02.40)

There is no statistically significant difference between the percentage frequency distribution of AB0 blood group in pregnant women with GDM and healthy pregnant women ($p>0.05$).

Rhesus factor (Rh factor) was positive in 580 (86.83%) of 668 healthy pregnant women. Rh factor was positive in 146 (87.43%) of 167 pregnant women with GDM. There was no difference between the two groups in terms of Rh factor positivity ($p>0.05$).

DISCUSSION

Approaches to the diagnosis and screening of GDM vary widely. According to IADPSG criteria, the regional and global prevalence of GDM varies. The combined global standardized prevalence of GDM is 14.0%. The regional

standardized prevalence of GDM is lowest in North America and the Caribbean at 7.1%. This prevalence was found to be 7.8% in Europe, 10.4% in South America, 14.7% in Africa, 20.8% in Western Pacific, 27.6% in Southeast Asia and Middle East and North Africa (14). In this study, OGTT data of 1468 pregnant women were obtained and GDM prevalence was found to be 15.94% according to IADPSG criteria.

Considering the prevalence of AB0 blood group phenotypes, blood group 0 is the most common phenotype in most populations. This prevalence is 44% in Caucasians, 49% in Blacks and 43% in Asians. Furthermore, the prevalence of AB0 blood group antigens is 27% for antigen A and 20% for antigen B in Caucasians, compared to 43% for antigen A and 9% for antigen B in Blacks. In Asians, A antigen is 28% and B antigen is 27% (15). The most common phenotype in pregnant women included in this study was blood group A with 47.43%. The second most common phenotype was blood group 0 with 31.73%. In addition, the rate of pregnant women with only B antigen was found to be 14.25%.

Advanced maternal age (≥35 years) is a known risk factor for GDM. Research suggests that GDM occurs from specific metabolic entities and suggests an individualized approach based on early pregnancy characteristics (maternal age, 75-gram OGTT values, obstetric history) (16). The average childbearing age of women is increasing due to improvement in social and economic status, prolonged schooling, work pressure and other reasons. In parallel, the prevalence of GDM in pregnant women shows a sharp upward trend. Similarly, mothers' long-term health concerns, such as those associated with type II DM and metabolic syndrome, are significantly affected by GDM. Moreover, unfavorable pregnancy outcomes and obesity in children after growing up constitute a major hidden risk for the development of DM and other diseases (17). In this study, the mean age of pregnant women with GDM was found to be higher than the mean age of healthy pregnant women.

In a systematic literature analysis examining the association between AB0 blood type and pregnancy complications, “pregnancy”, “AB0 blood type”, “preeclampsia”, “venous thromboembolism”, “eclampsia”, “pulmonary embolism”, “deep vein thrombosis”, A literature review was conducted using the keywords “gestational diabetes”, “postpartum hemorrhage”, “pregnancy-induced hypertension”, “HELLP syndrome” and “intrauterine fetal growth restriction”. The results of the systematic review reported that AB0 status had a consistent effect on the risk of developing pre-eclampsia. No effect of AB0 blood type on the risk of developing gestational diabetes has been reported (9). In another review examining the association between AB0 blood type and pregnancy complications, it was concluded that, in general, AB blood type may be associated with the pathogenesis of GDM in different populations (10).

In a study conducted in Turkey and including 233 GDM patients, it was reported that the 0-blood group significantly increased the risk of postpartum diabetes in women with GDM, the AB blood group showed a relatively mild increase, and the B blood group had the lowest risk. In addition, the Rh-positive blood group may also increase the risk of postpartum diabetes in GDM (11). On the other hand, in a systematic literature consisting of 15 studies, it was determined that individuals with the B blood group were at higher risk for type II DM and those with the 0-blood group had a lower risk of developing type II diabetes (7). In addition, in a retrospective cohort study conducted on 5320 Thai pregnant women, no significant relationship was found between the AB0 blood group and the risk of GDM (12). In this study, which included a total of 835 pregnant women, no significant difference was found between the blood group distributions of pregnant women with GDM and healthy pregnant women. In addition, no significant difference was found in terms of Rh factor positivity.

This study was a single-center study. In addition, although the sample included in the study was large (n=835), the sample size of pregnant women with B Rh (negative) and AB Rh (negative) blood groups was low. These two situations can be considered as limitations of the study. On the other hand, it is a reference for future multicenter studies with larger samples.

CONCLUSION

As a result, no relationship was found between GDM pathogenesis and AB0 blood group phenotypes and Rh factor. The different results in the literature regarding this relationship may be due to the diversity of the sample consisting of different populations. Further research is also needed to understand the mechanisms underlying the possible causal relationship of these different results.

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RESEARCH ARTICLE

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Investigation of Possible Protective Effects of Resveratrol on Oxidative Stress and Ferroptosis in PFOA Exposure in HepG-2 Cells

ABSTRACT

Objective: Exposure to perfluorooctanoic acid (PFOA) is linked to adverse health effects, including cancer and hepatic diseases. PFOA induces reactive oxygen species generation in human hepatic cells, causing oxidative stress and cell death. Resveratrol (RSV) has garnered attention for its protective effects against xenobiotic-induced damage, yet its impact on PFOA-induced oxidative stress and ferroptosis in the liver remains understudied. This study investigates RSV's protective mechanisms against oxidative stress and ferroptosis in HepG2 cells exposed to PFOA.

Method: HepG2 cells were cultured in DMEM with 10% FBS and 1% penicillin/streptomycin in a 5% CO2 incubator at 37°C. PFOA was added to the cells at concentrations ranging from 0 to 450 µM and incubated at 37°C for 24 hours. The IC50 was determined to be 457 µM. To examine RSV's protective effects, cells were treated with 60 µM RSV. Following treatment with PFOA, RSV, and the combination of PFOA+RSV, cell lysates were prepared for analysis. Oxidative stress and ferroptosis parameters were measured spectrophotometrically using ELISA.

Results: In the PFOA+RSV group, antioxidant capacity increased, and ferroptosis was suppressed compared to the control. Conversely, the PFOA group showed decreased antioxidant capacity, increased oxidant capacity, and induced ferroptosis compared to the control and RSV-treated groups.

Conclusion: PFOA exposure heightens oxidative stress and ferroptosis, whereas RSV treatment significantly reduces hepatic oxidative stress and protects against ferroptosis during PFOA exposure.

Keywords: PFOA, Resveratrol, HepG2, Oxidative Stress, Ferroptosis.

PFOA Maruziyetinde Resveratrol'ün Oksidatif Stres ve Ferroptosis Üzerindeki Olası Koruyucu Etkilerinin HepG2 Hücrelerinde Araştırılması

ÖZET

Amaç: Perflorooktanoik asit (PFOA) maruziyeti, kanser ve karaciğer hastalıkları dahil olmak üzere çeşitli olumsuz sağlık etkileri ile ilişkilendirilmiştir. PFOA, insan karaciğer hücrelerinde reaktif oksijen türlerinin oluşumunu indükleyerek oksidatif strese ve hücre ölümüne neden olur. Son yıllarda, Resveratrolün (RSV) ksenobiyotiklerin neden olduğu hasarlara karşı koruyucu etkisi üzerine çalışmalar önem kazanmıştır. Ancak, RSV'nin karaciğerde PFOA'nın neden olduğu oksidatif stres ve ferroptozis üzerindeki koruyucu etkileri hakkında yeterli çalışma bulunmamaktadır. Bu çalışmada, PFOA maruziyeti sonucu HepG2 hücrelerinde oluşabilecek oksidatif stres ve ferroptozis üzerine RSV'nin koruyucu etki mekanizmalarını araştırmayı amaçladık.

Yöntem: HepG2 hücreleri, %5 CO2 inkübatöründe 37°C'de %10 FBS ve %1 penisilin/streptomisin içeren DMEM'de kültürlendi. PFOA, 0-450 µM konsantrasyonlarında hücrelere eklendi ve 37°C'de 24 saat inkübe edildi. IC50, 457 µM olarak belirlendi. RSV'nin koruyucu etkilerini değerlendirmek için hücreler 60 µM RSV ile muamele edildi. PFOA, RSV ve PFOA+RSV ile muamele sonrasında, hücre lizatı hazırlandı ve analizler için kullanıldı. Oksidatif stres ve ferroptozis parametreleri, ELISA yöntemiyle spektrofotometrik olarak belirlendi.

Bulgular: PFOA+RSV grubunda, kontrol grubuna kıyasla antioksidan kapasite artmış ve ferroptozis baskılanmıştır. Buna karşılık, PFOA grubunda antioksidan kapasite azalmış, oksidan kapasite artmış ve kontrol ve RSV ile muamele edilen gruplara kıyasla ferroptozis indüklenmiştir.

Sonuç: PFOA maruziyeti oksidatif stresi ve ferroptozisi artırırken, RSV tedavisi karaciğer oksidatif stresini önemli ölçüde azaltır ve PFOA maruziyeti sırasında ferroptozise karşı korur.

Anahtar Kelimeler: PFOA, Resveratrol, Oksidatif Stres, HepG2, Ferroptoz.

INTRODUCTION

Perfluorinated alkylated substances (PFAS) are highly fluorinated organic pollutants, exceeding 4700 chemicals that find in environment (1). These compounds exhibit a unique configuration, comprising a hydrophilic end-group and a hydrophobic alkyl chain, setting them apart from conventional persistent organic pollutants. Their solubility in aqueous solutions surpasses that of traditional persistent organic pollutants, and they exhibit non-biodegradable and bioaccumulative traits (2). Perfluorooctanoic acid (PFOA) serves primarily as a chemical intermediate in fluoroacrylic ester production, while its salts act as processing aids in the manufacture of fluoropolymers, fluoroelastomers, and other surfactants (3). PFOA's stability stems from its eight-carbon chain, housing a hydrophilic functional group and a hydrophobic alkyl chain (4,5). Notably persistent, detectable levels of PFOA are detectable in humans and wildlife due to its slow excretion, with an average half-life in humans ranging from 3 to 5 years and a concentration-dependent elimination rate (6,7). This slow elimination may lead to accumulation, potentially triggering long-term health effects. Human exposure to PFOA can occur via food, water, and workplaces, with the highest distribution in lung, kidney, liver, and blood samples, while lower levels are found in the nervous system. PFOA has been detected in cord blood and breast milk among the general population, accumulating in the liver, kidney, and serum post-absorption, resulting in various toxicities (7). Acute exposure to PFOA may induce mild to moderate toxicity, whereas chronic exposure could lead to severe adverse effects such as hepatomegaly, liver damage, and cardiovascular diseases. Additionally, it has carcinogenic potential on organs like the liver, pancreas, and testes (8).

Studies have linked PFOA exposure to human liver enzymes (9), with the liver identified as the primary site for PFOA accumulation in animals, characterized by hepatocellular hypertrophy and necrosis at different exposure levels. In rodents and non-human primates, high liver concentrations of PFOA correspond with liver enlargement, potentially leading to hepatocellular adenomas in rats. Animal research has suggested that PFOA accumulation may trigger genotoxicity, immunotoxicity, neurotoxicity, and hepatotoxicity (10). Evidence from human studies suggests a positive association between PFOA exposure and elevated liver enzymes without conclusive evidence of liver diseases or cancers (7-9). Xu M. et al. reported that PFOA and PFOS alter antioxidant enzyme activities, induce oxidative stress, leading to cytotoxicity in mouse primary hepatocytes, whereby reduced cell viability, apoptosis, and increased oxidative stress levels were observed. These compounds directly interact with superoxide dismutase, resulting in oxidative stress production and apoptosis (11).

Ferroptosis, a cell death pathway catalyzing unsaturated fatty acids primarily found in cell membranes, triggers lipid peroxidation, inducing apoptosis through divalent iron or ester oxygenase action (12). Immediate exposure to PFOA is suggested to disrupt liver cells and induce cell death, although studiesare are inadequate for detailing the associated cell death mechanisms. Resveratrol (RSV), a polyphenol from grapes and other fruits, offers diverse benefits encompassing chemopreventive, antioxidant, tissue differentiation promotion, adipogenesis modulation, and antiproliferative effects in experimental tumor models (13). Although studies highlight the therapeutic potential of resveratrol in liver damage and chronic liver diseases, research gaps persist concerning its protective effects against PFOA-induced oxidative stress and the mechanisms of cell death associated with PFOA exposure. This study aims to unveil the protective mechanisms of resveratrol against potential oxidative stress and ferroptosis in HepG-2 cells following exposure to PFOA.

MATERIALS AND METHODS

Chemicals and Test Reagents: The ammonium salt form of PFOA, (Cas No. 3825-26-1) of ≥98.0% purity was purchased from Sigma-Aldrich Corporation (St. Louis, MO, USA). It was dissolved in dimethyl sulfoxide (DMSO; Cas No. D8418) from Sigma-Aldrich. Resveratrol was purchased from Santa Cruz Biotechnology (Dallas, TX). Lipid peroxidation (MDA) assay kit was purchased from Sigma-Aldrich (Saint Louis, MO; Cat no MAK085). Reduced glutathione (GSH), human glutathione peroxidase 4 (GPx4) and human acyl-CoA synthetase long-chain family member 4 (ACSL4) ELISA kits were purchased from MyBioSource (Cat no MBS727656, MBS2000338 and MBS9331516, respectively). Total oxidant (TOS) and antioxidant (TAS) ELISA Kits were purchased from Rel Assay Diagnostic (Gaziantep, Turkey). Caspase 3 (CASP3) and cytochrome C (CYCS) ELISA kits were purchased from Cloud-Clone Corp (Cat no SEA626Hu and SEA594Hu, respectively).

Cell Culture: HepG2 cell line, (ATCC® HB-8065™) was obtained from the American Type Culture Collection (ATCC; Manassas, VA, USA). The HepG2 cell line was cultured in Dulbecco's Modified Eagle's Medium (DMEM) containing 10% FBS and 1% penicillin/streptomycin in a %5 CO_2 incubator at 37 °C. For sub-cultivation, the cells were trypsinized and washed with diphosphate-buffered saline (DPBS, pH 7.4), subsequently centrifuged at 2000×g for 5 min, and divided.

Determination of PFOA's IC_{50} Concentration: HepG2 cells were seeded into a 96-well plate with each well of 1 x 10^6 cells. When the confluence of the cells reached 70–80%, PFOA was added to the cells at concentrations of 0 -450 µM and incubated 5% CO_2 at 37 °C for 24 h.

Study Groups:

- ✓ Control group: Untreated HepG2 cells
- ✓ PFOA group: HepG2 cells treated with IC_{50} dose (572 µM) of PFOA
- ✓ RSV group: HepG2 cells treated with 60 µM) of RSV
- ✓ PFOA + RSV group: HepG2 cells treated with 572 µM dose of PFOA (IC_{50}) and 60 µM dose of RSV (572 µM+ 60 µM)

Cell Viability: Cytotoxicity of PFOA was determined with the MTT assay. Briefly, HepG2 cells were seeded into 96-well microplates (10,000 cells/well). After overnight incubation at 37 °C, the growth medium was replaced with fresh medium containing 75, 150, 300, and 450 µmol/ml of PFOA and 75 mol/ml PFOA + 60 µmol/ml RSV, 150 mol/ml PFOA + 60 µmol/ml RSV, 300 mol/ml PFOA + 60 µmol/ml RSV, 450 mol/ml PFOA + 60 µmol/ml RSV in 96 well plates. The cells were incubated for an additional 24 hours. MTT was then added to a final concentration of 0.5 mg/mL and the cells were incubated at 37 °C for 3 h. After 3 h, the medium was removed, and formazan crystals were dissolved with DMSO. The optical density (OD) of the solution in each well was measured at 570 nm by a microplate reader.

Cell Lysate Preparation: Cell lysates for MDA, GSH, TAS, TOS, GPx4, ACSL4, cytochrome C (CYCS), and caspase 3 (CASP3) assays were prepared based on the following method. 527 µM PFOA and/or 527 µM PFOA+60 µM RSV were used in all the assays mentioned above. 24 hours after respective PFOA and/or RSV application, adherent cells were washed with PBS (pH 7.4) then detached with trypsin, and collected by centrifugation at 3000 x g for 10 min at 4°C. The supernatant was discarded and the pellet was collected. Protein levels were measured by the biuret method (14). The prepared cell lysates were stored at -80^{0}C until using for the assays.

TOS and TAS Measurements: TOS and TAS measurements were performed according to the manufacturer's instructions for RelAssay Diagnostic® commercial kits. TOS measurement depends on the oxidation process. The TOS method involves the oxidation of ferrous ions to ferric ions facilitated by various oxidizing agents within an acidic medium, with the subsequent quantification of ferric ions performed using xylenol orange. The results were evaluated as mmol Trolox equiv. /L.

The TAS level in the cell lysate was assessed using an automated method, specifically the Rel Assay (Rel Assay® Diagnostics kit, Mega Tip, Gaziantep, Turkey), which generates a hydroxyl radical. In this assay, a ferrous ion solution from reagent 1 is combined with hydrogen peroxide from reagent 2. The assay results in the formation of sequential radicals, including the brownish dianisidinyl radical cation, produced by the hydroxyl radical, which is a potent radical. This method measures the sample's antioxidative effect against the potent free radical reactions initiated by the hydroxyl radical. The results are expressed in micromolar Trolox equivalents per liter (mmol Trolox equivalents/L).

GSH Measurement: GSH levels were measurements were performed according to the manufacturer's instructions. Briefly, GSH levels in cells were incubated with GSH-horseradish peroxidase (HRP) conjugate in the pre-coated plate for one hour, and then the wells were emptied and washed five times. Then, the wells were incubated with a substrate for HRP enzyme. The product of the enzyme-substrate reaction formed a blue colored complex. Finally, a stop solution was added to stop the reaction. Following the reaction, the intensity of the color is measured spectrophotometrically in a microplate reader at 450 nm. The results were presented as µg/ml.

Lipid Peroxidation Measurement: MDA is a key parameter that is ordinarily used as a marker of lipid peroxidation. Lipid peroxidation in cell lysates was analyzed at 532 nm colorimetrically using a method based on the reaction of MDA with thiobarbituric acid (TBA) to form a compound. MDA level measurements were performed according to the manufacturer's instructions and were evaluated as nmol/mg protein.

GPx4 and ACSL4 Measurements: GPx4 and ACSL4 proteins were analyzed according to the manufacturer's instructions. The protein concentrations were calculated by measuring absorbance values using a microplate reader at the recommended wavelengths. The results were presented as ng/ml.

CYC and CASP3 Measurements: CYC and CASP3 levels in HepG2 cell lysates were measured using colorimetric commercial kits, pre-coated with an antibody specific to either CYC or CASP3. The cells were lysed depending on the manufacturer's protocol. The enzyme-substrate reactions for CYC and CASP3 were performed according to the manufacturer's instructions and then color changes were determined spectrophotometrically at 450 nm. CASP3 and CYCS levels results are presented as ng/ml and pg/ml respectively.

Statistical Analysis: The experiments were replicated three times for each group, with triplicate samples in each repetation. Statistical analysis was carried out using GraphPad 8, employing one-way analysis of variance (ANOVA) to examine the distribution of values. The data were presented as mean±standard deviation (SD), and statistical significance was determined at p values <0.05.

RESULTS

Cell Viability: The viability of HepG2 cells exposed to various concentrations of PFOA and PFOA+RSV was assessed using the MTT assay, and the results are illustrated in Figure 1A–D. PFOA exhibited toxicity in the micromolar dose range, displaying a variable dose–response curve. PFOA showed dose-dependent toxicity in the micromolar dose range. At a concentration of 450 μM PFOA, cell survival decreased by 50%. PFOA demonstrated a dose-dependent reduction in cell proliferation. However, when RSV was applied at a concentration of 60 μM, cell viability significantly increased, as depicted in Figure 1.

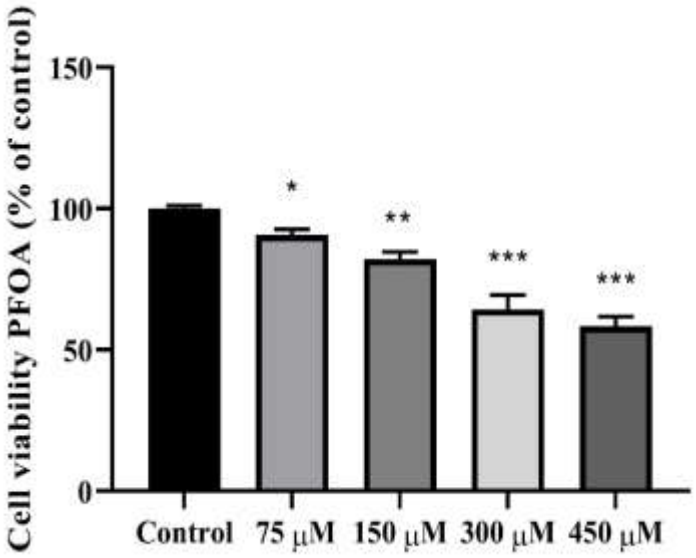

Figure 1. HepG2 cells were cultured with 0-450 μM concentrations of PFOA for 24 h**.** PFOA was toxic in the micromolar dose range showing a variable dose-response curve. At 450 μM PFOA concentration, cell survival was lower by 50%. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0001$ vs. control

TOS, TAS, and Oxidative Stress Biomarkers: In the total oxidant status measurements, we observed a 17.71% increase in total oxidant capacity in the PFOA group compared to the control. In the RSV and PFOA+RSV groups, TOS decreased by 14.57% and 9.85%, respectively, relative to the control group. Conversely, TAS decreased by 15.16% in the PFOA group and increased by 13.81% and 8.51% in the RSV and PFOA+RSV groups, respectively (Figure 2 and Figure 3). Notably, there was a 27% increase in the PFOA+RSV group compared to the PFOA group.

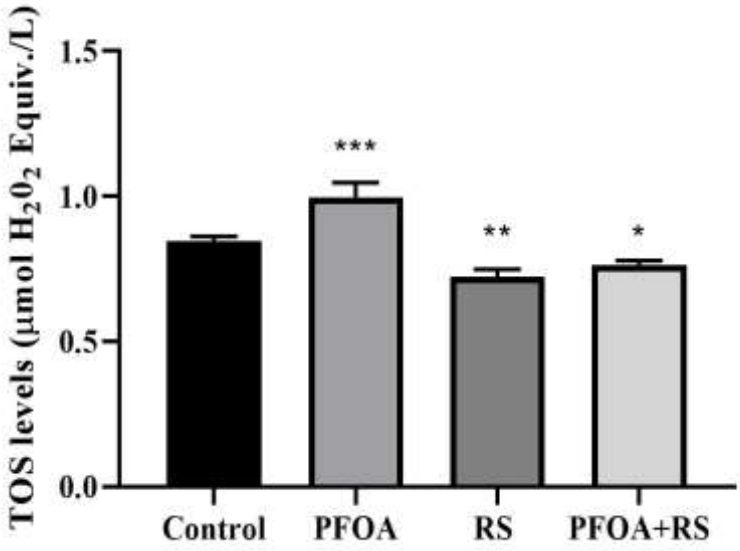

Figure 2. Effect of PFOA and RSV on TOS levels in HepG2 cells. Mean and standard mean values were found 8.4±0.008 in control group, 0.99±0.029 in PFOA group, 0.72±0.014 in RSV group and 0.76 ±0.008 in PFOA+RSV group. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0001$ vs. control

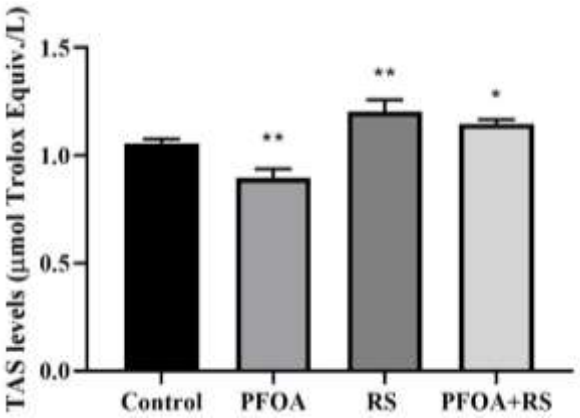

Figure 3. Effect of PFOA and RSV on TAS levels in HepG2 cells. Mean and standard mean values were found; 1.06±0.01 in control group, 0.90±0.02 in PFOA group, 1.20±0.03 in RSV group and, 1.47 ±0.012 in PFOA+RSV group. * $p < 0.05$; ** $p < 0.001$ vs. control

GSH and MDA carbonyl group levels are presented in Figure 4 and Figure 5. Total glutathione (GSH) levels decreased by 28.37% in the PFOA group compared to the control group ($p < 0.05$). In the PFOA+RSV and RSV groups, there was a significant increase by 32% and 62%, respectively, compared to the control group ($p < 0.05$ and $p < 0.0001$). Regarding MDA levels, a significant increase of 32.9% was observed in the PFOA group. In contrast, in the RSV and PFOA+RSV groups, MDA levels decreased by 32.9% and 26.5% compared to the control, respectively (Figure 4 and Figure 5).

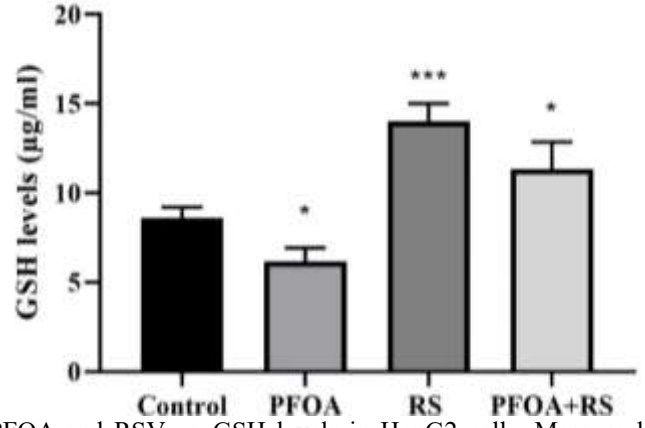

Figure 4. Effect of PFOA and RSV on GSH levels in HepG2 cells. Mean and standard mean values were found; 8.60±0.34 in control group, 6.167±0.44 in PFOA group, 14.0±0.57 in RSV group and 11.33 ±0.88 in PFOA+RSV group. * $p < 0.05$; *** $p < 0.0001$ vs. control

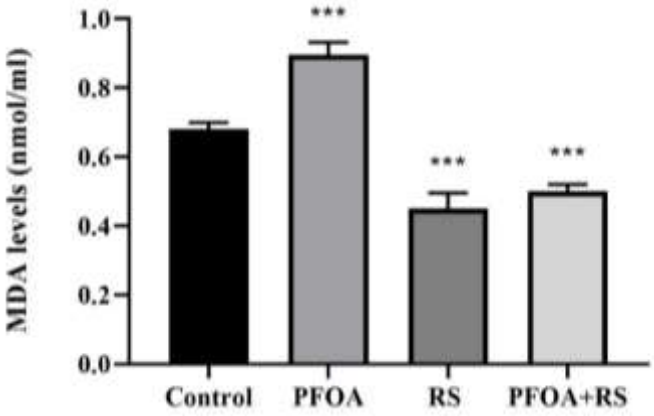

Figure 5. Effect of PFOA and RSV on MDA levels in HepG2 cells. Mean and standard mean values were found; 0.6 ±0.011 in control group, 0.89±0.02 in PFOA group, 0.45±0.02 in RSV group and 0.50 ±0.01 in PFOA+RSV group. *** $p < 0.0001$ vs. control

GPx4 and ACSL4 levels: In the PFOA group, GPx4 levels decreased by 28.69% compared to the control. These levels were found to decrease by 23.71% and 14.9% in the RSV and PFOA+RSV groups, respectively. Moreover, there was a 61.2% increase in the PFOA+RSV group compared to the PFOA group (Figure 6).

ASCL4 levels were significantly higher in the PFOA group, showing a 33.52% increase compared to the control. In the RSV group, an insignificant decrease of 29.41% was observed compared to the control (Figure 7). Additionally, there was a 15.88% decrease in the PFOA+RSV group compared to the control. Importantly, we found a substantial 37% decrease in the PFOA+RSV group compared to the PFOA group.

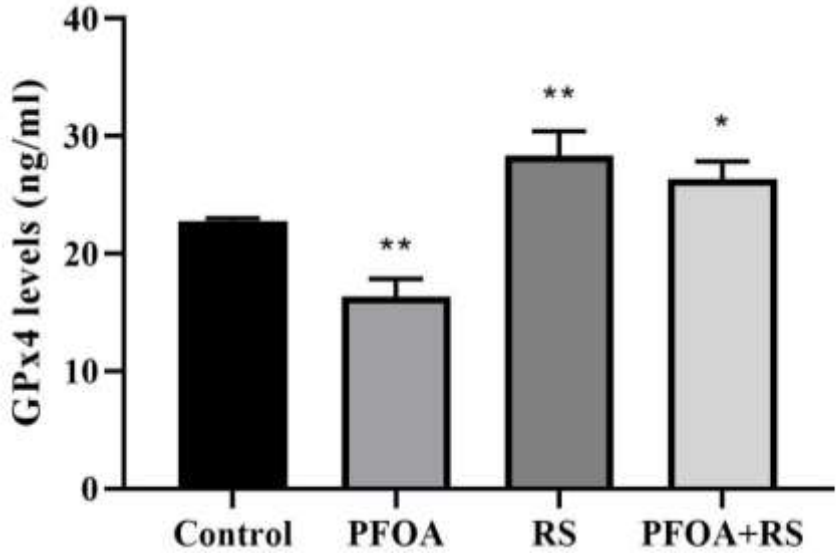

Figure 6. Effect of PFOA and RSV on GPx4 levels in HepG2 cells. Mean and standard mean values were found; 22.77±0.14 in control group, 16.33±0.88 in PFOA group, 28.33±1.2 in RSV group, and 26.33 ±0.86 in PFOA and RSV group. * $p < 0.05$; ** $p < 0.001$ vs. control

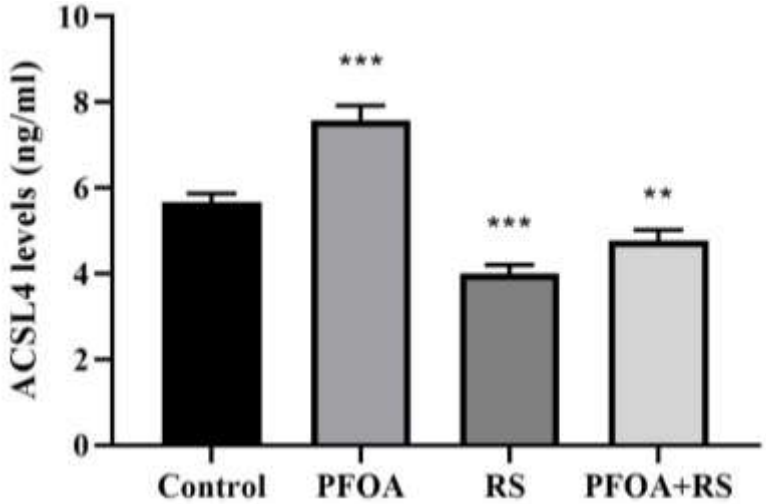

Figure 7. Effect of PFOA and RSV on GPx4 levels in HepG2 cells. Mean and standard mean values were found; 5.67 ±0.12 in control group, 7.6±0.2 in PFOA group, 4.01±0.11 in RSV group and 4.8±0.14 in PFOA+RSV group. ** $p < 0.001$; *** $p < 0.0001$ vs. control

CYC and CASP3 Levels: CYC levels increased in the PFOA group by 37.31% and in the PFOA+RSV group by 10.49% compared to the control group ($p < 0.0001$ and $p < 0.05$). There were no significant changes in the RSV group compared to the control. However, there was a notable 19.54% decrease in the PFOA+RSV group compared to the PFOA group (Figure 8).

For CASP3 activity, decreases were detected in the PFOA group (74%) and PFOA+RSV group (29.1%) compared to the control ($p < 0.0001$ and $p < 0.05$). In the RSV group, there was a 14.45% increase compared to the control. When comparing the PFOA group and the PFOA+RSV group, caspase 3 activity was lower by about 34.81% in the PFOA+RSV group compared to the PFOA group (Figure 9). All results have been summarized in Table 1.

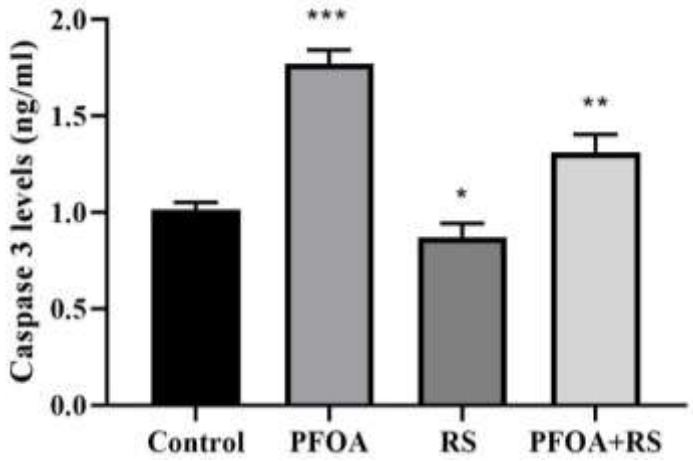

Figure 8. Effect of PFOA and RSV on ACSL4 levels in HepG2 cells. Mean and standard mean values were found; 1.02±0.02 in control group,1.77±0.04 in PFOA group, 0.87±0.04 in RSV group and 1.31±0.05 in PFOA+RSV group. * $p < 0.05$; ** $p < 0.001$; *** $p < 0.0001$ vs. control

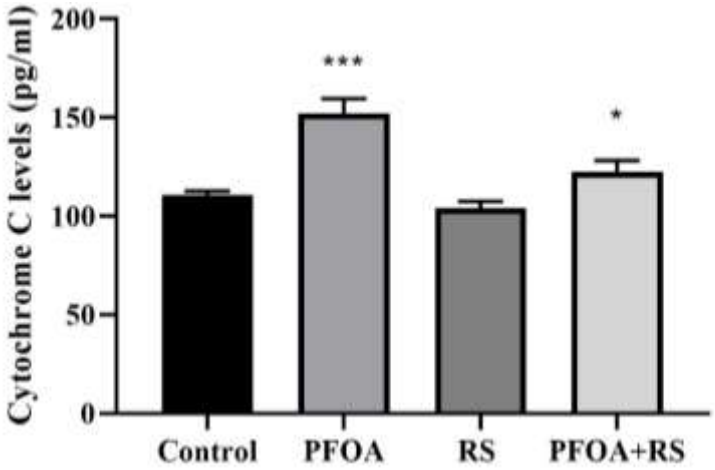

Figure 9. Effect of PFOA and RSV on caspase 3 levels in HepG2 cells. Mean and standard mean values were found; 110.7±1.2 in control group, 152±4.4 in PFOA group, 104±2.1 in RSV group and 122.3±3.4 in PFOA+RSV group. * $p < 0.05$; *** $p < 0.0001$ vs. control.

Table 1. General focus on the results

Parameter	Control	PFOA	RSV	PFOA+RSV
TOS	8.4 ±0.008	0.99 ±0.029^{a}	0.72 ±0.014^{b}	0.76 ±0.008^{c}
TAS	1.06 ±0.01	0.90 ±0.02^{c}	1.20 ±0.03^{b}	1.47 ±0.012^{b}
GSH	8.60 ±0.34	6.167 ±0.44^{c}	14.0 ±0.57^{a}	11.33 ±0.88^{c}
MDA	0,68 ±0,011	0,89 ±0,02^{a}	0,45 ±0,02^{a}	0,50 ±0,01^{a}
GpX4	22.77 ±0,14	16.33 ±0.88^{b}	28.33 ±1.2^{b}	26.33 ±0.86^{c}
ACSL4	5.67 ±0.12	7.6 ±0.2^{a}	4.01 ±0.11^{a}	4.8 ±0.14^{b}
Caspase 3	1.02 ±0.02	1.77 ±0.04$^{'a}$	0.87 ±0.04^{c}	1.31 ±0.05^{b}
Cytochrome C	110.7 ±1,2	152 ±4.4^{a}	104 ±2.1	122.3 ±3.4^{c}

Note. PFOA group, HepG2 cells cultured with IC50 dose of PFOA for 24 h; RSV group, HepG2 cells cultured with 60 µM RSV for 24 h; PFOA+RSV group, HepG2 cells cultured with IC50 dose of PFOA and 60 µM RSV for 24 h. Values are given as mean ± SD of n = 9 experiments and triplicate measurements a, b, c Lines that do not share the same letters (superscripts) are significantly different from each other ($p < 0.0001$; $p< 0.001$; $p < 0.05$, respectively).

DISCUSSION

PFCs are synthetic fluorinated compounds with a carbon backbone, and one of the widely used PFCs is PFOA with an eight-carbon structure (15). PFOA has been identified as resistant to metabolic and environmental degradation, exhibiting bioaccumulation and biopersistence, and has been detected in wildlife and human populations (16). The liver has been recognized as the primary target organ for PFOA-induced toxicity in the body, as demonstrated by in vivo and in vitro studies indicating toxic effects on the liver (17). RSV, a naturally occurring polyphenolic compound found in grapes and other plant sources, possesses potent free radical scavenging and antioxidative properties. RSV has been observed to protect

against proliferation through apoptosis in various cell models, modulating key mediators of the cell cycle and survival. It is known for its antioxidant, anti-inflammatory, and immunomodulatory properties (18). In the present study, the aim was to investigate the protective mechanisms of RSV against potential oxidative stress and cell death in HepG-2 cells resulting from PFOA exposure. The study found that PFOA led to a dose-dependent increase (1.17-fold) in oxidative capacity compared to the control. However, when 60 μM RSV was added along with PFOA at the same concentration (572 μM), a significant decrease in oxidative capacity (0.90-fold) was observed compared to the control group. Additionally, oxidant capacity decreased in the group where only RSV was added (0.80-fold) compared to the control group. In the PFOA+RSV group, total oxidant capacity decreased by 1.3-fold compared to the PFOA group. In antioxidant capacity measurements, PFOA dose-dependently decreased antioxidant capacity compared to RSV-added groups and the control group. In the PFOA group, total antioxidant capacity decreased by 0.84-fold compared to the control. However, there was a 1.08-fold increase in PFOA+RSV and a 1.13-fold increase in the RSV group compared to the control, respectively. GSH levels decreased by 0.28-fold in the PFOA group compared to the control. When RSV was added, these levels increased by 1.63-fold and 1.32-fold in the PFOA+RSV group and RSV group, respectively. MDA levels increased by 1.32-fold compared to the control in the PFOA group, while in the RSV and PFOA+RSV groups, these levels decreased by 0.66-fold and 0.73-fold, respectively (Table 1). The study suggests that PFOA administration increases oxidative stress markers, while RSV treatment significantly reduces hepatic oxidative stress caused by PFOA exposure. This reduction is attributed to the suppression of lipid peroxidation and enhancement of antioxidant enzyme activities, indicating that RSV has a hepatoprotective effect as an antioxidant against PFOA-induced oxidative liver injury. In a related study by Naderi et al., the protective effect of resveratrol against PFOA-induced mitochondrial toxicity in rat liver mitochondria was evaluated. The results indicated that resveratrol has a protective effect against PFOA-induced hepatotoxicity due to its antioxidant activity. The study suggests that RSV can be an effective supplement against oxidative stress and mitochondrial dysfunction in PFOA-induced hepatotoxicity (19).

Studies have demonstrated that PFOA can induce cell death mechanisms (20,21). Conversely, polyphenolic compounds have been suggested to have protective effects against apoptosis and other cell death mechanisms. In the current study, the effects of treatment with PFOA and RSV on cell death mechanisms were investigated. CYC levels were found to increase by 1.37-fold in the PFOA group and by about 1.1-fold in the PFOA+RSV group compared to the control. Conversely, there was a 0.9-fold decrease in the RSV group. Additionally, in the RSV group, there was a 0.86-fold increase versus the control. Regarding CASP3 levels, a 1.74-fold decrease was observed in the PFOA group, and a 1.26-fold decrease in the PFOA+RSV group. Interestingly, this decrease was 1.51-fold in the PFOA+RSV group compared to the PFOA group. These findings suggest that PFOA induces an increase in CYC levels and caspase-3 activity, indicative of apoptosis, while RSV treatment appears to mitigate these effects, as demonstrated by the decrease in CYC levels and CASP3 activity in the PFOA+RSV group compared to the PFOA group. These results underscore the potential of RSV in ameliorating PFOA-induced cellular responses, shedding light on promising avenues for further research in therapeutic interventions.

Ferroptosis is recognized as a distinct form of cell death, separate from apoptosis, autophagy, and necrosis. The current study indicates that PFOA reduces the levels of GPx4 and ACSL4. However, these levels were even lower in the PFOA+RSV group compared to the PFOA group. This suggests that RSV may alleviate the toxic effects of PFOA by further decreasing GPx4 and ACSL4 levels. This mechanism could indicate a potential protective role of RSV against ferroptosis induced by PFOA. In a related study by Wang et al., the role of ferroptosis in deoxynivalenol (DON)-exposed HepG2 cytotoxicity and the antagonistic effect of resveratrol (RSV) were investigated. HepG2 cells were treated with RSV (8 μM) and/or deoxynivalenol (0.4 μM) for 12 hours. The study measured various parameters including cell viability, cell proliferation, expression of ferroptosis-related genes, levels of lipid peroxidation, and Fe (II). The results showed that deoxynivalenol reduced the expression levels of GPX4, SLC7A11, GCLC, NQO1, and Nrf2, while increasing the expression of TFR1, causing GSH depletion, accumulation of MDA, and total reactive oxygen species (ROS). Deoxynivalenol also increased the production of 4-hydroxynonenal (4-HNE), ROS, and excess Fe (II), leading to ferroptosis. However, retreatment with resveratrol reversed these changes, alleviating deoxynivalenol-induced ferroptosis and improving cell viability and proliferation. The study suggested that resveratrol can protect against ferroptosis by activating the SLC7A11-GSH-GPx4 signaling pathway in the HepG2 cell line (22). Together, these findings in both studies imply that resveratrol may have a protective role in mitigating ferroptosis induced by environmental stressors, such as PFOA or deoxynivalenol, through its impact on key molecular pathways involved in ferroptosis regulation.

CONCLUSION

The current study indicates that PFOA decreases antioxidant parameters such as TAS, MDA, and GSH. Conversely, it increases TOS, GPX4, ACSL4, cytochrome C, and caspase 3, particularly in the RSV and PFOA+RSV groups. This suggests that oxidative stress may mediate the onset of ferroptosis, and ferroptosis could play a significant role in PFOA-induced hepatotoxicity. Ferroptosis might be a crucial factor that dictates the detoxification process in response to PFOA exposure. The intricate interplay between oxidative stress, ferroptosis, and the observed changes in antioxidant parameters underscores the complexity of the cellular response to PFOA and highlights the potential involvement of ferroptosis in the liver's reaction to PFOA-induced stress. Further investigation into the molecular mechanisms underlying these interactions could provide valuable insights into the detoxification processes and potential therapeutic strategies for mitigating the hepatotoxic effects of PFOA.

Conflict of Interest Statement: The authors declared no conflict of interest.

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RESEARCH ARTICLE

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Evaluation of Body Weight Perception Using Body Size Guides

ABSTRACT

Objective: The search for new approaches in the fight against obesity has resulted in the idea of examining the characteristics of body weight perception. The aim of this study was to determine individuals' body weight perceptions and to observe the association between such perceptions and their socio-demographic characteristics and weight loss-oriented behaviors.

Method: A cross-sectional study was conducted using the Body Size Guide and the Body Weight Attitude and Behavior Questionnaire to assess body weight perception among participants. We assessed the frequency of accurate, under- or over-perception of participants' own body weights and their association with socio-demographic characteristics Data were analyzed using Chi-square tests, Student's t-tests, and one-way ANOVA to determine associations between weight perception and socio-demographic characteristics.

Results: Of the 283 participants, 50.2% (142) exhibited inaccurate body weight perception (IBWP). Significant associations were found between IBWP and gender, education level, and BMI classification ($p<0.05$). The frequency of accurate body weight perception (ABWP) in participants with a normal actual body mass index (BMI) was 76.6% (66), but only 30.8% (33) in pre-obese, 41.1% (23) in class I obese and 31.6% (6) in class II obese individuals. In addition, 52.1% (74) of participants with IBWP under-perceived their body weight. Forty-seven (64.4%) women with IBWP under-perceived themselves, while 42 (60.9%) of men IBWP over-perceived themselves ($p=0.004$). There was a significant difference between actual BMI classes in terms of ABWP ($p<0.001$). Significant differences were determined between perceived BMI classes in terms of diet, exercise and seeking expert advice in order to lose weight ($p<0.001$, $p=0.005$, and $p<0.001$, respectively).

Conclusion: This study provides new insights into the prevalence and factors associated with inaccurate body weight perception. These findings can inform targeted public health interventions to promote accurate self-perception and encourage healthier behaviors, particularly among populations at higher risk of obesity.

Keywords: Body Mass Index, Obesity, Weight Loss, Body Weight Perception.

Vücut Ölçüsü Kılavuzlarını Kullanarak Vücut Ağırlığı Algısının Değerlendirilmesi

ÖZET

Amaç: Obeziteyle mücadelede yeni yaklaşımların arayışı vücut ağırlığı algısının incelenmesi fikrini doğurmuştur. Bu çalışmanın amacı, bireylerin vücut ağırlığı algılarını belirlemek ve bu algılar ile sosyo-demografik özellikleri ve kilo verme odaklı davranışları arasındaki ilişkiyi gözlemlemektir.

Yöntem: Katılımcılarda vücut ağırlığı algısını değerlendirmek için Vücut Ölçüsü Rehberi ve Vücut Ağırlığı Tutum ve Davranış Anketi kullanarak kesitsel bir çalışma yürütüldü. Katılımcıların kendi vücut ağırlıklarını doğru, az veya çok algılama sıklığını ve bunların sosyo-demografik özelliklerle ilişkisini değerlendirdik. Veriler, kilo algısı ile sosyo-demografik özellikler arasındaki ilişkileri belirlemek için Ki-kare testleri, Student t-testleri ve tek yönlü ANOVA kullanılarak analiz edildi.

Bulgular: 283 katılımcının %50,2'si (142) yanlış vücut ağırlığı algısı (YVAA) sergiledi. YVAA ile cinsiyet, eğitim düzeyi ve BKİ sınıflandırması arasında anlamlı ilişkiler bulundu ($p<0,05$). Normal vücut kitle indeksi (VKİ) olan katılımcılarda doğru vücut ağırlığı algısı (DVAA) sıklığı %76,6 (66) iken, pre-obezlerde bu oran yalnızca %30,8 (33), sınıf 1 obezlerde %41,1 (23) ve sınıf 2 obezlerde %31,6 (6) idi. Ayrıca, YVAA'lı katılımcıların %52,1'i (74) vücut ağırlıklarını olduğundan az algıladı. YVAA'lı kırk yedi kadın (%64,4) kendilerini olduğundan az algılarken, YVAA'lı erkeklerin 42'si (%60,9) kendilerini olduğundan fazla algıladı ($p=0,004$). Gerçek BKI sınıfları arasında DVAA açısından anlamlı fark bulundu ($p<0,001$). Diyet, egzersiz ve kilo vermek için uzman görüşü alma açısından algılanan BKI sınıfları arasında anlamlı fark bulundu (sırasıyla $p<0,001$, $p=0,005$ ve $p<0,001$).

Sonuç: Bu çalışma, yanlış vücut ağırlığı algısının yaygınlığı ve bununla ilişkili faktörler hakkında yeni bakış açıları sunmaktadır. Bu bulgular, özellikle obezite riski daha yüksek olan popülasyonlarda doğru öz algıyı teşvik etmek ve daha sağlıklı davranışları desteklemek için halk sağlığı müdahalelerine bilgi sağlayabilir.

Anahtar Kelimeler: Vücut Kitle İndeksi, Obezite, Ağırlık Kaybı, Vücut Ağırlığı Algısı.

INTRODUCTION

Body perception refers to the body image that individuals shape in their own minds (1). It is a subjective, rather than objective assessment, and reflects how one perceives oneself. However, it may not actually reflect reality (2). Body perception depends on many factors, such as psychological components, sociodemographic characteristics and cultural differences (3). Variables such as gender, age, ethnicity, anthropometric measurements and mass media can affect the perception of one's body (4).

Body weight perception refers to body weight perception (5). Awareness of body weight, in other words accurate body weight perception (AWBP), is defined as agreement between individuals' actual measurable weight and their perceived body weight. ABWP also helps individuals to be aware of potential health risks associated with their weight status (6). AWBP was assessed in the Turkey Body Weight Perception Survey, and incompatibility between participants' weight and perceived weight was defined as inaccurate body weight perception (IBWP) (7). IBWP may assume one of two forms – under-perception of one's actual weight, or over-perception.

According to the health belief model, the motivation needed to change a habit depends on the degree of perceived health risk associated with it (8). Therefore, failure to perceive one's health status accurately will result in a tendency not to alter health-threatening behaviors (8). While overweight individuals 20 years ago thought of themselves as overweight or obese, today they regard themselves as being of normal weight (9). This normalization of overweight and obesity suggests that patients fail to accurately perceive their own health status and will therefore not modify their weight loss-oriented behaviors in order to reduce health risks (10). ABWP plays an important role in the success of obesity prevention programs (11). Brener et al. reported that while healthy or overweight participants who described themselves as overweight or obese adhered to weight loss programs, participants who did not perceive themselves as overweight were unable to exhibit weight loss-oriented behaviors (12).

Understanding body weight perception can be a key tool in developing methods for reduce obesity (6). The aim of this study was to determine individuals' own body weight perceptions and to examine their relationship with various sociodemographic characteristics and weight loss-oriented behaviors.

MATERIALS AND METHODS

This cross-sectional was performed between July and December 2018 in three different family health centers in the Kalkınma region of Trabzon, Turkey. Participants' sociodemographic characteristics were investigated, and they were grouped according to World Health Organization (WHO) body mass index (BMI) classifications by measuring body weight and height and calculating actual BMI from these.

Participants were recruited from three family health care centers using a stratified random sampling technique to ensure a representative sample of the target population. The sample size was calculated using power analysis to ensure sufficient statistical power for detecting significant associations. Confounders such as age, gender, and socio-economic status were controlled through multivariate analysis.

Participants were asked to specify the image that most closely resembled their own body shape from images contained in the body mass index-based Body Size Guide (BSG). The BMI class in which participants perceived themselves was thus identified. The BSG was developed by Harris et al. and contains 10 different body images created using real photographs. Image A represents the 'underweight' class, images B and D the 'normal' class, image D the 'pre-obese' class, images E and F the 'class I obese' class, images G and H the 'class II obese' class, and images I and J the 'class III obese' class. High correlation exists between these images and measured BMI values (Pearson's correlation coefficient r:0.94 for men and r:0.86 for women, $p<0.001$) (13).

Exact agreement between actual BMI classes and perceived BMI classes was defined as ABWP, while inconsistency between the two was defined as IBWP. Participants with IBWP were divided into two groups based on comparison of actual BMI classes and perceived BMI classes at BSG analysis. The term 'over-perceiving' was employed to describe participants whose actual BMI classes were above the perceived BMI class at BSG. We also employed the term 'under-perceiving' for participants whose actual BMI classes were below the perceived BMI class at BSG.

We calculated the frequency of participants' own body weight perception, and also evaluated the association between body weight perception status and sociodemographic data. Associations between accurate or inaccurate body weight perception and actual BMI classes were also analyzed. When evaluating associations between actual BMI class and under- and over-perception of weight among participants with IBWP, we excluded participants in the 'underweight; and 'class III obese' groups. This is because it was not possible for participants in the 'underweight' actual BMI class to choose a BSG image lower than that category, nor for individuals in the 'class III obese' class to choose a higher category of BSG image. The prevalence of over- or under-perception among participants with IBWP in was thus investigated only in the 'normal,

pre-obese, class I obese and class II obese' actual BMI classes.

Participants were asked to select those images from the BSG most closely matching their ideal body shape in the words 'In your opinion, which is the most suitable image for the ideal body structure? Please specify.' The association between participants' ideal body choice and age and gender was then subjected to analysis.

We applied a Body Weight Attitude and Behavior Questionnaire (BABQ) prepared on the basis of a search of the existing literature. This was used to investigate participants' attitudes concerning whether their body weights were healthy, knowledge concerning whether obesity is a health problem using a five-point Likert-type scale, and diet and exercise-related behaviors and histories of consulting a specialist. Exercising for at least 20 minutes at moderate intensity three days per week was considered to represent appropriate exercise. The frequency of these attitude and behaviors was determined on the basis of perceived BMI classes, while the frequency of behaviors concerning weight loss was based on body weight perception.

Individuals aged 18 with sufficient intellectual capacity to understand the questionnaire were included. Exclusion criteria were the presence of a neurological or psychological illness, any condition capable of preventing exercise, pregnancy, and involvement in bodybuilding.

Statistical analysis was carried out on Statistical Package for the Social Sciences (SPSS) software. Descriptive statistics were applied, and normality of data distribution was assessed using the Kolmogorov-Smirnov test. The Chi-square test, Student's t test and one-way ANOVA were then used to evaluate the significance of intergroup differences.

All individuals taking part received verbal explanations of the study, and provided written consent. The study was approved by the Karadeniz Technical University Medical Faculty Ethical Committee. A Research Permits Cooperation Protocol was signed between the Trabzon Provincial Health Directorate and the Karadeniz Technical University Medical Faculty Dean's Office.

RESULTS

Sociodemographic Characteristics: Two hundred eighty-three participants with a mean age of 36.77 ± 12.77 years were enrolled in the study. Other sociodemographic data are shown in Table 1.

Table 1. Participants' Socio-demographic Characteristics

Sociodemographic data	%	Number
Gender		
Female	54.8	155
Male	45.2	128
Education status		
Illiterate	1.1	3
Literate	1.8	5
Primary school graduate	26.5	75
High school graduate	30.0	85
University and above	40.6	115
Actual body mass index classes		
Underweight	3.9	11
Normal	30.4	86
Pre-obese	37.8	107
Class I obese	19.8	56
Class II obese	6.7	19
Class III obese	1.4	4

Perceived BMI Classes

Participants' perceived BMI classes are shown in Figure 1.

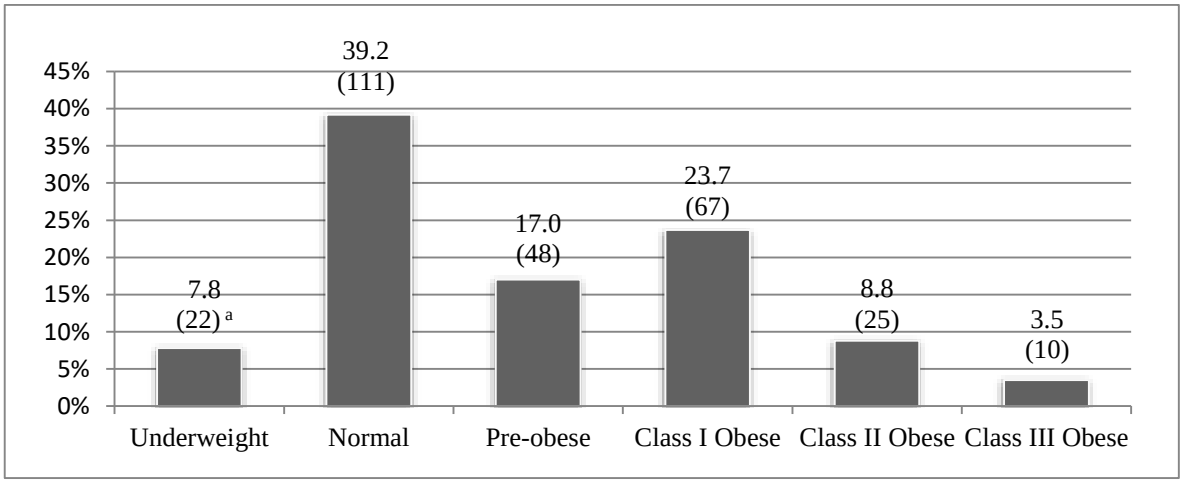

Figure 1. Distributions of perceived BMI classes.[a] % (n)

Body Weight Perception Status: ABWP was detected in 49.8% (141) of participants and IBWP in 50.2% (142), while under-perception was determined in 52.1% (74) of participants with IBWP and over-perception in 47.9% (68). Associations between participants' body weight perception status and sociodemographic data are shown in Table 2.

Table 2. Participants' body weight perception status and sociodemographic data

	Body Weight Perception Status			Inaccurate Body Weight Perception (IBWP)		
	ABWP*	IBWP	P value	Under-perception	Over-perception	p value
Mean age ± standard deviation[a]	34.14 ± 11.86	39.37 ± 13.14	0.001	40.20 ± 12.96	38.47 ± 13.36	0.434
Gender						
Female % (n)	52.9 (82)	47.1 (73)	0.283	64.4 (47)	35.6 (26)	0.004
Male % (n)	46.1 (59)	53.9 (69)		39.1 (27)	60.9 (42)	
Education status % (n)						
Illiterate	33.3 (1)	66.7 (2)	0.025	100.0 (2)	0.0 (0)	0.015
Literate	20.0 (1)	80.0 (4)		100.0 (4)	0.0 (0)	
Primary school graduate	40.0 (30)	60.0 (45)		39.2 (29)	35.6 (16)	
High school graduate	45.9 (39)	54.1 (46)		47.8 (22)	52.2 (24)	
University and above	60.9 (70)	39.1 (45)		37.8 (17)	62.2 (28)	

*Accurate body weight perception [a]: A significant difference was found between ABWP and under-perception (p=0.002). No significant difference was found between ABWP and over-perception, or between under- and over- (p=0.052 and p=0.689, respectively).

Participants' body weight perception status in terms of actual BMI classes is shown in Figure 2.

A significant difference was observed between actual BMI classes and whether perception of body weight was accurate or inaccurate (p<0.001). In the actual BMI classes, there were significant differences between normal and pre-obese classes (p<0.001), normal and class I obese classes (p<0.001), and normal and class II obese classes (p<0.001) in terms of accurate or inaccurate body weight perception. No significant difference was determined in actual BMI classes between pre-obese, class I obese and class II obese groups in terms of accurate or inaccurate body weight perception (p=0.412).

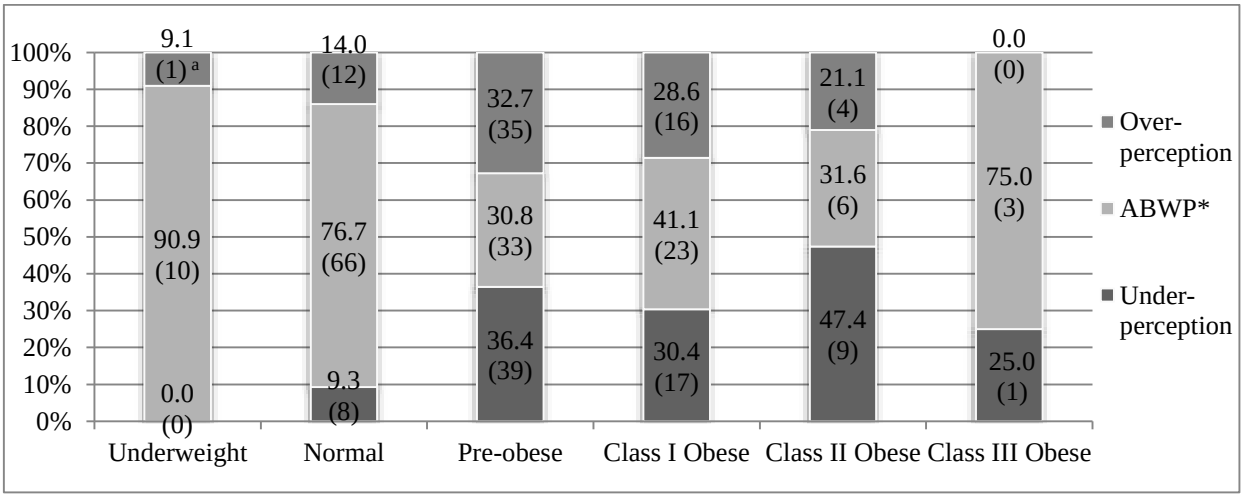

Figure 2. Distribution of Body Weight Perception Status Based on Actual BMI Classes
[a:] % (n) * Accurate body weight perception

Among the IBWP participants, in terms of actual BMI classes, under-perception was found in 40% (8) of the normal class, 52.7% of (39) the pre-obese class, 51.5% (17) of the class I obese class, and 69.2% (9) of the class II obese class. There was no significant difference between these classes in terms of under-perception status (p=0.437).

Ideal Body Image Preferences: While 70.7% (200) of participants preferred a 'normal' class image, 12.7% (36) selected an 'underweight' image, 13.1% (37) a 'pre-obese' image and 3.5% (10) a 'class I obese' image as an ideal body image. Participants' age and gender characteristics depending on ideal body preferences are shown in Table 3.

Table 3. Participants' age and gender characteristics depending on ideal body preferences

	Ideal body preferences				p value
	Underweight	Normal	Pre-obese	Class I obese	
Mean age ± standard deviation	33.50 ± 10.73	36.40 ± 12.41	39.27 ± 14.13	46.60 ± 16.68	0.019*
Gender					<0.001
Female % (n)	22.6 (35)	72.9 (113)	2.6 (4)	1.9 (3)	
Male % (n)	0.8 (1)	68.0 (87)	25.8 (33)	5.5 (7)	

* A significant difference was observed between the underweight and class I obese classes chosen as an ideal body in terms of mean age (p=0.020).

BABQ Outcomes and Their Association with Body Weight Perception: A significant difference was observed between perceived BMI classes in terms of participants' attitudes concerning whether their body weight was healthy (p<0.001, Figure 3).

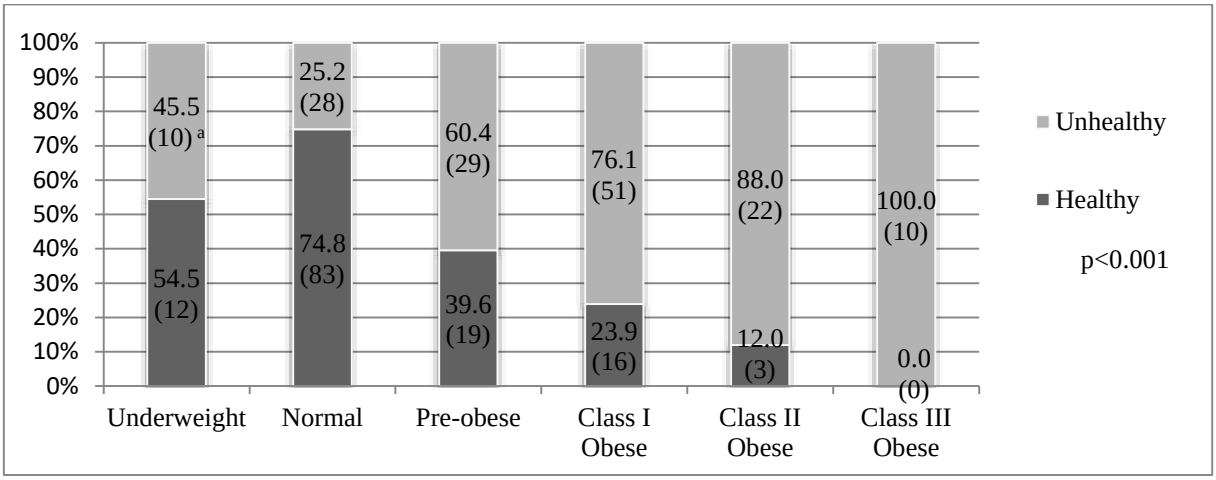

Figure 3. Participants' attitudes concerning body weight in terms of perceived body mass index classes
[a] % (n)

The study findings showed that 95.1% (269) of participants agreed or strongly agreed with the proposition that 'Obesity is a health problem,' while 0.7% (2) stated 'I have no opinion,' and 4.2% (12) responded 'I disagree.' No participants answered 'I strongly disagree'.

The findings also showed that 40.3% (114) of participants had dieted to lose weight in the past, 43.8% (124) exercised, and 23.7% (67) of participants had sought expert advice. There were significant differences between the perceived BMI classes in terms of diet, exercise and seeking expert advice (p<0.001, p=0.005, and p<0.001, respectively, Figure 4).

Frequencies of weight loss-oriented behaviors (diet, exercise and seeking expert advice) according to body weight perception status are shown in Table 4.

Table 4. Frequencies of previous weight loss-oriented behavior according to body weight perception status

	Previous weight loss-oriented behaviors		
	Diet	Exercise	Seeking expert advice
Body weight perception status			
ABWP*	37.6 (53)	41.1 (58)	21.3 (30)
IBWP**	43.0 (61)	46.5 (66)	26.1 (37)
p value	0.397	0.402	0.402
IBWP			
Under-perception	37.8 (28)	39.2 (29)	20.3 (15)
Over-perception	48.5 (33)	54.4 (37)	32.4 (22)
p value	0.236	0.092	0.126

*Accurate body weight perception, % (n) **Inaccurate body weight perception, % (n)

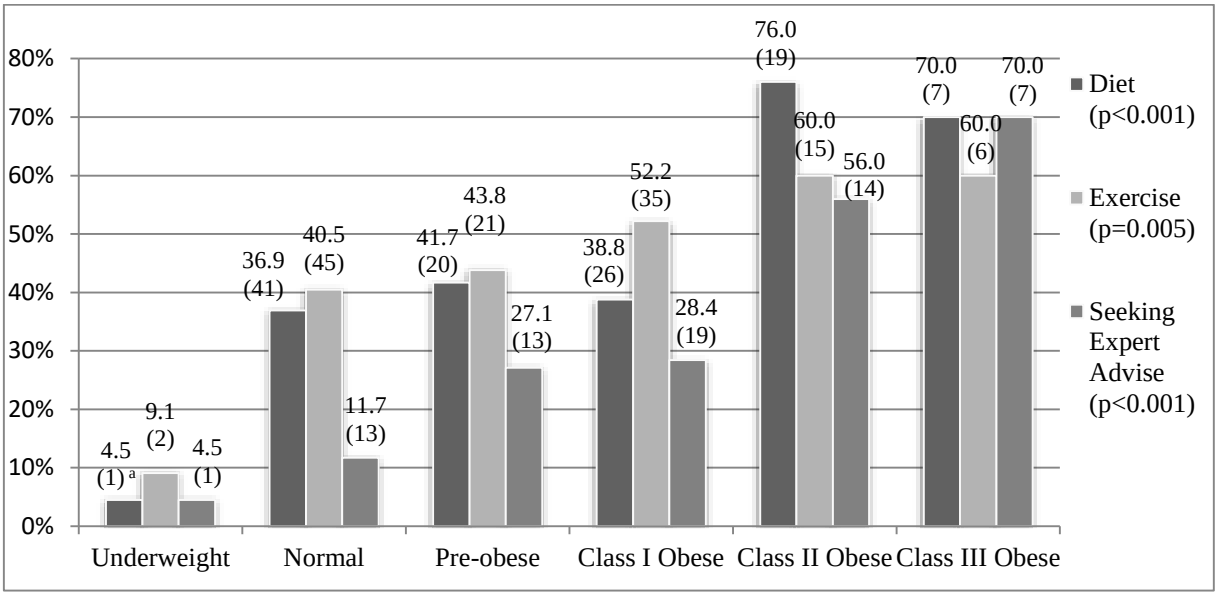

Figure 4. Frequencies of previous weight loss-oriented behaviors according to perceived body mass index classes

[a] % (n)

DISCUSSION

The prevalence of obesity in childhood and adulthood is increasing both in Turkey and worldwide (14). The most effective way to stop this increase is to prevent obesity and to raise awareness of the disease. The fact that overweight individuals perceive themselves as being of normal weight represents a risk factor for obesity (10). Efforts for weight management were associated with misperception of body weight (15). The present study therefore investigated sociodemographic features that may be related to body weight perception, together with individuals' knowledge of and attitudes and behaviors toward obesity.

Compared with the TURDEP-II study conducted in 2010, higher rates of membership of the actual BMI 'underweight, normal and pre-obese' classes were observed in the present study, while rates of membership of the actual BMI 'class I obese, class II obese and class III obese' classes were lower (16). In the Turkey Body Weight Perception Survey, which used participants' own statements when calculating actual BMI, 3.6% of participants were underweight, 39.7% were normal weight, 33.3% were pre-obese, and 23.4% were obese (7). According to the Turkish Health Interview Survey performed by the Turkish Statistical Institute in 2016, 4% of individuals aged 15 years and older were underweight, 42.1% were normal weight, 34.3% were pre-obese, and 19.6% were obese (17). The proportions of pre-obese and obese individuals in the present study were higher than in those two studies. A meta-analysis evaluating studies from Turkey in the previous 15 years reported variations in obesity prevalences between different studies was emphasized and attributed this to the general characteristics of the TURDEP study population (18). This may also explain the lower prevalence of obesity in our study than in TURDEP-II.

ABWP was determined in 49.8% of the participants in the present study. The frequency of ABWP in the Turkey Body Weight Perception Survey was 49.7%, which was very close to our own figure (7). And also Khalesi et al.'s found similar ABWP frequency (%48.6) as ours (19). In Inoue et al.'s study from Japan, the frequency of ABWP was 55.2%, higher than the value in the present study (20). In a study conducted among university freshmen by Stock et al., the frequency of ABWP was 56.7%, again higher than our figure (21). In the present study, the mean age of participants with ABWP was lower than that of individuals with under-perception. This finding is supported by previous studies showing that ABWP decreases with age (7, 22). There was no statistically significant difference between the genders in terms of ABWP or IBWP in the present study. Other studies have also reported similar rates of ABWP among females and males (7, 23, 24). Among our participants with IBWP, males tended to over-perceive their own weight, while females tended to under-perception. However, Stock et al. reported a higher rate of over-perception in females compared to males (84.8% among females with IBWP and 33.6% in males with IBWP) (21). Similarly, Kim at al. reported over-perception among 84.8% of females with IBWP (25). We think that the variations between studies may be due to differences in sociodemographic characteristics (age, education status, BMI values, ethnic origin etc.) of the study samples, as well as the differences in the methods employed to detect body weight perception. The highest frequencies of ABWP and of over-perception were observed among

individuals studying at university level or above, while the highest frequency of under-perception was observed among illiterate and merely literate individuals. In recent studies also demonstrated that underestimation body weight was associated with lower education level (15, 23, 24, 26, 27). Previous studies have shown that the frequency of ABWP increases in line with education levels (7, 11, 22, 28). The prevalence of obesity also increases as education levels decrease (29). This may be partly explained by the higher frequency of under-perception among primary school graduates and others with lower levels of education.

The two actual BMI classes with the highest frequencies of ABWP in the present study were 'underweight and normal.' The frequencies of ABWP in the 'pre-obese, class I obese and class II obese' classes were statistically significantly lower than in the 'normal' class ($p<0.001$, $p<0.001$ and $p<0.001$ for all). Karakaya et al. similarly observed found the highest ABWP frequency in the 'normal' class (71.8%) (7). In accordance with other research in China, Malaysia, Saudi Arabia shows that obese people were more likely to misperceive their weight than people with normal BMI (24, 30, 31). The lower prevalence of ABWP in overweight or obese individuals than in individuals with normal BMI values indicates impaired body weight perception. On the other hand, studies have also reported higher rates of ABWP in pre-obese or obese individuals. In Duncan et al.'s study, the prevalence of ABWP in pre-obese and obese individuals was approximately 77% (32). In another study, the reported rate of ABWP in pre-obese and obese individuals was 73.1% (22). Body weight perception is known to be affected by variables such as ethnicity, gender, and education (11, 32-35). The different prevalences of ABWP in these studies may result from variations in the sample characteristics. Randomized controlled studies are now needed to clarify the relationship between BMI and body weight perception.

In the present study, one out of every three members of the pre-obese and class I obese classes and one out of every two members of the class II obese class exhibited under-perception. This suggests impairment of body awareness. Pre-obese and obese individuals who under-perceive are unaware of their own health risks (35). The first step in the fight against obesity should be to improve individuals' body weight perception. If one is unable to regard oneself as pre-obese or obese, then one may be indifferent to all interventions aimed at preventing and treating obesity.

In the present study, men's ideal body preference mostly consisted of normal and pre-obese images, whereas women largely preferred normal and underweight images. This finding is consistent with Alipour et al.'s study of 184 women aged 18 to 35, in which women's ideal body preferences also consisted of normal and underweight body images (4). The mean age of individuals who selected the class I obese image as their ideal body image was higher than that of those who chose the underweight image. The fact that individuals with ABWP are younger, and that younger individuals select images from lower BMI classes as their ideal body preferences indicates that priority should be attached to middle age and above in terms of improving body weight perception in the fight against obesity.

Based on perceived BMI classes, one out of every 10 class II obese, one out of every five class I obese, and two out of every five pre-obese individuals evaluated their body weight as healthy. While 95.1% of participants agreed that obesity is a health problem, they were unable to exhibit the same judgment in terms of their own bodies. Irrespective of actual BMI, individuals who evaluate their own bodies as pre-obese or obese, and who also evaluate their body weights as healthy, have an insufficient level of perception and knowledge regarding healthy body weight. In the context of the fight against obesity, steps should be taken to improve the perception of healthy body weight in addition to ABWP.

In literature, weight loss-targeted behavior were associated with misperception of body weight (15). Frequencies of previous weight loss-targeted behaviors (dieting, exercising and seeking expert advice) differed significant differently between perceived BMI classes in the present study. The perceived BMI classes with the highest frequencies of dieting, exercising and seeking expert advice were 'class II obese and class III obese', while the lowest frequencies were in the 'underweight class'. Karakaya et al. asked participants whether they had dieted to lose weight in the past year, and observed a frequency of dieting of 10.1% in the normal class among perceived BMI classes, compared to 29.4% in the pre-obese class (7). The frequency of dieting was also higher in these classes in the present study. The lower frequency of dieting in Karakaya et al.'s study may result from their investigating a period of only one year.

No significant difference was observed in this study between accurate or inaccurate body weight perception in terms of past weight loss-oriented behaviors. Among participants with IBWP, there was no significant difference between under- and over-perception of body weight in terms of weight loss-oriented behaviors. In the light of these data, we conclude that the relationship between body weight perception and weight loss-oriented behaviors is related to the BMI class to which the individual perceives himself to belong, rather than perceiving himself to belong to the correct BMI class. In support of this thesis, Lemon et al. found that individuals who perceive themselves as overweight or obese attempt to lose weight more than those who perceive themselves as normal (36).

In another study a discrepancy between body weight perception and BMI among middle-aged children was found (29). Enabling individuals to perceive themselves as obese can be used as a motivation for overweight and obese individuals to engage in various weight loss-oriented behaviors. Studies are therefore now needed to reveal the effects of body weight perception on attempts to lose weight.

Limitations of the Study: One limitation of this study is we did not investigate the use of social media and other mass media, which may affect societies' ideal body perceptions. Individuals in participants' immediate environments – such as family members, colleagues, and other households – were also not investigated.

Strengths of the Study: One particular strength of this study is that we used the BSG when determining body weight perception. We think that the BSG is superior to methods of measuring body weight perception involving pictures or drawings in the literature and to methods in which subjects are asked to express how they perceive themselves in writing or verbally.

Although this study was not designed to reflect households, we think that it does reflect society, since it was conducted in primary health care facilities, those which are most accessible to the general community.

CONCLUSION

Half of the participants in this study had IBWP. Individuals' sociodemographic characteristics affect their body weight perception, and that perception affects weight loss-oriented behaviors. More efforts are needed to raise awareness of the health problems caused by obesity. Public health strategies should focus on promoting accurate body weight perception through education and awareness campaigns, targeting high-risk groups such as those with lower education levels. Within the scope of primary and secondary protections, accurate body weight perception should be inculcated, and efforts need to be made to increase individuals' awareness of their own bodies, especially in terms of pre-obesity and obesity. We recommend that further studies be performed to reveal the cause-effect relationship between body weight perception and obesity and socio-demographic features, and to produce methods for improving body perception. This study provides new insights into the prevalence and factors associated with inaccurate body weight perception. These findings can inform targeted public health interventions to promote accurate self-perception and encourage healthier behaviors, particularly among populations at higher risk of obesity.

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RESEARCH ARTICLE

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Validity and Reliability Testing of the Turkish Version of the Self-Acceptance Scale for Pregnant Women

ABSTRACT

Objective: This study was conducted to adapt the Self-Acceptance Scale for Pregnant Women (SAS-PW), which was developed in Brazil, to Turkish and test the psychometric properties of its Turkish version.

Method: This methodological study was carried out with 576 pregnant women who presented to the pregnancy outpatient clinics of a Research and Training Hospital in northern Turkey between December 2021 and April 2022. The validity of the Turkish version of SAS-PW was tested by conducting linguistic, content, and construct validity analyses, while its reliability was tested by conducting internal consistency and test-retest analyses.

Results: According to the results of the exploratory factor analysis, the factor load values of the items and the rates of the total variance in scale scores explained by the factors were sufficient. The confirmatory factor analysis results demonstrated that the goodness-of-fit indices of the scale were within suitable ranges. The 2-factor and 10-item construct of the original SAS-PW was confirmed based on the factor analyses. The item-total score correlations of the scale were found sufficient, and the total Cronbach's alpha coefficient of SAS-PW was determined to be 0.93. The test-retest analysis of the scale scores revealed a strong correlation between the scores of the two implementations.

Conclusion: The Turkish version of SAS-PW is a valid and reliable measurement instrument to evaluate the self-acceptance levels of pregnant women in Turkish society.

Keywords: Pregnancy, Reliability, Validity, Midwifery.

Gebelerde Kendini Kabul Ölçeği Türkçe Versiyonunun Geçerlik ve Güvenirlik Çalışması

ÖZET

Amaç: Araştırma Brezilya'da geliştirilen Gebelerde Kendini Kabul Ölçeği (GKKÖ)'nin Türkçe versiyonunu oluşturmak ve psikometrik özelliklerini test etmek amacıyla yapıldı.

Yöntem: Metodolojik türde olan araştırma Aralık 2021-Nisan 2022 tarihleri arasında, Türkiye'nin kuzeyinde bir Eğitim Araştırma Hastanesinin gebe polikliniklerine başvuran 576 gebe ile gerçekleştirildi. Araştırmada GKKÖ'nün geçerlik analizinde dil, kapsam, yapı; güvenirlik analizinde iç tutarlılık ve test-tekrar test analizleri kullanıldı.

Bulgular: Açıklayıcı faktör analizi sonrasında ölçeğin açıklanan varyans yüzdesi ve maddelerin faktör yükleri yeterli; doğrulayıcı faktör analizi sonrasında ölçeğin uyum indeksleri uygun aralıkta bulundu. Orijinal GKKÖ'nün iki alt boyut ve 10 maddelik yapısı faktör analizleri ile doğrulandı. İç tutarlılık analizinde ölçek maddelerinin madde toplam puan korelasyonları yeterli ve GKKÖ toplam Cronbach alfa katsayısı 0.93 olarak hesaplandı. Ölçeğin test-tekrar test sonuçları arasındaki ilişkiye ait korelasyon değeri ise yüksek bulundu.

Sonuç: GKKÖ'nün Türkçe versiyonunun gebelerde kendini kabul düzeylerinin değerlendirilmesinde Türk toplumu için geçerli ve güvenilir bir araç olduğunu göstermektedir.

Anahtar Kelimeler: Gebelik, Güvenilirlilik, Geçerlilik, Ebelik.

INTRODUCTION

Self-acceptance is defined as the individual's acceptance of oneself as a whole, comprising one's positive and negative characteristics, including past experiences (1, 2). Li et al. (2021) argued that self-acceptance comprises self-assessment and the self-experiences and attitudes that emerge as a result of it (3). Individuals who show self-acceptance can express themselves more accurately in social situations, establish interpersonal relationships more effectively, have higher self-worth, and experience less loneliness (1). Considering several biopsychosocial changes that occur in a short time during pregnancy (4, 5), the antenatal period is a critical period for the pregnant woman in terms of "self-acceptance" (6, 7).

Pregnancy and childbirth are significant events that lead to substantial physical, psychological, social, and existential changes in women's lives (8-10). In this period, in addition to physiological changes, the women experience body image changes, especially those such as weight gain and skin changes (4, 11, 12). While it was stated that some physiological changes brought about by pregnancy such as abdominal growth have positive effects on the feeling of motherhood (13), these changes may also increase the dissatisfaction of women with their body image (4).

Problems associated with body image during pregnancy can affect maternal and fetal health (5). In the study in which they examined the relationship between psychological well-being and body image in pregnant women, Fahami et al., (2018) found a significant positive relationship between these two variables (14). Similarly, Przybyła-Basista et al. (2020) reported that dissatisfaction with one's body image increased the likelihood of depression among pregnant women (15). Tsuchiya et al. (2019) investigated dissatisfaction with body image among Japanese pregnant women in the second trimester of pregnancy and revealed that body dissatisfaction increased in proportion to body mass index (BMI) (16). In their study in Turkey, Küçükkaya et al. (2020) reported that with an increase in weight during pregnancy, the body perceptions of women and their acceptance of pregnancy were negatively affected, and positive body perceptions related to pregnancy increased the acceptance of pregnancy (11).

In line with current studies, the acceptance of pregnancy and the relationships among the psychosocial aspects of pregnancy-related changes are a matter of curiosity (11, 14-16). The universal acknowledgment of the gap in scientific knowledge regarding the construct of self-acceptance among pregnant women emphasizes the need to investigate measurement instruments to be used in the screening of this issue. Measurement tools are necessary to help health professionals improve the mental health of pregnant women and provide them with better health services (2). Some studies in Turkey have examined the acceptance of pregnancy, the perception of motherhood, and body perceptions using different measurement instruments (11, 12, 17). The positive attitudes of pregnant women toward their current status (pregnancy) can be considered their acceptance of pregnancy, and they fundamentally reflect self-acceptance (2, 10, 14). The Self-Acceptance Scale for Pregnant Women (SAS-PW), which is different from other current measurement instruments, evaluates two aspects of self-acceptance in pregnant women, namely body acceptance and pregnancy acceptance (2). It is important to investigate whether SAS-PW, which is considered functional in this regard, is appropriate for different cultural structures. The purpose of our study is to create the Turkish version of SAS-PW and test its psychometric properties.

MATERIALS AND METHODS

Design and Participants: This study was conducted with a methodological design to test the validity and reliability of the Turkish version of the SAS-PW. It was conducted at the pregnancy outpatient clinics of a Research and Training Hospital in northern Turkey between December 2021 and April 2022. The population of the study consisted of pregnant women who presented to these outpatient clinics on the specified dates. A sample that can sufficiently reveal the psychometric structure of a scale is recommended to include at least 500 participants (18, 19). The research was completed with 576 pregnant volunteers. The simple random sampling method was used to include pregnant women in the sample. The sample included pregnant women who were literate, had singleton fetuses and did not have a risk factor in their pregnancies.

Data Collection Instruments: A "Personal Information Form" and the SAS-PW were used to collect data.

Personal Information Form: This form was developed by the researchers in line with the relevant literature to identify some sociodemographic characteristics (age, education level, occupation, family income, gestational week) of the participants (2, 11, 14).

Self-Acceptance Scale for Pregnant Women: SAS-PW was developed by Meireles et al. (2021). The scale consists of 10 items and two dimensions, namely Body Acceptance (BAc) (items 1, 2, 4, 5, 7, 8, and 9) and Pregnancy Acceptance (PA) (items 3, 6, and 10). Each item of the 5-point Likert-type scale has the response options of "Always (5)", "Often (4)", "Sometimes (3)", "Rarely (2)", and "Never (1)". The scale has a score range of 10-50, and higher scores indicate higher levels of self-acceptance. The Cronbach's alpha

internal consistency coefficient of the original scale was reported as 0.90 (2). In this study, the total Cronbach's alpha coefficient of SAS-PW was determined to be 0.93.

Cultural Adaptation: The cultural adaptation process of the scale was conducted in three stages: linguistic validity, content validity, and pilot application. The translation and back-translation methods were used to determine the linguistic validity of SAS-PW. The scale was translated from English into Turkish by the researchers (three faculty members specialized in the field of midwifery). As a result of this group translation process, the Turkish form of the scale was obtained. This form was evaluated by a Turkish language expert. The back-translation of the scale from Turkish into English was carried out by two translators who are native speakers of English and fluent in Turkish. The form obtained after the back-translation process and the original form of the scale were submitted for the review of expert linguists. After the examinations and analyses of these experts, it was concluded that there was no semantic shift in the items, the scale was applicable in Turkish, and the linguistic validity of the Turkish version of SAS-PW (henceforth Turkish SAS-PW) was demonstrated. To test the content validity of the Turkish SAS-PW, the form obtained as a result of linguistic validity testing was submitted for the reviews of 12 experts who are specialized in their field (Department of Midwifery). The Davis (1992) technique was used to calculate the content validity ratio (CVR) values based on expert opinions (20). Because the opinions of 12 experts were obtained for the analysis of the content validity of the scale, it was aimed to find CVR values greater than 0.66 (21). The CVR values of the items of the Turkish SAS-PW were in the range of 0.83-1.00. The content validity index (CVI) value of a scale is calculated by taking the average of the CVR values of the items remaining in the item pool (22). The total CVI value of the Turkish SAS-PW was calculated as 0.97. CVI values greater than 0.67 are desired (22). Because the calculated CVI value was greater than 0.67, the scale was found statistically significant, and no item was removed in the context of the content validity analyses. After the expert opinion and review processes, the scale was applied to a group of 28 individuals as a pilot implementation to determine whether the statements included in the scale were comprehensible. After the pilot implementation, it was concluded that all items were comprehensible. The data of the 28 pregnant women who participated in the pilot implementation were not included in the main sample. In this way, the final version of the Turkish SAS-PW form was created.

Psychometric Testing of the Turkish SAS-PW Validity: The exploratory factor analysis (EFA) and confirmatory factor analysis (CFA) methods were used to test the construct validity of the scale (18). Before EFA and CFA, to determine the adequacy of the sample and the suitability of the data for factor analysis, the Kaiser-Meyer-Olkin (KMO) test and Bartlett's test of sphericity were carried out. While KMO statistic values greater than 0.70 are considered sufficient in the literature, those in the range of 0.90-1.00 are considered excellent (23). Additionally, a statistically significant result of the Bartlett's test of sphericity shows that the data are suitable for factor analysis (24). In this study, it was aimed to obtain factor load values of at least 0.30 based on EFA results and remove the items with lower values from the scale, if any (23). The ratio of the total variance in the measured variable explained by the factors determined by EFA is considered sufficient in the range of 0.50-0.70 (22, 25). A scree plot was also examined, looking for a change in the slope of the line connecting the eigenvalues of the factors (25). After the EFA, a CFA was carried out to support the results on the factors of the scale (26). In structural equation modeling, which uses multiple goodness-of-fit indices to reveal whether a model that is established regarding factors is confirmed, rather than focusing on a single goodness-of-fit index, all indices are evaluated together (27). In the literature, desirable values for CFA goodness-of-fit indices have been reported as RMSEA<0.06-0.08, χ^2/df=2-5, GFI≥0.95, NFI≥0.95, and IFI and CFI≥0.95 (27-30).

Reliability: To measure the internal consistency of the scale, the Cronbach's alpha coefficient was used, and item-total score correlations were calculated as a part of the reliability analyses. The Cronbach's alpha coefficient varies between 0 and 1. Values closer to 1 indicate higher reliability regarding the internal consistency of the items of the scale that is being tested. Cronbach's alpha coefficients higher than 0.70 are considered an indicator of good internal consistency in the literature (19, 31). In this study, the criterion for the exclusion of items was determined as having item-total score correlation values that are negative or lower than 0.25 (22). The time-invariance of the scale was analyzed using the test-retest analysis method (26). It is important to re-administer a measurement instrument for test-retest analysis within an optimal time interval. For the test-retest analysis of the Turkish SAS-PW, the scale was administered again to 30 pregnant women two weeks later (26, 31). For this analysis, the correlation coefficient between the scores of the two implementations was calculated (18). In the literature, correlation coefficients (r) in the range of 0.00-0.49 are considered weak, those in the range of 0.50-0.69 are considered moderate, and those in the range of 0.70-1.00 are considered strong (32).

Data Analysis: The collected data were analyzed using the "Statistical Package for the Social Sciences" (SPSS) for Windows 26.0 statistical package program and the "Analysis of

Moment Structures" (AMOS) 24.0 program. Using the SPSS program, EFA and reliability analyses were carried out on the dataset. To test the significance of the construct, a CFA was carried out using the AMOS program. The test statistics and goodness-of-fit indices of the model that was obtained as a result of the analyses were interpreted to establish the final model. The descriptive statistics of the variables that were used in the study are presented as frequency, percentage, mean, and standard deviation values. The results were interpreted in a 95% confidence interval and at a statistical significance level of $p<0.05$.

Ethical Aspect of the Study: In the process of adapting SAS-PW to Turkish culture, Juliana Fernandes Filgueiras Meireles was first contacted via e-mail, and permission was obtained to use the scale. Next, to carry out the study, ethical approval was obtained from the Scientific Research and Publication Ethics Committee of Inonu University (Decision no: 2021/2723). The relevant hospital's permission and the informed consent of the participants were also obtained.

RESULTS

Participant Characteristics: The mean age of the participants was 27.75±4.83, while their mean gestational week was 31.96±8.36. It was found that 40.1% of the participants had high school degrees, 82.3% were not working, and 88.7% stated their income level as moderate (Table 1).

Table 1. Sociodemographic characteristics of the participants (n =576)

Sociodemographic characteristics			
Age (years) (mean ± SD)		27.75±4.83	
Gestational week (mean ± SD)		31.96±8.36	
		n	**%**
Educational level	Literate	6	1.0
	Primary school	47	8.2
	Secondary school	103	17.9
	High school	231	40.1
	University	189	32.8
Occupation	Employed	102	17.7
	Unemployed	474	82.3
Family income	Low	32	5.6
	Moderate	511	88.7
	High	33	5.7

SD: Standard deviation

Validity Analyses

Multivariate Normal Distribution Testing for the Construct Validity Analyses of the Scale: One of the most frequently used methods for checking multivariate normal distribution in the AMOS program is the Mahalanobis distance. In this approach, a plot is drawn and examined for each variable. The existence of an outlier value in the dataset is tested based on the distances of the observed data on the plots to the centroid, the mean values of the samples, and their variances (33). The study started with 611 data collection forms, and 35 of these forms were eliminated as their values were under the $p<0.01$ in terms of the Mahalanobis distance results. Consequently, validity and reliability analyses were conducted with 576 forms. The multivariate normal distribution of the data was tested using the "observations farthest from the centroid (Mahalanobis distance) menu" in the AMOS program. The skewness value for the model was calculated as 6.149, and multivariate normal distribution was provided as this value was smaller than 8 (33).

Construct Validity: The EFA and CFA methods were used to test the construct validity of the scale. Before EFA and CFA, to determine the adequacy of the sample and the suitability of the data for factor analysis, the KM test and Bartlett's test of sphericity were carried out. As a result of these tests, the KMO statistic was found as 0.923, and the result of the Bartlett's test of sphericity was $\chi^2=4336.291$ and significant at $p<0.001$.

Exploratory Factor Analysis: An EFA was conducted to investigate the Turkish SAS-PW, whose original version had 10 items and two factors. It was determined that 48.798% of the total variance in the scale scores was explained by the BAc dimension, while 25.015% of this variance was explained by the PA dimension. The rate of the total variance explained by these two factors was 73.813%. According to the EFA results, the factor load values were 0.708-0.891 in the BAc dimension and 0.597-0.906 in the PA dimension (Table 2). The scree-plot drawn for the scale is given in Figure 1. The number of segments in the plot clearly showed the two-factor structure of the scale, and the construct that was obtained as a result of the analyses was also similar to the plot.

Table 2. Item Factor Loads, Descriptive Statistics, and Corrected Item-Total Correlations of the Turkish SAS-PW

Scale Items	BAc	PA	Mean ± SD	Corrected Item-total correlations
Q1	0.891		3.72 ± 1.17	0.788
Q2	0.857		3.78 ± 1.11	0.773
Q4	0.834		3.81 ± 1.08	0.794
Q5	0.773		3.88 ± 1.11	0.793
Q8	0.766		3.9 ± 1.06	0.822
Q9	0.749		4.01 ± 1.03	0.831
Q7	0.708		3.36 ± 1.25	0.706
Q6		0.906	4.56 ± 0.72	0.516
Q3		0.883	4.34 ± 0.88	0.607
Q10		0.597	4.22 ± 0.95	0.716
% variance explained	48.798	25.015	**Total = 73.813**	

SD: Standard deviation

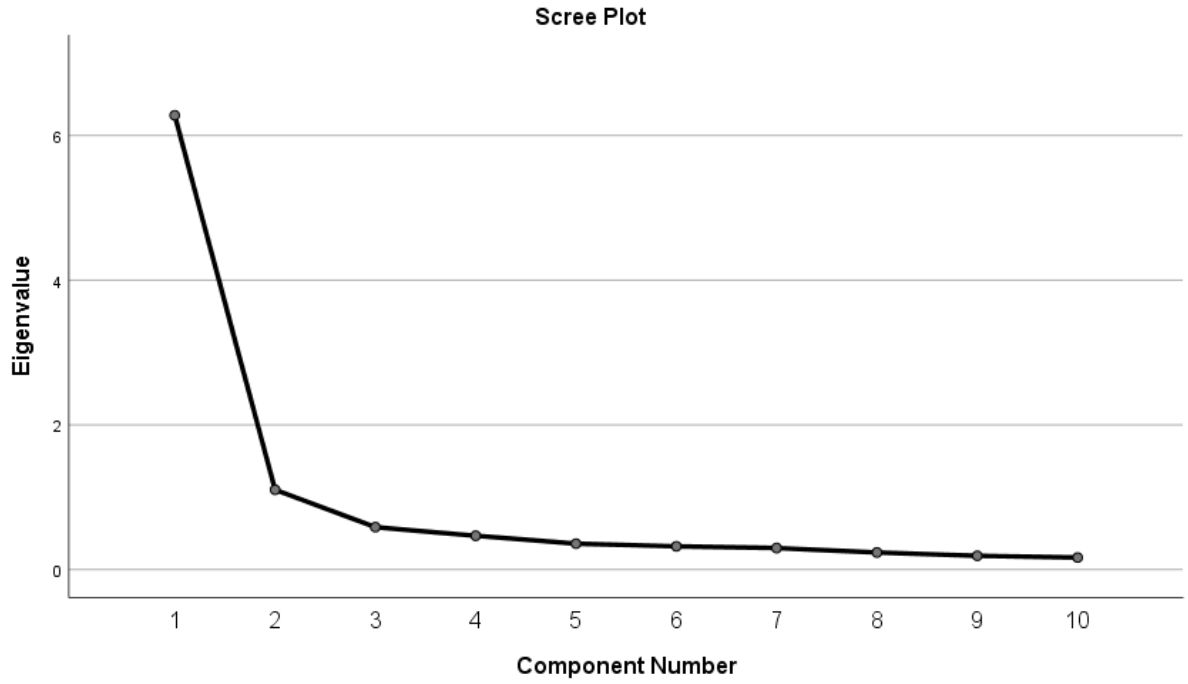


Figure 1. Turkish SAS-PW Scree-Plot

Confirmatory Factor Analysis: To test the accuracy of the 10-item two-factor Turkish SAS-PW model that was calculated with the EFA and confirm the construct, a CFA was carried out. The initial goodness-of-fit values of the Turkish SAS-PW were found as χ^2=478.943, df=34 ($p<0.05$), χ^2/df=14.087, RMSEA=0.151, GFI=0.843, CFI=0.898, NFI=0.891, and IFI=0.898 (Table 3). Accordingly, the desired result could not be achieved based on the goodness-of-fit indices obtained from the first model. When the modification indices of the model were examined, it was determined that the residual term pairs with the highest values were e1-e2, e4-e9, e7-e8, e8-e9, e3-e6, and e3-e10. A new model was created by drawing covariances between these pairs, and calculations were made. A second CFA model was obtained by correlating the error covariances of the items in question. The χ^2 value based on the modified CFA model's diagram was found as 132.208. The degree of freedom for the model was 28, and the χ^2/df value was found as 4.722. The RMSEA value, which indicates the adequacy of the sample size, was found as 0.080. Among other goodness-of-fit indices, GFI was determined to be 0.956, NFI was 0.970, and IFI and CFI were 0.976 (Table 3). The factor structure that was obtained based on the second CFA model of the scale items is presented in the form of a path diagram in Figure 2.

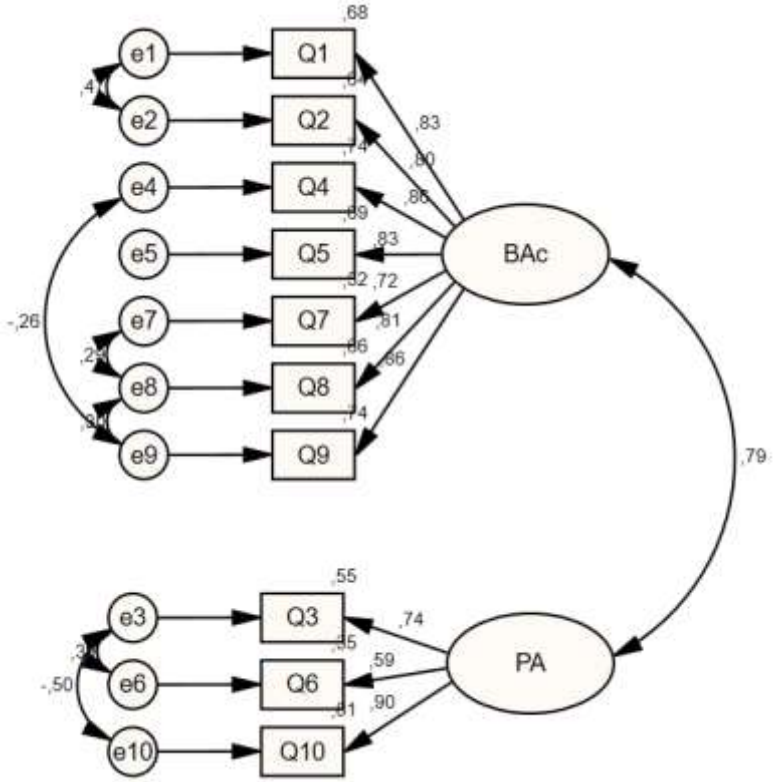


Figure 2. Factor structure model of the Turkish SAS-PW

Table 3. Fit indices for confirmatory factor models in the Turkish SAS-PW

Fit indices	First Model	Modified Model	Acceptable fit indices
CMIN	478.943	132.208	The model with the smallest value is more compatible.
p	<0.001*	<0.001*	<0.05
χ^2 / sd	14.087	4.722	2-5
IFI	0.898	0.976	≥0.95
CFI	0.898	0.976	≥0.95
NFI	0.891	0.970	≥0.95
GFI	0.843	0.956	≥0.95
RMSEA	0.151	0.080	<0.06-0.08

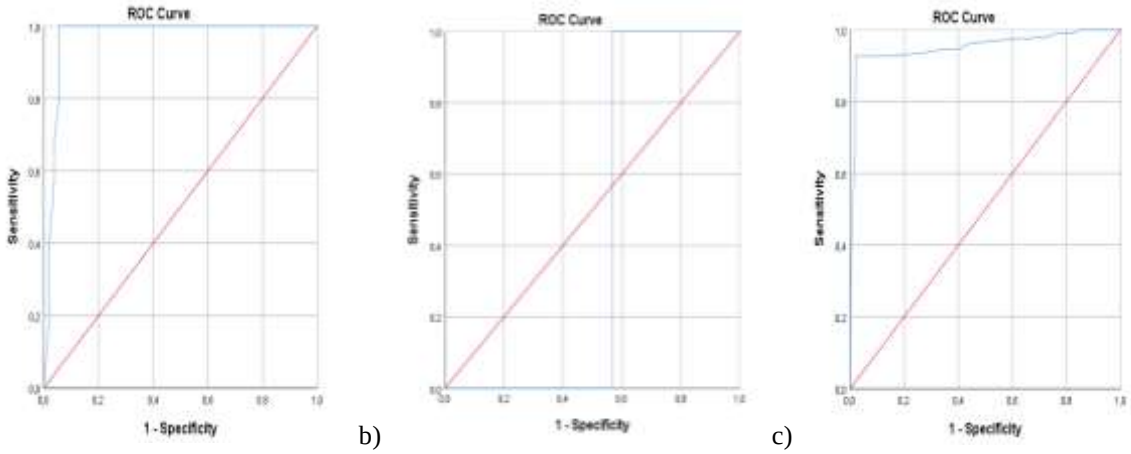
The 10-item Turkish SAS-PW consisting of the dimensions of BAc (items 1, 2, 4, 5, 7, 8, and 9) and PA (items 3, 6, and 10) in the EFA was confirmed with the CFA.

Reliability Analyses: To test the reliability of the Turkish SAS-PW, internal consistency (item-total score correlation and Cronbach's alpha coefficients) and test-retest analyses were conducted.

Internal Consistency Analyses: According to the results of the Cronbach's alpha reliability analysis conducted to measure the internal consistency of the scale, the Cronbach's alpha coefficient of the BAc dimension was found as 0.93, the coefficient of the PA dimension was found as 0.78, and the coefficient of the total SAS-PW was found as 0.93. The item-total correlation coefficient ranges for the dimensions were determined to be 0.706-0.831 for BAc and 0.516-0.716 for PA.

Test-Retest Analysis: The test-retest analysis method was used to test the time-invariance of the scale. Thirty pregnant women were included in this analysis, and the same scale was administered to these participants again two weeks later. The test-retest correlation coefficients were determined to be 0.893 for the BAc dimension, 0.901 for the PA dimension, and 0.902 for the total scale ($p<0.001$).

Cutoff Point Calculation: An ROC analysis was carried out to determine the cutoff points of the scale. The evaluation categories for the Turkish SAS-PW were found as low self-acceptance for scores of 10-35, moderate self-acceptance for scores of 36-45, and high self-acceptance for scores of 46-50 (Figure 3).



a) b) c)

Figure 3. Cutoff points based on ROC analysis results a) low, b) moderate, c) high

DISCUSSION

Validity: Construct validity shows the capacity of a measurement instrument to measure the construct for which it is designed to measure (34). The EFA and CFA methods were used in the construct validity analyses of the Turkish SAS-PW. Before EFA and CFA, KMO and Bartlett's tests were carried out. The results of these tests showed the KMO statistic of the scale as 0.923, and the result of the Bartlett's test was χ^2=4336.291, which was significant at p<0.001. These results demonstrated the adequacy of the sample and the suitability of the dataset for factor analysis (23, 24).

EFA is a multivariate statistical method that is used to create a new construct by investigating the relationships between variables (35, 36). The original SAS-PW consists of two dimensions and 10 items (2). In the literature, the lower limit of factor loads for items in a measurement instrument was recommended to be 0.30 (23). According to the results of the EFA in this study, because the factor loads of all items were greater than 0.30, no item was removed, and these results were compatible with the EFA results of the study in which the original SAS-PW was developed (2). Like the original SAS-PW, the Turkish SAS-PW was also two-dimensional. According to the EFA results of the original scale, the rates of the total variance in the scale scores explained by the factors were 42.519% for the BAc dimension and 10.611% for the PA dimension (2). In this study, for the Turkish SAS-PW, 48.798% of the total variance was explained by the BAc dimension, while 25.015% of this variance was explained by the PA dimension, which constituted a total variance explanation ratio of 73.813%. The results of this study showed similarities to the results of the original scale development study. Considering the variance explanation rates of this study, sufficient construct validity was achieved (22, 25). The two-factor scale construct that was found as a result of the EFA was checked using the CFA method. The CFA results of the original scale showed goodness-of-fit index values of RMSEA=0.079, χ^2/df=4.04, CFI=0.994, GFI=0.991, AGFI=0.985, and NFI=0.986 (2). In this study, the desired outcome could not be achieved in terms of goodness-of-fit indices based on the model that was established first. The modification indices for the model were examined, covariances between residual term pairs were drawn, and a new model was established. According to the results of the second CFA, the goodness-of-fit indices of the Turkish SAS-PW were found as RMSEA=0.080, χ^2/df=4.722, GFI=0.956, NFI=0.970, and IFI and CFI=0.976. After the modifications, it was seen that the goodness-of-fit indices of the Turkish SAS-PW were within suitable ranges, and the scale had sufficient construct validity (27- 30) (Table 3).

Reliability: Reliability is considered an indicator of the consistency of results obtained from a measurement instrument in implementations repeated under the same conditions (34). For the Turkish SAS-PW, internal consistency and test-retest analyses were carried out (18). The Cronbach's alpha coefficient is one of the most prevalently used psychometric indicators of the reliability and internal consistency of a measurement instrument (18, 26). The Cronbach's alpha coefficients of the original scale were reported as 0.91 for the BAc dimension, 0.76 for the PA dimension, and 0.90 for the total SAS-PW (2). In this study, the Cronbach's alpha coefficients of the Turkish SAS-PW were found as 0.93 for the BAc dimension, 0.78 for the PA dimension, and 0.93 for the total Turkish SAS-PW. These results were in agreement with the results of the original version of the scale. Moreover, considering the Cronbach's alpha coefficients of the Turkish SAS-PW, the internal consistency levels of the dimensions of the scale and the total scale were very high, and the scale was found reliable (19, 31). A high correlation coefficient for each item with the total scale shows that the relevant item is effective and adequate in measuring the result that is aimed to be measured (24). In this study, the item-total

score correlation coefficient ranges were found as 0.706-0.831 for the BAc dimension and 0.516-0.716 for the PA dimension. Therefore, as the item-total correlation coefficients of all items were positive and greater than 0.25, no item was removed from the scale (22).

The consistency of the responses of individuals to a measurement instrument at different times indicates the time-invariance of the instrument (19, 26). In the literature, it is recommended to have a time interval of 1-2 weeks between two implementations (31). In this study, after the Turkish SAS-PW was administered to 30 pregnant women again after two weeks for the test-retest analysis, positive, statistically significant, and strong correlations were found between the results of the two implementations for the total scale and both of its dimensions ($p<0.001$). According to these results, because there was sufficient time between the two measurements, and the agreement of outcomes in this time interval was preserved, the Turkish SAS-PW was found to be a consistent scale.

In the original development study of the scale, cutoff scores were calculated. Accordingly, self-acceptance levels were categorized as low for scores of 10-34, moderate for scores of 35-44, and high for scores of 45-50 (2). In this study, an ROC analysis was carried out to determine the cutoff points of the Turkish SAS-PW, and the evaluation categories were found as low self-acceptance for scores of 10-35, moderate self-acceptance for scores of 36-45, and high self-acceptance for scores of 46-50. While these results were not exactly the same as the results of the original scale, they were very close. The small difference between these cutoff points may have originated from the samples of the two studies that were selected from two different cultures.

The strong aspects of the study include the fact that it was conducted with a broad sample of individuals, and a valid and reliable measurement instrument was adapted to Turkish society for healthcare professionals in Turkey. Despite the strengths of the study, the limitation of the study was that the data were collected in only one province in Turkey, and the results were dependent on the self-reports of the participants. This situation is susceptible to bias.

CONCLUSION

The results of the analyses demonstrated that the Turkish SAS-PW had a good agreement with the original SAS-PW, and it was a valid and reliable measurement instrument in the assessment of the self-acceptance levels of Turkish pregnant women.

SAS-PW can be used as a short, accurate, and beneficial measurement instrument by healthcare professionals and researchers for evaluating the adaptation of pregnant women to the pregnancy process in the antenatal stage, planning education and support interventions to improve their self-acceptance levels, and providing individual-centered care services.

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RESEARCH ARTICLE

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How Does Metabolic Syndrome Affect Sexual Function in Obese Women?

ABSTRACT

Objective: Metabolic syndrome (MetS) is significant public health concern with a rising prevalence. MetS leads to diseases such as diabetes mellitus, arterial hypertension (HTN) and atherosclerotic heart disease, as well as female sexual dysfunction (FSD). However, the relationship of MetS to female sexual function in obese woman is unclear. In our study, obese women and obese women with MetS were compared. We aimed to determine whether there was a difference between the two groups in terms of FSD.

Method: The study included 114 patients, aged 21-51, who visited the obesity outpatient clinic of our center from January to April 2022. Patients who met the study criteria answered the sociodemographic data questionnaire, Female Sexual Function Index (FSFI), and the Beck Depression Inventory (BDI). Anthropometric measurements and blood pressure assessments were conducted during the visit, and blood tests were recorded.

Results: Seventy-three (64%) patients were only obese, and 41 (36%) had a diagnosis of MetS with obesity. There was no significant difference between the two groups in terms of demographic data, clinical features, BDI scores, and FSFI total score. Lubrication, one of the FSFI subparameters, was found to be low in the group with MetS (p=0.028), while there was no difference in other subparameters.

Conclusion: In this study, we showed that lubrication as a sign of arousal problem is affected by MetS. Patients with risk factors for FSD such as MetS, obesity, HTN, diabetes mellitus should not be ignored. Thus, it will be possible to prevent the effects of FSD on general health.

Keywords: Bioelectrical Impedance, Female Sexual Dysfunction, Metabolic Syndrome, Obesity.

Metabolik Sendrom Obez Kadınlarda Cinsel İşlevi Nasıl Etkiler?

ÖZET

Amaç: Metabolik sendrom (MetS), gitgide yaygınlaşan önemli bir halk sağlığı sorunudur. MetS; diabetes mellitus, arteriyel hipertansiyon ve aterosklerotik kalp hastalığı gibi hastalıklara ve kadın cinsel işlev bozukluğuna (FSD) yol açar. Ancak obez bireylerde MetS'un kadın cinsel işleviyle ilişkisi belirsizdir. Çalışmamızda obez kadınlar ve MetS'li obez kadınlar karşılaştırıldı. Her iki grup arasında cinsel işlev bozukluğu açısından fark olup olmadığını saptamayı amaçladık.

Yöntem: Çalışmaya Ocak-Nisan 2022 tarihleri arasında merkezimizin obezite polikliniğine başvuran 21-51 yaş aralığındaki 114 hasta dahil edildi. Çalışma kriterlerini karşılayan hastalar sosyodemografik veri anketi, Kadın Cinsel İşlev İndeksi (FSFI) ve Beck Depresyon Envanteri'ni (BDI) yanıtladılar. Ziyaret sırasında antropometrik ölçümler ile kan basıncı ölçümleri yapıldı ve laboratuvar sonuçları kaydedildi.

Bulgular: Hastaların 73'ü (%64) sadece obez iken 41'i (%36) obezite ile birlikte MetS tanısı almıştı. İki grup arasında demografik veriler, klinik özellikler, BDI puanları ve FSFI toplam puanı açısından anlamlı fark saptanmadı. FSFI alt parametrelerinden biri olan lubrikasyon MetS'li grupta düşük bulunurken (p=0,028), diğer alt parametrelerde fark görülmedi.

Sonuç: Bu çalışmada, uyarılma sorununun bir işareti olan lubrikasyonun MetS'dan etkilendiğini gösterdik. MetS, obezite, arteriyel hipertansiyon, diabetes mellitus gibi FSD için risk faktörleri olan hastalar göz ardı edilmemelidir. Böylece FSD'nin genel sağlık üzerine olası etkilerinin önüne geçmek mümkün olacaktır.

Anahtar Kelimeler: Biyoelektrik Empedans, Kadın Cinsel İşlev Bozukluğu, Metabolik Sendrom, Obezite.

INTRODUCTION

Female sexual dysfunction (FSD) is a health issue influenced by various factors, including psychological, biological, and interpersonal components. It is affected by many factors such as age, ethnicity, sociocultural level, general health (1). According to the definition made by the World Health Organization (WHO), sexuality; it consists of a combination of effects that enrich personality, communication and emotions in physical, psychological and social aspects. The female sexual response cycle is a multifaceted process influenced by various factors, such as vasculogenic, neurogenic, hormonal, and psychogenic elements (1). The disturbance of any of these factors may lead to sexual dysfunction. It is known that nearly half of women in the United States of America (USA) face at least one sexual health problem (2).

Obesity is characterized by the accumulation of excess fat in the body. It is a chronic disease that affects all systems, especially the cardiac and endocrine systems. Obesity, recognized as a complex and multifactorial disease that adversely impacts health, is the second leading cause of preventable deaths after smoking (3). According to WHO 2016 data, the estimated number of obese adults worldwide is 650 million and the number of overweight people is 1.9 billion. Among the adult population, 13.1% are classified as obese, while 39% are considered overweight (4). Metabolic syndrome (MetS) is an endocrinological disease in which diseases such as hyperglycemia, obesity, insulin resistance, arterial hypertension (HTN), hyperlipidemia, and coronary artery disease coexist (5). The most widely used definitions for MetS have been established by WHO, European Group for the Study of Insulin Resistance, and National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) (6). Adult Treatment Panel III (ATP III) diagnostic criteria are as follows; abdominal obesity; waist circumference >88 cm in women, >102 cm in men, triglyceride (TG) ≥150 mg/dl, high-density lipoprotein (HDL) level <40 mg/dl in men, <50 mg/dl in women, fasting plasma glucose >100 mg/dl, arterial blood pressure ≥ 130/85 mm Hg. Three of the five criteria are sufficient for the diagnosis of MetS (6).

MetS, defined as a pandemic by Grundy, is increasing globally in many countries and affects 20-30% of the adult population (7,8). MetS leads to diseases such as diabetes mellitus, HTN and atherosclerotic heart disease, as well as FSD. However, the relationship of MetS to female sexual function in obese woman is unclear. Consequently, this study aims to explore the potential association between the presence of MetS and sexual dysfunction among women of reproductive age who are being monitored at an obesity outpatient clinic. Another aim was to analyze the relationship between depression and FSD in this selected patient group.

MATERIALS AND METHODS

After the approval of the Ethics Committee of University (Approval No: 2021/0622, Date: 8/12/2021), the patients who were followed up and treated in the obesity outpatient clinic were prospectively enrolled in the study. Patients were screened according to the study criteria and first interview was made with 160 of 2488 patients who applied to the outpatient clinic between January 2022 and April 2022. The use of drugs causing sexual dysfunction was an exclusion criterion. Being in menopause, having urinary tract infection or genital infection in the last one month, having a history of pelvic surgery were determined as exclusion criteria. Thirty-four of the interviewed patients were excluded from the study due to their personal problems with their spouses and irregular relationship. Three patients were excluded from the study because they were previously diagnosed with vaginismus or had previously been treated for this reason. Seven patients were excluded from the study due to their social and mental status affecting their sexual life; three patients had recently lost a first-degree relative, four patients were in active patient care. Study was completed with 114 patients remaining after exclusion criteria.

Female Sexual Function Index (FSFI) and Beck Depression Inventory (BDI) were used. FSFI was developed in 2000 by Rosen et al (9). In 2005, a validation study was conducted for the Turkish population, and the Turkish version of FSFI is reliable and valid (10). It is a questionnaire consisting of 19 questions about the woman's sexual life in the last four weeks. The total score range of the scale is 2 – 36. Scale's structure includes 6 main subparameters: sexual desire, arousal, lubrication, orgasm, satisfaction, and pain. Six subparameters are defined as: *sexual desire* to measure the degree of sexual desire and interest of the patient; *arousal* to ensure the state of arousal, to measure the frequency and level of arousal; *orgasm* to measure difficulty in reaching orgasm, satisfaction at that moment and its frequency; *lubrication* to measure the frequency of lubrication, the frequency of maintaining this condition in the relationship, and the difficulty; *satisfaction* to measure the rate of intimacy with her partner, satisfaction with sexual and general life and *pain* during vaginal penetration, to measure the feeling of discomfort afterwards. The cut-off value of the FSFI total score for sexual dysfunction was accepted as 26.55 (11).

The psychological aspect of sexual dysfunction is significant and cannot be overlooked; therefore, depressive symptoms were also evaluated. BDI is a 21-item questionnaire that measures emotional, somatic, cognitive and motivational symptoms related to depression. Turkish validation was published by Hisli et al (12). The score ranges for minimal, mild, moderate, and severe depression are 0-9, 10-16, 17-29, and 30-63,

respectively. In our study, these questionnaires were read and filled by the physician in a separate room where the patients could talk comfortably.

Bioelectrical impedance analysis (BIA) is based on the difference in electrical permeability of lean tissue mass and fat. It is effective with its ease of measurement and low cost. Tanita MC 780 was used for BIA. Body weight, fat and muscle ratio measurements were made with the device. Then the patients were divided into two groups as obese with MetS and obese only.

Statistical Analysis: The data were analyzed using SPSS version 18 (IBM, NY, USA). Conformity of continuous variables to normal distribution was examined by Kolmogorov Smirnov test. Categorical variables in the study were presented with frequency (n) and percentage (%), and continuous variables with mean deviation to standard (mean±SD) and median (IQR: 25th-75th percentile) values. For the analysis of categorical variables, Pearson's Chi-square, Yates correction, Fisher Freeman Halton Exact Test were used in comparison of the two groups mean. Independent Samples T test was used when parametric test assumptions were met, and Mann Whitney U test was used when not. The statistical significance level was accepted as 0,05 in the study.

RESULTS

The mean age of the 114 participants included in the study was 38.99±7.23 years, and the mean age of onset of obesity was calculated as 25.21±7.73 years. The comorbidities of the patients and the drugs they used were examined; 56 patients (49.1%) had no comorbid disease. The most common comorbid disease was prediabetes (41.2%). Nine patients had HTN (7.8%) and three patients (2.6%) had hyperlipidemia. Patients with a total score of less than 26.55 on the FSFI scale were diagnosed with sexual dysfunction. According to the analyses conducted, sexual dysfunction was identified in 46 of the participants, which accounts for 40% of the study population.

Patients were found to be statistically similar in terms of age, age of onset of obesity, and employment status. Smoking status shows a significant difference among the groups (p=0.035). While 6.8% of obese patients were actively smoking, this rate was found to be significantly higher (24.4%) in obese patients with MetS (Table 1).

Table 1. Demographic characteristics, anthropometric measurements, laboratory findings, bioelectrical impedance measurements, FSFI scores and Beck depression scale scores by study groups

Variables (n=114)	Groups: Obese (n=73)	Obese+MetS (n=41)	p value
Demographic features			
Age (years), *Median(IQR)*	40(33-44)	40(35-46)	0.732
Age at diagnosis of obesity (years), *Median(IQR)*	24(20-30)	24(20-28)	0.290
Working status (n, %)			
Not working	54(74)	32(78)	0.796
Working	19(26)	9(22)	
Smoking (n, %)			
Never	63(86.3)[a]	29(70.7)[b]	**0.035**
Ex smoker	5(6.8)[a]	2(4.9)[a]	
Active smoker	5(6.8)[a]	10(24.4)[b]	
Anthropometric measurements			
Body mass index (kg/m^2), *Mean±SD*	34.63±4.74	35.91±4.82	0.170
Waist circumference (cm), *Mean±SD*	102.78±10.32	107.1±10.21	**0.034**
Hip circumference (cm), *Mean±SD*	119.88±10.19	122.9±10.16	0.131
Laboratory findings			
HbA1c (%), *Median(IQR)*	5.6(5.3-5.8)	5.9(5.6-6)	**0.002**
Fasting plasma glucose (mg/dl), *Median(IQR)*	91(87-98)	100(91-106)	**0.001**
HDL (mg/dl), *Median(IQR)*	56(49-67)	45(39-50)	**<0.001**
LDL (mg/dl), *Median(IQR)*	117(86-133)	109(95-136)	0.920
Triglyceride (mg/dl), *Median(IQR)*	90(71-120)	182(142-219)	**<0.001**
Bioelectrical impedance measurements			
TANITA fat (%), *Median(IQR)*	38.4(33.4-40.1)	37.9(35.4-42)	0.186
TANITA fat (kg), *Mean±SD*	33.47±8.34	37.32±10.17	**0.031**
Body, fat (kg), *Mean±D*	14.06±4.13	15.92±4.89	**0.033**
FSFI scores			
Desire, *Median(IQR)*	3(3-3.6)	3(2.4-3.6)	0.860
Arousal, *Mean±SD*	3.84±1.16	3.73±1.11	0.631
Lubrication, *Median(IQR)*	5.4(4.2-6)	4.8(4.2-5.4)	**0.028**
Orgasm, *Median(IQR)*	4.4(4-5.2)	4.4(3.6-5.2)	0.907
Satisfaction, *Median(IQR)*	5.2(4.4-6)	4.8(4-5.6)	0.139
Pain/discomfort, *Median(IQR)*	5.6(4.8-6)	5.6(4-6)	0.509
Total score, *Median(IQR)*	27.5(24.2-30.3)	26.7(23.1-29.4)	0.336
Beck depression scale scores			
Minimal depression, 0-9, (n, %)	33(45.2)	20(48.8)	0.827
Mild depression, 10-16, (n, %)	29(39.7)	13(31.7)	
Moderate depression, 17-29, (n, %)	9(12.3)	7(17.1)	
Severe depression, 30-63, (n, %)	2(2.7)	1(2.4)	

FSFI: Female Sexual Function Index, MetS: Metabolic syndrome, HDL: High-density lipoprotein, LDL: Low-density lipoprotein; Mann Whitney U test, Independent samples T test, Pearson's chi-squared test, Fisher Exact test, Yates' correction. a,b: Differences between groups are shown in lower case letters.

Anthropometric measurements were analyzed according to the study groups and the results of the analysis were shown. Waist circumference (cm) (102.78 vs 107.1; p=0.034) was found to be significantly higher in obese patients with MetS than in patients with only obesity. HbA1c (%) (5.6 and 5.9; p=0.002), fasting plasma glucose (mg/dl) (91 and 100; p=0.001), triglyceride (mg/dl) (90 and 182; p<0.001)), body fat weight (kg) (14.06±4.13 and 15.92±4.89; p=0.033) was significantly higher in obese patients with MetS than in patients who were only obese; HDL (mg/dl) was found to be significantly lower (56 and 45; p<0.001). TANITA fat weight was 33.47±8.34 kg in obese patients and 37.32±10.17 kg in obese patients with MetS, and this difference was statistically significant (p=0.031). TANITA fat percentage was similar in both groups (p=0.0186). When the scores of the patients from the FSFI scale were analyzed, it was determined that the lubrication score was 5.4 (4.2-6) in obese patients and 4.8 (4.2-5.4) in obese patients with MetS, and this difference was statistically significant (p=0.028). There was no significant difference found between the groups in terms of the total score and scores obtained from other subparameters. Sexual dysfunction was observed in 38.4% of obese patients and 43.9% of obese patients with MetS, but this difference was not statistically significant (p=0.562). The median score obtained from the BDI was determined as 10 for both groups (p=0.981). When the relationships between the presence of sexual dysfunction and other independent variables are examined; there was a difference between the two groups in terms of the scores obtained from the BDI and the scale classification (Table 2). The mean scores of the patients from the BDI were calculated as 11.53±6.58. According to the analysis, minimal depression was found in 53 patients (46.5%), mild depression in 42 patients (36.8%), moderate depression in 16 patients (14%), and severe depression in 3 patients (2.6%)

Table 2. Beck depression scale scores and scale classification according to sexual dysfunction

	Sexual dysfunction, *n(%)*		
Variables (n=114)	**No (n=68)**	**Yes (n=46)**	**p value**
Beck depression scale score, *Median(IQR)*	9(7-12)	14(9-19)	**<0.001**
Beck depression scale scores			
Minimal depression (0-9)	40(58.8)[a]	13(28.3)[b]	**<0.001**
Mild depression (10-16)	24(35.3)[a]	18(39.1)[a]	
Moderate depression (17-29)	4(5.9)[a]	12(26.1)[b]	
Severe depression (30-63)	0(0)[a]	3(6.5)[b]	

Mann Whitney U test, Pearson's chi-squared test, Fisher Exact test.
a, b: Differences between groups are shown in lower case letters

DISCUSSION

Epidemiological data are needed to determine the etiology of diseases, to define risk factors, and to evaluate their prevalence in the population. Oksuz et al. detected FSD in 48.3% of 518 women and reported age, smoking, diet, menopause and marital status as risk factor (13). In another study conducted with 2467 participants, the FSD rate was found to be 46.9% and it was reported that female sexual function was affected by age, low education level, unemployment status, chronic disease, multiparity and menopause (14). Other studies have shown that it is affected by many factors such as chronic diseases, neurotransmitters, sex hormones, age, marital status, income level and mood disorders (15) (16) (17). In our study, it was shown that the group with FSD had a more depressive mood, but no difference was found between the two groups in terms of sociodemographic characteristics defined in the literature. This situation may have been caused by the evaluation of only the patients in the reproductive period in our study.

In a study conducted by Kirchengast et al. in 1990 with 171 postmenopausal female patients without a control group, it was shown that the increase in body mass index (BMI) and subcutaneous fat ratio was significantly associated with sexual reluctance, independent of the hormonal effect (18). On the other hand, Adolfsson et al. did not find a relationship between BMI and FSD in their study. This study was based on a Swedish population of 840 women aged 18-49 (18% overweight, 6% obese) and 426 women aged 50-74 (32% overweight and 11% obese). There was no difference in satisfaction with sexual life between obese and normal weight women in both groups, but a trend was detected in the younger group towards a decrease in sexual satisfaction and sexual desire as weight increased (19). In a study conducted with 5535 women in France, no difference was found between those with normal BMI and those who were obese or overweight in terms of sexual dysfunction. However, sexual desire was observed to be lower in patients with high BMI (p=0.01) (20). Esposito et al. showed that BMI and FSFI score were significantly correlated when they compared 52 women with an FSFI score <23 to 66 women with a score of >23. It has been shown that sexual desire and pain are not correlated with BMI, but arousal, vaginal dryness, orgasm and sexual satisfaction are correlated with BMI (21). In

our study, which focused exclusively on women in the reproductive period, no significant differences in anthropometric measurements were observed between the groups with and without sexual dysfunction. We think that the main reason for this result is that we evaluated only obese patients.

In study by Esposito et al., 120 female patients with MetS and 80 without MetS with similar BMIs were evaluated with the FSFI score. Total FSFI score was found to be significantly lower ($p<0.001$) in the group with MetS. It has been shown that orgasm, arousal and lubrication scores, which are subparameters, are low in women with MetS (21). In their study published in 2010, Kadioglu et al. detected FSD in 32 (50%) of obese patients and 11 (41%) of 27 control cases among patients with similar sociodemographic characteristics, age, and menopausal status. When all subparameters were compared, no difference was found between obese patients and healthy controls. It was shown that all FSFI subparameter scores except lubrication were similar between patients with MetS and patients without MetS, but the median score of the lubrication parameter was found to be significantly lower in patients with MetS ($p=0.04$) (22). Female genital arousal response is a neurovascular event involving genital engorgement, swelling, and lubrication. Vaginal lubrication occurs as a result of increased clitoral, vaginal and labial blood flow. Women with sexual arousal disorder experience problems such as delayed arousal, decreased vaginal/clitoral sensation, difficulty in orgasm, and decreased lubrication. It is thought that these problems may result from insufficiency in the ilio-hypogastric arterial bed (23). We can attribute the reason for the significantly lower lubrication score in the MetS group in our study to the higher incidence of atherosclerotic events. Clitoral and vaginal vascular insufficiency due to atherosclerosis may have led to decreased genital blood flow, decreased muscle relaxation, and decreased response of the genital organs to sexual stimulation.

HTN is one of the main MetS components that cause FSD. In the literature, the FSFI score of patients diagnosed with HTN was found to be significantly lower than those without (24). In our study, 9 of 114 patients were diagnosed with HTN, and we detected FSD (77%) in 7 of these 9 patients. Among the drugs, the main agents causing sexual dysfunction are selective serotonin reuptake inhibitors, they cause orgasmic disorders in female patients (25). Since it is known that antihypertensive drugs such as thiazide diuretics, irbesertan, felodipine, and metoprolol may also cause sexual dysfunction, patients using these drugs were not included in our study (26).

In our study, we wanted to touch on female sexuality, which is quite complex, and its relationship with MetS. From a pathophysiological perspective, MetS would be expected to have an impact on arousal function or pain. We should consider that our sample size may have been insufficient to show the effect of MetS on FSD. This may have caused the relationships between variables to be statistically insignificant. Another limitation of our study is that it was conducted in a single center and it was not a randomized study. Patients with serious comorbidities were not included in the study, so our patient group may not have well reflected those with MetS and obesity in the society. Sexual dysfunctions in the partners of the participants could not be questioned, which is one of the limitations of our study. When comparing the findings of our study with studies in the literature, we should not forget the cultural and social differences between the study populations.

CONCLUSION

In our study, there was no difference in FSFI total scores between obese participants with MetS and only obese participants. No significant difference was found in the other FSFI subparameters except lubrication. We showed that lubrication as a sign of arousal problem is affected by MetS. It was also revealed that patients with sexual dysfunction were in a more depressed mood. Patients with risk factors for FSD such as MetS, obesity, HTN, diabetes mellitus should not be ignored. Thus, it will be possible to prevent the possible effects of FSD on general health.

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RESEARCH ARTICLE

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Evaluation of the Differences in Parameters Obtained from the Computed Tomography Images of the Eyeball and the Structures in the Orbit by Age and Gender

ABSTRACT

Objective: The aim of this study is to show the variation of eyeball and orbital structures according to different age groups and gender.

Method: The study was conducted on computerized tomography (CT) images of 4 age groups: 30-40, 41-50, 51-60, and over 61 years old. The parameters were, the angle between the optic nerve and axis of eyeball (A-Cr2AA), the length of the medial rectus muscle (MRML) and the length of the lateral rectus muscle (LRML) up to the Zinn ring, the thickness of the lens (LT), the length of the optic nerve from the Zinn ring (Cr2L), optic nerve thickness (Cr2T), distance between two eyeballs (BOD) and the others.

Results: As a result of the study, in the comparison of males in four groups, significant difference was found between the groups in LT, Cr2L, A-Cr2AA, MRML parameters in the right eyeball and Cr2L and LRML parameters in the left eyeball ($p<0.05$). In the comparison of females in four groups, significant difference was found between the groups in BOD, LT, Cr2L, LRML, MRML in the right and left eyeball and Cr2T parameter in the left eyeball ($p<0.05$).

Conclusion: As a result of the study, it was determined that age and gender differed in the determined parameters.

Keywords: Bulbus Oculi, Orbit, Computed Tomography, Age and Gender Difference.

Göz Küresi ve Orbitadaki Yapıların Bilgisayarlı Tomografi Görüntülerinden Elde Edilen Parametrelerdeki Farklılıkların Yaş ve Cinsiyete Göre Değerlendirilmesi

ÖZET

Amaç: Bu çalışmanın amacı göz küresi ve yörünge yapılarının farklı yaş gruplarına ve cinsiyete göre değişimini ortaya koymaktır.

Yöntem: Çalışma 30-40, 41-50, 51-60, 61 yaş üzeri 4 yaş grubuna ait bilgisayarlı tomografi (BT) görüntüleri üzerinden gerçekleştirildi. Parametreler, optik sinir ile göz küresi ekseni arasındaki açı (A-Cr2AA), medial rektus kasının uzunluğu (MRML) ve lateral rektus kasının uzunluğu (LRML) Zinn halkasına kadar, lensin kalınlığı (LT), optik sinirin Zinn halkasından itibaren uzunluğu (Cr2L), optik sinir kalınlığı (Cr2T), iki göz küresi arasındaki mesafe (BOD) ve diğerleri idi.

Bulgular: Çalışma sonucunda erkeklerde dört grup karşılaştırıldığında, sağ göz küresinde LT, Cr2L, A-Cr2AA, MRML parametreleri ile sol göz küresinde Cr2L ve LRML parametrelerinde gruplar arasında anlamlı fark bulundu ($p< 0,05$). Kadınlarda dört grup karşılaştırıldığında sağ ve sol göz küresinde BOD, LT, Cr2L, LRML, MRML ve sol göz küresinde Cr2T parametresinde gruplar arasında anlamlı fark bulundu ($p<0,05$).

Sonuç: Araştırma sonucunda belirlenen parametrelerde yaş ve cinsiyetin farklılık gösterdiği belirlendi.

Anahtar Kelimeler: Bulbus Oculi, Orbita, Bilgisayarlı Tomografi, Yaş ve Cinsiyet Farkı

INTRODUCTION

The orbit is a complex and important anatomical structure that contains the eyeball, lacrimal gland, adipose tissue, muscle tissue, vascular and nerve structures. It frequently becomes the subject of studies since it has the potential for many diseases due to its complex structure in the orbit (1). Ocular parameters have a significant of ophthalmology. For example, axial length (AL) (2, 3) in cataract surgery and in the detection of some eye-related clinical pictures, the parameter of length of anterior chamber (ACL) before and during intraocular surgery (4, 5), lens thickness (LT) (6) in the evaluation of lens weight and volume are of great importance and knowing the anatomy of these parameters fully affects the diagnosis, treatment and surgical intervention process of the clinician seriously.

The aim of the surgical intervention for diplopia is to restore the deteriorated parallelism of the eyes. Surgical treatment is provided by strengthening or relaxing the functions of the extraocular muscles. For this reason, it is important to know the radioanatomical structures of the rectus muscles (7). Although the length of vitreous body (VL) parameter is not used much in the clinic, it can provide clinically important information and important data for the literature since it is associated with AL (8).

It has been seen the optic nerve is frequently examined in literature in terms of being a cranial nerve that contains special somatic afferent fibres related to vision, has dense fibre count, complex crosses and has important neighbourhoods. A good knowledge of the anatomy is essential for the surgery of problems that arise in itself or in neighbouring structures (9-11).

Computed Tomography (CT) is based on dividing the projection of the object from different angles into cross-sectional images. Unlike other imaging methods, CT can also display soft tissue differences. Thanks to the developing technology, the fast and easy use of CT facilitates the examination of patients in emergency situations and the quick decision on surgical intervention (12-14).

The relationship of eyeball and structures of the orbit with age has been a matter of interest for many years. As a result of different studies conducted, it was found that the anterior-posterior diameter, transverse diameter, height, LT, ACL, VL, AL parameters of the eyeball vary depending on age (14-16).

The study was undertaken to demonstrate the changes in 13 parameters derived from CT imaging of structures in the eyeball and orbit in different age groups and gender

MATERIALS AND METHODS

Population Sample: The study was designed as 4 groups: 30-40 years old (Group 1), 41-50 years old (Group 2), 51-60 years old (Group 3) and 61 years and older (Group 4) with 20F, 20M in each group. Retrospective CT images of the individuals were used. Individuals who had pathologies such as orbital anomaly, uveitis, cataract, and trauma and those who had undergone surgical intervention were not included in the study.

Multidetector CT Protocol: Images were acquired by a 16-row Toshiba multidetector CT (Aquilion 16; Otawara, Japan) in the Radiology Department of the hospital. We retrospectively screened the images that met our exclusion criteria for different conditions.

Image Analysis: CT images in Digital Imaging and Communications in Medicine format were imported into Horos Medical Image Viewer (Version 3.0, USA). 3D Curved Multiplanar Reconstruction (3D-MPR) was then applied. All images were orthogonalized by determining the line passing through the nasion and inion of the axial, sagittal and coronal images (Figure 1).

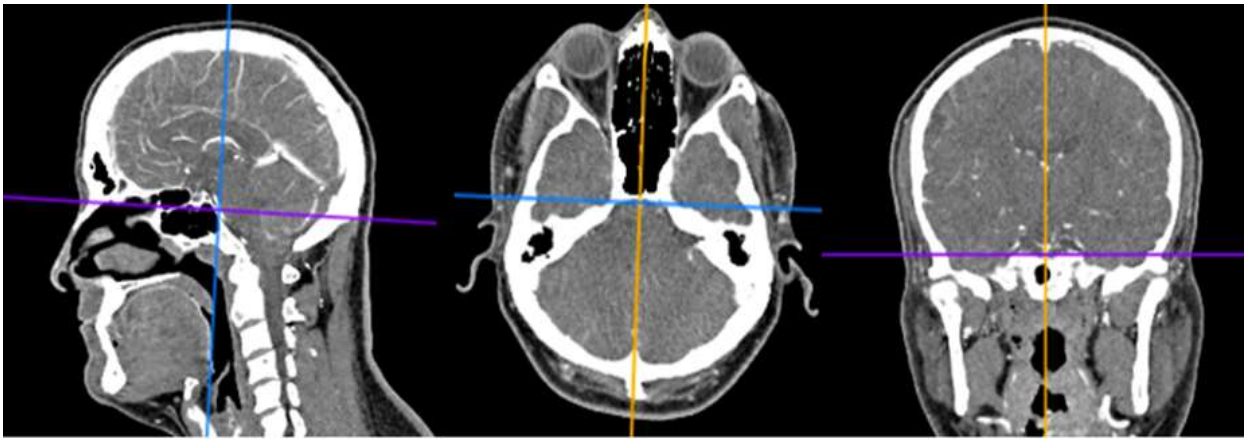

Figure 1. Bringing to the orthogonal plane

The measurement of the width of bulbus oculi (BOW), the length of the axis of eyeball (AL), the angle between the optic nerve and axis of eyeball (A-Cr2AA), the length of the medial rectus muscle (MRML) and the length of the lateral rectus (LRML) up to the Zinn ring, the length of the

anterior chambers of eyeball (ACL), the thickness of the lens (LT), the length of the lens (LL), the length of the vitreous body (VL), the length of the optic nerve from the Zinn ring (Cr2L), optic nerve thickness (Cr2T), distance between orbits (OD), distance between two bulbus oculi (BOD) were made by the same radiologist (Figure 2, 3).

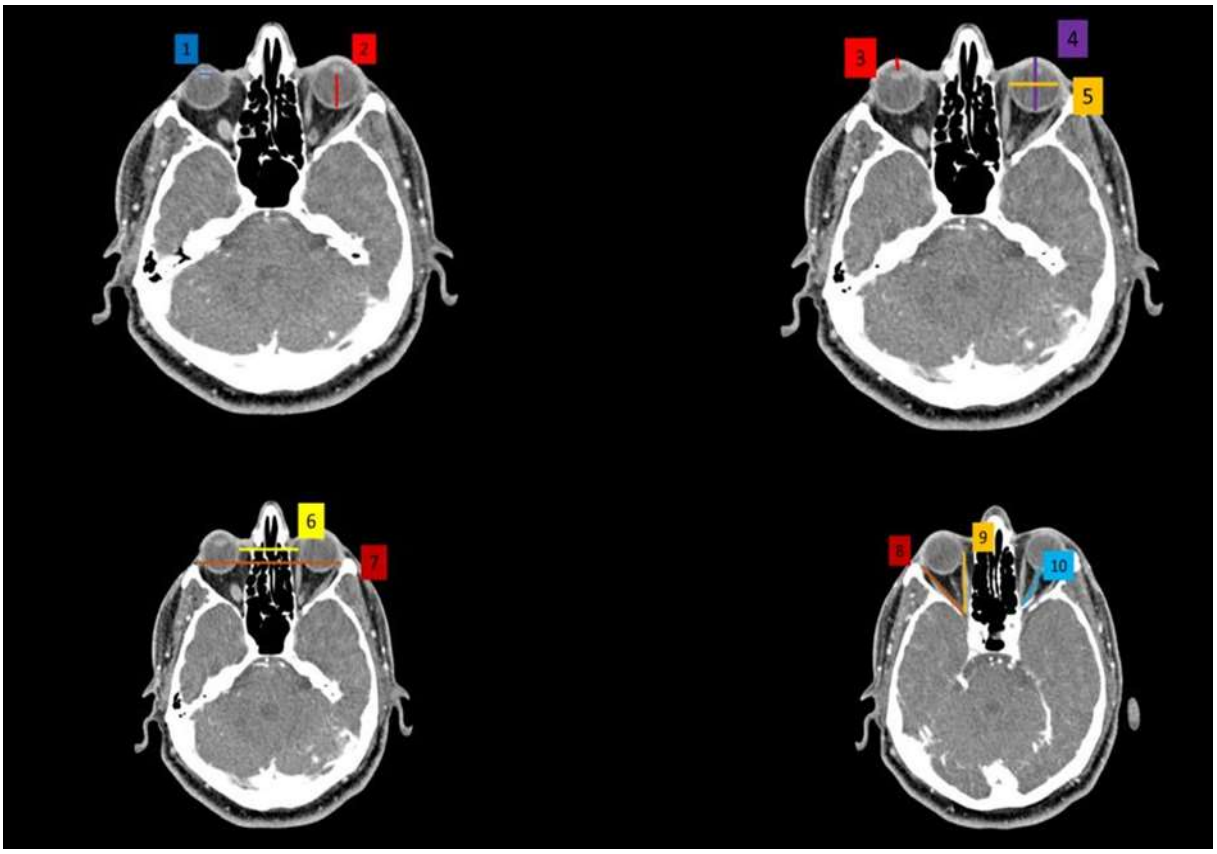

Figure 2. Measurement of LL (1), VL (2), ACL (3), AL (4), BOW (5), BOD (6), OD (7), LRML (8), MRML (9), Cr2L (10) parameters

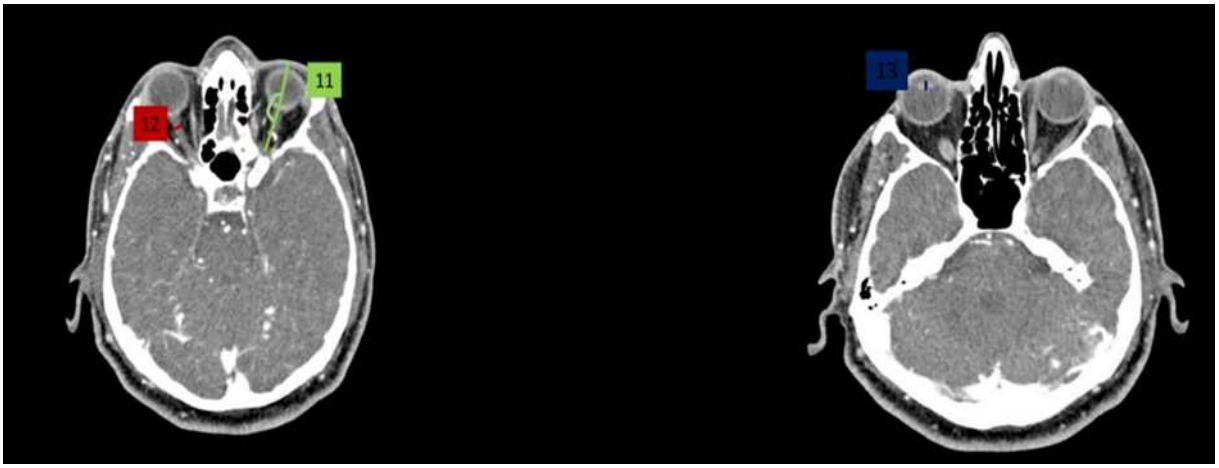

Figure 3. Measurement of A- Cr2AA (11), Cr2T (12), LT (13) parameters

Statistical Analysis: Median, minimum (min) and maximum (max) values of the data were used. Mann-Whitney U test was applied to all data obtained for gender comparison. The relationship between the groups was revealed by Kruskal-Wallis H test. Pairwise Comparison test was preferred as the post-hoc test of Kruskal-Wallis H test. IBM SPSS Statistics 22.0 program running on Windows-based computers was used in the analyses and $p<0.05$ was used as the significance level.

RESULTS

In the study, 13 parameters were evaluated from CT images of 160 people. Table 1 shows the descriptive statistics of the parameters of the right side, which were found to be significant as a result of the comparisons between the genders. No statistically significant difference was found between genders in parameters in group 3 ($p>0.05$).

Table 1. Comparison of the parameters found to be significant in the right eyeball by gender

Parameters	Group	Gender	Median	Minimum	Maximum
Cr2T (mm)	Group 1	Female	3.79	3.10	5.63
		Male	4.65	3.27	6.53
VL (mm)	Group 1	Female	14.72	13.42	16.68
		Male	15.67	14.07	18.59
AL (mm)	Group 2	Female	23.99	21.10	27.03
		Male	25.15	22.54	27.10
Cr2L (mm)	Group 2	Female	21.94	17.79	27.26
		Male	25.80	21.59	35.02
Cr2T (mm)	Group 2	Female	4.13	3.08	6.28
		Male	4.54	3.78	7.71
A- Cr2AA (°)	Group 2	Female	168.60	155.64	176.48
		Male	173.86	164.09	177.81
LRML (mm)	Group 2	Female	37.00	31.12	42.11
		Male	38.44	34.26	48.93
MRML (mm)	Group 2	Female	30.66	27.02	33.20
		Male	33.45	28.38	43.08
LT (mm)	Group 4	Female	3.73	2.19	5.31
		Male	3.29	2.53	4.34
AL (mm)	Group 4	Female	24.23	21.29	25.35
		Male	24.89	22.58	26.79

Table 2 includes the descriptive statistics of the parameters of the left side, which were found to be significant in terms of gender as a result of the comparisons between the genders. It was concluded that the parameters found to be significant were greater in males than females.

Table 2. Comparison of the parameters found to be significant in the left eyeball by gender.

Parameters	Group	Gender	Median	Minimum	Maximum
Cr2L (mm)	Group 1	Female	21.41	15.96	25.08
		Male	23.30	17.63	26.96
Cr2T (mm)	Group 1	Female	3.73	3.16	5.45
		Male	4.77	2.70	5.99
MRML (mm)	Group 1	Female	30.01	25.48	34.52
		Male	32.23	26.42	36.07
ACL (mm)	Group 2	Female	3.69	2.42	4.87
		Male	4.34	2.74	5.37
Cr2L (mm)	Group 2	Female	23.16	18.27	33.34
		Male	25.84	18.98	36.15
Cr2T (mm)	Group 2	Female	4.07	3.31	5.42
		Male	4.88	3.29	6.30
BOW (mm)	Group 2	Female	22.88	21.93	25.46
		Male	23.99	21.10	26.92
LRML (mm)	Group 2	Female	34.69	30.80	43.08
		Male	37.73	28.86	43.72
MRML (mm)	Group 2	Female	31.21	25.35	34.82
		Male	33.48	28.68	42.84
Cr2L (mm)	Group 3	Female	23.09	17.62	29.05
		Male	25.45	20.15	29.29
Cr2T (mm)	Group 3	Female	3.75	2.70	5.39
		Male	4.73	3.46	6.87
MRML (mm)	Group 4	Female	33.31	29.10	40.31
		Male	31.17	28.74	42.31

Table 3 includes the descriptive statistics of the parameters of the midline, which were found to be significant in terms of gender as a result of the comparisons between the genders. It was concluded that the parameters found to be significant were greater in males than females.

Table 3. Comparison of the parameters found to be significant in midline by gender

Parameters	Group	Gender	Median	Minimum	Maximum
BOD (mm)	Group 1	Female	36.88	29.13	40.91
		Male	38.78	32.68	45.75
OD (mm)	Group 1	Female	91.28	81.72	100.99
		Male	92.92	87.88	101.00
BOD (mm)	Group 2	Female	36.44	29.68	41.32
		Male	39.58	35.04	47.15
OD (mm)	Group 2	Female	90.07	83.17	95.08
		Male	95.61	88.04	99.43
OD (mm)	Group 3	Female	89.74	84.52	95.04
		Male	93.17	85.12	99.57

The parameters of male and female individuals in four groups were tested with the Kruskal-Wallis H test and the p values of the parameters that were found to be statistically significant were included ($p<0.05$), (Table 4, 5). Of the parameters in the midline, BOD parameter was found to be statistically significant in females, and it was statistically significantly higher in males than in females ($p=0.04$).

Table 4. Comparison of right eyeball parameters of male and female individuals

Parameters	Gender	p
LT (mm)	Female	**0.00**
	Male	**0.01**
Cr2L (mm)	Female	**0.00**
	Male	**0.00**
A- Cr2AA (˚)	Female	0.68
	Male	**0.03**
LRML (mm)	Female	**0.00**
	Male	0.06
MRML (mm)	Female	**0.01**
	Male	**0.01**

Table 5. Comparison of left eyeball parameters of male and female individuals

Parameters	Gender	P
LT (mm)	Female	**0.02**
	Male	0.06
Cr2L (mm)	Female	**0.00**
	Male	**0.03**
Cr2T (mm)	Female	**0.05**
	Male	0.98
LRML (mm)	Female	**0.00**
	Male	**0.00**
MRML (mm)	Female	**0.00**
	Male	0.07

According to the Pairwise Comparison test, statistically significant difference was found between Group 1 and Group 2 in LT, Cr2L, A-Cr2AA, MRML parameters and between Group 1 and Group 4 in LT parameter ($p<0.05$). Statistically significant difference was found between Group 1 and Group 2 and Group 1 and Group 4 in LRML parameter in the left eyeball ($p<0.05$), (Table 6).

Table 6. Parameters found to be significant in male individuals in the comparison between groups

Right Bulbus Oculi	Groups	p
LT (mm)	1 vs 2	**0.01**
LT (mm)	1 vs 4	**0.04**
Cr2L (mm)	1 vs 2	**0.00**
A- Cr2AA (˚)	1 vs 2	**0.02**
MRML (mm)	1 vs 2	**0.00**
Left Bulbus Oculi	Groups	p
LRML (mm)	1 vs 2	**0.01**
LRML (mm)	1 vs 4	**0.04**

DISCUSSION

This study was conducted to show the differences in the parameters obtained from the structures in the eyeball and orbit according to age and gender. As a result of the study, in the comparisons between genders, significant difference was found in BOD, OD, Cr2T, VL in right eyeball, Cr2T, Cr2L, MRML in left eyeball in Group 1; BOD, OD, AL, Cr2L, Cr2T, A-Cr2AA, LRML, MRML in right eyeball, ACL, Cr2L, Cr2T, LRML, MRML and BOW in left eyeball in Group 2; OD, Cr2L, Cr2T in left eyeball in Group 3 and AL and LT in right eyeball in Group 4 ($p<0.05$). In the analysis conducted according to age groups, significant correlation was found between first and second groups of LT, Cr2L, A-Cr2AA, MRML parameters in the right eyeball, between the first and fourth groups of LT parameter, and between the first and second and first and fourth groups of LRML parameter in the left eyeball ($p<0.05$).

Chan et al. found that the diameter of the optic nerve sheath complex in the right and left eyeball did not differ significantly between males and females (17). Shen et al. measured the diameter of the optic nerve-sheath complex from behind the eyeball using MRI and found as 5.4; while it was found as 4.2 mm in another measured from 7 mm behind the eyeball (18). In a study they conducted on male cadavers with ages between 3 and 69, Tunahan et al. measured Cr2L as 11 mm on the right and as 9.9 mm on the left and they concluded that the difference they found between right and left optical nerves was not statistically significant (19). Cr2T and Cr2L parameters were measured in this study and it was found that the median value of Cr2T parameter varied between 3 and 5 mm, while the median value of Cr2L parameter varied between 21 and 26 mm. We think that this difference is due to the population, different methods used and the number of sample. Statistically significant difference was found between genders in both right and left eyeball of Group 1 and Group 2 ($p<0.05$). While no statistically significant difference was found between genders in the parameters measured in right eyeball in Group 3, statistically significant difference was found between genders as a result of measurements in the left eyeball ($p<0.05$). In values which were found to be statistically significant, Cr2L was found to be longer in males than in females, and Cr2T was found to be thicker in males than in females. When comparison was made in male individuals of the four groups in terms of age, Cr2L in right and left eyeball was found to have significant difference in Group 1, Group 2, Group 3 and Group 4 ($p<0.05$). When comparison was made in male individuals of the four groups in terms of age, statistically significant difference was found in Cr2L in right and left eyeball in Group 1, Group 2, Group 3 and Group 4 ($p=0.00$ in both sides); in addition, statistically significant difference was found in Cr2T in left eyeball between Groups 1,2,3,4 and groups and Cr2L and Cr2T values were found to increase with age ($p=0.05$).

In CT studies on interzygomatic line length, it was found to be between 97 and 101.5 mm in females and between 101 and 103.8 mm in males (20-22). In our study, length of interzygomatic line, which we determined as OD, was 91.28 mm in female and 92.92 mm in male in Group 1, 90.07 mm in female and 95.61 mm in male in Group 2, 89.74 mm in male and 93.17 mm in female in Group 3. These measurements showed that there was a statistically significant difference between genders and females were found to have more OD than males ($p<0.05$). OD parameter was also found to increase with age. The results found support the literature.

Uygur et al. found that the anteroposterior diameter of the right eyeball, the transverse diameter of the right-left eyeball, and the height of the right-left eyeball decreased significantly with age (14). In our study, there was a significant gender difference in the BOW parameter in Group 2 of only the left eyeball ($p=0.04$). We think that this difference is due to the number of samples.

Tuncer et al. investigated age- and sex-related changes in ocular biometric data from healthy eyes, and it was found that ACL decreased as age increased (15). In their study, Özdemir et al. found the ACL parameter to be statistically significant in terms of gender and higher in males ($p<0.05$) and reported that ACL and LT parameters in healthy eyes changed with advancing age, while VL and AL parameters did not change according to age. When each group was compared separately, no significant gender-related difference was found in age groups (16). In our study, statistically significant difference was found between genders in the AL parameter in the right eyeball in Group 2 and in LT and AL parameters in Group 4. AL was found to be longer in males, while LT was found to be longer in females ($p<0.05$). As a result of measurement in male individuals in four groups, statistical significance was found in right eyeball, LT parameter, Group 1, 2, 3 and 4, while as a result of measurement in female individuals in four groups, statistical significance was found in LT parameter in right-left eyeball, in Group 1, 2, 3 and 4 and LT parameter was found to increase in left eyeball in terms of age ($p<0.05$). These results found support the literature.

Mean length of lateral rectus muscle has been reported to be 40 mm (23). Kocabıyık et al. measured it as 36.38 mm on average in right eyeball, as 37.01 on average in left eyeball. No statistically significant difference was found in another study conducted between right and left eyes ($p\geq0.05$) (24). Our study measured the length of lateral rectus and medial rectus muscles from Zinn ring. The median values of LRML and MRML parameters were found to vary between 30 mm and 38 mm. We think that this difference is due to the

population and sample size. In Group 1, the MRML parameter in the left eyeball was found to be longer in males than in females. In group 4, the MRML parameter in the left eyeball was found to be longer in females than in males. In group 2, LRML and MRML parameters in the right-left eyeball were found to be longer in males ($p<0.05$).

CONCLUSION

The limited number of images in the age groups included in the study is a limitation of this study. We believe that the age- and sex-related differences obtained in our study will contribute to the understanding of eye and orbital morphometry in basic and forensic sciences and in the surgical intervention at different ages in clinical sciences.

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Ethics Committee Approval: This study was conducted with the 2021/459 numbered decision of Karabük University Non-interventional Clinic Research Ethics Committee.

Informed Consent: The study is a retrospective study and was carried out by scanning images in the hospital archive system.

Peer-review: Externally peer-reviewed.

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RESEARCH ARTICLE

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Evaluation of the Relationship between Sociodemographic Factors, COVID-19 Fear Levels and Vaccination Status in Patients Applying to Family Medicine Outpatient Clinics in a University Hospital

ABSTRACT

Objective: This study has aimed to examine the relationship between sociodemographic factors and COVID-19 fear levels in patients aged 18-65 years and their COVID-19 vaccination status.

Method: The study sample consists of 866 patients aged 18-65 who applied to the Family Medicine Polyclinics of a university hospital between 01.03.2022 and 01.06.2022. Personal Information Form and Fear of COVID-19 Scale were used to collect data. As the score obtained from the scale increases, the level of fear of COVID-19 increases. The analyzes of the study were done in SPSS 21.0 package program. Kruskal Wallis test and Mann Whitney U test were used for comparisons.

Results: 52.3% of the participants in the study were women and the mean age was 36.59±12.32 years. Compared to men, women's fear of coronavirus was statistically significantly higher. The coronavirus fear levels of those who received at least one dose of vaccine compared to those who did not get vaccinated at all and those who received more doses of vaccines compared to those who received only one dose were found to be statistically significantly higher.

Conclusion: As the level of fear of COVID-19 increased, it was determined that the vaccination behavior of individuals was positively affected. COVID-19 is a vaccine preventable disease. With vaccination in all healthcare institutions, it will be possible to prevent morbidity and mortality, as well as economic and social losses that may be caused by the COVID-19 pandemic.

Keywords: COVID-19, Pandemic, Fear, Vaccine.

Bir Üniversite Hastanesinde Aile Hekimliği Polikliniklerine Başvuran Hastalarda Sosyodemografik Faktörler, COVID-19 Korku Düzeyleri ve Aşılanma Durumu Arasındaki İlişkinin Değerlendirilmesi

ÖZET

Amaç: Bu çalışmada 18-65 yaş arası hastalarda sosyodemografik faktörler ve COVID-19 korkusu düzeylerinin, COVID-19 aşılanma durumu ile ilişkisini incelemek amaçlanmıştır.

Yöntem: Çalışma örneklemi bir üniversite hastanesinin Aile Hekimliği Polikliniklerine 01.03.2022-01.06.2022 tarihleri arasında başvuran 18-65 yaş arası 866 hastadan oluşmaktadır. Veri toplamada Kişisel Bilgi Formu ve COVID-19 Korkusu Ölçeği kullanıldı. Ölçekten alınan puan arttıkça COVID-19 korkusu düzeyi yükselmektedir. Çalışmanın analizleri SPSS 21.0 paket programında yapıldı. Karşılaştırmalarda Kruskal Wallis testi ve Mann Whitney U testi kullanıldı.

Bulgular: Çalışmaya katılanların %52.,3'ü kadındı ve yaş ortalaması 36.,59±12.,32 yıldı. Erkeklerle karşılaştırıldığında kadınların koronavirüs korkusu düzeyi istatistiksel olarak anlamlı düzeyde daha fazlaydı. Hiç aşı yaptırmayanlarla karşılaştırıldığında en az bir doz aşı yaptıranların ve sadece bir doz aşı yaptıranlarla karşılaştırıldığında, daha fazla doz aşı yaptıranların koronavirüs korkusu düzeyleri istatistiksel olarak anlamlı düzeyde daha yüksek bulundu.

Sonuç: COVID-19 korkusu düzeyi yükseldikçe bireylerin aşı olma davranışlarının pozitif yönde etkilendiği belirlendi. COVID-19 aşı ile önlenebilir bir hastalıktır. Sağlık hizmeti verilen tüm kurumlarda aşılama ile COVID-19 pandemisinin neden olabileceği morbidite, mortalitenin yanı sıra ekonomik ve sosyal kayıpların önüne geçilmesi mümkün olacaktır.

Anahtar Kelimeler: COVID-19, Pandemi, Korku, Aşı

INTRODUCTION

Declared as a pandemic by the World Health Organization (WHO) on March 11, 2020; COVID-19 has caused fear and anxiety among people worldwide (1,2). The lack of a definitive treatment for the infection has led to uncertainty; this has increased the fear levels of societies towards COVID-19 (3). People resort to protective measures such as masks, distance, and hygiene to protect themselves from the COVID-19 epidemic (4). One of the best ways to prevent the epidemic is to develop and distribute the vaccine. The number of people vaccinated here is also significant. Vaccines not only limit the signs and symptoms of COVID-19 infection; but also help prevent transmission (4). Vaccination against all diseases, especially COVID-19; it is the best cost-effective method for providing herd immunity against infections and for the development of healthy communities (5). The aim of this study is to evaluate the relationships between the behaviors of being vaccinated in individuals during the COVID-19 pandemic and their fear levels towards the transmission of COVID-19. In addition, it was aimed to examine the relationship between these parameters and sociodemographic factors and to determine the factors affecting the COVID-19 vaccine behavior. We think that these factors can make a supportive contribution to the development of vaccination policies.

Coronaviruses are enveloped, single-stranded, positive polarity Ribonucleic Acid (RNA) viruses. The COVID-19 virus causes symptoms such as runny nose, dry cough, and shortness of breath in patients by binding to the Angiotensin Converting Enzyme-2 (ACE-2) receptors in the respiratory system mucosa (6). COVID-19 infection can be overcome with asymptomatic or mild symptoms; pneumonia, septic shock, multi-organ dysfunction and eventually mortality may occur (7). The gold standard in diagnosis is Polymerase Chain Reaction (PCR) test (8). Many drugs mainly used in different indications such as hydroxychloroquine, favipiravir, remdesivir, lopinavir/ritonavir have been tried in treating COVID-19 with special permissions (9). Similar to other viral infection treatments, it is recommended to start antiviral therapy as early as possible. However, there is no antiviral agent whose safety and efficacy have been definitively proven (10). Vaccination is the most effective way to end the pandemic, as it was in the past. Since the end of 2020, different vaccines have been developed and some of them have been approved for emergency use. These are whole virus vaccines, protein-based vaccines, viral vector vaccines and nucleic acid vaccines. Among the vaccines used in our country, Sinovac and Turkovac vaccines are complete virus vaccines; BioNTech is a nucleic acid vaccine (11).

COVID-19 has caused the world to be perceived as an uncertain, confused and volatile place; fear of this infection has arisen. The thought of being unable to access healthcare facilities, long quarantine periods, constant exposure to media news about the pandemic, illness or death of relatives have caused a serious increase in anxiety and fear about COVID-19 (12).

MATERIALS AND METHODS

Study Design and Sample Size: This research is a descriptive cross-sectional study. Considering the distribution of vaccine numbers, 866 patients between the ages of 18-65 who applied to Eskisehir Osmangazi University Health Practice and Research Hospital Family Medicine Polyclinics between 01.03.2022 and 01.06.2022 were included in the study. This article was produced from the specialty thesis in medicine. Approval was obtained from Eskisehir Osmangazi University Non-Interventional Clinical Research Ethics Committee with the decision number 28 on 28.09.2021. Also necessary permissions were obtained from the Republic of Turkey Ministry of Health and the responsible author of the scale used. The questionnaire form of the study was applied to the patients by face-to-face interview method.

Data Collection Tools: Participants were asked in the personal information form; age, gender, education level, marital status, working status, presence of chronic and/or psychological illness, status of being vaccinated against COVID-19, if so how many doses, whether or not she/he had COVID-19 infection, how she/he survived, his/her relative whether or not had the disease, and if she/he had, how did she/he end up. The participants were directed to Fear of COVID-19 Scale along with the personal information form. The Fear of COVID-19 Scale was developed by Ahorsu (2020) and his friends to determine the level of fear of COVID-19 experienced by individuals during the pandemic period. The Turkish validity and reliability study of the scale was carried out by Bakioğlu, Korkmaz, Ercan. In the Turkish validity and reliability study, the Cronbach Alpha reliability coefficient of the scale was found to be 0.82. The Fear of COVID-19 Scale is a one-dimensional 5-point Likert-type scale consisting of 7 items (1: Strongly Disagree, 5: Strongly Agree). There is no reverse item in the scale. The total score obtained from all items of the scale determines the level of coronavirus fear experienced by the individual. A minimum of 7 and a maximum of 35 points can be obtained from the scale. An increase in the score obtained from the scale means an increase in the level of fear of COVID-19 (13).

Statistical Analysis of Data: The analyzes of the study were made in the SPSS 21.0 package program. Categorical variables were summarized as numbers, percentages, continuous numerical variables as mean±standard deviation, and median

(min–max) values. Chi-square test and Fisher's exact test were used to compare categorical variables between groups. Conformity of continuous numerical variables to normal distribution was checked with the Shapiro Wilk test. It was determined that the numerical data were not normally distributed among the categories. Mann-Whitney U test was used for comparison of continuous numerical variables between two groups, and Kruskal Wallis test was used for comparison between more than two groups. In determining the groups from which statistical significance originates, p values are presented by making Bonferroni correction. The relationship of continuous numerical variables with each other was checked with the Spearman Correlation test. Statistically, p value less than 0.05 was accepted as the limit of significance.

RESULTS

Descriptive Features of the Cases:866 patients between the ages of 18-65 who applied to family medicine outpatient clinics were included in the study. 52.3% of the patients were female and the mean age was 36.59±12.32 years. 68.3% of the individuals had a bachelor's degree or higher, 58.2% were married, 71.9% were working, and 17.9% had at least one chronic or psychological illness.

Table 1. Some sociodemographic characteristics and chronic disease status of the participants

Variables	Number	Percent
Gender		
Male	413	47.7
Female	453	52.3
Education level		
Illiterate	2	0.2
Primary school	33	3.9
Middle school	52	6.0
High school	91	10.5
Associate degree	96	11.1
Undergraduate and above	591	68.3
Marital status		
Single	362	41.8
Married	504	58.2
Working Status		
Working	623	71.9
Not working	243	28.1
Chronic or psychological illness		
Yes	155	17.9
None	711	82.1

When the vaccination status was examined, it was seen that 89% of the participants had at least one dose, and 10.5% had 4 doses or more. When examining the situations of affected by COVID-19 infection, 31.9% of the people stated that they, 83.2% of a relative had COVID-19, 2.2% of them stated that they were hospitalized, 7.5% of them stated that their relative died due to COVID-19.

Table 2. Participants' experiences with COVID-19 infection and COVID-19 vaccine

Variables	Number	Percent
COVID-19 vaccine		
At least one dose vaccinated	770	89.0
Never done	96	11.0
Number of COVID-19 vaccine doses		
1	49	5.7
2	463	53.5
3	167	19.3
4 and above	91	10.5
COVID-19 infection		
Get the illness	276	31.9
Not get the illness	590	68.1
How she/he survived COVID 19		
At home	257	29.7
At hospital	19	2.2
The status of relative get the illness		
Don’t know	24	2.8
Yes	721	83.2
None	121	14.0
How did his/her relative survive the illness?		
At home	551	63.9
At hospital	84	9.6
Died	66	7.5
In the intensive care unit	20	2.2

Conclusions on Fear of Coronavirus: Compared to men, women's fear of coronavirus was statistically significantly higher ($p<0.001$). There was no statistically significant correlation between the age of the subjects and their FVC-19S score ($r=-0.043$, $p=0.215$). No correlation was found between education level, marital status, employment status, presence of chronic disease and FCV-19S score ($p>0.05$).

Those who had at least one dose of vaccinated compared to those who had never been vaccinated and those who had only one dose of vaccinated had a statistically significant higher FCV-19S score ($p<0.001$). Among those whose relatives had COVID-19, compared to those whose relatives had the disease at home or in the hospital, the FCV-19S score of those whose relatives died was statistically significantly higher ($p=0.001$).

Table 3. Comparison of COVID-19 fear level according to some sociodemographic characteristics and chronic disease status of the participants

Variables	FCV-19S Score		
	Mean±SD	Median (min-max)	*p*
Gender			
Male	14.71±4.15	14 (8-35)	**<0.001**
Female	17.25±5.07	17 (8-35)	
Education level			
Illiterate	22.5±10.61	22.5 (15-30)	0.216*
Primary school	16.33±5.04	17 (8-28)	
Middle school	15.35±4.49	14.5 (8-32)	
High school	15.24±4.81	14 (8-30)	
Associate degree	15.65±4.55	15 (8-30)	
Undergraduate and above	16.23±4.85	15 (8-35)	
Marital status			
Single	16.19±4.81	15 (8-35)	0.322
Married	15.92±4.83	15 (8-35)	
Working status			
Working	15.88±4.62	15 (8-35)	0.330
Not working	16.42± 5.31	15 (8-35)	
Chronic or psychological illness			
Yes	16.39±5.04	16 (8-35)	0.366
None	15.95±4.77	15 (8-35)	

*Kruskal Wallis test was used for comparisons. Mann Whitney U test was used for other comparisons.

Table 4. Comparison of COVID-19 fear level according to participants' experiences with COVID-19 infection and vaccine

Variables	FCV-19S Score		
	Mean±SD	Median (min-max)	*p*
COVID-19 vaccine			
Never vaccinated	14.1±4.47	12 (8-30)	**<0.001**
At least 1 dose vaccinated	16.27±4.81	15 (8-35)	
Number of COVID-19 vaccine doses			
1	14.4±3.49	13.5 (10-24)	**<0.001***
2	16.55±5.01	16 (8-35)	
3	16.39±4.81	15 (8-30)	
4 and above	15.68±4.13	15 (9-25)	
COVID-19 infection			
Not get the illness	16.12±4.68	15 (8-35)	0.167
Get the illness	15.84 ± 5.12	15 (8-35)	
How she/he survived COVID 19			
At home	15.7±5.06	15 (8-35)	0.102
At hospital	17.68±5.63	17 (10-30)	
The status of relative get the illness			
Don't know	17.78±5.11	17 (11-35)	0.108*
None	16.37±4.85	15 (8-31)	
Yes	15.92±4.8	15 (8-35)	
How did his/her relative survive the illness?			
At home	15.71±4.64	15 (8-32)	**0.001***
At hospital	15.22±4.25	14 (8-30)	
Died	18.38±5.87	18 (9-35)	
In intensive care unit	16.1±5.36	14.5 (10-29)	

Comparison of Sociodemographic Factors and Vaccination Status: 87.4% of female participants and 90.6% of male participants received at least 1 dose of vaccine. The frequency of vaccination among primary school graduates was 90.9%, similar to those with a bachelor's degree or higher (91%). In addition, 2 illiterate people participated in our study, and both of them had at least 1 dose of vaccine (100%, p=0.015). When we excluded 2 illiterate people from the evaluation, no significant relationship was found between education level and vaccination status. Compared with married, singles (p<0.001); vaccination frequency among working people were statistically significantly higher (p=0.015) compared to non working people.

Table 5. COVID-19 vaccination status according to sociodemographic characteristics

	COVID-19 vaccine				
	At least one dose		Never done		
Variables	**Number**	**Percent**	**Number**	**Percent**	***p***
Gender					
Male	374	90.6	39	9.4	0.142
Female	396	87.4	57	12.6	
Education level					
Illiterate	2	100.0	0	0.0	**0.015**
Primary school	30	90.9	3	9.1	
Middle school	40	76.9	12	23.1	
High school	79	86.8	12	13.2	
Associate degree	80	83.3	16	16.7	
Undergraduate and above	538	91.0	53	9.0	
Marital status					
Single	338	93.4	24	6.6	**<0.001**
Married	432	85.7	72	14.3	
Working Status					
Working	564	90.5	59	9.5	**0.015**
Not working	206	84.8	37	15.2	
Chronic or psychological illness					
Yes	140	90.3	15	9.7	0.538
None	630	88.6	81	11.4	

Row percentage is given. Chi-square test was used for comparisons.

Compared to men, women's fear of coronavirus was statistically significantly higher (p<0.001). Those who had at least one dose of vaccinated compared to those who had never been vaccinated and those who had only one dose of vaccinated had a statistically significant higher FCV-19S score (p<0.001) (Figure 1). Among those whose relatives had COVID-19, compared to those whose relatives had the disease at home or in the hospital, the FCV-19S score of those whose relatives died was statistically significantly higher (p=0.001) (Figure 2).

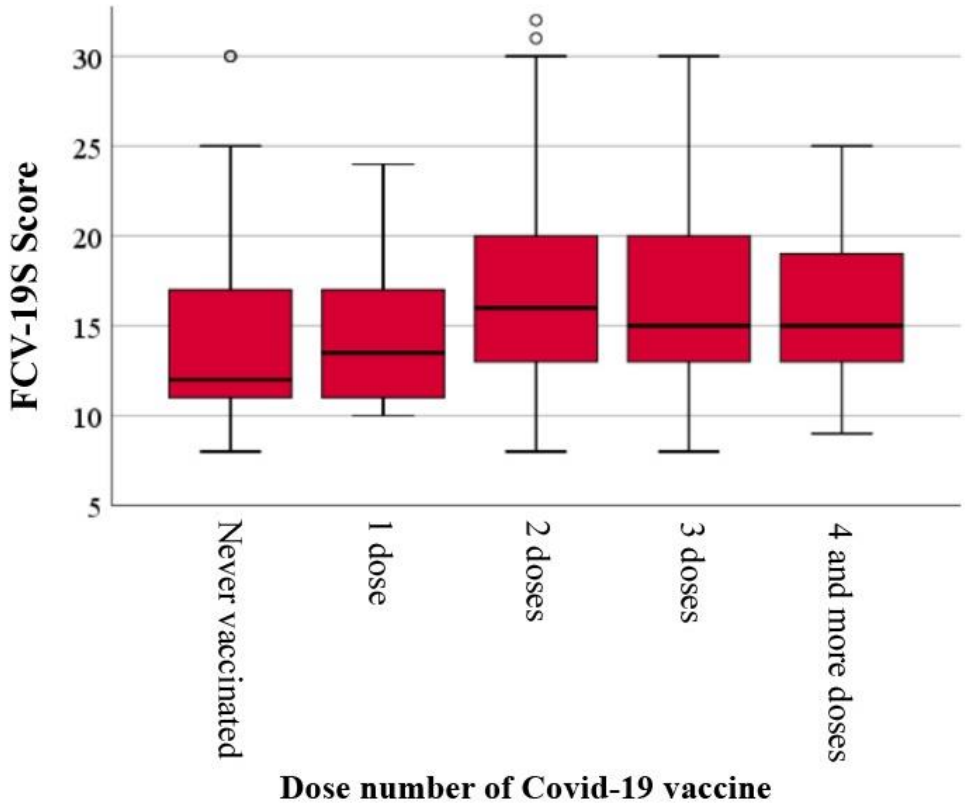

Figure 1. Graphical representation of the distribution of the number of COVID-19 vaccine doses and FCV-19S scores of the participants

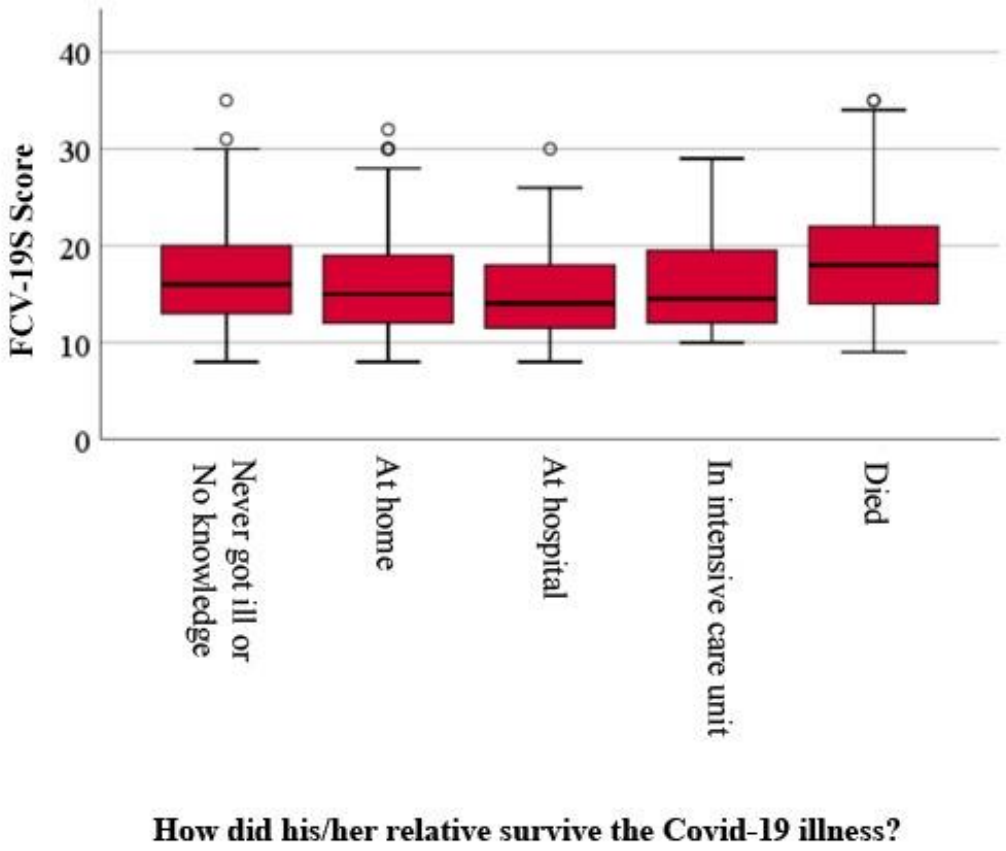

Figure 2. The relationship between the outcome of the disease of the relatives of the participants who had COVID-19 and the FCV-19S score

DISCUSSION

Since people between the ages of 18-65 are the population that contributes to production and provides economic value to the country, individuals from this age group were included in our research. In addition, since most of the people between the ages of 18-65 are involved in education and working life; it is more risky than childhood and old age in terms of being exposed to the transmission of COVID-19 or causing it to be transmitted to others. Therefore, vaccination of this age range is very important for the control of the pandemic. According to the results related to the fear of coronavirus; women had higher coronavirus fear levels than men. Although men have a higher risk of death due to this infection compared to women, women's fear of coronavirus is higher than men (14-17). When similar studies in the literature were examined, it was seen that they were in line with the results of this study. In the study, the level of fear of COVID-19 of those who lost a relative due to coronavirus was found to be significantly higher than those whose relative had the disease at home or in the hospital. Similar to the results obtained; in an article published in The Journal of Social Science, among university students; The COVID-19 fear levels of those whose relatives died due to coronavirus were found to be significantly higher than those of the students who did not experience a loss due to the same reason (18). Single people compared with married people and working people compared with non-working people were more likely to get at least 1 dose of the vaccine. The number of COVID-19 vaccination doses varied statistically significantly according to marital status and working status, similar to vaccination status. In a study conducted among healthcare professionals in China; being single was found to be associated with higher vaccine acceptance (19). In a study by Malik et al. in the USA, it was determined that working people were more likely to accept any COVID-19 vaccine than those who did not work (20). Based on the results of the study, it can be thought that the fact that people who take an active role in working life are more exposed to crowded environments and that single people do not have someone to care for them when they get sick may cause more vaccination behavior. Compared to those who have never been vaccinated, the fear of coronavirus was found to be higher in those who had at least 1 dose of vaccination. In addition, compared to those who received only 1 dose of vaccine, the fear of coronavirus was found to be higher in those who received more doses. According to the results of this study, as the level of fear of COVID-19 increases, the doses of vaccination against COVID-19 increase; it can be said that those who have

never been vaccinated decide to be vaccinated. In the study of Türktemiz et al., it was found that individuals' fears of COVID-19 caused positive vaccination attitudes; in the study of Bendau et al., subjective anxiety and fear were found to be important in vaccine acceptance (4,21). The available literature supports the results of this research.

CONCLUSION

The most important result obtained in this study; as the level of fear of COVID-19 rises, the vaccination behavior of individuals is positively affected. As the level of fear of COVID-19 rises; it can be said that people who have never been vaccinated decide to be vaccinated, while the vaccination doses of vaccinated people increase. Being single compared to being married; It was determined that being working can increase vaccine acceptance compared to not working. According to the results of the research; Women's fear of coronavirus was found to be higher than men. In addition, it was determined that losing a relative due to COVID-19 may cause the fear of COVID-19 to rise.

To effectively combat the pandemic; more informative studies on COVID-19 infection and vaccine should be organized. Public service announcements and social campaigns can be organized by the Ministry of Health to raise awareness on this issue. In addition, the COVID-19 pandemic can be limited by facilitating access to the vaccine by institutions and organizations affiliated with the Ministry of Health and by providing access to cheap, fast and reliable diagnostic tests in case of infection symptoms. The society's responsibility in this regard is to trust the health authorities; is to comply with the preventive measures implemented throughout the world and the country. COVID-19 can be prevented by vaccination and family physicians play an important role in vaccination. In particular, institutions providing primary health care bear the burden of vaccination. In addition to the morbidity and mortality that may develop secondary to COVID-19 infection with vaccination in all institutions providing health services, especially in primary care; it will be possible to prevent economic and social losses.

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CASE REPORT

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A Rare Case of Signet Ring Cell Lymphoma and Review of the Literature

ABSTRACT

Signet ring cell lymphoma (SRCL) is a non-Hodgkin's lymphoma with a very rare variant. Although this morphology is frequently seen in follicular lymphoma, it can also be observed in the group of diffuse large B-cell lymphomas. A seventy-six year old woman with known diagnosis of gastric adenocarcinoma, tubular type, moderately differentiate presented with a mesenteric lymphadenopathy with high FDG uptake (SUVmax: 21.3) in PET/CT during follow-up. A tru-cut biopsy was performed for histopathological diagnosis. Diffuse infiltrative singet ring neoplastic cells showed negativity for PanCK, CK7, CK20, S100, SMA, calretinin and vimentin. The panel was then expanded to include SRCL, a rare variant of lymphoma. Additional immunohistochemical evaluation revealed positivity for CD20, CD19, PAX-5 and Bcl-2. Ki-67 proliferation index was about 80%. CD3, CD30, Myc, Bcl-6, ALK, Cyclin-D1, CD23, CD10, CD21, and MUM-1 were negative. EBER was also negative by chromogen in situ hybridization (CISH). Based on these data, diffuse large B-cell lymphoma (DLBCL) was considered. We herein reported a case of signet ring cell lymphoma discussed its clinical and morphological features with regard to the literature.

Keywords: Signet Ring Cell, Lymphoma, Diffuse Large B-Cell Lymphoma, Post Transplant.

Nadir Bir Taşlı Yüzük Hücreli Lenfoma Olgusu ve Literatürün Gözden Geçirilmesi

ÖZET

Taşlı yüzük hücreli lenfoma, Hodgkin dışı lenfomaların oldukça nadir görülen bir varyantıdır. Bu morfoloji sıklıkla foliküler lenfomada görülmekle birlikte diffüz büyük B hücreli lenfomalar grubunda da görülebilmektedir. Bilinen tübüler tip mide adenokarsinomu tanısı olan 76 yaşında kadın hasta, takip sırasında PET/BT'de FDG tutulumu yüksek (SUVmax: 21,3) mezenterik lenfadenopati ile başvurdu. Histopatolojik tanı için tru-cut biyopsi yapıldı. Diffüz infiltrasyonlu taşlı yüzük görünümündeki neoplastik hücreler PanCK, CK7, CK20, S100, SMA, kalretinin ve vimentin için negatiflik gösterdi. Panel daha sonra nadir bir lenfoma çeşidi olan SRCL'yi içerecek şekilde genişletildi. Ek immünhistokimyasal incelemede CD20, CD19, PAX-5, Bcl-2'nin pozitif olduğu ve Ki-67 proliferasyon indeksinin %80 civarında olduğu görüldü. CD3, CD30, Myc, Bcl-6, ALK, Cyclin-D1, CD23, CD10, CD21, MUM-1 negatifti. EBER, kromojen in situ hibridizasyon (CISH) ayrıca negatifti. Bu verilere dayanarak diffüz büyük B hücreli lenfoma (DLBCL) düşünüldü. Burada taşlı yüzük hücreli bir lenfoma olgusu sunulmuş olup morfolojik ve klinik özelliği literatür eşliğinde tartışılmıştır.

Anahtar Kelimeler: Taşlı Yüzük Hücreli, Lenfoma, Diffüz Büyük B Hücreli Lenfoma, Transplantasyon Sonrası

INTRODUCTION

Signet ring cell morphology consists of cells with transparent cytoplasm and irregular nuclei that are pushed aside. Signet ring cell morphology is seen in many types of cancer such as melanoma (1-4), adenocarcinoma (5-7), mesothelioma (8,9), multiple myeloma (10,11), lymphoma, liposarcoma (7).

SRCL is a very rare morphologic variant of non-Hodgkin's lymphoma. In the literature, this variant is generally considered to be a follicular lymphoma. In some case reports (12, 13), this morphologic appearance is also present in DLBCL, although more rarely. Here, we presented a case of lymphoma with signet ring cell morphology and discussed with the literature.

CASE REPORT

Our case was seventy-six-year-old female patient with a history of chronic kidney disease (renal transplant 12 years ago), type 2 diabetes mellitus, primary hypertension, and a history of total abdominal hysterectomy and bilateral salpingo-oophorectomy due to endometrial carcinoma 20 years ago. A biopsy taken from the skin of the chin 2 years ago was reported as squamous cell carcinoma. Since it was an early stage squamous cell carcinoma, no specific treatment was clinically initiated.

The patient was referred to an external center with complaints of dyspepsia, heartburn and abdominal pain that started 2 years ago. The endoscopic biopsy result was interpreted as chronic inactive atrophic gastritis, intestinal metaplasia and mild to moderate dysplasia. Due to gastrointestinal bleeding, a biopsy performed 1 year ago at an external center revealed gastric adenocarcinoma, tubular type, moderately differentiated. After submucosal dissection, PET/CT showed a 1 cm lymphadenopathy with SUVmax: 8 in the mesenteric fat plane in the descending colon and was interpreted as a metastasis. When the patient returned for follow-up, the March 2024 PET/CT showed a mass lesion with an SUVmax of 15.2 in the jejunal wall and a 4 cm diameter lymphadenopathy with an SUVmax: 21.3 in the mesenteric fat planes, which was interpreted as a metastasis (***Figure 1***). Due to the progressive nature of the patient's disease, a tru-cut biopsy was performed for the diagnosis of lymphadenopathy. A large number of cells with signet ring morphology were observed in the biopsy specimen, and PanCK, CK7, CK20, S100, SMA, vimentin, and calretinin were interpreted as negative by immunohistochemistry. Considering the possibility of a rare SRCL, a lymphoma panel was performed. In the immunohistochemical panel, CD20, PAX5, CD19, Bcl-2 were interpreted as positive and the Ki-67 proliferation index was evaluated as 80% (***Figure 2 A-F***). CD3, CD10, ALK, Cyclin-D1, Bcl-6, MUM-1, CD23, CD21, CD30, Myc were interpreted as negative. CISH performed on the patient was negative for EBER. Based on the morphologic findings, immunohistochemistry, and CISH, the patient was diagnosed with DLBCL. The patient was then referred to in our hematology clinic. Hematology accepted a different primary tumor and initiated the R-CHOP protocol.

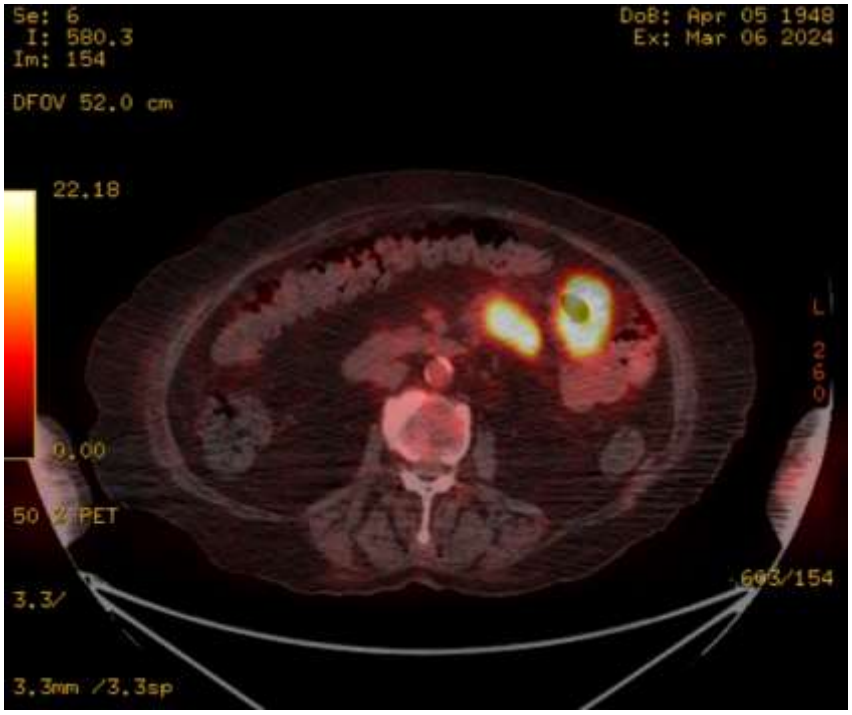

Figure 1. The patient has lymphadenopathies with SUVmax: 21.3 on PET-CT.

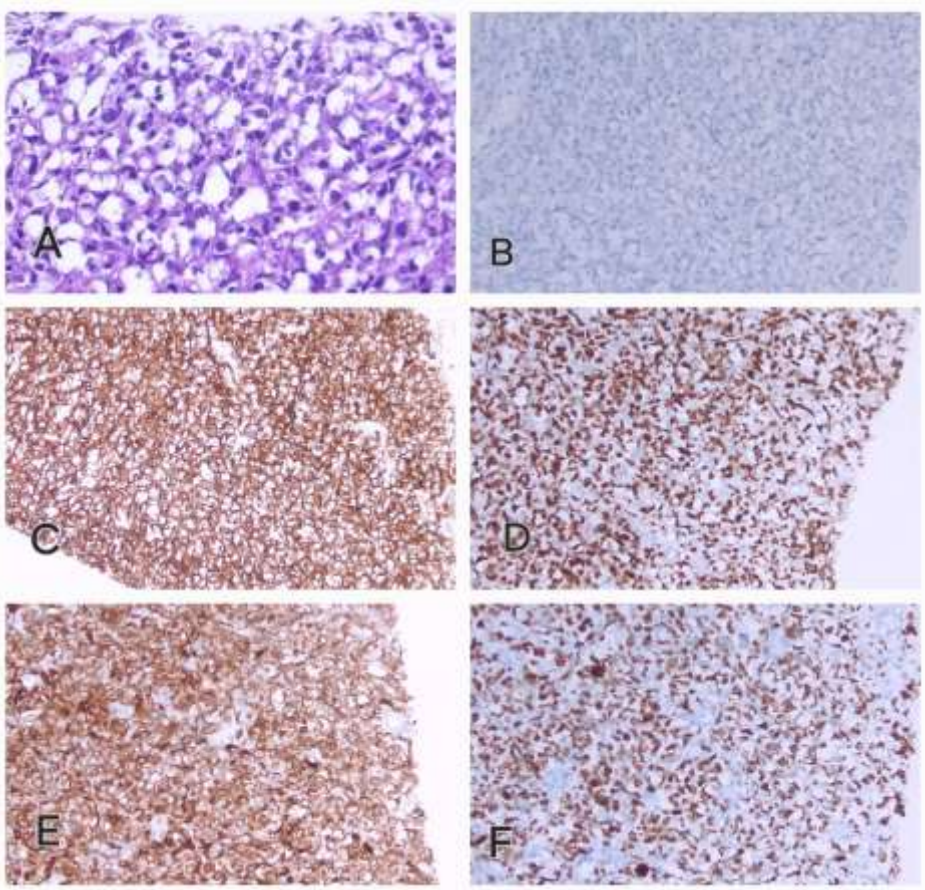

Figure 2 A= High magnification (H&E, ×200) of cells with signet ring cell morphology., B= PanCK-negative in tumor cells (x100), C= CD20 positive in signet ring cells (x100), D= PAX-5 positive in tumor cells (x100), E= Bcl-2 positive in cells with the morphology of a signet ring (x100), F= Ki-67 proliferation index is about 80% (x100).

DISCUSSION

Signet ring cell morphology can be seen in many types of cancer. Although adenocarcinoma is the first to come to mind for malignant lesions of the cell group with this morphology, lymphomas may rarely have this cell morphology and this possibility should be considered.

SRCL has been reported in most cases to belong to the subtypes of non-Hodgkin lymphoma. Diagnoses to date have included follicular lymphoma, but also small lymphocytic lymphoma(14), lymphoplasmacytic lymphoma, MALT-associated marginal zone lymphoma, diffuse large B-cell lymphoma, T-cell lymphoma(15,16), anaplastic large cell lymphoma(17), and plasma cell myeloma(10,11). Signet ring cell lymphoma most commonly arises from the lymph nodes, but there are also cases from extranodal sites such as skin (18), gastrointestinal tract(19), salivary gland, breast(12), central nervous system(20), thyroid(21), and bone marrow(22).

In our case, PanCK negativity showed that the neoplastic cells were not epithelial origin. Immunohistochemical studies for CK7, CK20, S100, SMA, vimentin, and calretinin were performed to exclude other diseases with signet ring cell morphology in the differential diagnosis. When these were negative, immunohistochemical panels for lymphoid cells were ordered, considering that the neoplastic cells could be lymphoid origin. CD3 negativity and CD20 positivity suggested that the neoplastic cells were B cell origin. No Reed-Sternberg cells in the tumor and MUM-1 or CD30 negativity excluded the possibility of Hodgkin lymphoma.The high Ki-67 proliferation index suggested a high-grade lymphoma. Diffuse infiltration of neoplastic cells and negativity for follicular dendritic cell markers such as CD21 and CD23 excluded posibilty of follicular lymphoma. Cyclin-D1 and Sox11 negativity ruled out mantle cell lymphoma. The diffuse infiltration pattern in neoplastic cells, high Ki-67 proliferation index, negativity of EBV and follicular dendritic cell markers, rapid clinic progression were consistent with DLBCL. ALK and Myc were found to be negative.

There are less than 100 cases of lymphoma with signet ring cell morphology in the literature, and very few of these cases are DLBCL. The characteristics of lymphoma cases in the literature are summarized in the table (***Table 1***).

Table 1. Signet Ring Cell Lymphoma - List of case reports and case series. DLBCL=Diffuse Large B-Cell Lymphoma, LN=Lymph Node.

Reference	Number of cases	Diagnosis	Anatomic Location
Kim et al.[7]	7 cases	Follicular Lymphoma	2 Mesenteric LN, 1 Submaxillary LN, 1 Post Auricular LN, 1 Supraclavicular LN, 1 Inguinal LN
Van den Tweel et al.[23]	3 cases	Follicular Lymphoma	1 Mesenteric LN, 1 Cervical LN, 1 Pelvic LN
Moir et al.[24]	1 case	Follicular Lymphoma	Inguinal LN
Iossifides et al.[25]	1 case	Follicular Lymphoma	Supraclavicular LN
Harris et al.[26]	1 case	Follicular Lymphoma	Femoral LN
Pileri et al.[27]	1 case	Follicular Lymphoma	Axillary LN
Spagnolo et al.[28]	3 cases	Follicular Lymphoma	
Navas-Palacios[29]	3 cases	Follicular Lymphoma	1 Retroperitoneal LN, 1 Submandibular LN, 1 Supraclavicular LN
Vernon et al.[30]	1 case	Lymphocytic Lymphoma	Pelvic mass
Silberman et al.[31]	1 case	Follicular Lymphoma	Cervical LN
Allevato et al.[21]	1 case	Follicular Lymphoma	Thyroid
Weiss et al.[32]	2 cases	T-cell Lymphoma	Skin
Grogan et al.[33]	1 case	T-cell Lymphoma	Skin
Hanna et al.[34]	1 case	Follicular Lymphoma	Skin
Manivel-Rodriguez et al.[35]	1 case	B-cell Lymphoma (Not specified)	Cervical LN
Lee et al.[36]	1 case	Burkitt's-like Lymphoma	Cervical LN
Uccini et al.[37]	1 case	Follicular Lymphoma	Axillary LN
Pappas et al.[20]	1 case	Not specified	Brain
Cross et al.[15]	1 case	T-cell Lymphoma	Skin
Bellas et al.[16]	1 case	T-cell Lymphoma	Inguinal LN
Vaillant et al.[38]	1 case	T-cell Lymphoma	Skin
Talbot et al.[39]	1 case	DLBCL	Bone marrow
Mc Cluggage et al.[22]	1 case	High Grade Centroblastic Lymphoma	Bone marrow
Yu et al.[40]	1 case	DLBCL with Follicular Lymphoma	Mesenteric Mass
Zamboni et al.[3]	26 cases	MALT Lymphoma	Gastric associated Lymphoid Tissue
Fallini et al.[17]	1 case	ALCL	Supraclavicular LN
Cangiarella et al.[41]	1 case	Follicular Lymphoma	Paraaortic Mass
Ramnani et al.[14]	1 case	CLL/SLL	Axillary LN
Jaeger et al.[42]	1 case	DLBCL	Mandible
Chim et al.[43]	1 case	Follicular Lymphoma	Bone Marrow
Moran et al.[18]	3 cases	Cutaneous B Cell Lymphoma	Skin
Masir et al.[44]	1 case	Follicular Lymphoma	Inguinal LN
Nakamura et al.[45]	1 case	Immunoblastic Post Germinal Center	Cervical LN
Nagasaki et al.[46]	1 case	Follicular Lymphoma	Cervical LN
Coffing and Lim[47]	1 case	Follicular Lymphoma	Cervical LN
Sarro et al.[48]	1 case	Follicular Lymphoma	Uterine
Basir et al.[19]	1 case	Follicular Lymphoma	Small Bowel
Wu et al.[49]	3 cases	Follicular Lymphoma	1 Inguinal LN, 1 Mesenteric LN, 1 Peripancreatic Mass
Krause et al.[50]	2 cases	Follicular Lymphoma	1 Inguinal LN, 1 Mesenteric LN
Wang et al.[51]	7 cases	5 Follicular Lymphomas,	1 Mesenteric LN,

		1 DLBCL Follicular Center Cell Origin, 1 B-cell Lymphoma with Plasmocytoid features low grade.	2 Retroperitoneal LN, 1 11th Vertebra, 1 Inguinal LN, 1 Lung, Hilar Mass 1 Inferior Auricular Mass
Bogusz et al.[52]	1 case	DLBCL with Follicular Lymphoma origin	Femoral LN
Mulay et al.[53]	1 case	DLBCL	Orbital Mass
Venkateshwar et al.[54]	1 case	B-cell Lymphoma (Not Specified)	Gastric Tissue
Murakami et al.[55]	1 case	MALT Lymphoma	Omentum
Machado et al.[56]	1 case	DLBCL with Marginal Zone Lymphoma	Supraclavicular LN
Sakai et al.[13]	1 case	DLBCL	Gastric Tissue
Dardick et al.[57]	1 case	DLBCL	Tonsil
Zhang et al.[12]	7 cases	4 Follicular Lymphomas, 1 Germinal Center DLBCL, 1 DLBCL with Follicular Lymphoma, 1 DLBCL with Marginal Zone Lymphoma	1 Submandibular LN, 2 Not location specified LNs, 1 Thigh Mass, 1 Breast, 1 Parotid LN, 1 Tonsil
Gore et al.[58]	1 case	Follicular Lymphoma	Cervical LN
Patel et al.[59]	1 case	Germinal Center DLBCL with minor Follicular Lymphoma	Inguinal LN
Mishra et al.[60]	1 case	Follicular Lymphoma	Presacral mass
Younes et al.[61]	1 case	Non-Germinal Center DLBCL	Thigh/Groin Mass
Zhang and Min et al.[62]	1 case	DLBCL	Breast

In these case series, a history of colon adenocarcinoma (21), early-stage gastric adenocarcinoma (55), skin cancer (subtype not specified) (40), renal failure (no history of renal transplantation) (13, 44), and of immunosuppression (one under steroid treatment, two HIV-positive patients) (22, 36, 54) were previously reported. We consider our case may develop with the effect of immunosuppression secondary to transplantation.

Post-transplant lymphoproliferative disorders (PTLDs) are lymphoid or plasmacytic proliferations that develop as a result of immunosuppression in a solid organ or stem cell allograft recipient(63). PTLDs are further categorized by the lymphoma they resemble, such as monomorphic and classical types of Hodgkin's lymphoma, as seen in non-immunosuppressed patients. EBV-negative PTLDs are more common in adults, present with transplantation, and are more likely to be monomorphic than EBV-positive cases. The etiology of EBV-negative PTLDs is unknown. Some may be due to EBV that is no longer detectable, some to other unknown viruses, and some to the transplant itself.

Monomorphic PTLDs are post-transplant lymphoproliferative disorders recognized in immunocompetent hosts that meet the criteria for either B-cell or T/NK-cell neoplasms. Monomorphic B-cell PTLDs are B-lymphocytic or plasmacytic proliferations with monoclonal transformation that meet the criteria for DLBCL or, less commonly, Burkitt lymphoma or plasma cell neoplasm. The clinical picture of these cases is generally similar to that of the lymphomas or plasma cell neoplasms. On microscopic examination, monomorphic B-PTLDs often fulfill the traditional criteria for diffuse large B-cell lymphoma. EBV-negative cases are more likely to have a germinal center-type phenotype. Consistent with phenotypic findings, EBV+ PTLDs are of the activated B-cell type, but 45% of EBV-negative cases are of the germinal center type. Furthermore, EBV-negative monomorphic PTLDs often lack expression of the cyclin-dependent kinase inhibitor CDKN2A (p16INK4a). In our case, the patient was a transplant recipient and immunosuppressed. The patient has monomorphic cells and is classified as EBV-negative PTLD based on negative EBER studies and a diagnosis of DLBCL in the B-cell population.

As a result, in small biopsies, the possibility of lymphoma should be considered in panCK-negative tumors with signet ring cell morphology.

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