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Mushroom Poisonings in Turkey: A Meta-Analysis Study

ABSTRACT

Objective: The aim of this research is to examine the characteristics of mushroom poisoning (MP) seen in Turkey and to evaluate the results of clinical studies conducted on this subject in the last 20 years.

Methods: Google Scholar, PubMed, Science Direct and Scopus databases were scanned with the phrases "mushroom poisoning, mushroom poisoning in Turkey". 17 studies including sample volume, gender distribution, age average, complaint to the health institution, transplantation and full recovery rates were included in the analysis. In statistical data, random effects model was used.

Results: 17 different studies have been identified which give the average age of MP cases, nausea, vomiting, diarrhea and abdominal pain symptoms, liver and kidney failure, complete recovery and transpantation rates. The average age in studies involving MP cases was 38.2 years (95Cl% 36.1-40.3). The average age determined as to whether the family members are adults, elderly or childhood is as expected.

Conclusions: Although the rates of admission to hospital according to gender distribution of MP patients are similar, the signs and symptoms at admission, the distribution of liver and kidney failure, and the rates of complete remission after transplantation vary significantly.

Keywords: Meta-Analysis, Mushroom Poisoning, Toxins.

Türkiye'deki Mantar Zehirlenmeleri: Bir Meta-Analiz Çalışması

ÖZET

Amaç: Bu araştırmanın amacı, Türkiye'de görülen mantar zehirlenmelerinin (MZ) özelliklerini incelemek ve son 20 yılda bu konuyla ilgili yapılan yapılan klinik çalışmaların sonuçlarını değerlendirmektir.

Gereç ve Yöntem: Google Scholar, PubMed, Science Direct ve Scopus veri tabanları "mantar zehirlenmesi, Türkiye'de mantar zehirlenmesi " ibareleri ile tarandı. Örneklem hacmi, cinsiyet dağılımı, yaş ortalaması, sağlık kuruluşuna başvuru şikayeti, transplantasyon ve tam iyileşme oranlarını içeren 17 çalışma analize dahil edildi. İstatistiksel verilerde rastgele etkiler modeli kullanılmıştır.

Bulgular: MZ vakalarının ortalama yaşını, bulantı, kusma, ishal ve karın ağrısı semptomlarını, karaciğer ve böbrek yetmezliğini, tam iyileşme ve transpantasyon oranlarını veren 17 farklı çalışma tespit edilmiştir. MZ olgularını içeren çalışmalarda ortalama yaş 38.2'dir (%95Cl %36.1-40.3). Aile bireylerinin çocuk, yetişkin ya da yaşlı olup olmamasına göre belirlenen yaş ortalaması beklendiği gibidir.

Sonuç: MZ hastalarının cinsiyet dağılımına göre hastaneye başvuru oranları benzer olsa da, başvuru sırasındaki belirti ve bulgular, karaciğer ve böbrek yetmezliği dağılımları ve transplantasyon sonrası tam remisyon oranları önemli ölçüde değişmektedir.

Anahtar Kelimeler: Mantar Zehirlenmesi, Meta-Analiz, Toksinler.

INTRODUCTION

Mushroom poisoning (MP) is an important life-threatening health problem with the potential to affect blood values (1). Depending on the variety of mushrooms consumed, a wide variety of clinical symptoms may occur (2). There are approximately 5000 poisonous mushroom species in the world and especially around 100 fungal species are responsible for most of the poisonings (3). Although the clinical picture that occurs in patients mostly complain of gastrointestinal system, in some cases, liver, kidney and nervous system damage and even death may be encountered. MP should be considered as a medical emergency from the first diagnosis and treatment should be applied quickly for a successful treatment result (4).

Fungi are examined in two categories as poisonous and nonpoisonous mushrooms (5). Cultured mushrooms are a non-poisonous (toxin-free) mushroom that grows under special conditions. The improper storage conditions of the cultivated mushroom and keeping it at an inappropriate temperature causes the growth of microorganisms. As a result, a gastroenteritis tabloid appears (6). The main poisonous toxins are; amanitis, ibotenic acid, giromitrin, mussimol, orellanin, psilosibin, muscarin and coprin (7).

Collecting and consuming wild mushrooms is a historical tradition in many European countries (8). A significant portion of the population in Turkey live in rural areas and are benefiting from some of the plants growing in the environment for various reasons. Consumption of poisonous ones, especially of these products consumed as food and medicine, causes poisoning. Although it varies very widely consumed in Turkey according to the types of wild mushrooms. However, mushroom pickers generally do not have sufficient information to distinguish poisonous mushrooms from non-toxic ones (9). Amanita mushroom poisonings are frequent in Turkey. Amatoxins (α-amanitis and β-amanitis) produced by Amanita phalloides cause severe liver, kidney and central nervous system damage. Amanita phalloides has been reported to be responsible for 90% of fatal cases (10,11). The lack of a comprehensive meta-analysis about mushroom poisoning in Turkey in the literature directed us to this research.

The main aim of this research is to examine the characteristics of MP in Turkey in the last 20 years and evaluate the clinical results of MP.

MATERIAL AND METHODS

Since our study will examine mushroom poisonings in our country, research results related to mushroom poisoning between 1999-2019 were needed. To this end, Google Scholar, PubMed, Science Direct and Scopus databases were scanned with the phrases "mushroom poisoning, mushroom poisoning in Turkey" and article results analyzed studies conducted in Turkey were evaluated. The references of the articles and abstracts were also searched. The data in the articles included in the study were recorded on the SPSS program, no additional form was used for the data.

Compliance Criteria of the Studies: Original research papers that analyzed the cases of mushroom poisoning in Turkey were included in the study. The necessity of the studies to be included in the meta-analysis to have common parameters and statistical data for analysis was determined as the inclusion criteria in the years we investigated (12). The following parameters were included in our study: Giving the average age of MP cases, evaluating the symptoms of nausea, vomiting, diarrhea and abdominal pain, determining the rates of liver and kidney failure, complete with recovery or transplantation. Our limitation when researching studies was publication date and country. Native or refugee status was not used when examining studies. Scanned in Turkish and English. We didn't collect unpublished data.

Selection and Data Extraction: All the sources of information were searched by three authors (I.U., E.F.O.P. and H.B.). After the copies, titles and abstracts were removed, the full texts of the studies were scanned for the eligibility criteria. The appropriate study was included in the analysis after being evaluated by both researchers. A study that was deemed unsuitable for inclusion by one researcher was also evaluated by two other researchers. It was defined as a study not suitable for practice that did not meet the inclusion criteria. The study, which was determined as inappropriate by two researchers or led to disagreement between the three researchers for any reasons, was evaluated by the other researcher (E.C.). After than it was determined appropriate or inappropriate to be excluded from the analysis.

One of the two separate studies by Cevik AA et al. was published in 2007 and poisoning severity scores were evaluated. In their other study published in 2014, Cevik AA and colleagues examined the mortality and complication rates of mushroom poisoning cases that came to their clinics in the last 20 years. Studies have not been combined. Other than, there was no combinable studies.

Analysis of Data: In our study we have taken into consideration studies which evaluated the MP in Turkey. We planned to determine which complaints the poisonings apply to the health institution, the rates of organ failure, full recovery or transplantation. Each parameter determined for meta-analysis needs to be extracted and adjusted from the data obtained. For this reason, while we included those who have common parameters from 36 studies scanned from databases, we had to exclude other studies from analysis. While 17 studies including sample volume, gender distribution, age average, complaint to the health institution, transplantation and full recovery rates

were included in the analysis, 19 studies have common parameters according to the sample characteristics adapted to meta-analytical statistics in acceptable criteria since all or some of these values are not specified. They were excluded from the analysis.

A statistical model should be chosen for meta analysis (13). If all studies are similar, a fixed-effect model will be appropriate. If the studies are changing in ways that may affect the effect size, the random effects model will be appropriate in the analysis. For this reason, it has been deemed appropriate to use the random effects model in this study. Model selection was determined based on the sampling frame, not on the result. Comprehensive Meta Analysis (CMA) Software Version (CMA V3, Biostat Inc, NJ, USA) was used for data synthesis. In statistical data, random effects model was used, standardized mean difference (SD) and 95% confidence interval (Cl) were given in the analysis.

If the P value for Begg and Mazumdar Rank Correlation p value for Publication Bias is higher than 0.05, it indicates that there is no “publication bias”. Begg and Mazumdar p values were calculated for all analyzes and added to the tables as the last column. Since all p values are greater than 0.05, there is no "publication bias" in this study.

RESULTS

We scanned 2120 studies from databases by as a result of the electronic search with keywords. As a result of detailed examination, it was observed that 2084 studies were excluded from the scope of the research. By examining the summary information, 36 studies were included in the research. Detailed with inclusion criteria, 17 studies were included in the meta-analysis. 17 different studies have been identified suitable in our research (Figure 1). These studies includes the average age of MP cases, nausea, vomiting, diarrhea and abdominal pain symptoms statues, liver and kidney failure rates and complete with recovery and transplantation rates. The cities where mushroom poisoning studies are carried out are Bolu, Bursa, Denizli, Eskişehir, İstanbul, Karabük, Malatya and Sivas. The Black Sea and Thrace regions were determined as the regions where the studies were carried out.

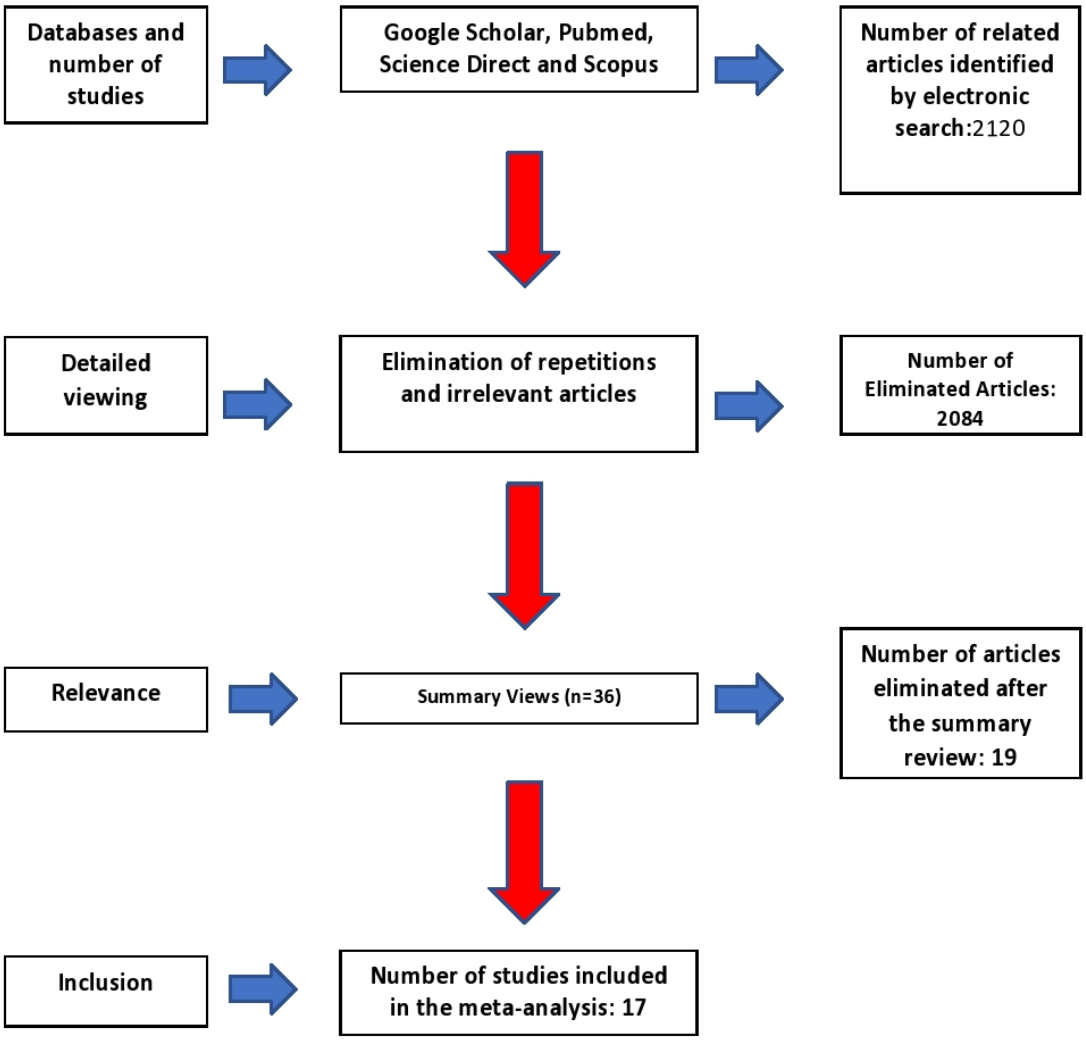

Figure 1. Flow chart showing the selection of reviews.

Descriptive statistics of these studies for categorical independent variables are given in Table 1. Homogeneous distribution value according to the effect model of the studies, average effect size and confidence intervals are given in Table 2 and Table 3.

Table 1. Average Values of Studies Containing Mushroom Poisoning Data According to Sample Volume, Provinces and Gender Distribution

Studies	Sample volume	City or region where the research was conducted	Gender distribution	
			Woman	Man
Ahishali (2012)[14]	77	İstanbul	46	31
Bilir (2006)[15]	23	Eskişehir	13	10
Cevik (2007)[16]	307	Eskişehir	172	135
Cevik (2014)[17]	599	Eskişehir	319	280
Colak (2015)[18]	58	İstanbul	37	21
Erdur (2007)[19]	154	Denizli	77	77
Eren (2010)[20]	294	Sivas	173	121
Kavalci (2010)[21]	75	Trakya	40	35
Kiziltas (2013)[22]	84	İstanbul	52	32
Koksal (2013)[23]	53	Bursa	28	25
Koyuncu (2014)[24]	64	Karabük	32	32
Ozdemir (2004)[25]	26	Sivas	19	7
Petekkaya (2016)[26]	6	Malatya	2	4
Sonmez (2013)[27]	135	Other	90	45
Trabulus (2011)[28]	144	İstanbul	72	72
Yardan (2010)[29]	317	Karadeniz	214	103
Yilmaz (2015)[30]	648	Bolu	391	257

Table 2. Table of Homogeneous Distribution Value, Average Effect Size and Confidence Intervals in the Effect Models of the Studies Included in the Meta Analysis According to the Average Age

Model Type	n	Z	p	Q	Average Effect Size	For Impact Size 95% Confidence Interval		Begg and Mazumdar Rank Correlation p value for Publication Bias
						Lower Limit	Upper Limit	
Fixed	17	127.546	<0.001	181.926	37.380	36.806	37.955	0.537

Table 3. Table of homogeneous distribution value, average effect size and confidence intervals in the effect models of the studies included in the meta-analysis according to the complaint and symptom.

Complaint and Symptom	Model Type	n	Z	p	Q	Average Impact Size	For Impact Size 95% Confidence Interval		Begg and Mazumdar Rank Correlation p value for Publication Bias
Nausea	Fixed	17	6.389	<0.001	757.213	0.574	0.551	0.596	0.902
	Random	17	2.400	0.016		0.700	0.539	0.823	
Vomiting	Fixed	17	-0.672	0.502	1131.749	0.491	0.463	0.518	0.837
	Random	17	1.254	0.210		0.649	0.414	0.829	
Abdominal Pain	Fixed	17	-8.367	<0.001	474.044	0.414	0.394	0.434	0.202
	Random	17	-4.463	<0.001		0.244	0.165	0.347	
Diarrhea	Fixed	17	-13.045	<0.001	477.272	0.359	0.339	0.379	0.773
	Random	17	-5.058	<0.001		0.200	0.128	0.300	
Recovery	Fixed	17	29.269	<0.001	31.373	0.939	0.928	0.949	0.092
	Random	17	17.233	<0.001		0.950	0.932	0.964	
Acute Liver Failure	Fixed	17	-27.515	<0.001	63.340	0.042	0.034	0.051	0.711
	Random	17	-12.496	<0.001		0.033	0.020	0.055	
Acute Kidney Failure	Fixed	17	-24.073	<0.001	61.694	0.050	0.040	0.063	0.537
	Random	17	-11.594	<0.001		0.024	0.013	0.044	
Transplantation	Fixed	17	-16.579	<0.001	20.990	0.010	0.006	0.016	0.232
	Random	17	-14.419	<0.001		0.008	0.004	0.016	

The effect size and confidence intervals of the studies included in the meta-analysis according to the condition of acute liver failure, transplantation statues and the average effect size chart according to the Random Effects Model are given in Figure 2 and Figure 3.

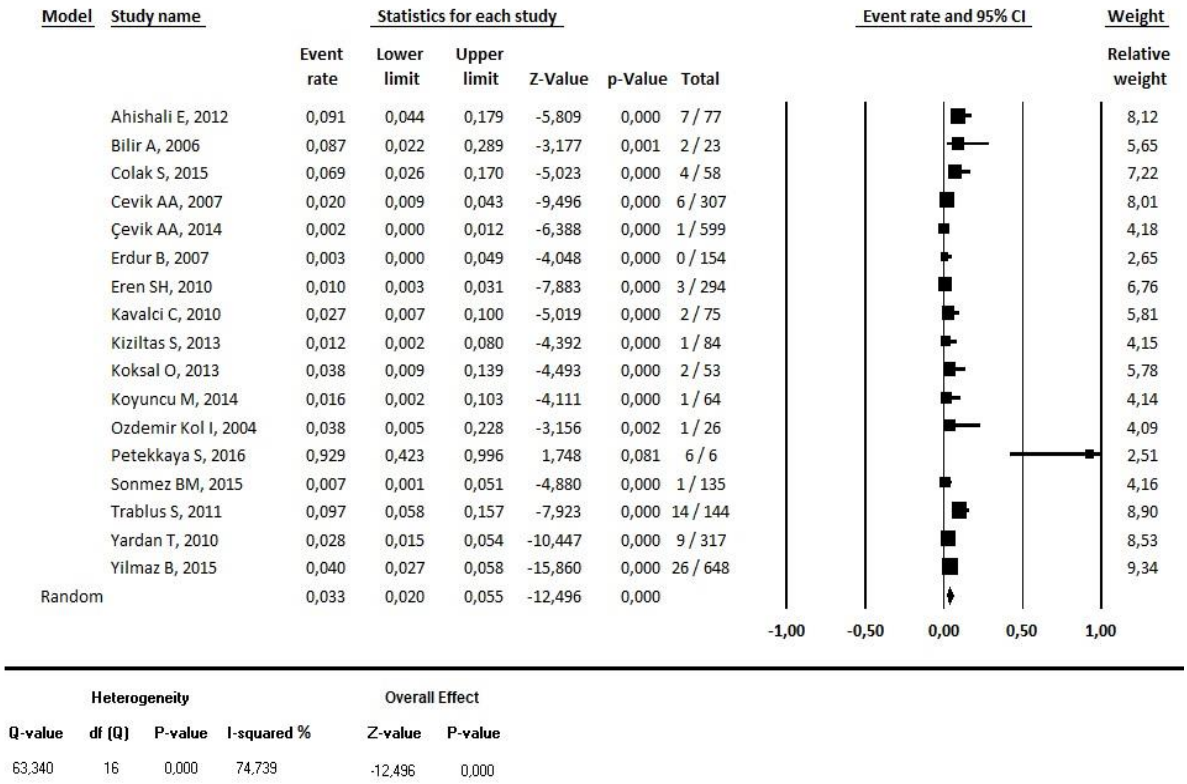

Figure 2. The effect size and confidence intervals of the studies included in the meta-analysis according to the condition of acute liver failure and the average effect size chart according to the Random Effects Model.

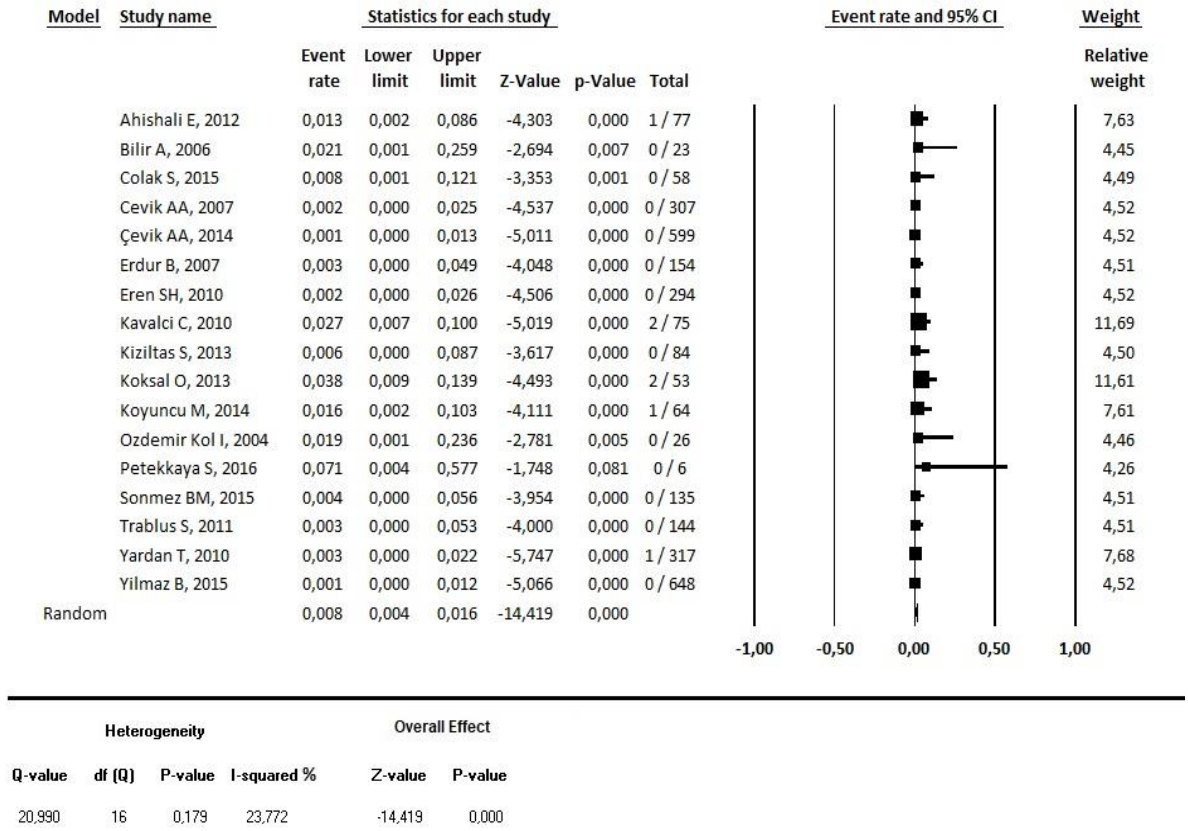

Figure 3. The effect size and confidence intervals of the studies included in the meta-analysis according to the transplantation status and the average effect size chart according to the Random Effects Model.

DISCUSSION

Poisoning is a common cause of applying to the emergency room by patients. According to data from European hospitals, about 1% of all emergency room entries are related to poisoning. Although this is not seen as a very high rate at first glance, it becomes an important health problem considering the potential risk of death in most cases (14,15). For this reason, our systematic meta analysis study's purposes are examine the distribution of poisoning in Turkey and the symptoms and what the findings to the relevant period together by setting transplantation rates with the cure rates and organ failure cases about MP.

The quality of the conclusions and generalizations to be drawn from a meta-analysis depends on how the studies included in the meta-analysis are presented (16). At the same time, one of the biggest difficulties in meta-analysis studies is that printed publications are considered suitable for printing if they have a strong effect or statistically significant (17). The absence of a strong impact or statistical significance of the studies carried out causes them to be deemed unsuitable to print. This prevents the homogenous distribution in the studies included in the analysis.

Seventeen studies were included in our study because they had the criterias(18-34). In all of these studies in which mushroom poisoning cases were evaluated; the average age of the sample, gender distribution, nausea, vomiting, abdominal pain and diarrhea symptoms, and the rates of referral to health institutions, liver and kidney failure, and transplantation and complete recovery rates are specified. Mushroom poisoning often causes a picture of gastroenteritis. Hepatotoxicity is associated with a limited group of fungi. Kidney failure; may be due to severe dehydration or specific toxin damage. Early syndromes (nausea and vomiting within 6 hours) are generally associated with a good prognosis, while delayed syndromes carry the risk of liver and kidney failure (35). In the studies included in the analysis, the rates of nausea and vomiting were higher than the random effects model among the complaints of applicants, compared to the rates of abdominal pain and diarrhea. While almost all of the studies included in the analysis were found to have liver and kidney failure in MP cases, in one study (23) they stated that they did not find the organ failure table in the cases they investigated.

Especially after rainy weather, a wide variety of wild mushrooms grow spontaneously in forest areas and often leads to potentially fatal consequences by being consumed by local communities (36). Although it is known that fungi grow mostly after rainy weather, most of the studies included in the meta-analysis reported that MP cases were observed in the autumn season. In three studies in summer (20,24,29), in one study in spring (21) and in one study in winter (28) MP cases were reported more frequently.

Located in the traditional culture dishes in Turkey is carried out with public participation in the household. With the family elders, all adults and children in the house are replaced at the table (37). For this reason, it will be meaningful to evaluate the food cultures in the regions where the study is performed. As a result of the analysis, the average age in studies involving MP cases was 38.2 years (95Cl% 36.1-40.3). The average age determined as to whether the family members are adults, elderly or childhood is as expected.

Limitations: There are many limitations on meta-analysis studies and integrity on the subject. We tried to make an extensive electronic search for this study, but some studies may have been missed during the searches. In addition, the studies were conducted on the pediatric and adult population, and we conducted our analysis without categorizing them by age group. We are of the opinion that evaluating studies in pediatric and adult populations in separate groups may be better in terms of elucidating the main approaches in MP cases.

As a result, a heterogeneous result set was encountered in our meta analysis as a result of the studies performed in different regions and with different sample volumes. Although patients vary in age and gender distribution of MP Turkey, symptoms and findings in admission to the hospital, liver and kidney failure distributions, and transplantation complete remission rates vary significantly.

Türkiye consists of various regions in terms of its natural structure and mushroom diversity is very high. For this reason, the clinical findings and results of mushroom poisoning cases seen in the regions are very diverse. In general, it is important to analyze mushroom poisoning cases in all cities and regions.

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RESEARCH ARTICLE

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The Results of Liver Transplantation Performed In a Single Center Due To Hepatocellular Carcinoma

ABSTRACT

Objective: Hepatocellular cancer (HCC) is the most common malignancy of the hepatobiliary system. There are significant differences in the global spread of HCC. It is the major cause of death in patients with cirrhosis. Its molecular pathogenesis is highly complex and heterogeneous. Major risk factors for the development of HCC are chronic hepatitis B virus (HBV) infection, chronic hepatitis C virus (HCV) infection and alcohol-related liver cirrhosis. Hepatocellular cancer is rarely seen in the first 4 decades of life, except in communities where HBV infection is hyperendemic.

Methods: The study was conducted by retrospectively scanning the files of 204 patients diagnosed with HCC who applied to Organ Transplantation Center between 21.09.2014 and 13.04.2019. Patients were transplanted liver by being classified according to Milan criteria, San Francisco [University of California San Francisco (UCSF)] criteria, and Barcelona Clinic Liver Cancer (BCLC) criteria.

Results: The median age of the patients was 58.03 (range 31 to 72). 170 of the patients were men and 34 of them were female. Liver transplantation (LT) was performed from cadaveric donors to 31 patients and from living donors to 173 patients. There is a significant relationship between the life span of the patients and their gender. Female patients have a longer life expectancy [t (202) = 2.963, p =0.003]. A significant relationship was found between life expectancy and surgical classification [F (3) = 3.008, (p =0.031)].

Conclusions: In patients diagnosed with HCC and undergoing LT; the gender being female and the classification method before transplantation affect life expectancy.

Keywords: Transplantation, Liver, Hepatocellular Carcinoma.

Hepatosellüler Kanser Nedeniyle Tek Merkezde Yapılan Karaciğer Nakli Sonuçları

ÖZET

Amaç: Hepatosellüler kanser (HSK), hepatobiliyer sistemin en sık görülen malignitesidir. HSK'nin küresel yayılımında önemli farklılıklar vardır. Sirozlu hastalarda en önemli ölüm nedenidir. Moleküler patogenezi oldukça karmaşık ve heterojendir. HSK gelişimi için başlıca risk faktörleri kronik hepatit B virüsü (HBV) enfeksiyonu, kronik hepatit C virüsü (HCV) enfeksiyonu ve alkole bağlı karaciğer sirozudur. HSK, HBV enfeksiyonunun hiperendemik olduğu bölgeler dışında, genellikle hayatın ilk dört dekadı içerisinde görülmez.

Gereç ve Yöntem: Çalışma, 21.09.2014-13.04.2019 tarihleri arasında organ nakli merkezine başvuran HSK tanılı 204 hastanın dosyaları geriye dönük olarak taranarak gerçekleştirildi. Hastalara Milan kriterlerine, San Francisco [University of California San Francisco (UCSF)] kriterlerine ve Barcelona Clinic Liver Cancer (BCLC) kriterlerine göre sınıflandırılarak karaciğer nakli yapıldı.

Bulgular: Hastaların medyan yaşı 58.03 (31-72 aralığında) idi. Hastaların 170'i erkek, 34'ü kadındı. Kadavra vericisinden 31 hastaya, canlı vericiden ise 173 hastaya karaciğer nakli yapıldı. Hastaların yaşam süreleri ile cinsiyetleri arasında anlamlı bir ilişki olduğu görüldü. Kadın hastaların yaşam beklentisi daha uzundur [t (202) = 2.963, p =0.003]. Yaşam beklentisi ile cerrahi sınıflandırma arasında anlamlı bir ilişki bulundu [F (3) = 3.008, (p =0.031)].

Sonuç: HSK tanılı olup karaciğer nakli yapılan hastalarda; cinsiyetin kadın olması ve nakil öncesi yapılan sınıflandırma yöntemi, yaşam beklentisini etkilemektedir.

Anahtar Kelimeler: Transplantasyon, Karaciğer, Hepatosellüler Karsinom.

INTRODUCTION

Hepatocellular cancer (HCC) is the primary tumor of the liver that can be seen frequently in chronic liver diseases that occur due to various etiological reasons, especially viral infections such as chronic hepatitis B or hepatitis C. Hepatocellular carcinoma (HCC) is originating from hepatocytes and it is the most common primary malignant tumor of the liver. 250 thousand to 1 million people died because of it annually worldwide (1-4). The biggest risk factor of the hepatocellular carcinoma is cirrhosis. In our country are viral hepatitis (HBV, HCV) and alcohol are the most common causes of cirrhosis. Other causes which increasing the risk of hepatoma are male gender, nonalcoholic fatty liver, diabetes mellitus, smoking, hemochromatosis, alpha-1-antitrypsin deficiency (5). According to new epidemiological data, the incidence of HCC is constantly increasing (1-3). Incidence of HCC is increasing in the Western population because of the high prevalence of HCV. This increase is related to frequency of HCV infection, the increased incidence of a migraine from HBV endemic countries, and the increase in the incidence of non-alcoholic fatty liver disease. HCC is rarely seen in the first four decades of life, except in communities where HBV infection is hyper endemic (3). The incidence of HCC is higher in men. The most valid reasons for this are high testosterone level, low estrogen level, and the fact that liver diseases are more common to men. The widespread use of HBV vaccination can reduce the HCC incidence in some regions.

Early diagnosis is very important for curative treatment approaches, and in developing countries, it is only possible with a good surveillance program (1). It is quite important to determine accurately whether the nodules detected in the liver are pre-neoplastic or early HCC. In the follow-up of dysplastic lesions with imaging methods, the malignant phenotype can be observed in approximately one-third of the lesions (2,3). Ideally, all treatment alternatives can be used if tumors are detected when they are 2 cm or less. However, one or more imaging methods are usually required to diagnose tumors in this size (4,5). Since small tumors do not have pathognomonic symptoms, the diagnosis is usually made in the more advanced stages of the disease and the patient loses the treatment options that can be curative (6). The median life span of patients diagnosed with HCC is approximately 6-20 months. Great tumor diameter, vascular invasion, poor functional status, lymph node, and/or distant metastasis are bad prognostic indicators (7-9).

MATERIAL AND METHODS

Our study was approved by Hospital Ethics Committee's decision dated 23.02.2021 and numbered 7. The study was conducted by retrospectively analyzing the files of 204 patients diagnosed with HCC who applied to Organ Transplantation Center between 21.09.2014 and 13.04.2019. Patients which performed liver transplantation (LT) were classified according to Milan criteria, San Francisco [University of California San Francisco (UCSF)] criteria, and Barcelona Clinic Liver Cancer (BCLC) criteria. The information in the files and hospital resources were analyzed. The survival status of the patients was learned from the file information, from the automation system, and by accessing with phones when necessary. Overall survival was determined as the time elapsed from the time of diagnosis to death or to the last control date and it was calculated in months.

Statistical Analysis: Statistical Package for Social Sciences 23 (SPSS for Windows 23.0) was used for statistical processes. The life expectancy (Survey) was calculated based on the time between transport and death for dead patients, and the time between transport and analysis (15.12.2020) for patients who are still alive. Independent samples t-test or one-way ANOVA was used to determine the difference between groups for variables showing normal distribution characteristics. Since the variables AFP and Mass size did not show normal distribution, the correlations were performed by Spearman Correlation Analysis. A bivariate logistic regression analysis was performed to determine the size of the mass and the survival status of the patient. Two-sided p-values less than 0.05 were defined as statistically as significant.

RESULTS

The median age of the patients was 58.03 (range 31 to 72). 170 of the patients were men and 34 of them were female. LT was performed from cadaveric donors to 31 patients and from living donors to 173 patients. There is a significant relationship between the life span of the patients and their gender. Female patients have a longer life expectancy [t (202) = 2.963, p =0.003]. A significant relationship was found between life expectancy and surgical classification [F (3) = 3.008, (p =0.031)]. There is a difference between mixed and Milan, patients with Milan have a longer life expectancy than mixed category. There was not a significant relationship between the survey and the etiological cause [F (3) = 2.214; p = 0.088]. Also, there was not a significant relationship between tumor differentiation and survey [F (2) = 2.185; p =0.115)], between perinodal invasion and survey [t (200) =0.552, p =0.581] and between the number of tumor focus in liver and survey [t (202) =0.656, p =0.513] (Table 1).

Table 1. Difference analysis of variables

Variable		N	%	Mean	SD	CI	p
Sex	Female	34	16.7	1.83	7.175	1.78-1.88	0.003
	Male	170	83.3				
Surgical Classification	Milan	131	64.2	1.49	0.797	1.38-1.61	0.031
	Beyond	47	23.0				
	UCSF	16	7.8				
	Mixed	9	4.4				
Etiological Cause	Autoimmune HCC	10	4.9	2.9157	0.75065	2.80-3.02	0.088
	Cryptogenic HCC	32	15.7				
	HBV+ HCC	120	58.8				
	HCV+ HCC	39	19.1				
Tumor differentiation	Good	58	28.4	1.80	0.623	1.71-1.89	0.115
	Medium	105	51.5				
	Bad	20	9.8				
Perinodal invasion	Perineural invasion is absent	192	94.1	0.04	0.195	0.01-0.07	0.581
	Perineural invasion is present	10	4.9				
Number of focus	1 focus	124	60.8	1.83	0.380	1.77-1.88	0.513
	Foci more than 2	80	39.2				

No significant relationship was found between the survey and AFP level and age (Table 2). Tumor size affects survival chances of the patients. The predictor variable explains 0.4% of the variance. One-unit increase in size decreases the chance of survival by 0.81 (p = 0.01) (Table 3) (Table 4).

Table 2. Spearman correlation results

			Age	Life expectancy day	AFP	Size 1
Spearman's rho	Age	Correlation Coefficient	1,000			
		P	.			
		N	203			
	Life expectancy day	Correlation Coefficient	-0.024	1.000		
		P	0.735	.		
		N	203	204		
	AFP	Correlation Coefficient	-0.123	-0.089	1.000	
		P	0.109	0.247	.	
		N	172	172	172	
	Tumor size	Correlation Coefficient	0.004	-0.094	0.066	1.000
		P	0.953	0.188	0.398	.
		N	198	199	167	199
Mean			58.03	1379.43	297.224	1.9284
Std. Deviation			7.175	894.525	2048.0211	1.9284

N: number; SD: standard deviation; CI: confidence interval; AFP: alpha feto protein

Table 3. Statistics and accuracies of logistic regression models

	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square	Hosmer and Lemeshow test		
LR	237.386[a]	.031	.044	$\chi 2$	df	p
				2.415	7	0.933

Table 4. Summary of multiple binary logistic regression analysis

Variable	B	Wald	Standard Error	p	Odds Ratio	95% CI	
						Lower	Upper
Tumor Size	-0.199	5.718	1	0.017	0.819	0.696	0.965
Constant	1.491	21.926	1	0.000	4.444		

DISCUSSION

The curative treatment options accepted for HCC are resection and LT (10). Advances in imaging methods and follow-up programs give a chance to patients with cirrhosis to surgical resection (7,8). Despite all these innovations, only a small group of patient with HCC can undergo hepatic resection (9,11).

Early detected or small HCC, are defined as lesions smaller than 2 cm or lesions smaller than 4 cm, and even HCCs that are within the Milan criteria (12,13). In recent years, the postoperative risks have decreased, postoperative mortality rate has decreased to 0.7%, and postoperative major complication rate has decreased to 7.3% as a result of improvement of patient selection criteria, advances in surgical technique and technology, and improvement of postoperative care (12,14,15). Dependent to these developments, 5-year disease-free survival rates after resections have also increased up to 70% (11). The chance of success of hepatic resection is high in small HCCs (≤5 cm) (16,17). Although some authors emphasize that the results of hepatic resection are similar to small masses in terms of disease-free survival, especially in HCCs above 5 cm developing on a non-cirrhotic background, the 5-year disease-free survival rate after resection of masses above 5 cm ranges between 20% and 30% (6,7). In univariate analysis, the factors determining disease-free survival rates after resection were determined as tumor size, high MELD score, vascular invasion and high tumor grade (6). Risk of the recurrence after hepatic resection was depended on the size and degree of differentiation of the primary tumor, and it was concluded that portal vein invasion in the resected liver was the biggest risk factor for recurrence (18). In some studies, high telomerase activity of the tumor is also emphasized as an independent recurrence factor (19).

Recurrence generally occurs in postoperative 3 years, and unfortunately, there is not an effective neo-adjuvant or adjuvant treatment to reduce the recurrence (20,21). The most important factor that increases postoperative mortality and morbidity after hepatic resections is a possible decompensated liver failure. Considering the size and cell reserve, this risk is higher in right lobe resections than in left lobe resections (22,23).

The Child-Pugh staging system, does not completely show the liver reserve in HCC patients developing on the basis of cirrhosis. It has been concluded that normal serum bilirubin level and portal vein pressure below 10 mmHg is the most important parameters for post-operative liver failure risk estimation regardless of Child-Pugh stages (23).

The factors determining the limits of hepatic resection are the degree of the underlying cirrhosis and size, location and the number of tumor respectively. While major resections (lobectomies) are at the forefront in masses larger than 5 cm, minor and non-anatomic resections gain significance in masses less than 5 cm (24). Major resections provide advantages such as complete oncological removal, removal of the portal vein branches together with the mass, and low recurrence rates, while minor resections offer advantages such as preserving liver reserve and low risk of hepatic failure that may develop after surgery (25).

LT became accepted worldwide as the definitive treatment of liver failure in the mid-1980s. With the effective use of immunosuppressive treatments, its success has gradually increased and nowadays 5-year survival rates have increased up to 85% (26). In patients with HCC, due to the advanced underlying liver failure and the inability to perform resection, LT is a good option.

CONCLUSION

In the first years, the debate on which patient should be transplanted was focused on the criteria known as Milan criteria (single nodule smaller than 5 cm or 3 nodules smaller than 3 cm) were put forward. These criteria were followed for many years and consequently, disease-free survival rates of LT are high. In the studies conducted, 5-year survival rates were found to be 70% and recurrence rates below 10%. As a result of increasing the experience and success in LT over the years, Milan criteria and expanded San Francisco criteria with successful results has also begun in patients have a single nodule smaller than 6 cm, or 3 or fewer nodules with the largest size smaller than 4.5 cm, and the total nodule sizes smaller than 8.5 cm and they are all limited in the liver (6,26-29).

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RESEARCH ARTICLE

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The Effect of Iron Replacement on Cognitive Functions in Reproductive Women with Iron Deficiency

ABSTRACT

Objective: Iron plays key role in brain development including neurogenesis, myelination, synaptic development, energy and neurotransmitter metabolism as well as normal brain functioning. The aim of this study is to examine the effect of iron replacement on cognitive functions in women with iron deficiency.

Methods: An intervention study was conducted in 165 women aged 15-49 years with low iron levels (ID;hemoglobin >12 gr/dl, ferritin <15 ng/mL) or iron deficiency anemia (IDA; hemoglobin <12 gr/dl, ferritin <15 ng/mL). 165 participants were subjected to 1st Montreal Cognitive Assessment (MoCA) scale in order to determine their preliminary cognitive function status. The women were given ferrous glycine sulfate at 100 mg/day (for those with ID) and 200 mg/day (for those with IDA), respectively, for eight weeks. Eight weeks later, the 2nd MoCA scale and control hemogram and ferritin tests were administered to 81 patients who came for follow-up and used iron treatment appropriately. Wilcoxon Signed Ranks Test was preferred when two dependent groups were compared, and Mann-Whitney U test was used when two independent groups were compared, and Kruskal Wallis test was used when three or more independent groups were compared. The analyze between age and cognitive function scores was evaluated with the Spearman correlation test.

Results: There was not a significant difference between the 1st MoCA scores of patients with ID or IDA in 165 women at the onset of the study. There was a significant increase in hemogram and ferritin levels of 81 patients who received a 200 mg/day iron replacement as expected (p<0.001). Cognitive functions were found to be significantly lower in single women with a high education level and a low body mass index (p<0.001). Average pretreatment MoCA score was 21 (min: 18- max:21), whereas post treatment average score was 26 (min:23- max:27) (p<0.001). For all cognitive functions, subgroup scores significantly increased after treatment. This improvement in cognitive functions was determined independently of demographic data. A low negative correlation also was found between age and total cognitive function score (r:-0.335, p <0.001).

Conclusions: In this study, we observed that after replacement therapy there was a significant increase in total and subgroup scores corresponding to cognitive functions of women diagnosed as iron deficiency or anemia. Considering the effect of iron replacement therapy on cognitive functions in women in the reproductive period, it should not be neglected.

Keywords: Iron Deficiency, Iron Replacement, Cognitive Functions, Female.

Demir Eksikliği Olan Üreme Dönemindeki Kadınlarda Demir Replasmanının Bilişsel İşlevlere Etkisi

ÖZET

Amaç: Demir normal beyin fonksiyonunda olduğu gibi, nörogenez, miyelinasyon, sinaptik gelişim, enerji ve nörotransmitter metabolizması dahil olmak üzere beyin gelişim süreçlerinde kilit rollere sahiptir. Bu araştırmanın amacı, demir eksikliği olan kadınlarda demir replasmanın zihinsel fonksiyonlar üzerine etkisini incelemektir.

Gereç ve Yöntem: Demir düzeyi düşük (hemoglobin >12 g/dl, ferritin <15 ng/mL) veya demir eksikliği anemisi (hemoglobin <12 g/dl, ferritin <15 ng/mL) olan 15-49 yaş arası 165 kadında müdahale çalışması yapılmıştır. 165 katılımcıya ön bilişsel işlev durumlarını belirlemek amacıyla 1. Montreal Bilişsel Değerlendirme (MoCA) ölçeği uygulandı. Kadınlara, sekiz hafta süreyle sırasıyla 100 mg/gün (DE olanlara) ve 200 mg/gün (DEA olanlara) demir glisin sülfat verildi. Sekiz hafta sonra kontrole gelen ve demir tedavisini uygun şekilde kullanan 81 hastaya 2. MoCA skalası ile kontrol hemogram ve ferritin testleri uygulandı. Bağımlı iki grubun karşılaştırılmasında Wilcoxon İşaretli Sıralar Testi, bağımsız iki grubun karşılaştırılmasında Mann-Whitney U testi, üç ve daha fazla bağımsız grubun karşılaştırılmasında ise Kruskal Wallis testi tercih edildi. Yaş ve bilişsel fonksiyon puanları arasındaki ilişki Spearman korelasyon testi ile değerlendirildi.

Bulgular: Çalışma başlangıcında DE veya DEA olan 165 kadının ilk MoCA skorları arasında anlamlı fark saptanmadı. 200 mg/gün demir replasmanı alan 81 hastanın hemogram ve ferritin düzeylerinde beklendiği gibi anlamlı artış oldu (p<0.001). Bekar, yüksek eğitim düzeyi ve düşük beden kitle indeksi olan kadınlarda bilişsel fonksiyonlar anlamlı düşük saptandı (p<0.001). Tedavi öncesi MoCA skor ortalaması 21(min:18-max:23) iken tedavi sonrası 26 (min:23-max:27) olarak saptandı (p<0,001) ve tüm fonksiyon alt grup skorlarında da tedavi sonrasında anlamlı yükselme görüldü. Bilişsel fonksiyonlardaki bu iyileşme demografik verilerden bağımsız olarak saptandı. Yaş ile toplam bilişselfonksiyon skoru arasında negatif yönde düşük düzeyde bir ilişki saptandı r:-0,335,p <0,001).

Sonuç: Bu çalışmada demir eksikliği veya anemi tanısı alan kadınlarda replasman tedavisi sonrası bilişsel işlevlere karşılık gelen toplam ve alt grup puanlarında anlamlı artış olduğunu gözlemledik. Reproduktif dönemdeki kadınlarda demir replasman tedavisi bilişsel fonksiyonlara etkisi göz önünde bulundurularak, ihmal edilmemelidir.

Anahtar Kelimeler: Demir Eksikliği, Demir Replasmanı, Bilişsel Fonksiyon, Kadın.

INTRODUCTION

Anemia affects roughly one third of World population, where half of the cases are caused by iron deficiency (ID)(1). World Health Organization (WHO) determined that, prevalence of anemia is 38.2% for pregnant women and 29.4 % for reproductive women and severe anemia is strongly associated with mortality and has cognitive and functional consequences(2). ID hinders cognitive and motor development, and causes fatigue and loss of productivity (2,3).

As far as its effects on brain are considered, iron (Fe) plays key roles in brain development processes including neurogenesis, myelination, synaptic development, mitochondrial energy and neurotransmitter metabolism. Neurodegenerative disorders are strongly associated with impaired homeostasis of iron (4).

Between the ages of 15-50, when women are most active and productive, they also encounter with nutritional deficiencies such as IDA(5,6). It is controversial whether ID has detrimental effects on cognition, mental health, and fatigue in women of childbearing age and iron replacement contributes positively to cognitive functions in these women(5). The aims of this paper was to find three answers regarding effects of IDA on cognitive functions in women of childbearing age;

1. Is the change in iron status related to cognitive functions?

3. Is there any difference in terms of cognitive between women of childbearing age with ID or IDA?

4. Is there any correlation between hemoglobin level and mental functioning in women of childbearing age with ID or IDA?

MATERIAL AND METHODS

Between the April 1,2018 and October 1,2018 a total of 165 women aged 15-49 and had either ID or IDA were enrolled and underwent to scale in Family medicine outpatient clinics. It was planned to direct patients who had hemoglobin (Hb) levels lower than 10 gr/dl and whose hemoglobin levels did not increase after treatment to hematology clinic. Together with hemoglobin and ferritin values of patients, data such as age, marital status, education level, occupation, current chronic conditions and body weight were recorded. Each participant provided informed written consent.

Sample Population – Participants: Participants are summarized in Figure 1.

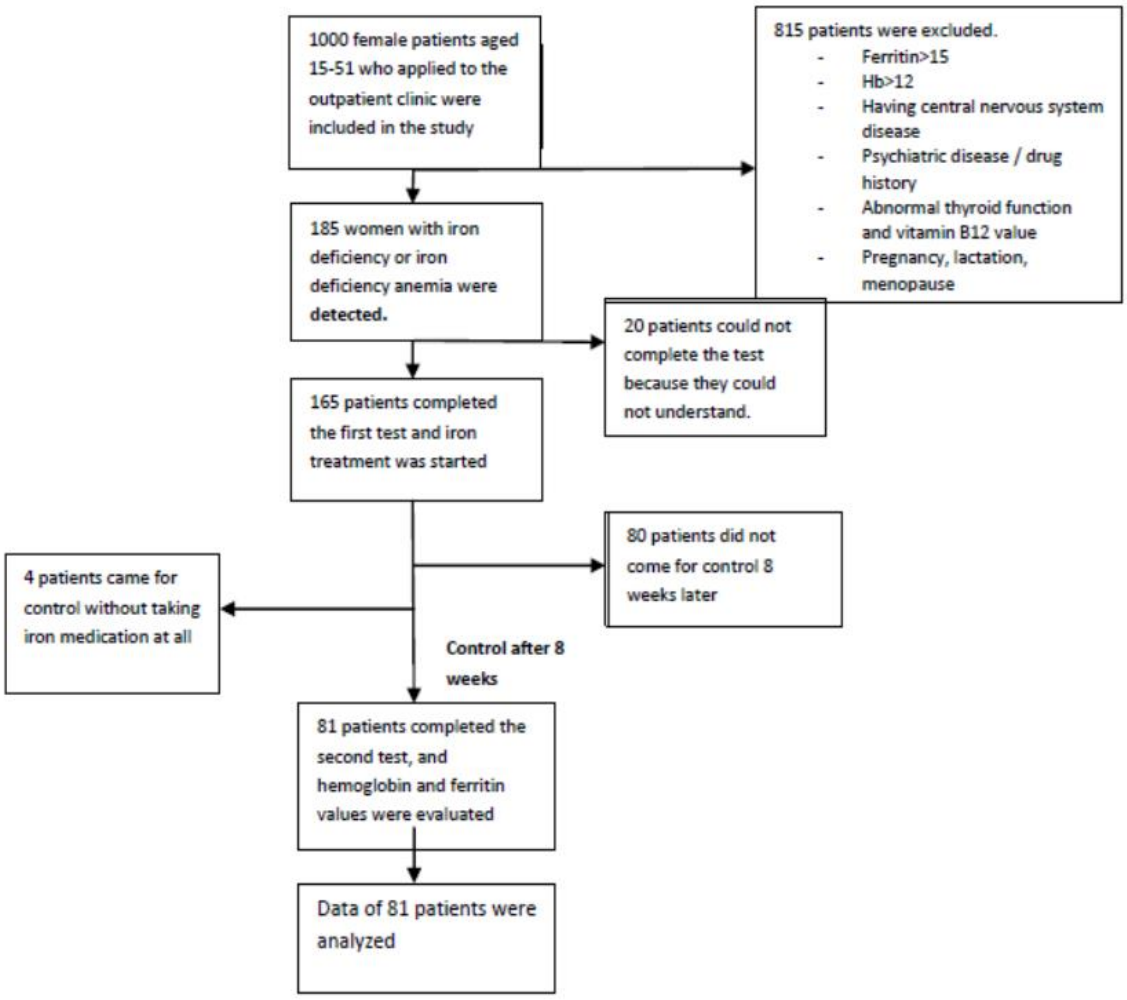

Figure 1. The scheme of choice for women with iron deficiency or iron deficiency anemia.

Study Design: 165 women had ID or IDA were subjected to a MoCA scale in order to assess cognitive function levels initially. The eight-week iron supplementation was provided to the participants in ID and group. The ferrous glycine sulfate doses were planned for ID as 100 mg/day and IDA as 200 mg/day. Participants were invited for a follow up after 8 week. Only 85 of the participants came back to the outpatient clinic for control. 4 women were excluded from the second phase of the study because they did not use the treatment as described. 81 participants completed assessments of MoCA scale and the analysis of hemogram and ferritin tests.

Laboratory Analysis: Blood samples were taken by experienced nurses. Purple-top EDTA coated tubes were used for hemogram and yellow-top heparin tubes were used for ferritin analysis. Blood samples were analyzed in Hospital Biochemistry Laboratory. The method for hemogram analysis was electrical impedance, volumetric technique with a Beckman Coulter LH780 (Houston, USA 2014) analyzer, and chemiluminescence technique was applied with a Beckman Coulter DXI 800 (California, USA 2014) analyzer. In the preparation of the study, support of Scientific Researches and Projects Commission (SRPC) was received for hemogram and ferritin tests after 8 weeks iron treatment of patients(On 04/01/2018. Decision number: 67).

Instruments: The socio-demographic questionnaire involved questions about the participants' age, education, occupation, body mass index and presence of chronic disease.

A Turkish version of MoCA scale translated by Selekler et al (7) who repeated reliability and validity analyses was employed for determining cognitive function levels. MoCA is an easy to apply scanning test for detecting minor cognitive disorders and is utilized for assessing a set of cognitive functions. Among these functions are short-term memory, visuospatial skills, executive functions, attention, language and orientation. MoCA scale can be administered in approximately 10 minutes.

Statistical Methods: Data were presented in the form of descriptive statistics, such as frequency, percentages, mean, and standard deviation were performed with SPSS® IBM 20.0 software((IBM Corp., Armonk, NY, USA). The Kolmogorov–Smirnov test was used to verify the normality of distribution. The Mann–Whitney U test was performed to compare data with non-normal distributions. The Wilcoxon signed-rank test was used for abnormally distributed quantitative variables to compare the measurements taken at the baseline and after three months (Hemoglobin, ferritin and MoCA scores). If there was a significant difference in the comparison of three or more groups, the group that caused the difference was determined by making multiple comparisons between the two groups with Mann-Whitney U test. The correlation of total cognitive function scores with age was analyzed by Spearman correlation test. The results were considered significant at $p < 0.05$.

Ethical Consideration: The ethics committee of the University of Health Sciences, Dışkapı Yıldırım Beyazıt Health Training and Research Hospital approved the study protocol (IRB number 47/11 and date of March 19,2018).The Scientific Research Support Board supported for hemogram and ferritin kit(Decision no: 67 and date of Jan 4, 2018). The directives and content of study were explained to all participants and provided to written informed consent.

RESULTS

Initially, 1000 female patients aged 15-51 years who applied to the outpatient clinic were included in the study. ID or IDA were occurred in 185 women. 20 participants could not complete the scale due to not comprehend. 81 of 165 females included in the study were between the ages of 15-49 (Median=34,13) (Figure 1). 14,8% (n=12) of the participants had a chronic disease and 18.5% (n=15) were also working. According to body mass index (BMI) 3.6% of the patients were underweight, 50.9% was in normal range, 30.3% was overweight, 12.7% was obese class I, 1.2% was obese class II and 1.2% was obese class III. 38.3%(n=50) of them had ID and 61,7%(n=31) of those had IDA. Participants' data is summarized in Table 1.

According to the results of the independent sample t-test to see if the treatment was effective, both hemoglobin and Ferritin measurements increased significantly ($p<0.001$)(Table 2). MoCA scores of the groups were also analyzed separately to determine whether demographic parameters were related to mental status. Group comparisons are summarized in Table 1. It was observed that MoCA scores of married patients were higher as compared to single patients and the difference was statistically significant.

Table 1. Comparison of MoCA Scores of Demographic Groups

	Demographic data	TotalMoCA Score	*p*	MoCA Score difference	*p*
Marital Status	**n , %**		**<0.001***		0.299
Married	58 (71.5)	20 (17-23)		3 (2-5)	
Single	23 (28.5)	23 (21-26)		3 (1.5-4.5)	
Employment State	**n , %**		0.136		0.956
Employed	15 (18.5)	21 (18-24)		4 (2.5-4)	
Unemployed	66 (81.5)	21 (18-24)		3 (2-5)	
Chronic Condition	**n , %**		0.063		0.478
Yes	12 (14.8)	21 (16-22)		4 (3-5)	
No	69 (85.2)	22 (19-24)		3 (2-5)	
Education Level	**n , %**		**<0.001****		0.872
Primary Education	19 (23.5)	17 (15-20)		3 (2,5-4.5)	
Secondary Education	15 (18.5)	19 (18-21)		4 (2-5)	
Higher Education	26 (32.1)	22 (20-24)		3 (2-4)	
University	21 (25.9)	24 (22-26)		3 (2-4)	
BMI	**n , %**		**<0.001***		0.556
Normal Range	43 (53.1)	22 (20-25)		3 (2-4.5)	
Overweight	27 (33.3)	21 (18-23)		4 (3-5)	
Obese	11 (13.6)	18 (15-20)		4 (3-4)	
Anemia Condition	**n , %**		0,718		**0.019***
Iron deficiency	50 (61.7)	21(14-28)		3(0-8)	
Iron deficiency anemia	31 (38.3)	22(11-29)		4 (1-8)	

MoCA: Montreal Cognitive Assessment ; BMI. body mass index
*Mann Whitney U Test, ** Kruskal Wallis test, p < 0.05 was were considered significant

Occupational status, having whether a chronic condition or not had no significant effect, also. For education levels, a statistically significant direct relationship with several subgroup scores was observed except Total Scores and subgroup of orientation. A low negative correlation was found between age and total cognitive function score (r:-0.335, p <0.001).When MoCA scores of ID and IDA patients were compared, there were no statistically significant differences between ID and IDA groups for all subgroups of MoCA tests (p>0,05).

*Independent-samples t-test

Table 2. Comparision of Test Results Before and After Iron Replacement Therapy *

	Before Replacement(n=81)	After Replacement(n=81)	p	Z
Measurements	Median (min-max)	Median (min-max)		
Hemoglobin(g/dL)	12.4(10.5-13.6)	13.3 (12.4-14.1)	**0.000**	-6.656
Ferritin(µg/L)	5.7(3.5-7.9)	11.4(7.7-16.5)	**0.000**	-7.803
MoCA score	21(19-24)	26 (23-27)	**0.000**	-7.238

*Independent-samples t-test

Average pretreatment MoCA score was 21 (min: 18- max:21), whereas post treatment average score was 26 (min: 23- max:27) (p<0.001). A statistically significant increase for both total MoCA scores and subgroup scores were observed (p<0.001). For all cognitive functions, subgroup scores significantly increased after treatment. 1st and 2nd MoCA scores of 81 patients were summarized in Figure 2.

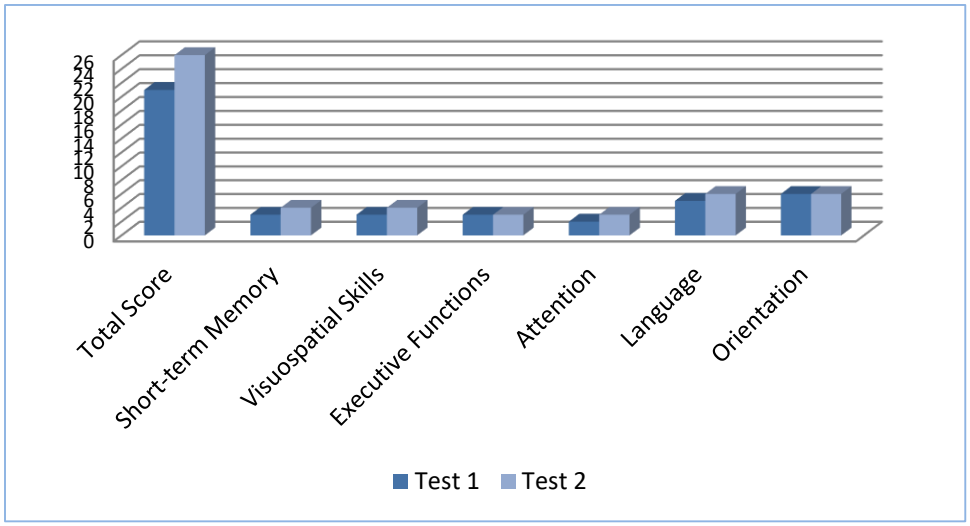

Figure 2. A comparison of Total and Subgroup MoCA Scores Before and After Treatment

Hemoglobin and ferritin measurements and MoCA scores of 81 women increased significantly after iron replacement, as expected ($p<0.000$) (Table 2). Additionally, the scatterplot referring the relationship between MoCA scores and Hemoglobin is given in Figure 3.

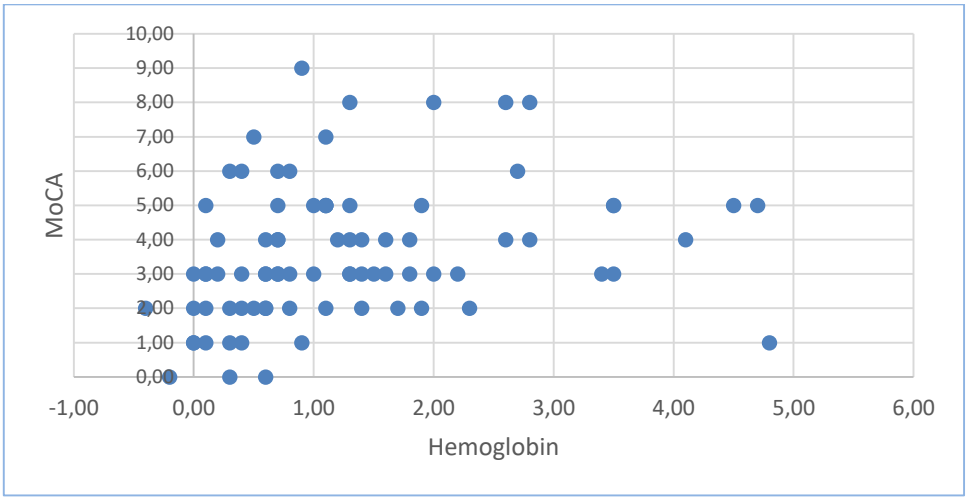

Figure 3. Scatterplot of Hemoglobin vs. MoCA scores after intervention

DISCUSSION

The young and middle-aged women are at risk of ID and IDA because of the increased iron requirement due to menstruation and pregnancy (2). The most of studies investigating the relationship between nutrient, element deficiency and cognitive functions are concentrated in childhood, antenatal period or adolescents (8-13). However, in the reproductive period of women, the most active and productive age of life, women's cognitive performances attracted the attention of few researchers (3,5,6,14) In women in this age group, researchers were generally interested in the relationship of iron in pregnancy with children's intelligence tests after birth (9,15). In 1970, Elwood et al. conducted a study in which anemic women aged 20 or older were randomized as a daily iron supplement group and a placebo group for 8 weeks and were applied cognitive test; they found that there was a reduction in the number of mistakes made when completing a maze in women taking iron, but there were no differences for cognitive tests (16). In 1996, Bruner et al. found that 81 adolescents with IDA performed better than girls in the control group in special learning and memory tests after 650 mg of iron supplementation against placebo. He did not find any difference attributable to iron in the Symbol Digit Modalities Test, Visual Search and Attention Test, or Short Attention Test (10). In 2007, Murray-Kolb and Beard found that 42 women with ID between the ages of 18-35 completed cognitive functions in a shorter time (5-7 times) with Detterman's Cognitive Ability Test (11). In 2014, Leonard et al. administered 60 and 80 mg of ferrous sulphate and compared with placebo, with 24 women aged 18 to 35 years with iron deficiency and taking no iron replacement. IntegNeuro Cognitive Scale was applied initially; women treated with iron (at both doses) had a significant reduction in impulsivity, but researchers could not find any difference in memory, response speed, attention, information processing, executive function or emotion identification. The increase in hemoglobin was associated with the time to complete the test (12). Gençay-Can et al., conducted a study in 33 anemic women 18-50 years of age is nearly accepted as fertility period in Turkey and 32 non-anemic control group with neuropsychological tests and life quality tests to determine the cognitive functions of women (6). They found a correlation with education, serum Fe, ferritin, and hemoglobin levels were associated with cognitive test scores and fatigue. But they didn't execute and observe the test scores after treatment of IDA. In our study, a total of 81 female patients diagnosed with ID or IDA were compared before and after the iron replacement with MoCA scale total score and MoCA scale sub scores, which are close memory, visual-spatial skills, executive functions, attention, language and orientation scores. There was a significant increase in total score and all subgroup scores. The increase in hemoglobin and ferritin after replacement therapy was also significant. Considering the correlation of this significant increase in hemoglobin and ferritin with the increase in MoCA scores, there was a significant correlation between the increase in hemoglobin and the MoCA scores, but no correlation between ferritin and MoCa scores. It was found that a strong positive correlation between hemoglobin increase and increases in MoCa score differences. These results correspond to the majority of previous studies (11, 12).

In the past few years, most of the studies investigating the relationship between iron and cognitive status have used iron-rich foods. In 2017, Murray-Colb et al. reported that 150 women aged

18-27 showed a 17% greater improvement in spatial attention speed, a 68% greater improvement in productivity, and > 2 times greater improvement in memory intake specifity and speed after consuming iron-biologically treated beans (86.1 ppm iron) or control beans (50.1 ppm iron) daily for 18 weeks (3). According to the present study, a statistically significant increase in hemoglobin and ferritin levels was achieved before and after iron replacement in 81 female patients. Unlike others, 8-week replacement treatment was provided with Ferrous sulfate preparation, which has high dose (200 mg/day) and high bioavailability instead of foods with high iron content. This method may have been effective in providing clear data and clinical recovery quickly.

Higher iron levels in women are associated with better attention and planning. However, it is not related to all cognitive sub-features (17). In the first phase of the study, there was no difference in cognitive functions between women with ID and IDA. In this respect, the results were consistent with literature on this subject (10).

There is only one cross-sectional study about the association of IDA with cognitive functions in a similar sample group in Turkey. They found middle positive correlation between education, serum iron, ferritin, and hemoglobin levels were associated with cognitive test scores and fatigue (6). We think that we carry the contributions of this study forward in terms of revealing the results of the post-intervention tests, as well as overlapping with the results of the first part of our study.

Despite the fact that the occupations and development of brain capacity is affected by many unmeasured confounders from a large number of demographic, dietary, environmental, and lifestyle factors (18,19). However, in our study, we showed the positive contribution of iron, regardless of demographic characteristics. In the first stage of our study, it was observed a statistically significant difference between the groups in terms of educational status, marital status and BMI in women with ID and IDA. It has been found that single individuals have higher MoCA scale scores than married ones, and there was a positive correlation with education level. According the study by Liu et al., divorced and widowed older adults are particularly vulnerable to cognitive impairment (19). The reason of this contradiction might be higher education and younger age of single participants. Another finding is positive correlation between MoCA scores and education level which was unsurprising. In certain studies, obesity is negatively related to cognitive performance in humans and that deterioration may increase over time and cause dementia (20). Verdejo-García et al. demonstrated that the performances of inhibition and mental flexibility in executive areas were significantly lower in obese compared to healthy ones in adolescents (21). However, significant differences were not found in the executive functions such as working memory, planning, and reasoning between these two groups. These results were interpreted as indication of selective alterations of executive functions in overweight adolescents. Similar to this study, it was concluded that as BMI increased, cognitive functions decreased. It was precipitated that normal weight individuals scored significantly higher than overweight and obese individuals, and overweight individuals were scored significantly higher than obese individuals. According to a meta-analysis, replacement in all age groups regardless of iron status enhances cognitive performance (22). This results have given countenance to previous substantial researches. In contrary to the 1st MoCA scores iron was found to contribute positively to the cognitive function levels of the participants, regardless of individual characteristics including age, marital status, occupation, chronic disease, education level, and BMI, after replacement.

The strengths of the present study are the improvement in cognitive functions 8 weeks after being treated with high dose ferrous sulfate, and there are no studies comparing the cognitive functions of women with ID and IDA. The limitations of the study that are small number of samples, only half of patients at the start completed phases of the study and the absence of a control group. In addition, control levels could not be observed 6 months after the initiation of the treatment.

CONCLUSION

We have corroborated others' previous findings and contributed to them by demonstrating improvement in cognitive functions, as independence of demographic characteristics even if iron replacement was given for a short-time. In this study, we would like to emphasize that cognitive capacity is affected by the lack of iron mineral, which is one of the components of the diet, and also iron replacement has a positive contribution to mental functions in women with or without anemia. We think that our study might have reflect the importance of iron supplementation in terms of cognitive clinical reflection and be a step for prospective cohort studies in women reproductive age.

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RESEARCH ARTICLE

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Anatolian Women's Opinions Attitudes and Behaviors toward Violence against Women

ABSTRACT

Objective: Violence against women is a global humanitarian problem. The present study evaluates the opinions, attitudes and behaviors of women living in the Kars province of Turkey toward violence against women, and analyses the socio-demographic factors that influence both physical violence, and the opinions, attitudes and behaviors of women toward such violence.

Methods: This cross-sectional research was conducted with 183 volunteer women aged 17–83 years who benefited from healthcare services in a family health center clinic in the Kars province of Türkiye. The survey questions were prepared based on a Turkish report on domestic violence against women (2014).

Results: Of the women in the study sample, 71.7% had been subjected to physical violence (41.3% moderate physical violence and 30.4% some form of severe physical violence), and a younger age ($p<0023$), relatively short relationship duration ($p<0.041$), low educational level of the partner ($p<0.029$) and low family income ($p<0.002$) were all found to significantly increase the risk of physical violence against women. Low family income in particular increased the risk of physical violence 3.152-fold. Women with a higher level of education and with greater economic independence, those in employment and those in the relatively younger age group (≤45 years) mostly considered violence against women to be "never acceptable". Furthermore, the women who sought legal aid when exposed to violence by their partners were predominantly in the well-educated and economically independent groups, to a significant degree.

Conclusions: Culture, education and economic status are the main risk factors for violence against women. Multidimensional studies are required to better understand the root causes of such behaviors..

Keywords: Culture, Domestic Violence, Education, Violence Against Women.

Anadolu Kadınlarının Kadına Yönelik Şiddete İlişkin Görüş Tutum Ve Davranışları

ÖZET

Amaç: Kadına yönelik şiddet, küresel bir insanlık sorunudur. Bu çalışma; Türkiye'nin Kars ilinde yaşayan kadınların, kadına yönelik şiddete ilişkin görüş, tutum ve davranışlarını değerlendirmekte ve hem fiziksel şiddeti hem de kadınların bu şiddete yönelik görüş, tutum ve davranışlarını etkileyen sosyo-demografik unsurları incelemektedir.

Gereç ve Yöntem: Bu kesitsel araştırma, Kars ilinde aile sağlığı merkezinde sağlık hizmtinden yaralanan 18-83 yaş arası 183 gönüllü kadında yapılmıştır. Araştırma verisini toplamak için kullanılan anket, Türkiye'de Kadına Yönelik Aile Içi Şiddet Raporu (2014) temel alınarak hazırlanmıştır.

Bulgular: Çalışma grubumuzda fiziksel şiddete maruz kalan kadınların oranı %71,7' dir (%41,3 orta ve %30,4 ağır fiziksel şiddetin bazı şekilleri), kadının görece genç yaşı ($p<0.023$), görece kısa olan ilişki süresi ($p<0.041$), eşin düşük eğitim düzeyi ($p<0.029$) ve düşük aile geliri ($p<0.002$) ile kadına yönelik fiziksel şiddet arasında istatistiksel olarak anlamlı ilişkili bulunmuştur. Düşük aile gelirinin fiziksel şiddet riskini 3.152 kat arttırdığı görülmüştür. Eğitim düzeyi yüksek, ekonomik bağımsızlığı olan, çalışan ve daha genç yaş gruplarındaki kadınlar, yüksek oranda, kadına yönelik şiddeti "asla kabul edilemez" olarak değerlendirmişlerdir. Eşlerinden şiddet gördüklerinde adli yardım arayan kadınlar da önemli ölçüde iyi eğitimli ve ekonomik olarak bağımsız olan kadın grupları arasındaydı.

Sonuç: Kültür, eğitim ve ekonomik durum, kadına yönelik şiddetin başlıca risk faktörleridir. Bu tür davranışların temel nedenini anlamak için çok boyutlu araştırmalara gereksinim vardır.

Anahtar Kelimeler: Kültür, Aile İçi Şiddet, Eğitim, Kadına Yönelik Şiddet.

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INTRODUCTION

Like any other type of violence (violence against children, men, nature and animals), violence against women (VAW) is a human behavioral disorder (1). Despite being mostly derived from psychological issues and thus requiring therapy, this disorder is considered almost "normal" in some cultures (2,3). Several studies to date have shown reported VAW to be more prevalent in societies with low socio-economic and education levels (4-6). Although its prevalence varies depending on the level of development and the cultural characteristics of a society, it has been reported that 35% of women around the world have experienced some form of violence, whether physical, emotional, economic or sexual, in their lifetime (7,8). A rapid increase in the prevalence VAW has been witnessed in Turkey, especially over the last 10 years (9,10), and many contributing factors have been identified, from jealousy to economic issues, although all of these factors seek to attribute violence to an excusable cause. Violence, however, is primarily a behavioral problem that needs to be fixed. It is well known that human behaviors, as well as individual characteristics (such as education, talent, intelligence, vision, values and personal philosophies), are shaped by one's culture (1,11-14). Cultures develop out of common beliefs, values and behaviors, among which, behaviors are the most visible aspects of a culture. Behaviors manifest within the mutual interactions of humans, and just as cultures produce behaviors, behaviors also produce cultures. It's clear that the behaviors of men and women interact in a society and create culture together in the process. Unfortunately, VAW is often seen as "ordinary", especially in the lower socio-economic and less educated segments of society in Turkey, and is frequently normalized in such Turkish proverbs as "If you don't beat your daughter, you beat your knee" (making use of the rhyming of the Turkish words for daughter [kız] and knee [diz]), "The husband both loves and beats" and "Roses bloom where the husband hits". To understand the causes of violent behavior among men, it is necessary to comprehend the cultural characteristics of the society in question, and the opinions, attitudes and behaviors of women toward violence.

Accordingly, the present study seeks to understand the opinions, attitudes and behaviors of women toward violence against women, and to examine the associated socio-demographic factors affecting the issue through a study of women living in a developing city in Türkiye.

MATERIAL AND METHODS

This cross-sectional study was conducted among women (who applied for healthcare services) registered with a family health center clinic in the Kars province of Türkiye. The outpatient clinic from which the data were garnered is located in the center of the city, but provides services to people from across the metropolitan area meaning that the beneficiaries were homogeneous socio-economically. The data were collected in compliance with ethical standards, and the Kafkas University Medical Faculty Ethics Committee approved the study (protocol number: 80576354-050-99/114). No appropriate sample size was calculated, as all women who agreed to participate in the study were included in the survey (n=183). The survey questions were prepared based on a Turkish report on the subject of domestic violence against women (2014) (9). The data were collected over a period of three months through face-to-face interviews, conducted in a private room to ensure the confidentiality of the respondent, and began after the respondent had been informed about the study and had given verbal informed consent for their participation in the study. As all of the respondents had been registered with the same doctor in the same family health center for a long time, there was a close relationship and a high level of intimacy between the doctor and the respondents, and this served to increase their trust in the researcher, and to answer the questions sincerely. The questionnaire forms were responded to in full by all the respondents. A10-item questionnaire form was used to assess the socio-demographic characteristics (age, marital status, relationship duration, education level, education level of the husband or intimate partner, monthly family income, employment status of the respondent, employment status of the partner, number of children and level of economic independence) of the respondents, after which a 5-item questionnaire form comprising closed-ended questions was used to identify exposure to violence of any kind (physical, emotional, economic, sexual), and whether the respondent had been exposed to domestic gender-based (father, brother, etc.) violence in their birth family. The women were also asked if they had divorced due to violence. The types of violence encountered by the respondents were examined in four categories: physical violence, emotional violence, economic violence and sexual violence (9,15,16). Physical violence was categorized as either moderate or severe, with moderate physical violence defined as slapping, throwing objects, pushing or pulling hair; while severe physical violence was defined as striking with a fist or object, kicking, dragging, beating, choking, burning or threats of use, or actual use, of

a weapon, such as a gun, knife, etc.; Emotional violence was defined as insults, swearing, humiliation in front of others, scare tactics, threatening behavior and threats of physical violence; Economic violence was defined as prevention from working, forcing the person to quit their job, not give money for household expenses and depriving of income; and Sexual violence was defined as the use of physical force to have sexual intercourse and intercourse without consent (9,15,16). The present study, besides addressing the issue of physical violence, examined also the emotional, economic and sexual violence encountered by women living in a developing region of Türkiye. As almost all of the victims of physical violence in the study were exposed also to economic, emotional and sexual violence, and almost at the same rate, only the prevalence of physical violence was analyzed based on the yes/no responses of the respondents. To evaluate the opinions of VAW among the respondents, one simple question was asked: "Is violence acceptable to women?", which produced five common answers: "never acceptable", "it depends on the situation", "maybe some moderate physical violence", "on rare occasions" and "no idea". The attitudes of the women were then evaluated with the question, "When faced with violence, what do/did you do?", which also produced five common answers: "hide from everyone", "ask for legal aid", "ask for help from a family member", "ask for help from friends" and "separate immediately". To evaluate the behavioral dynamics of the women who had been subjected to violence, the open-ended question "Why do you remain in a violent relationship?" was asked, producing four common answers: "social pressure", "for the children", "for economic reasons" and "due to dependence on the relationship". The respondents were divided into two groups based on the mean age of the sample (≤45 and ≥46); and into three groups based on their education level, as: no formal education/elementary school; secondary school/high school; and university and above. In the analysis of the data, the education level variable was based on none/high school and university/above, employment status was defined as either unemployed or employed, and marital status was defined as married or living with a partner, and others (divorced, widowed or currently without a partner). Women who had been single throughout their lives were excluded from the study. The relationship duration variable was based on the mean duration of the relationship of the respondents (≤19 and ≥20 years). The economic status variable was based on the stated monthly family income, and statistical evaluations of economic status were based on the average monthly income for a family of four, divided for the analysis into a set of two variables based on the poverty line (less than $800/month) (17), leading to groups ≤$800 and >$800. The number of children value was dichotomized as ≤two and >three, based on the mean number of children (mean 2.53±1.89).

Statistical Analysis: The SPSS Statistics Version 20.0. (University of Kafkas, IP number: 194.27.41.6) was used for the data analysis. Descriptive statistics were expressed and examined as percentage distributions, frequencies, arithmetic means and standard deviations (SD). Depending on the type of variable (continuous or categorical, respectively), the characteristics of the respondents were expressed as mean and SD, or frequencies and percentages. For the comparison of variables, Pearson's Chi-square and Fisher's exact tests were used. The odds ratio (OR) values were calculated between the categorical variables for risk evaluation (sc. the ratio of differences was calculated for the risk evaluation in crosstabs, not logistic regression) and a 95% confidence interval (CI) of the OR values was also determined. The threshold for statistical significance was set at $p<0.05$.

RESULTS

The study group was aged 17-83 years (mean: 44.77±14.69 years) and 11.5% of the respondents reported currently having no partner (1.2% divorced, 10.3% widowed). The relationship duration of the study group ranged from 1–51 years (mean: 18.90±13.33), and 73.6% of the respondents had been married for more than 20 years, while 18.6% had been in their relationship for less than 5 years. The education levels of the respondents were 67.2% none/elementary school, 18.6% secondary school/high school, and 14.2% university/above; while the education level of the respondents' partners were 49.3% none/elementary school, 32.8% secondary school/high school, and 17.9% university/above. The proportion of the respondents in the study group reporting a monthly family income below $800 was 63.9%, and the proportion of women in work (employed) was 29.5%, while 71.6% had an employed partner. Of the total, 26% of the respondents stated that they worked with their partners in agriculture as seasonal workers. The mean number of children in the study group was 2.53 (min: 0, max: 7, SD: 1.89). A total of 56.8% of the respondents had ≥2 children and 13.7% of the respondents had no children. Of the total, 71% of the women reported being economically dependent. Table 1 presents a summary of the socio-demographic data of the

Table 1. Relationship between socio-demographic characteristics and physical violence

Socio-demographic characteristics (n=183)	n	%	SD Standard Deviation	95% CI		P (PV)
				Min	Max	
Age						
≤45	116	63.4	14.69 (mean:44.77)	17	83	**0.023**
≥46	67	36.6				
Marital Status						
Married	162	88.5				0.958
Other	21	11.5				
Relationship Duration						
≤19	34	18.6	13.33 (mean:18.90)	1	51	**0.041**
≥20	149	81.4				
Women Education Level						
None-High School	157	85.8				0.066
University-Above	26	14.2				
Partner Education Level						
None-High School	150	82.1				**0.029**
University-Above	33	17.9				
Monthly Family Income						
≤$800	117	63.9	2674.69 (mean:5562.84)	2.700	12.000	**0.002**
>$800	66	36.1				
Women Employment Status						
Employed	54	29.5				0.083
Unemployed	129	70.5				
Partner Employment Status						
Employed	131	71.6				**0.004**
Unemployed	52	28.4				
Number of Children						
≤2	104	56.8	1.89 (mean:2.53)	0	7	**0.046**
≥3	79	43.2				
Women Economic Dependency						
Yes	130	71.1				0.078
No	53	28.9				

n: Frequency, %: Percentage, CI: Confidence Interval, Min: Minimum, Max: Maximum, PV: Physical Violence, p<0.05.

study group. The proportion of the respondents who had encountered physical violence was 71.7% (41.3% moderate physical violence and 30.4% some form of severe physical violence - striking with a fist or object). No women reported exposure to choking, burning, or threats of, or actually, use of a gun, knife or other weapon among those exposed to physical violence. Of the total, 72% stated that they had been exposed to emotional violence, 76.8% to economic violence and 64.7% to sexual violence. The proportion of women exposed to domestic violence in their birth family was 76.2% in the study group, and the vast majority of women who were exposed to physical violence had also been exposed to domestic violence in their birth family (78.4%). Among the victims of physical violence, the rate of economic violence was 99.2%, the rate of emotional violence was 98.7% and the rate of sexual violence was 73.1%, indicating that almost all of the women who had been exposed to physical violence had also been exposed to economic, emotional and sexual violence in the study group. The responses of the participants when asked their opinions of domestic violence were, in order, "never acceptable" (33.7%), "it depends on the situation" (26.2%), "possibly some moderate physical violence" (20.8%), "on rare occasions" (15.6%) and "I have no idea" (3.7%). When asked how they responded to such violence, the most common answers from the respondents were, in order, "I hide from everyone" (68.3%), "I turn to my family for help" (19.7%), "I turn to friends for help" (8.7%)" "I seek legal help" (2.1%) and "I separated immediately" (1.2%). All of the women who stated that they had "separated immediately" were already divorced in the study group. When asked "why do/did you remain in a violent relationship", the responses of the appropriate respondents were "social pressure" (36%), "for the children" (30.4%), "for economic reasons" (31.5%) and "dependency on the relationship" (2.1%). A significant relationship was identified between physical violence and age, with a higher rate of physical violence reported in the ≤45 years age group. There was also a significant relationship between duration of marriage of less than 5 years and physical violence, while no significant relationship was identified between the level of education of the respondents and exposure to physical violence, although the rate of physical

violence was relatively lower among the women with higher education levels. In contrast, the rate of physical violence was significantly higher among women whose partners had a low level of education, and a significant relationship was also found between economic status and physical violence, with the rate of physical violence being significantly higher in the low-income group. An analysis of the relationship between employment status and physical violence revealed that women with unemployed partners were subjected to significantly higher rates of physical violence, while no significant relationship was identified between unemployment in women and physical violence. A statistically significant relationship was detected between physical violence and the number of children, as the rate of physical violence was significantly lower among the respondents with three or more children. The rate of physical violence was also low among the economically independent respondents, although this difference was not statistically significant. The relationships between socio-demographic characteristics and physical violence are presented in Table 1. Among the higher educated, economically independent, employed, relationship duration less than 5 years and younger age women groups, the level of the response "violence against women is never acceptable" was close to statistical significance. The older age and three or more children groups were significantly associated with the response "violence could be acceptable in certain situations". The less educated, low family income and economically dependent women groups said that they remained in violent relationships due to "social stigma", to a significant degree. In the economically dependent and low family income women groups, the respondents stated that they remained in their violent relationships due to the "children" to a significant degree. The response "for reasons of economy" to the question "why you remain in a violent relationship" was significantly higher in the low family income, three or more children, and economically dependent groups. A significant relationship was also identified between the response "I hide the violence from everyone" and the older age, low family income and economically dependent groups. Significantly more women seek legal aid among the well-educated and economically independent women groups when violence is encountered. Among the younger age, relationship duration of less than 5 years and well-educated women groups, the response to physical violence of "separated immediately" was higher, to a statistically significant degree. The results of a comparative analysis of the socio-demographic characteristics of the respondents and their opinions/attitudes/behaviors toward violence against women are broadly presented in Table 2.

Table 2. The relationships between the socio-demographic characteristics and women's opinion-attitude-behavior toward violence against women

Characteristic →	AGE	RD	WEL	PEL	MFI	WES	PES	NC	WEI
	p	p	p	p	p	p	p	p	p
Women's Opinions of Violence Against Women									
Never Acceptable	0.055	0.051	0.053	0.896	0.143	0.057	0.259	0.391	0.054
Depends on the Situation	**0.041**	0.076	0.157	0.264	0.457	0.955	0.854	**0.048**	0.386
Moderate Could be Possible	0.383	0.092	0.083	0.748	0.256	0.469	0.559	0.185	0.843
On Rare Occasions	0.562	0.376	0.474	0.843	0.185	0.694	0.386	0.366	0.379
No Idea	0.524	0.422	0.236	0.381	0.811	0.653	0.583	0.642	0.588
Women's Attitudes Toward Violence Against Women									
Social Stigma	0.056	0.129	**0.041**	0.834	**0.026**	0.096	0.758	0.382	**0.043**
Children	0.389	0.982	0.353	0.867	**0.047**	0.375	0.465	0.754	**0.038**
Economy	0.664	0.742	0.256	0.750	**0.034**	0.583	0.885	**0.033**	**0.026**
Dependency	0.348	0.511	0.482	0.634	0.381	0.745	0.476	0.343	0.271
Women's Behaviors toward Violence Against Women									
Hide	**0.047**	0.324	0.547	0.965	**0.046**	0.253	0.128	0.116	**0.023**
Legal Aid	0.856	0.765	**0.029**	0.443	0.549	0.852	0.648	0.784	**0.047**
Family Aid	0.485	0.586	0.548	0.575	0.853	0.931	0.942	0.387	0.643
Friends Aid	0.975	0.487	0.637	0.837	0.489	0.506	0.574	0.641	0.561
Separate Immediately	**0.032**	**0.026**	**0.048**	0.653	0.387	0.092	0.549	0.645	0.059

RD: Relationship Duration, WEL: Women Education Level, PEL: Partner Education Level, MFI: Monthly Family Income, WES: Women Employment Status, PES: Partner Employment Status, NC: Number of Children, WEI: Women Economic Dependency.

The risk of physical violence was 2.328 (95% CI, 1.890–3.494) times higher in the ≤45 years age group than in the ≥46 age group. The risk of physical violence was 1.532 (95% CI, 1.103–2.758) times greater among the respondents in relationships for fewer than 5 years. A relatively low educational level of the partner meant a 2.981-fold (95% CI, 1.603-4.981) increase in the risk of physical violence. The risk of physical violence was 2.974 (95% CI, 1.705-4.953) times greater in women with an unemployed partner; and a low family income increased the risk of physical violence 3.152-fold (95% CI, 1.901-5.234). It was further observed in the present study that having two children or less increased the risk of physical violence 1.526-fold (95% CI, 1.112–2.659) (Table 3).

Table 3. Risk of physical violence with the socio-demographic characteristics

Characteristic	Categorization	Physical Violence	
		OR	(95% CI)
Age	≤45	**2.328**	**(1.890-3.494)**
	≥46		
Relationship Duration	≤19	**1.532**	**(1.103-2.758)**
	≥20		
Women Education Level	None-High School	1.211	(0.954-2.218)
	University-Above		
Partner Education Level	None-High School	**2.981**	**(1.603-4.981)**
	University-Above		
Women Employment Status	Employed	1.185	(0.896-1.986)
	Unemployed		
Partner Employment Status	Employed	**2.974**	**(1.705-4.953)**
	Unemployed		
Monthly Family Income	≤$800	**3.152**	**(1.901-5.234).**
	>$800		
Number of Children	≤2	**1.526**	**(1.112-2.659)**
	≥3		
Women Economic Dependency	Yes	1.297	(0.948-2.090)
	No		

OR: Odds Ratio, CI: Confidence Interval, $p<0.05$.

DISCUSSION

This study's results showed that a large proportion of the women in the study sample had been subjected to physical violence. A significant association was identified between a younger age, a relatively short relationship duration, a low educational level of the partner and low family income and physical violence against women. This concurs with the findings of earlier studies reporting a decrease in the risk of physical violence with older age, and identifying a low economic level as a risk factor for violence (4,5,18-21). As is the case in the rest of the world, Türkiye is experiencing an economic recession and an increase in youth unemployment, exacerbated by the fact that Türkiye's population is considerably young (22). The north-eastern Region of Türkiye ranks below the national average in all socio-economic criteria (22,23), and cultural habits are maintained here more intensely than in other Anatolian regions. All the above factors could contribute to the higher rate of VAW among the respondents in the present study. It has been reported in several studies around the world that economic and socio-demographic factors play a leading role in the prevalence of VAW (5,24,25). Women with low educated, unemployed partners and with a low family income were found to be exposed to significantly higher rates of violence in the present study, and the economic dependency of women was one of the main factors identified preventing women from escaping abusive relationships. In an examination of the risk factors associated with VAW in the present study, greater risk was identified in the low family income, low-educated partner groups. It is well known, however, that, regardless of the societal level, it is not only men with a low level of education and a low economic level who commit violence against women (6-8). Although no statistically significant relationship was identified in the higher educated, economically independent and employed women groups, these groups reported a lower rate of physical violence, which suggests that if women are well educated and participate in the labor force, they are better able to shield themselves from exposure to violence. There have been several studies to date reporting that it is the intimate partner that is the most frequent perpetrator of VAW (6,24,25). To examine the cause of male violence, an integrated model was developed by Heise in 1998 that was revised in 2011, proposing that intimate partner violence (IPV) is influenced by interconnected factors at four different levels: individual (experience of childhood violence, low social support, socio-demographic characteristics), relationship/interaction (non-egalitarian decision-making, poor communication, high relationship conflict), community (norms e.g. acceptance of wife-beating, stigma of divorce, family privacy, lack of sanctions, neighborhood characteristics), and macro-social (gender order e.g. discriminatory family law; cultural factors, e.g. collectivist vs individual; economic factors, e.g. level of development) (13,14). In this widely accepted model, the influence of culture on IPV is clearly observable. Anthropological studies view violence as a part of human behavior that can become normalized by an underlying cultural logic (11). To understand "how violence is affected by cultural factors", it is important to understand the ideology of masculinity in a society. The hegemonic masculinity in Türkiye promotes the domination and control of women by the male sex.

VAW is mostly an expression of power that is encouraged by other men, and even elderly women, as men may otherwise suffer humiliation among their peers. This compelling role ascribed to men can also be a burden and an undesired situation for men. As stated by Fulu et al., violence is a compensatory action in men when they feel that their authority is waning, and unemployed and financially embarrassed men may project their masculinity as a means of compensating for failure (12). The reconstruction of the cultural concept of a society in which violence is tolerated is only possible through education and the enactment of long-term social policies. It is clearly apparent that there is a need to change and transform the cultural infrastructure related to VAW in the long term. The increased violence against women in Türkiye is certainly worrying, but we believe it is inevitable given the declining economy and also the lack of progress in education. That said, the increase in VAW can be attributed to multidimensional elements, and not only to education, economy and culture. Understanding the effects of the opinions, attitudes and behaviors of women toward VAW on the violent behaviors of men requires follow-up cohort studies, which falls outside the scope of the present study. The aim of the present study was to determine the frequency of VAW and to garner data on the opinions, attitudes and behaviors of women on the subject of VAW through a small group analysis. The cross-sectional nature of the present study served to identify some significant relationships between risk factors and physical violence, but failed to reveal any casual relationships. Understanding the reason for the dramatic increase in VAW in Türkiye, especially over the last 10 years, will require multidimensional research. The strength of the present study lies in the fact that all of the respondents were given the opportunity to express their opinions candidly, and to explain their approaches and responses to violence in their personal lives. They had no fear of repercussion when describing their experiences due to the assured confidentiality, and this intimacy facilitated in-depth interviews and ensured high reliability in the findings. Future studies should include a qualitative study to gain a better understanding of the context and causes of violence against women. The findings of the present study offer clear evidence that the lives of women are not easy in this region. If we are to improve women's lives, promote their participation in social life and increase community development, VAW must be given greater emphasis and subjected to academic study in all of its dimensions. To the best of our knowledge, this is the first study to date of this issue to be conducted in this specific region, and in this country. As the study was not based on a nationwide sample from Türkiye, the results cannot be generalized for the country as a whole.

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RESEARCH ARTICLE

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Comparison of Anterior Segment Measurements in Obese Children and Healthy Control Group

ABSTRACT

Objective: To evaluate anterior segment parameters in obese children.

Methods: Fifty-five obese and 30 control group children subjects participated. All participants and the control group were examined and anthropometric measurements were made. The measurements of fasting blood glucose (FBG), systolic blood pressure (SBP) triglyceride (TG), total cholesterol (TC), high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), and insulin values were performed. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated. Each participant underwent a detailed ophthalmic examination and intraocular pressure (IOP), central corneal thickness (CCT), anterior chamber depth (ACD) and lens thickness (LT) were measured.

Results: The gender distribution of the groups was similar (p=0.893). The mean of CCT and LT were significantly higher in the obese group (572.9 ± 14.5 vs. 559.5 ± 10.1 µm, p=0.001; 3.6 ± 0.14 vs. 3.48 ± 0.25 mm, p=0.007). No significant difference was found between the obese and control groups in terms of other parameters. Body mass index (BMI) and waist circumference (WC) had a significant negative correlation with LT control groups. The obese group showed a significant positive correlation between IOP and TG (r=0.276, p=0.042), and a significant negative correlation with HDL-C (r=-0.273, p=0.043). In the control group, there was a significant positive correlation between IOP and BMI (r=0.389, p=0.034), WC (r=0.497, p=0.005), HOMA-IR (r=0.384, p=0.036), Insulin (r=0.407, p=0.026), and a significant negative correlation with TC (r=-0.511, p=0.004). A significantly positive correlation between ACD and LDL-C (r=0.371, p=0.043) and a significantly negative correlation between HOMA-IR in the control group were detected (r=-0.682, p=0.000).

Conclusions: The obese group had higher CCT and LT than the control groups.

Keywords: Obese Children, Corneal Thickness, Anterior Chamber Depth, Lens Thickness, Intra Ocular Pressure.

Obez Çocuklarda ve Sağlıklı Kontrol Grubunda Ön Segment Ölçümlerinin Karşılaştırılması

ÖZET

Amaç: Obez çocuklarda ön segment parametrelerinin değerlendirilmesi.

Gereç ve Yöntem: Elli beş obez ve 30 kontrol grubu çocuk denek katıldı. Tüm katılımcılar ve kontrol grubu incelendi ve antropometrik ölçümler yapıldı. Açlık kan şekeri (AKŞ), trigliserit (TG), toplam kolesterol (TK), yüksek yoğunluklu lipoprotein-kolesterol (HDL-K), düşük yoğunluklu lipoprotein-kolesterol (LDL-K) ve insülin değerleri ölçümleri yapıldı. . İnsülin direncinin (HOMA-IR) homeostaz modeli değerlendirmesi hesaplandı. Her katılımcıya detaylı bir göz muayenesi yapıldı ve Göz içi basıncı (GİB), Santral kornea kalınlığı (SKK), Ön kamara derinliği (ÖKD) ve Lens kalınlığı (LK) ölçüldü.

Bulgular: Grupların cinsiyet dağılımı benzerdi (p=0,893). SKK ve LK ortalaması obez grupta anlamlı olarak daha yüksekti (572.9 ± 14.5'e karşılık 559.5 ± 10.1 µm, p=0.001; 3.6 ± 0.14'e karşı 3.48 ± 0.25 mm, p=0.007). Obez ve kontrol grupları arasında diğer parametreler açısından anlamlı fark bulunmadı. Vücut kitle indeksi (VKİ) ve bel çevresi (BÇ), LK kontrol grupları ile anlamlı bir negatif korelasyona sahipti. Obez grup, GİB ile TG arasında anlamlı bir pozitif korelasyon (r=0.276, p=0.042) ve HDL-K ile anlamlı bir negatif korelasyon gösterdi (r=-0.273, p=0.043). Kontrol grubunda GİB ile VKİ (r=0.389, p=0.034), WC (r=0.497, p=0.005), HOMA-IR (r=0.384, p=0.036), İnsülin arasında anlamlı pozitif ilişki vardı. (r=0.407, p=0.026) ve TK ile anlamlı bir negatif korelasyon (r=-0.511, p=0.004). Kontrol grubunda ÖKD ile LDL-K arasında anlamlı pozitif korelasyon (r=0.371, p=0.043) ve HOMA-IR arasında anlamlı derecede negatif korelasyon saptandı (r=-0.682, p=0.000).

Sonuç: Obez grup, kontrol gruplarına göre daha yüksek SKK ve LK'ye sahipti.

Anahtar Kelimeler: Obez Çocuklar, Kornea Kalınlığı, Ön Kamara Derinliği, Lens Kalınlığı, Göz İçi Basıncı.

INTRODUCTION

Obesity is a condition characterized by excessive weight that is associated with negative health outcomes (1). The prevalence of obesity in the United States continues to rise at an alarming rate, affecting approximately 10% of infants and toddlers, 17% of children and teenagers, and over 30% of adults (2). The interplay of physical and environmental factors lays the foundation for childhood obesity. The regulation of weight through neuroendocrine mechanisms involves various instances where genetic variations may influence an individual's weight status. Unfortunately, children are more vulnerable than ever to obesity and related weight disorders due to inadequate dietary and exercise environments.

The long-term consequences of childhood obesity on an individual's health are significant. Obesity negatively impacts both physical and mental well-being and increases the risk of various conditions, including atherosclerosis, diabetes mellitus, hypertension, sleep apnea, nonalcoholic fatty liver disease (NAFLD), precocious puberty, gynecomastia, polycystic ovary syndrome, and steatohepatitis (3). In a study by Bergman et al., it was suggested that a higher body mass index (BMI) may be associated with decreased visual acuity, although the exact ocular conditions contributing to this relationship and their underlying mechanisms remain unclear (4). Furthermore, obesity also raises the risk of vision loss associated with age-related macular degeneration, diabetic retinopathy, cataracts, and glaucoma (5).

Ocular problems in obesity may be related to disorders of the mechanical and vascular functions of the eye, which may be due to chronic oxidative stress. Therefore, obesity may worsen visual function even in the absence of related diseases or in the preclinical phases(6,7). While the cornea of a child reaches adult thickness by the age of 3, there have been few reports documenting normal central corneal thickness (CCT) measurements in children's eyes(8). Although intraocular pressure (IOP) and CCT have been extensively studied in relation to obesity, there is no definitive data on whether obesity affects anterior chamber depth (ACD). Only a few studies have evaluated anterior segment measurements in children with obesity. The aim of this study is to assess BMI and adiposity markers, metabolic parameters, and ocular parameters such as IOP, CCT, ACD, and lens thickness (LT) in obese children compared to healthy children. CCT has emerged as an important predictor of progression in glaucomatous damage.

MATERIAL AND METHODS

This prospective study was conducted at the Departments of Ophthalmology and Pediatric Endocrinology at the University School of Medicine. The study received approval from the ethics committee (Clinical Research Registration number: 2017-34) and was conducted in accordance with the principles of the Declaration of Helsinki. Informed consent and oral assent were obtained from each patient and/or their legal guardians.

Fifty-five obese children and 30 age- and gender-matched subjects from a control group participated in the study. Participants who had been diagnosed with systemic diseases, had a history of ocular pathology that could affect central corneal thickness (CCT) and intraocular pressure (IOP) (such as irregular astigmatism or large regular astigmatism ≥3 diopters), ocular hypertension, glaucoma, uveitis, corneal pathology, or were uncooperative during ophthalmic measurements, were excluded from the study.

All participants, including those in the control group, underwent physical examinations, and anthropometric measurements were taken. The children's weight and height were measured with light clothing and without shoes. Body mass index (BMI) is the most commonly used method in clinics to determine overweight and obesity. The BMI formula used for each child was: weight (kg) / height (m)2. BMI above the 95th percentile for age and gender was defined as obesity (8). Waist circumference (WC) was calculated using a measuring tape, with the measurement taken as the nearest half-centimeter midway between the iliac crest and lower rib margin. Blood pressure was measured using a digital automatic sphygmomanometer (Omron® M2 HEM-7121-E, Omron® Healthcare Co, Japan) after a resting period, and measurements were repeated at least three times with a 10-minute interval. Systolic and/or diastolic blood pressure higher than the 95th percentile was defined as hypertensive (9).

A comprehensive ophthalmic examination was performed on all participants, including assessment of best corrected visual acuity using a Snellen chart, slit-lamp biomicroscopy for examination of the anterior and posterior segments of the eye. The measurements were conducted by an experienced ophthalmologist (MTE). Following the ophthalmological examination, intraocular pressure (IOP) and central corneal thickness (CCT) were measured using a non-contact tonometer (Canon TX-20P, Tokyo, Japan). Three measurements were taken for each eye using the non-contact tono/pachymeter devices, and the averages were used for statistical analysis. Anterior chamber depth (ACD) and lens thickness (LT) were measured using the IOL Master 700 (Carl Zeiss Meditec AG, Jena, Germany). A single measurement was taken for each eye using the IOL Master 700.

Statistical Analysis: Descriptive statistics of the data were given as mean, standard deviation (SD), median, first quartile and third quartile, minimum and maximum values for numerical variables, while numbers and percentage frequencies were given for categorical features. The

Shapiro-Wilks test was used to analyze whether the numerical variables fit the normal distribution in both groups. Since the values of numerical variables did not show the normal distribution in at least one group, nonparametric tests were used in data analysis. The two groups were compared for numerical characteristics using the Mann-Whitney U test and correlations between numerical characteristics in each group were analyzed using Spearman rank correlation analysis. The distribution of genders into groups was evaluated by Pearson chi-square analysis. The statistical significance level was considered as P<0.05 and SPSS (ver. 23) program was used for calculations.

RESULTS

Fifty five obese patients, 23 of whom were male (41.8%) and 30 people of the control group, 13 of whom were male (43.3%) participated in the study. The gender distribution of both groups was similar (P=0.893). Descriptive statistics of demographic measurements and group comparison results are given in Table 1. When the table is examined, the obese and control groups showed no difference in terms of systolic and diastolic blood pressures and age, while the mean HDL-C was found to be significantly lower in the patients (46.11 ± 10.45 vs. 55.60 ± 15.13 mg/dl, p=0.020) and WC (90.74. ± 12.18 vs. 56,97 ± 5.27 cm, p<0.001), fasting blood glucose (FBG) (94.16 ± 7.42 vs. 87.40 ± 7.83 mg/dl, p=0.01), TG (121.42 ± 77.10 vs. 52.80 ± 10.68 mg/dl, p<0.001), TC (165.27 ± 51.97 vs. 128.87 ± 16.86 mg/dl, p<0.001), LDL-C (94.32 ± 38.45 vs. 57.77 ± 13.11 mg/dl, p<0.001), HOMA-IR (3.85 ± 212. vs. 1.34 ± 0.34, p<0.001), insülin (16.31 ± 9.10 vs. 6.16 ± 1.78 µIU/ml, p<0.001) significantly higher in the obese group in all the remaining measurements.

Table 1. Descriptive statistics of demographic measurements and group comparison results

	Groups	N	Mean	SD	Min	Max	Percentiles			P
							1st Quartile	Median	3rd Quartile	
Age	ObeseGrup	55	11.15	3.14	6.00	17.00	8.00	11.00	14.00	0.135
	Control Grup	30	10.03	2.44	6.00	17.00	8.00	11.00	12.00	
BMI	ObeseGrup	55	27.17	4.70	19.43	38.81	23.37	26.38	31.31	**<0.001**
	Control Grup	30	19.30	1.58	16.40	22.00	18.50	19.75	20.00	
WC	Obese Grup	55	90.74	12.18	65.00	114.00	80.00	93.00	99.00	**<0.001**
	Control Grup	30	56.97	5.27	50.00	65.00	51.00	58.00	61.00	
Systolic BP	Obese Grup	55	115.82	11.34	90.00	135.00	110.00	115.00	125.00	0.998
	Control Grup	30	115.67	3.88	110.00	120.00	113.75	115.00	120.00	
Diastolic BP	Obese Grup	55	75.73	9.59	50.00	90.00	70.00	80.00	80.00	0.218
	Control Grup	30	74.67	3.92	70.00	80.00	70.00	75.00	80.00	
FBG	Obese Grup	55	94.16	7.42	80.00	112.00	88.00	93.00	99.00	**0.001**
	Control Grup	30	87.40	7.83	71.00	99.00	84.75	90.00	91.25	
TG	Obese Grup	55	121.42	77.10	45.00	434.00	76.00	100.00	147.00	**<0.001**
	Control Grup	30	52.80	10.68	36.00	80.00	44.00	54.50	57.00	
TC	Obese Grup	55	165.27	51.97	48.00	377.00	134.00	150.00	174.00	**<0.001**
	Control Grup	30	128.87	16.86	94.00	162.00	118.60	128.00	141.50	
HDL-C	Obese Grup	55	46.11	10.45	25.00	73.00	40.00	46.00	51.00	**0.020**
	Control Grup	30	55.60	15.13	38.00	83.00	40.00	55.00	67.25	
LDL-C	Obese Grup	55	94.32	38.45	54.20	296.60	70.40	84.40	108.40	**<0.001**
	Control Grup	30	57.77	13.11	38.00	90.00	45.00	58.00	63.25	
HOMA-IR	Obese Grup	55	3.85	2.12	1.01	9.83	2.08	3.68	4.96	**<0.001**
	Control Grup	30	1.34	.34	.84	2.05	1.19	1.28	1.51	
Insulin	Obese Grup	55	16.31	9.10	4.67	45.78	10.49	15.00	19.96	**<0.001**
	Control Grup	30	6.16	1.78	3.90	9.10	4.93	6.00	7.15	

Abbreviations: N,number; SD,standard deviation; BMI, body mass index (kg/m2); WC, waist circumference (in cm); SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg); FBG, fasting blood glucose (mg/dl); TG, triglycerides (mg/dl); TC, total cholesterol (mg/dl); HDL-C, high density lipoprotein- cholesterol (mg/dl); LDL-C, low density lipoprotein- cholesterol (mg/dl); HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; Insulin, µIU/ml.

Descriptive statistics and group comparison results of ocular measurements are given in Table 2. When the table was examined, it was seen that the mean of CCT and LT were significantly higher in the obese group (572.9 ± 14.5 vs. 559.5 ± 10.1 µm, p=0.001; 3.6 ± 0.14 vs. 3.48 ± 0.25 mm, p=0.007) . No significant difference was found between the obese and control groups in terms of other parameters.

Table 2. Descriptive statistics and group comparison results of ocular measurements

	Groups	N	Mean	SD	Min	Max	Percentiles			P
							1st Quartile	Median	3rd Quartile	
IOP	Obese Grup	55	16.0	2.92	9.0	21.0	14.0	16.0	18.0	0.067
	Control Grup	30	14.8	2.50	11.0	19.0	13.5	15.0	17.2	
CCT	Obese Grup	55	572.9	14.5	535.0	608.0	563.0	573.0	581.0	**0.001**
	Control Grup	30	559.5	10.1	545.0	576.0	552.5	558.0	565.0	
ACD	Obese Grup	55	3.4	0.2	2.7	4.3	3.2	3.4	3.6	0.133
	Control Grup	30	3.3	0.3	2.7	3.8	3.2	3.3	3.5	
LT	Obese Grup	55	3.6	0.14	3.28	3.85	3.49	3.62	3.69	**0.007**
	Control Grup	30	3.48	0.25	2.53	3.77	3.47	3.53	3.67	

Abbreviations:N,number; SD,standard deviation; IOP, intraocular pressure (mmHg); CCT, central corneal thickness (µm); ACD, anterior chamber depth (in mm); LT, lens thickness (in mm).

When the correlations between anthropometric and metabolic characteristics and Ocular measurements were examined separately in both groups, the results given in Table 3 were obtained. When Table 3 was examined, no ocular parameter was found that had a significant relationship with age, systolic blood pressure (SBP) and FBG in both groups. BMI and WC were found to have a significant negative correlation with LT control groups. The obese group showed a significant positive correlation between IOP and TG (r=0.276, p=0.042) and a significantly negative correlation with HDL-C (r=-0.273, p=0.043). In the control group, there was a significant positive correlation between IOP and BMI (r=0.389, p=0.034), WC (r=0.497, p=0.005), HOMA-IR (r=0.384, p=0.036), Insulin (r=0.407, p=0.026), and a significant negative correlation with TC (r=-0.511, p=0.004). It was determined that there was no correlation between the anthropometric and metabolic characteristics of the obese group and CCT and ACD, a significantly positive correlation between ACD and LDL-C (r=0.371, p=0.043) and a significantly negative correlation between HOMA-IR in the control group (r=-0.682, p=0.000).

Table 3. Correlations between demographic characteristics and Ocular measurements in obese and control groups.

		Obese Grup (n=55)				Control Grup (n=30)			
		IOP	CCT	ACD	LT	IOP	CCT	ACD	LT
Age	r	-.030	-.176	.023	-0.14	.260	-0.23	-.062	-.329
	P	.831	.197	.866	0.31	.166	0.09	.744	.076
BMI	r	.071	-.034	-.058	-0.20	**.389**	-0.01	.009	**-.633**
	P	.606	.804	.674	0.15	**.034**	0.94	.961	**.000**
WC	r	.044	-.093	.028	-0.25	**.497**	-0.16	-.193	**-.749**
	P	.749	.500	.839	0.07	**.005**	0.24	.307	**.000**
Systolic BP	r	.181	-.020	.041	-0.08	-.165	-0.01	-.241	-.315
	P	.186	.882	.765	0.58	.385	0.95	.200	.090
Diastolic BP	r	.150	-.127	-.007	-0.21	-.202	**-0.27**	-.163	.114
	P	.275	.356	.962	0.13	.285	**0.04**	.389	.547
FBG	r	.204	-.103	-.029	-0.11	-.131	-0.08	-.197	.122
	P	.135	.455	.833	0.44	.491	0.55	.297	.519
TG	r	**.276**	-.033	-.048	0.11	-.054	-0.16	.064	.016
	P	**.042**	.813	.728	0.43	.775	0.24	.735	.932
TC	r	.058	.030	.161	0.03	**-.511**	-0.04	.307	-.023
	P	.674	.826	.239	0.81	**.004**	0.78	.099	.905
HDL-C	r	**-.273**	.141	-.100	0.01	-.310	0.25	-.156	-.153
	P	**.043**	.306	.469	0.97	.096	0.07	.412	.420
LDL-C	r	.028	-.066	.194	0.04	-.329	-0.01	**.371**	-.220
	P	.839	.631	.157	0.77	.076	0.92	**.043**	.242
HOMA-IR	r	.125	-.122	.015	0.02	**.384**	-0.09	**-.682**	-.066
	P	.364	.375	.914	0.90	**.036**	0.51	**.000**	.729
Insulin	r	.134	-.132	.072	0.02	**.407**	-0.07	-.188	.088
	P	.331	.336	.603	0.88	**.026**	0.59	.320	.642

Abbreviations: N,number; BMI, body mass index (kg/m2); WC, waist circumference (in cm); SBP, systolic blood pressure (mmHg); DBP, diastolic blood pressure (mmHg); FBG, fasting blood glucose (mg/dl); TG, triglycerides (mg/dl); TC, total cholesterol (mg/dl); HDL-C, high density lipoprotein- cholesterol (mg/dl); LDL-C, low density lipoprotein- cholesterol (mg/dl); HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; Insulin, µIU/ml.

DISCUSSION

This study aimed to evaluate the effects of obesity and related metabolic changes on anterior segment parameters, intraocular pressure (IOP), and anterior chamber depth (ACD). No significant differences were found in IOP and ACD between the groups ($p>0.05$). However, significantly higher central corneal thickness (CCT) and lens thickness (LT) measurements were observed in the childhood obesity group compared to the healthy children. As expected, fasting blood glucose (FBG), total cholesterol (TC), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), homeostatic model assessment of insulin resistance (HOMA-IR), and insulin levels were significantly higher in the obese group.

Furthermore, there was a significant negative correlation between body mass index (BMI) and waist circumference (WC) with LT in the control group only. In the obese group, there was a significant positive correlation between IOP and TG, and a significant positive correlation was found between IOP and BMI, WC, HOMA-IR, and insulin in the control group. Additionally, a significant negative correlation was found between IOP and TC in the control group. However, no significant correlations were observed between anthropometric and metabolic characteristics and CCT or ACD in the obese group. In the control group, there was a significantly positive correlation between ACD and LDL-C, and a significantly negative correlation between ACD and HOMA-IR.

Previous studies have examined the relationship between obesity and IOP. Akıncı et al. found that obesity is a risk factor for increased IOP in pediatric patients (10). Baran et al. reported elevated IOP in obese children in a study involving 61 obese patients and 35 healthy control subjects (11). Pekel et al. reported similar IOP measurements in obese and non-obese children (12). Kocak et al. compared IOP values between obese and normal-weight children and found no significant difference in IOP values, visual field examinations, and cup/disc ratios between the two groups (5).

Obesity has emerged as a significant problem not only in adults but also in children. However, the impact of obesity on intraocular pressure (IOP) in children is not yet fully understood. Several possible mechanisms have been proposed to explain the association between obesity and elevated IOP. These include the presence of excess intraorbital fat tissue, increased episcleral venous pressure, and reduced outflow, which collectively contribute to higher IOP in obese individuals (13,14). Additionally, obesity can lead to increased blood viscosity due to elevated red blood cell count, hemoglobin, and hematocrit levels, resulting in increased resistance to outflow in the episcleral vessels. Elevated arterial blood pressure also contributes to increased IOP by raising ciliary artery pressure and promoting ultrafiltration of the aqueous humor (15,16). Furthermore, obesity, particularly in the presence of insulin resistance, can contribute to increased IOP (17). Autonomic dysfunction and hyperglycemia, which are commonly associated with insulin resistance, may create an osmotic gradient leading to fluid shift into the intraocular space, thus affecting IOP.

In this study, overweight/obese children with a mean BMI of 27.17 kg/m2 were included, as children with very high BMIs often exhibit insulin resistance. Previous research has shown a connection between obesity and IOP in both adults and children (18). Cohen et al. investigated the relationship between BMI and IOP in men and women and found obesity to be a risk factor for elevated IOP in both genders (19).

The study revealed that the mean central corneal thickness (CCT) and lens thickness (LT) were significantly higher in the obese group. However, a study conducted by Güneş et al. did not find a significant difference in CCT between the two groups (20). Similarly, studies by Erol et al. and Acer et al. also reported no significant differences in CCT and anterior chamber depth (ACD) between the obese and healthy groups (21,22).

Numerous studies have found a positive association between obesity and lens thickness, although the underlying mechanism is not fully understood. It is possible that oxidative stress plays a role in the development of obesity-related diseases, including cataracts (4,22,23). Similarly, in our study, LT was found to be statistically significant and higher in the obese group. The significant differences in fasting blood glucose, HOMA-IR, and insulin levels between the obese and control groups, as well as the association between LT and CCT, may be attributed to the osmotic balance mechanisms influenced by high blood glucose levels.

Another study that investigated changes in ocular measurements related to obesity found a positive correlation between intraocular pressure (IOP) and body mass index (BMI), as well as between BMI and anterior chamber depth (ACD). The results demonstrated that the obese group had significantly higher ACD and IOP compared to the control group (24).

In our study, a significant negative correlation was observed between diastolic blood pressure (DBP) and central corneal thickness (CCT) in the control group. However, no significant relationship was found between any ocular parameter and age, systolic blood pressure (SBP), or fasting blood glucose (FBG) in both groups. However, a study by Okosun et al. showed a positive correlation between waist circumference and blood pressure and FBG, indicating that as the

BMI index increases, the likelihood of increased FBG also rises (25). Previous studies have also reported an adverse link between BMI and parameters such as anterior chamber depth (ACD) and anterior chamber angle (ACA) (7,20).

A limitation of our study was the small number of patients, as some children exhibited low cooperation during the testing process. We believe that the lack of a significant difference in IOP values between the obese and control groups in our study may be attributed to the inclusion of obese individuals with relatively low BMI, the use of non-contact tonometry for intraocular pressure measurement, and differences in systemic parameters such as SBP, FBG, and HOMA-IR. It is important to note that obesity has been associated with various ocular diseases.

In conclusion, our study found higher CCT and LT in the obese group compared to the control group. However, no significant differences were observed in IOP and ACD between the obese and control groups. Further literature studies are necessary to gain a better understanding of the relationships between ocular parameters in children with obesity and those with a normal BMI.

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RESEARCH ARTICLE

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Evaluation of Academicians' Levels of Nutritional Knowledge and Adherence to the Mediterranean Diet

ABSTRACT

Objective: In this study, it was aimed to evaluate the nutritional knowledge levels of academicians and their adherence to the Mediterranean diet.

Methods: The research data were collected face to face with the help of a questionnaire created by the researchers. Demographic characteristics, anthropometric measurements, nutritional habits, nutritional knowledge levels and adherence to the Mediterranean diet were questioned with the questionnaire form. Nutritional knowledge levels of individuals were evaluated with the 'Nutrition Knowledge Level Scale for Adults (NKLSA)'. Mediterranean diet pattern characteristics were identified with the 'Mediterranean diet adherence score (MEDAS)'.

Results: The mean age of the individuals was 40.2±9.20 years, 42.2% of individuals were overweight and 7.8% are obese. 8.4% of the individuals had bad, 24.7% moderate, 44.8% good, 22.1% very good basic nutrition knowledge levels. 7.1% of the individuals had bad, 26.6% moderate, 27.9% good, 38.3% very good knowledge levels about food preference. 68.2% of individuals were in compliance with the Mediterranean diet. A statistically significant difference was found between individuals who did and did not comply with the Mediterranean diet in terms of the total score of NKLSA, basic nutrition knowledge score and food preference knowledge score ($p<0.05$).

Conclusions: It was determined that the majority of academicians were in compliance with the Mediterranean diet and their nutritional knowledge level was good. However, half of the academicians were determined to be overweight or obese, which is a risk factor for noncommunicable chronic diseases.

Keywords: Mediterranean Diet, Nutritional Knowledge, Academicians.

Akademisyenlerin Beslenme Bilgi Düzeylerinin ve Akdeniz Diyetine Uyumlarının Değerlendirilmesi

ÖZET

Amaç: Bu çalışmada, akademisyenlerin beslenme bilgi düzeylerinin ve Akdeniz diyetine uyumlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Araştırma verileri, araştırmacılar tarafından oluşturulan anket formu yardımıyla yüz yüze toplanmıştır. Anket formu ile demografik özellikler, antropometrik ölçümler, beslenme alışkanlıkları, beslenme bilgi düzeyleri ve Akdeniz diyetine uyum sorgulanmıştır. Bireylerin beslenme bilgi düzeyleri 'Yetişkinler İçin Beslenme Bilgi Düzeyi Ölçeği (YETBİD)' aracılığı ile değerlendirilmiştir. Akdeniz diyet örüntüsü özellikleri 'Akdeniz Diyeti Bağlılık Ölçeği (MEDAS)' ile belirlenmiştir.

Bulgular: Bireylerin yaş ortalaması 40,2±9,20 yıldır, bireylerin %42,2'si fazla kilolu ve %7,8'i obezdir. Bireylerin %8,4'ü kötü, %24,7'si orta, %44,8'i iyi, %22,1'i çok iyi temel beslenme bilgi düzeyine sahiptir. Bireylerin besin tercihi konusunda %7,1'i kötü, %26,6'sı orta, %27,9'u iyi, %38,3'ü çok iyi bilgi düzeyine sahiptir. Bireylerin %68,2'si Akdeniz diyetine uyum sağlamaktadır. Akdeniz diyetine uyum sağlayan ve sağlamayan bireyler arasında YETBİD toplam puanı, temel beslenme bilgi puanı ve besin tercihi bilgi puanı açısından istatiksel olarak anlamlı fark saptanmıştır ($p<0.05$).

Sonuç: Akademisyenlerin büyük çoğunluğunun Akdeniz diyetine uyum gösterdiği ve beslenme bilgi düzeyinin iyi derecede olduğu saptanmıştır. Ancak akademisyenlerin yarısının fazla kilolu veya obez olduğu belirlenmiştir, bu durum bulaşıcı olmayan kronik hastalıklar için bir risk faktörüdür.

Anahtar Kelimeler: Akdeniz Diyeti, Beslenme Bilgisi, Akademisyenler.

INTRODUCTION

Nutritional chronic diseases are a global epidemic. Nutrition is an important intervention method in both the prevention and treatment of chronic diseases (1). Overweight or obesity is defined as excessive accumulation of fat in the body. According to the latest report of the World Health Organization, the prevalence of obesity in our country is 32.1% and Turkey is the country with the highest obesity prevalence in Europe (2). Nutritional knowledge has an important place in exhibiting positive eating behaviors and plays a role in acquiring and maintaining healthier eating habits (3). In various studies in the literature, it has been determined that the level of education has a positive effect on nutritional knowledge and eating habits (4, 5).

In the Mediterranean diet, a high intake of fruits, vegetables, whole grains, legumes, nuts, and olive oil is combined with a moderate intake of meat and dairy products. This diet pattern is associated with a reduced incidence of obesity, hypertension, metabolic syndrome, cardiovascular diseases, neurodegenerative diseases, cancer, depression and respiratory diseases (6-8). The Mediterranean diet is adopted as a health-protective and ecologically sustainable diet model. Sustainability has become a major concern in recent years due to climate changes. The diets applied contribute to greenhouse gas emissions, water and land use, energy consumption and environmental pollution. The Mediterranean diet is a cultural model that includes the way food is produced, processed and distributed. The Mediterranean diet model is seen as a healthy and environmentally friendly approach (9, 10).

Academicians are individuals with the highest education level in society. For this reason, it is expected that their knowledge level will be high in parallel with their education level. In this study, it was aimed to evaluate the nutritional knowledge levels and adherence to the Mediterranean diet of the academicians, who are the group with the highest education level in the society.

MATERIAL AND METHODS

The population of this cross-sectional and descriptive study consisted of 321 academicians working at Trakya University Faculty of Medicine and Faculty of Health Sciences. It was aimed to reach the entire population without making a sample selection, but since there were those who could not be reached and did not want to participate in the study, the data of 154 (47.9%) volunteer academicians were obtained and the study was completed. Before starting the study, 'Ethics Committee Approval' with the decision number 18/22 was obtained from the Trakya University Faculty of Medicine Non-Invasive Scientific Research Ethics Committee. The Declaration of Helsinki was followed in every step of the study's protocols. Informed consent was obtained from all participants included in the study.

Data Collection Tools: The research data were collected face to face with the help of a questionnaire created by the researchers. Demographic characteristics, anthropometric measurements, nutritional habits, nutritional knowledge levels and adherence to the Mediterranean diet were questioned with the questionnaire form.

Nutritional knowledge levels of individuals were evaluated with the 'Nutrition Knowledge Level Scale for Adults (NKLSA)'. The scale was developed by Batmaz and Güneş (11), and its reliability and validity were made. The scale consists of 2 sub-factors: 'basic nutrition' and 'food preference'. The maximum score that can be obtained from the basic nutrition section is 80, and the maximum score that can be obtained from the food preference section is 48. Nutritional knowledge levels of individuals are evaluated as bad, moderate, good and very good according to the scores obtained from the scale.

The Mediterranean diet adherence score (MEDAS) was used to determine the participants' features related to the Mediterranean diet pattern. The scale consists of 14 questions, and a total score of 7 or higher shows that the subject adheres to the Mediterranean diet to an appropriate degree (12-14).

According to their methods, body weight was recorded using a calibrated scale, and height was taken using a stadiometer. In order to determine the body mass index (BMI) value, the body weight was divided by the square of the height. Underweight was defined as a body mass index below 18.50 kg/m^2, normal as between 18.50 and 24.99 kg/m^2, overweight as between 25.0 and 29.99 kg/m^2, and obese as above 30.0 kg/m^2 (15).

Statistical Analysis: The Statistics Package for Social Sciences (SPSS) 22.0 statistical package tool was used to analyze the research's data. Distribution analysis of the data was performed using the histogram, coefficient of variation ratio, Skewness, Kurtosis and Kolmogorov-Smirnov tests. In the comparison of paired groups, Mann Whitney U test was used for methods that were not suitable for normal distribution in independent groups. Relationships between numerical variables are given by Spearman correlation coefficient. The results were evaluated at the 95% confidence interval, statistically at $p<0.05$ significance level.

Post-hoc power analysis was performed using the G*Power (version 3.1.9.7, Universitat Düsseldorf, Düsseldorf, Germany), and the effect size was computed for the mean difference NKLSA score between the groups complying and not complying with the Mediterranean diet. The analysis determined that for the statistical

significance of 2-sided alpha of 5%, the study power (1- β) was 86%.

RESULTS

The general characteristics of the individuals were given in Table 1. A total of 154 individuals (95 female, 59 male) were included in the study. The mean age of the individuals was 40.2±9.20 years, and the mean BMI was 25.1±3.62 kg/m2. 42.2% (n=65) of individuals were overweight and 7.8% (n=12) are obese.

Table 1. General characteristics of individuals

Variables	**n (%)**
Gender	
Female	95 (61.7)
Male	59(38.3)
Marital status	
Married	101 (65.6)
Single	53 (34.4)
Chronic disease status	
Yes	65 (42.2)
No	89 (57.8)
Affiliated faculty	
Faculty of Medicine	98 (63.6)
Faculty of Health Sciences	56 (36.4)
	X̄±SD
Age (years)	40.2±9.20
BMI (kg/m^2)	25.1±3.62
BMI classification	
Underweight (<18.50 kg/m^2)	3 (1.9)
Normal (18.50-24.99 kg/m^2)	74 (48.1)
Overweight (25.00-29.99 kg/m^2)	65 (42.2)
Obese (≥30.0 kg/m^2)	12 (7.8)

Nutritional habits of individuals were given in Table 2. The average number of main meals was 2.7±0.49, and the number of snacks was 1.7±1.04. 53.9% (n=83) of the individuals were skipping meals. The most skipped main meal was breakfast (56.6%). 51.3% (n=79) of the individuals stated that they received education/information about healthy nutrition. 32.9% (n=26) of the individuals who received education /information about healthy nutrition stated that they received this education /information from a dietitian and 15.2% (n=12) of the individuals stated that they received it from other health personnel.

Table 2. Nutritional habits of individuals

	X̄±SD
Number of main meals	2.7±0.49
Number of snacks	1.7±1.04
	n (%)
Skipping the main meal	
Yes	83 (53.9)
No	71 (46.1)
Skipped meal	
Breakfast	47 (56.6)
Lunch	29 (34.9)
Dinner	7 (8.5)
Receiving education/information about healthy eating	
Yes	79(51.3)
No	75 (48.7)
Person/tool for education/ information	
Dietitian	26 (32.9)
Other health personnel	12 (15.2)
Undergraduate course	19 (24.1)
Social media tools	22 (27.8)

Nutritional knowledge levels of individuals were given in Table 3. 8.4% (n=13) of the individuals had bad, 24.7% (n=38) moderate, 44.8% (n=69) good, 22.1% (n=34) very good basic nutrition knowledge levels. 7.1% (n=11) of the individuals had bad, 26.6% (n=41) moderate, 27.9% (n=43) good, 38.3% (n=59) very good knowledge levels about food preference. There was a significant difference in NKLSA total score and food preference knowledge score according to the status of receiving education/information about healthy eating (p=0.036; p=0.023, respectively).

Table 3. Nutritional knowledge levels of individuals

	Total X̄±SD	**Receiving education/information about healthy eating**		**p-value**
		Yes	**No**	
NKLSA total score	97.7±14.47	100.2±14.88	95.2±13.64	**0.036***
Scale subfactors				
Basic nutrition knowledge score	58.1±10.80	59.5±11.48	56.6±9.89	0.091
Bad (<45 points)	13 (8.4)	6 (7.6)	7 (9.3)	
Moderate (45-55 points)	38 (24.7)	18 (22.8)	20 (26.7)	
Good (55-65 points)	69 (44.8)	34 (43.0)	35 (46.7)	
Very good (>65 points)	34 (22.1)	21 (26.6)	13 (17.3)	
Food preference knowledge score	39.6±5.77	40.6±5.59	38.5±5.78	**0.023***
Bad (<30 points)	11 (7.1)	2 (2.5)	9 (12.0)	
Moderate (30-36 points)	41 (26.6)	19 (24.1)	22 (29.3)	
Good (37-42 points)	43 (27.9)	22 (27.8)	21 (28.0)	
Very good (>42 points)	59 (38.3)	36 (45.6)	23 (30.7)	

Mann-Whitney U test, *p<0.05

The evaluation of nutritional knowledge levels of individuals according to their adherence to the Mediterranean diet was given in Table 4. 68.2% (n=105) of individuals were in compliance with the Mediterranean diet. A statistically significant difference was found between individuals who did and did not comply with the Mediterranean diet in terms of the total score of NKLSA, basic nutrition knowledge score and food preference knowledge score (p=0.003, p=0.004, p=0.038, respectively). The BMI values of the individuals did not differ according to their compliance with the Mediterranean diet (p>0.05).

Table 4. Evaluation of the nutritional knowledge level of individuals according to their adherence to the Mediterranean diet

	$\bar{X}$±SD		
	NKLSA total score	**Basic nutrition knowledge score**	**Food preference knowledge score**
Compliance with the Mediterranean diet (≥7 points) (n=105/68.2%)	100.1±14.02	59.9±10.51	40.2±5.70
No compliance with the Mediterranean diet (<7 points) (n=49/31.8%)	92.6±14.20	54.3±10.54	38.2±5.73
p-value	**p=0.003***	**p=0.004***	**p=0.038***

Mann-Whitney U test, *p<0.05

The relationship between nutritional knowledge level and some variables was given in Table 5. A statistically significant weak positive correlation was found between the number of snacks and the total score of NKLSA and basic nutrition knowledge score (p<0.05).

Table 5. Evaluation of the relationship between nutritional knowledge level and some variables

	NKLSA total score	**Basic nutrition knowledge score**	**Food preference knowledge score**
Age	r=0.101 p=0.212	r=0.084 p=0.300	r=0.132 p=0.102
BMI (kg/m^2)	r=-0.064 p=0.434	r=-0.103 p=0.202	r=0.025 p=0.760
MEDAS	r=0.100 p=0.218	r=0.083 p=0.308	r=0.111 p=0.169
Number of main meals	r=0.029 p=0.722	r=0.073 p=0.368	r=-0.033 p=0.683
Number of snacks	r=0.169 **p=0.036***	r=0.204 **p=0.011***	r=0.113 p=0.161

Spearman correlation, *p<0.05

DISCUSSION

In this study, the nutritional knowledge levels of Trakya University academicians and their adherence to the Mediterranean diet were evaluated. Almost half of the academicians (53.9%) skipped meals, and half of the academicians (50.0%) were overweight or obese. The number of studies evaluating the nutritional habits of academicians in our country is quite limited. In the study conducted by Bayramoğlu et al.(16), it was determined that 71.4% of the academicians skipped meals, and 45.7% were overweight or obese. In another study, it was found that 72.0% of the academicians skipped meals and 41.4% were overweight or obese (17). Similar to the studies conducted in this study, it was determined that the rate of skipping meals and overweight or obese individuals was high in academicians.

Nutrition education is effective on individuals' nutritional knowledge and nutrition-related behaviors. Nutrition education is the most common theory used to maintain sustainable and healthy eating behaviors (18-20). In this study, it was determined that individuals who received education/information about healthy eating had higher nutritional knowledge. Obtaining nutritional education/information from an accurate and reliable source is as important as obtaining nutritional education/information (18, 21). In this study, the majority of individuals (72.2%) stated that they received this information from any health personnel or as a course. According to the result of the study, it was determined that the academicians were aware of the reliable source of nutrition.

In this study, it was determined that the majority of the academicians had a good level of knowledge about basic nutrition and food preference (66.9% and 66.2%, respectively). In a study conducted with doctors in our country, it was determined that 53.3% of individuals had good nutritional knowledge (22). In another study conducted with adults, it was determined that 42.8% of the individuals had a good level of basic nutrition knowledge and 46.2% of them had a good

level of food preference (23). The fact that the level of nutritional knowledge was higher in this study than in other studies may be due to the higher education level of the individuals.

The Mediterranean diet is a healthy and sustainable diet model. Adherence to the Mediterranean diet is associated with a reduced risk of chronic disease (24-26). In this study, it was determined that the majority of the academicians (68.2%) compliance with the Mediterranean diet in parallel with their nutritional knowledge level. In addition, it was determined in the study that individuals who comply with the Mediterranean diet have higher nutritional knowledge than individuals who do not comply with the diet. Nutritional knowledge is effective on the nutritional behaviors of individuals (27). It is an expected situation that individuals with a high level of nutritional knowledge will tend to healthy and positive eating behaviors.

CONCLUSION

As a result, it was determined that the majority of Trakya University academicians were in compliance with the Mediterranean diet and their nutritional knowledge level was good. However, it was determined that half of the academicians were overweight or obese. Being overweight/obesity is a risk factor for the development of chronic diseases. Although the level of nutritional knowledge and compliance with the Mediterranean diet were high in our study, the high number of overweight/obese individuals may be due to the fact that the individuals are physically inactive. Academicians, like other individuals in the society, should be followed by family physicians in units providing primary care preventive health services in terms of obesity-related chronic diseases. It is very important for the academicians, who have the highest education level in the society, to have high nutritional knowledge and to display positive nutritional behaviors in terms of being social role models.

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RESEARCH ARTICLE

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Reliability and Validity of the Turkish Version of the Food Disgust Scale

ABSTRACT

Objective: The feeling of disgust for food plays an important role in many situations, especially in food choice and consumption. Since the feeling of disgust is effective in many events that affect individuals' daily-life, it is important to understand the role of this emotion in food-related behaviours. Recently, a 32-item instrument to Food Disgust Scale (FDS) developed and validated. This study aims to validate the FDS for the first time in Turkish population.

Methods: This cross-sectional study included 240 healthy Turkish individuals between the ages of 19-65. The research was carried out on the internet between July 2020-February 2021 with the survey method. The scale was evaluated with a six-point Likert scale as in the original. Statistical analyses were made with the R-Project program and lavaan packages. A Turkish version of the FDS (FDS-TR) was tested with confirmatory factor analysis (CFA) in order to test the original item.

Results: In this study, the Cronbach's Alpha coefficient of the scale was determined as 0.914. The Cronbach's Alpha reliability coefficients for FDS-TR subscales varied between 0.717-0.902. The fit indices provided by confirmatory factor analysis results were also within the acceptable range.

Conclusions: This study results indicate that FDS-TR is highly reliable in healthy individuals and can be used safely in future studies. It is recommended that the scale be used to determine the effects of food disgust on many issues such as food waste, obesity, eating behaviour in our country.

Keywords: Disgust, Likert Scale, Reliability, Turkish Society, Validity.

Gıda Tiksinme Ölçeğinin Türkçe Uyarlamasının Geçerlik ve Güvenirliği

ÖZET

Amaç: Gıdalardan tiksinme duygusu, özellikle gıda seçimi ve tüketimi olmak üzere birçok durumda önemli rol oynar. Bireylerin günlük yaşamı etkileyen pek çok olayda iğrenme duygusu etkili olduğundan, bu duygunun gıdalarla ilgili davranışlardaki rolünü anlamak önem arz etmektedir. Son zamanlarda, 32 maddelik bir Gıda Tiksinme Ölçeği (GTÖ) geliştirilmiş ve onaylanmıştır. Bu çalışma, Türk popülasyonunda ilk kez GTÖ'ni doğrulamayı amaçlamaktadır.

Gereç ve Yöntem: Bu kesitsel çalışmaya Türkiye'de yaşayan, 19-65 yaş arası sağlıklı 240 kişi dahil edilmiştir. Araştırma anket formu yöntemi ile Temmuz 2020-Şubat 2021 tarihleri arasında internet ortamında yürütülmüştür. Ölçek orijinalindeki gibi altılı Likert ile değerlendirilmiştir İstatistiksel analizler R-Project programı ve lavaan paketleri ile yapılmıştır. Orijinal ölçek maddelerini test etmek için GTÖ'nin Türkçe uyarlaması (GTÖ-TR) doğrulayıcı faktör analizi (DFA) ile test edilmiştir.

Bulgular: Bu çalışmada ölçeğin Cronbach's Alpha katsayısı 0.914 olarak belirlenmiştir. GTÖ-Tr alt boyutları için Cronbach's Alpha güvenirlik katsayıları 0.717-0.902 arasında değişmektedir. Doğrulayıcı faktör analizi sonucu hesaplanan uyum indeksleri de kabul edilebilir aralıktadır.

Sonuç: Çalışma sonuçları, GTÖ-TR'nin sağlıklı bireylerde oldukça güvenilir olduğunu ve gelecekteki çalışmalarda güvenle kullanılabileceğini göstermektedir. Ölçeğin, ülkemizde toplumun gıdadan tiksinmeye yönelik davranışlarının gıda israfı, obezite, yeme davranışı bozuklukları gibi pek çok konu üzerindeki etkisinin belirlenmesinde kullanılması önerilmektedir.

Anahtar Kelimeler: Tiksinme, Likert Ölçek, Güvenirlik, Türk Toplumu, Geçerlik.

INTRODUCTION

Disgust is a fundamental human emotion that acts as a defence against microbes and potentially harmful substances by triggering avoidance and that has an important role in our daily lives (1). For example, disgust may affect hand washing (2) prevention of diseases (3,4) adoption of new food products (5) eating behaviour (6) and food wastefulness (7).

Fundamentally, food disgust is the mechanism of rejecting food and it affects the methods of food processing, food consumption etc. (2,3,8). Studies have shown that individuals with more prominent food disgust have limited variety in their diets (2,8), obese individuals have less tendency towards food disgust compared to individuals with normal body weight (9). and more easily disgusted consumers cause more wasted food compared to consumers that are not disgusted easily (7).

It is important to understand the role of disgust in terms of food-related behaviours as it is one of the impactful factors affecting many parts of daily life. In order to understand this role of disgust, scientific interest has increased in the subject of food related disgust. Better understanding of the underlying mechanisms of food disgust will both provide better understanding of the behaviour and also contribute towards various subjects such as estimating food preferences of people, regulating eating behaviours of people, making the acceptance of newly developed food products easier and preventing food waste. Hartmann and Siegrist (8). developed the Food Disgust Scale (FDS) with 32 items to measure the sensitivity of disgust of people towards food and food related situations. FDS is the first scale that offers an insight to food disgust and that fills a void in the current literature. With this scale, individuals' reactions related to disgust towards food related situations such as food contamination, decay etc. are evaluated. Inter-cultural differences may affect food disgust sensitivity. Therefore, it is an interesting subject to show how the Food Disgust Scale (FDS) will provide results in different cultures. As far as we are aware, the validity and reliability of FDS for Turkish has not been researched. The purpose of this present research is to adapt the Food Disgust Scale developed by Hartmann and Siegrist (8) to Turkish.

MATERIAL AND METHODS

Type and Sample of the Research: This research is a methodological type research conducted in order to adapt Food Disgust Scale to Turkish and to evaluate its validity and reliability. Even though sample size can be estimated with relative criteria such as factor and number of items, sample size usually needs to be 5-10 times the number of items in the scale (10). Therefore, when it is considered that there are 32 items in the original scale, a sample size of 160 people is going to be sufficient for this research. A total of 240 healthy individuals between the ages of 19-63 participated in the study.

The research inclusion criteria are; acceptance of participation to the study by individuals, being older than 18 years of age, having no visual impairment, being literate in Turkish and having internet access. The research was conducted via questionnaire form method over the internet (Microsoft Forms) between July 2020-February 2021. Researchers announced the study by sharing the study link through their own social media platforms (Facebook®, WhatsApp® and Instagram®). Additionally, as the individuals that saw the study announcement and participants shared the study link through their own social media, the data collection process was completed in eight months. The information about the study was given to the individuals through an information text that was at the beginning of the questionnaire form and the individuals that had decided to participate in the study filled the form and submitted it online. On average, participants answered the questionnaire in 10-15 minutes.

Data Collection Tools: Sociodemographic information form and Food Disgust Scale (FDS) was used to collect data.

Sociodemographic Information Form: In the socio-demographic information form which is the first section of the questionnaire form, there are 7 questions that ask for general information such as "age, gender, level of education, occupation, marital status, level of income and family type" about the sample.

Food Disgust Scale (FDS): Food disgust scale is psychometrically validated scale that was developed by Hartmann and Siegrist in 2018 (8) that measures the food disgust of individuals. The scale consists of 32 items and 8 subscales. The subscales of the scale are; animal meat (4 items- situations associated with raw meat or certain parts of animals), poor hygiene (5 items- poor hygienic conditions in the preparation of food or eating), human contamination (4 items- shared use of cutlery or other people's contact with utensils and food,), mold (4 items- mold that has been removed from food), decaying fruit (4 items- fruits that are overripe and change their color or texture), fish (4 items- texture and smell of fish), decaying vegetables (4 items- vegetables that are overripe and change their color or texture) and living contaminants (3 items- exposure of food to worms). The participants are asked how disgusted they are about the products or situations given in the scale. The answers range from "Not Disgusting at All" -1- to "Extremely Disgusting" -6-. Higher score should state higher food disgust.

Ethical Aspect of the Research: Firstly, permission to adapt the scale was obtained from the authors of the "Food Disgust Scale" via e-mail.

Ethics Committee approval was obtained from Selcuk University Faculty of Health Sciences Ethics Committee for Non-Interventional Clinical Investigations with decision numbered 2020/597.

Data Analyses: All of the statistical analyses were completed using R-Project software (11) and lavaan (12) packages. To begin with, frequency analysis results of the demographic variables and descriptive statistics regarding scale items were given. Afterwards, for the subscales of the Food Disgust Scale, Cronbach's Alpha reliability analysis was applied. The adapted Food Disgust Scale was verified through a confirmatory factor analysis (CFA) using a maximum likelihood estimation method. The fit of the model was examined through the Chi-squared test, comparative fit index (CFI), goodness-of-fit index (GFI), adjusted goodness-of-fit index (AGFI), Tucker-Lewis index (TLI), nonnormed fit index (NNFI), incremental fit index (IFI) and root mean square error of approximation (RMSEA). The margin of error in the research was evaluated as 95% validity ($p<0.05$).

Research Application Plan: Permission for the Turkish adaptation of the Food Disgust Scale was obtained via e-mail from the researcher who developed the scale. As part of the adaptation process for the Food Disgust Scale to Turkish, Brislin's (1970) translation-back translation method has been applied (13). The Turkish translation of the scale had been carried out by two people who are researchers and language experts. Afterwards, researchers analysed the optimal translation for each item and jointly prepared a Turkish text. After the required editing had been done, the scale was translated back. After this reverse translation, the sentences in the original text were compared with the ones in the reverse translated text by the researchers, incomprehensible expressions were edited and form was made ready for expert review. In order to evaluate the content validity of the scale, expert opinion was obtained after language adaptation. In this regard, the scale was presented to three experts who had had related studies in the literature. The experts were asked to state their opinions, with explanations where necessary, in terms of suitability of the scale to the expression in the original form in terms of translation, the comprehensibility of the scale towards the targeted group, evaluation of the sufficiency of the scale in terms of evaluating food disgust. The opinions, suggestions and criticisms of the experts on the evaluation forms and each explanation regarding the items were evaluated and the scale was finalized (14,15).

Before the start of the study, 10 participants who complied with the inclusion criteria were contacted online to conduct a preliminary application in order to evaluate the comprehensibility of the scale. No changes were made to the items of the scale after this preliminary application. 10 participants in the preliminary application were not included in the sample.

RESULTS

The average age of the participants are 29.03 ± 9.17 years. Frequency distributions of demographic information of study participants are presented in Table 1. 80.8% of the participants were female, almost half of the participants had bachelor's degree (48.8%) and 40.8% of the participants had specialized professions (lawyer, doctor, engineer etc.). Moreover, 56.3% of the individuals were single, 37.5% had incomes of 6001 TL or more (440 USD or more), and most of them (90.4%) lived in a nuclear family.

Table 1. Demographic findings regarding the individuals.

Variable	n	%
Gender		
Female	194	80.8
Male	46	19.2
Level of education		
Elementary school	5	2.0
Junior high school	3	1.3
High school	20	8.3
Associate degree	21	8.8
Bachelor's degree	117	48.8
Postgraduate	74	30.8
Occupation		
Unemployed	78	32.5
Student	40	16.6
Specialized professions (lawyer, doctor, engineer etc.)	98	40.8
Self employed	9	3.8
Civil servant	15	6.3
Marital status		
Married	91	37.9
Single	135	56.3
Divorced / Widowed	14	5.8
Level of income		
Less than 1500 TL (less than 110 USD)	26	10.8
Between 1500-3000 TL (between 110 - 219 USD)	40	16.7
Between 3001-4500 TL (between 220 - 329 USD)	44	18.3
Between 4501-6000 TL (between 330 - 439 USD)	40	16.7
6001 TL or more (440 USD or more)	90	37.5

Descriptive statistics of the items of Food Disgust Scale and the results of the Cronbach's Alpha reliability analysis are presented in Table 2. As a result of Cronbach's Alpha reliability analysis, corrected correlation values for all of the items of Food Disgust Scale were found to be positive. As an increase cannot be observed in the reliability coefficient when an item is removed from the Food Disgust Scale, all of the items in the scale are included in the analysis. When the results are evaluated, the Cronbach's Alpha reliability coefficients for animal meat, poor hygiene, human contamination, mold, decaying fruit, fish, decaying vegetables and living contaminants were 0.717, 0.797, 0.828, 0.902, 0.841, 0.766, 0.827 and 0.824, respectively. In this study, the Cronbach's Alpha coefficient of the scale was determined as 0.914. When the obtained reliability coefficients are analysed, it is determined that the adapted scale is highly reliable as a compatible literature (16).

Table 2. Reliability analysis results of food disgust scale.

Subscales and Items	Med	R	Adjusted-R	MIC	α
Animal meat					
1. To put animal cartilage into my mouth	4	5	0.516		
2. To see raw meat	2	5	0.583	0.392	0.717
3. To eat a steak that is still bloody inside	5	5	0.408		
4. To see a whole pig (lamb) en brochette *	1	5	0.536		
Poor hygiene					
5. To eat with dirty silverware in a restaurant	6	5	0.607		
6. A meal prepared by a cook who has greasy hair and dirty fingernails	6	4	0.682		
7. If the cook in a restaurant has an open cut	6	5	0.555	0.473	0.797
8. If people blow their nose before they serve my meal	6	4	0.610		
9. Another person's hair in my soup	6	4	0.555		
Human contamination					
10. Food donated from a neighbor whom I barely know	3	5	0.474		
11. If a friend bites into my bread	4	5	0.698		
12. To drink from the same drinking glass a friend has already drunk from	4	5	0.751	0.543	0.828
13. If friends or acquaintance have touched my food	3	5	0.707		
Mold					
14. To eat the mold-free part of a moldy tomato	3	5	0.791		
15. To eat bread from which mold was cut away	3	5	0.813	0.700	0.902
16. To eat hard cheese from which mold was cut off	2	5	0.810		
17. To eat marmalade from which mold was removed from the surface	4	5	0.714		
Decaying fruit					
18. To eat overripe fruits	2	5	0.681		
19. To eat a banana that has black spots	1	5	0.740		
20. To eat fruits (e.g., apple and peach) with pressure marks	1	5	0.691	0.576	0.841
21. To eat apple slices that turned brown when exposed to air	2	5	0.606		
Fish					
22. To have a whole fish with its head on the plate	2	5	0.489		
23. To eat raw fish like sushi	4	5	0.500	0.454	0.766
24. The smell in a fish shop or in fish sections with fresh fish	4	5	0.645		
25. The texture of some kinds of fish in the mouth	3	5	0.644		
Decaying vegetables					
26. To eat brown-colored avocado pulp	3	5	0.548		
27. To eat an overripe cucumber that can already be bent	4	5	0.721	0.544	0.827
28. To eat shrunken radishes	3	5	0.755		
29. To eat salad that is not crispy	4	5	0.595		
Living contaminants					
30. There is a maggot in the cherry that I wanted to eat	5	5	0.772		
31. There is a little snail in the salad that I wanted to eat	6	5	0.582	0.613	0.824
32. There is a worm in my apple	5	5	0.724		

Med: Median, R: Range, Adjusted-R: Corrected item correlation, MIC: Median inter-item correlation, α: Cronbach's alpha coefficient
*The item adapted according to Turkish culture with the permission of the scale authors. In the Turkish adaptation of the scale, the word lamb was preferred instead of pig.

CFA statistics of Food Disgust Scale are shown in Table 3. When the results are analysed, standardized beta coefficients of path coefficients are statistically significant. Fit indices were calculated as a result of the CFA of Food Disgust Scale that had been adapted to Turkish. According to fit indices, Chi-squared statistic was calculated as $\chi^2=354.696$ (sd=436) and the ratio of

χ^2/sd=0.814 was found to be below 2. Other fit indices of the CFA of the Food Disgust Scale are calculated as CFI=1, GFI =0.975, adjusted goodness-of-fit AGFI =0.970, TLI =1, NNFI =1, IFI =1 and all the statistics are above 0.9. Among fit indices, it is calculated that RMSEA =0.000 and this error value is below 0.05. In general, it is seen that Turkish-adapted Food Disgust Scale is statistically valid when CFA findings are analysed (17).

Table 3. CFA statistics of food disgust scale.

Subscales and Items	β	STZ(β)	z-value	p
Animal meat				
1. To put animal cartilage into my mouth	1	0.648	-	-
2. To see raw meat	0.955	0.676	13.698	<0.001
3. To eat a steak that is still bloody inside	0.665	0.538	12.843	<0.001
4. To see a whole pig (lamb) en brochette *	0.706	0.616	13.397	<0.001
Poor hygiene				
5. To eat with dirty silverware in a restaurant	1	0.569	-	-
6. A meal prepared by a cook who has greasy hair and dirty fingernails	0.990	0.572	5.726	<0.001
7. If the cook in a restaurant has an open cut	1.903	0.694	6.418	<0.001
8. If people blow their nose before they serve my meal	1.173	0.740	6.387	<0.001
9. Another person's hair in my soup	1.657	0.750	6.540	<0.001
Human contamination				
10. Food donated from a neighbor whom I barely know	1	0.720	-	-
11. If a friend bites into my bread	1.041	0.706	13.380	<0.001
12. To drink from the same drinking glass a friend has already drunk from	1.057	0.689	13.317	<0.001
13. If friends or acquaintance have touched my food	1.216	0.834	13.979	<0.001
Mold				
14. To eat the mold-free part of a moldy tomato	1	0.836	-	-
15. To eat bread from which mold was cut away	1.058	0.866	19.860	<0.001
16. To eat hard cheese from which mold was cut off	1.093	0.880	20.019	<0.001
17. To eat marmalade from which mold was removed from the surface	0.979	0.766	19.008	<0.001
Decaying fruit				
18. To eat overripe fruits	1	0.811	-	-
19. To eat a banana that has black spots	0.815	0.726	16.316	<0.001
20. To eat fruits (e.g., apple and peach) with pressure marks	0.730	0.720	16.439	<0.001
21. To eat apple slices that turned brown when exposed to air	0.918	0.749	17.085	<0.001
Fish				
22. To have a whole fish with its head on the plate	1	0.644	-	-
23. To eat raw fish like sushi	0.736	0.457	12.082	<0.001
24. The smell in a fish shop or in fish sections with fresh fish	1.224	0.761	15.294	<0.001
25. The texture of some kinds of fish in the mouth	1.174	0.821	15.548	<0.001
Decaying vegetables				
26. To eat brown-colored avocado pulp	1	0.675	-	-
27. To eat an overripe cucumber that can already be bent	1.073	0.745	16.651	<0.001
28. To eat shrunken radishes	1.201	0.808	16.954	<0.001
29. To eat salad that is not crispy anymore	1.009	0.738	16.412	<0.001
Living contaminants				
30. There is a maggot in the cherry that I wanted to eat	1	0.820	-	-
31. There is a little snail in the salad that I wanted to eat	0.625	0.632	14.647	<0.001
32. There is a worm in my apple	1.203	0.901	17.006	<0.001

β: Beta coefficient; STZ(β): Standardized B-beta coefficient

*The item adapted according to Turkish culture with the permission of the scale authors. In the Turkish adaptation of the scale, the word lamb was preferred instead of pig.

DISCUSSION

In our daily lives, disgust plays a significant role. Many factors in our daily lives can be affected by disgust, including eating behaviour (6,18) and the production of food waste (7). In the case of exposure to new and unfamiliar food sources, disgust to food may lead to picky eating (19, 20). In the long run, individuals who exhibit excessively picky eating behaviours may suffer from nutritional deficiencies (21). As a disease avoidance mechanism, food disgust may also be triggered by cues that indicate potential contamination and food inedibility. As a result, people with high food aversion sensitivities may be more sensitive to cues of food spoilage and avoid consuming foods that appear to be deteriorating but may still be edible, resulting in food waste (22). Research has shown

that perception of risk and desire to consume expired food products are correlated (23), as are perceptions of health risk and the amount of food wasted (24).

As of recently, the Food Disgust Scale (FDS) has been developed specifically to measure sensitivity to food-related health-threatening situations (8). The purpose of this research was to adapt the Food Disgust Scale developed by Hartmann and Siegrist (8) to Turkish culture and to study the Turkish form of the scale in terms of validity and reliability. Aside from enabling us to generalize the collected data, scale adaptation studies also provide opportunities to research mutual and different properties between cultures measured (25). It is thought that this scale, adapted into Turkish, will fill a big void in the field. In the first step of the adaptation process, language equivalence study of the original scale was conducted. In this context, the original 32-item form of the scale was translated to Turkish by expert translators. After this step, reverse translation method was conducted and expert reviews was obtained again. It was seen that after the adaptation studies of the scale, equivalency of the Turkish form of the scale to the original scale was acceptable.

In the second step, it was tested if the original form of the scale was reliable and valid for Turkish culture. In the reliability analysis, Cronbach's alpha consistency coefficients were; 0.72 for animal meat, 0.79 for poor hygiene, 0.83 for human contaminants, 0.90 for mold subscale, 0.84 for decaying fruit subscale, 0.77 for fish subscale 0.83 for decaying vegetables and 0.82 for living contaminants subscale. Overall Cronbach's alpha coefficient for the scale was determined as 0.91. Generally, values over 0.70 are considered acceptable for reliability coefficients (26). When the fit indices as a result of confirmatory factor analysis, the ratio of chi-squared over degrees of freedom was below 2. Other fit indices were calculated as; RMSEA=0.000, CFI=1, GFI=0.975, AGFI=0.970, TLI=1, NNFI=1, IFI=1. Therefore, it is evident that Food Disgust Scale is validated through the data obtained from the Turkish sample. These results may be interpreted that the measuring tool will yield valid and reliable results in the future studies.

Through this study, it is determined that Food Disgust Scale is a valid and reliable measuring tool for Turkish culture. This scale, which was determined to be a valid and reliable measure for the Turkish public, might be a reference scale which may be used to develop policies regarding disease prevention, adoption of new foods, evaluation of eating behaviours and food waste reduction, in conducting clinical processes and in scientific studies.

One of the limitations of the study is the fact that research data was collected over the internet due to the COVID-19 pandemic. Moreover, as the scale data was collected online, the sample is limited to literate individuals with internet access. Additionally, due to the voluntary collection of study data, homogeneity was not achieved within the sample. It was observed that female participants showed great interest in the study. Obtaining a more homogeneous sample in future studies is important for comparing the results of the scale with other variables.

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RESEARCH ARTICLE

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Can Typical Cervical Vertebrae Be Distinguished from One Another by Using Machine Learning Algorithms? Radioanatomic New Markers

ABSTRACT

Objective: The aim of this study is to distinguish the typical cervical vertebrae that cannot be separated from one another with the naked eye by using machine algorithms (ML) with measurements made on computerized tomography (CT) images and to show the differences of these vertebrae.

Methods: This study was conducted by examining the 536 typical cervical vertebrae CT images of 134 (between the ages of 20 and 55) individuals. Measurements of cervical vertebrae were made on coronal, axial and sagittal section. 6 different combinations (Group 1: C3 – C4, Group 2: C3 – C5, Group 3: C3 – C6, Group 4: C4 – C5, Group 5: C4 – C6, Group 6: C5 – C6) were formed with parameters of each vertebrae and they were analyzed in ML algorithms. Accuracy (Acc), Matthews correlation coefficient (Mcc), Specificity (Spe), Sensitivity (Sen) values were obtained as a result of the analysis.

Results: As a result of this study, the highest success was obtained with Linear Discriminant Analysis (LDA) and Logistic Regression (LR) algorithms. The highest Acc rate was found as 0.94 with LDA and LR algorithm in Groups 3 and Group 4, the highest Spe value was found as 0.95 with LDA and LR algorithm in Group 5, the highest Mcc value was found as 0.90 with LDA and LR algorithm in Group 5 and the highest Sen value was found as 0.94 with LDA and LR algorithm in Groups 3 and 5.

Conclusions: As a conclusion, it was found that typical cervical vertebrae can be distinguished from each other with high accuracy by using ML algorithms.

Keywords: Typical Cervical Vertebrae, Machine Learning Algorithms, Computerized Tomography.

Tipik Servikal Omurlar Makine Öğrenimi Algoritmaları Kullanılarak Birbirinden Ayırt Edilebilir mi? Radyoanatomik Yeni Belirteçler

ÖZET

Amaç: Bu çalışmanın amacı, bilgisayarlı tomografi (BT) görüntülerinde yapılan ölçümlerle makine algoritmaları (ML) kullanılarak çıplak gözle birbirinden ayrılamayan tipik servikal omurları ayırt etmek ve bu omurların farklılıklarını göstermektir.

Gereç ve Yöntem: Bu çalışma 134 (20-55 yaş arası) bireyin 536 tipik servikal vertebra BT görüntüleri incelenerek yapıldı. Servikal vertebraların koronal, aksiyal ve sagital kesitlerinde ölçümleri yapıldı. Parametrelerle 6 farklı kombinasyon (Grup 1: C3 – C4, Grup 2: C3 – C5, Grup 3: C3 – C6, Grup 4: C4 – C5, Grup 5: C4 – C6, Grup 6: C5 – C6) oluşturulup her bir omur ML algoritmalarında analiz edildi. Analiz sonucunda Doğruluk (Acc), Matthews korelasyon katsayısı (Mcc), Özgüllük (Spe), Duyarlılık (Sen) değerleri elde edildi.

Bulgular: Bu çalışma sonucunda en yüksek başarı Linear Discriminant Analysis (LDA) ve Logistic Regresyon (LR) algoritmaları ile elde edildi. Grup 3 ve Grup 4'te en yüksek Acc oranı LDA ve LR algoritması ile 0.94, en yüksek Spe değeri Grup 5'te LDA ve LR algoritması ile 0.95, en yüksek Mcc değeri LDA ve LR algoritması ile 0.90 olarak bulundu. Grup 5'te en yüksek Sen değeri, Grup 3 ve 5'te LDA ve LR algoritması ile 0.94 olarak bulundu.

Sonuç: Sonuç olarak, tipik servikal vertebraların ML algoritmaları kullanılarak birbirinden yüksek doğruluk oranı ile ayırt edilebildiği bulundu.

Anahtar Kelimeler: Tipik Servikal Omurga, Makine Öğrenimi Algoritmaları, Bilgisayarlı Tomografi.

INTRODUCTION

Vertebral column is an important anatomical structure that is connected to intervertebral disc, formed by the combination of 33 vertebrae, extending from cranium to coccyx (1). The part of this structure in the neck region is called cervical vertebrae and there are 7 of these. Cervical vertebrae 1, 2 and 7 are called atypical, while the others are called typical. Although the basic features of typical vertebrae are the same, their sizes can vary and therefore they can show unique morphometric differences (2).

Cervical vertebrae surgery goes back to 1500s B.C. Although surgical intervention technologies in this area have made significant process up till now, many complications can still occur (3-5). The main reason for these complications is that the complex anatomy of cervical vertebrae limits surgical intervention. The close neighbourhood of cervical vertebrae to vital structures such as vertebral artery, spinal cord and spinal nerves create serious difficulties for surgeons performing interventional procedures in this region (6). It has been reported that transpedicular screw fixation is a surgical procedure that might create confusion for the cervical region and this practice becomes much more complex with the pedicular length and width that changes from individual to individual (7-9). Understanding the relationship between pedicle size and shape and vital adjacent structures increases the reliability of transpedicular screw fixation (10-15).

It has been reported in literature that the positions of vertebrae can be determined with intraoperative computed tomography (iCT) based systems by using intraoperative neuro-navigation methods and with this method, incorrect location of the screw to be used in the cervical area can be prevented (16). Although this information increases the safety of patient based operation, it may not be applied in all centres. This situation shows the importance of clarifying cervical vertebrae morphometry radioanatomically and distinguishing between typical cervical vertebrae.

Machine learning (ML) algorithms which have emerged with the close relationship of mathematics and computer science and it can be seen that they have begun to be used in the field of medicine and important results have been obtained today (17-21). Decision Tree (DT) is an algorithm that tries to find the estimators with the highest distinguishing feature by subdividing the relationships among multiple independent variables (22). Random Forest (RF) is an algorithm that shows higher accuracy in estimating nonlinear and complex data (23). Logistic regression (LR) is an algorithm that can highly predict and classify categorical data (24). Linear discriminant analysis (LDA) is an algorithm that can reveal the contribution of each parameter in the data set to the overall result (25). Ouadratic discriminant analysis (QDA) is a parametric classifier algorithm with higher efficiency than LDA. Extra Tree Classifier (ETC) is a tree algorithm that randomly splits nodes (26).

The aim of this study is to show on CT images the morphometric differences of typical cervical vertebrae which are very similar and difficult to distinguish with the naked eye and to try to distinguish between these vertebrae by using ML algorithms.

MATERIAL AND METHODS

Population and Image Samples: The present study was initiated with the 2021/484 numbered decision of Karabük University Non-Interventional Ethics Committee. 536 cervical CT images of a total of 134 individuals between the ages of 20 and 55 were included in the study.

Multidetector CT (MDCT) Protocol: The images were obtained by using 16 row multidetector computed tomography (Aquilion 16; Toshiba Medical Systems, Otawara, Japan) at Karabük University Training and Research Hospital Department of Radiology. Screening protocol values were found as pitch: 1,0 mm, tube voltage: 120 kV, gantry rotation: 0.75 s and image section thickness value: 1 mm.

Image Analysis: The images in Digital Imaging and Communications in Medicine (DICOM) format were transferred to Horos Medical Image Viewer (Version 3.0, USA) program and images were obtained in axial, coronal and sagittal plane by using 3D Curved Multiplanar Reconstruction (MPR). The line passing through the middle of vertebral body and spinous process was determined and all images were brought to ortogonal plane (Figure 1).

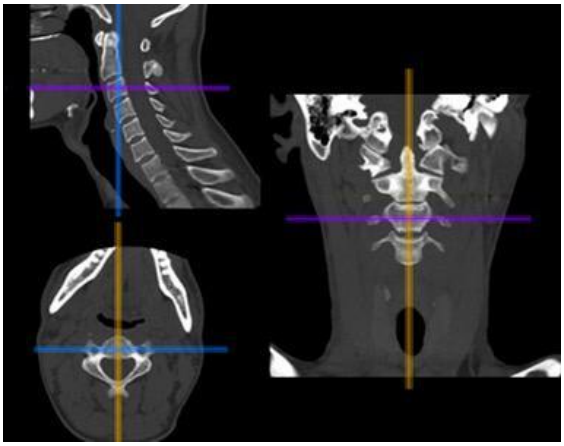

Figure 1. Method of bringing C3 vertebrae to ortogonal plane.

Length and angle measurements of certain anatomical points were made through MDCT brought to ortogonal plane (Figure 2).

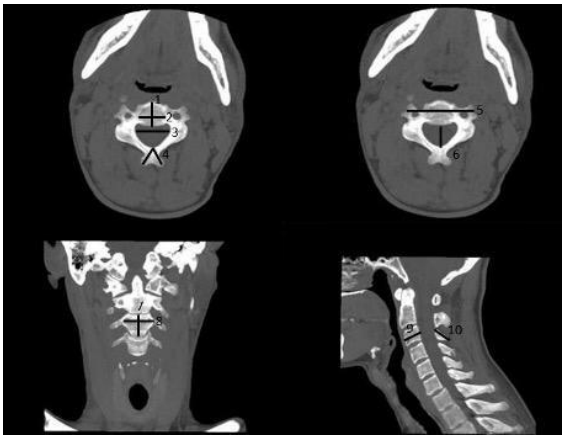

Figure 2. Measurements for C3 vertebrae on axial, coronal and sagittal plane (on axial image; 1: anterior posterior length of the vertebral body, 2: transverse length of the vertebral body, 3: transverse length of the vertebral foramen, 4: spinous process angle, 5: the distance between transverse processes, 6: anterior posterior length of the vertebral foramen; on coronal image; 7: vertebral body height, 8: vertebral body width; on sagittal image; 9: vertebral body thickness, 10: spinous process length measurement)

Measurement parameters were anterior posterior length of the vertebral body, transverse length of the vertebral body, transverse length of the vertebral foramen, spinous process angle, the distance between transverse processes and anterior posterior length of the vertebral foramen on axial section; vertebral body height and vertebral body width measurements on coronal section and vertebral body thickness and spinous process length measurement on sagittal section.

ML Algorithms: ML algorithms were performed by using an Hp-Folio 1040 model computer with i7 operating system and 8 Gb Ram. Python programming language (version 3.7.1) and scikit-learn library (version 0.20.0) were used for ML modelling (27). DT, RF, LR, LDA, QDA, ETC algorithms were used. Training set was determined as 80%, while test set was determined as 20%. In addition, groups of two were formed for each cervical vertebrae and analyses were made on these groups (Table 1).

Table 1. ML algorithms analysis groups

Analysis groups	
Group 1	C3 – C4
Group 2	C3 – C5
Group 3	C3 – C6
Group 4	C4 – C5
Group 5	C4 – C6
Group 6	C5 – C6

Performance Criteria: Accuracy (Acc), Matthews correlation coefficient (Mcc), Specificity (Spe), Sensitivity (Sen), F1 score (F1) values were used in this study.

$$Acc = \frac{TP}{TP+FN+FP+TN}$$

$$\text{Mcc} = \frac{TP \times TN - FP \times FN}{\sqrt{(TP+FP)\times(TP+FN)\times(TN+FP)\times(TN+FN)}}$$

$$\text{Sen} = \frac{TP}{TP+FN}$$

$$\text{Spe} = \frac{TN}{TN+FP}$$

$$\text{F1} = 2\frac{Spe \times Sen}{Spe+Sen}$$

Equation 1. (FP; False positive, FN; False negative, TP; True positive, TN; True negative)

Statistical Analysis: Mean and standard deviation values were used in the descriptive statistics of each cervical vertebrae. Minitab 17 program was used for descriptive statistics.

RESULTS

Parameters obtained from 134 analyzed images and descriptive statistical analyses obtained from C3, C4, C5 and C6 are shown in (Table 2, 3, 4, 5).

Table 2. C3 vertebrae descriptive statistics

Parameters (C3)	Sex	Mean	SD
Anterior posterior length of the vertebral body (cm)	Male	2.173	0.194
	Female	2.036	0.178
Transverse length of the vertebral body (cm)	Male	1.318	0.124
	Female	1.181	0.172
Transverse length of the vertebral foramen (cm)	Male	2.565	0.202
	Female	2.417	0.161
Spinous process angle (˚)	Male	35.590	10.970
	Female	38.830	11.200
The distance between transverse processes (cm)	Male	4.767	0.301
	Female	4.320	0.181
Anterior posterior length of the vertebral foramen (cm)	Male	1.456	0.188
	Female	1.411	0.138
Vertebral body height (cm)	Male	1.640	0.298
	Female	1.445	0.191
Vertebral body width (cm)	Male	2.536	0.233
	Female	2.399	0.184
Vertebral body thickness (cm)	Male	1.617	0.130
	Female	1.384	0.239
Spinous process length (cm)	Male	1.964	0.368
	Female	1.606	0.299

Table 3. C4 vertebrae descriptive statistics

Parameters (C4)	Sex	Mean	SD
Anterior posterior length of the vertebral body (cm)	Male	2.165	0.210
	Female	2.013	0.168
Transverse length of the vertebral body (cm)	Male	1.376	0.146
	Female	1.202	0.144
Transverse length of the vertebral foramen (cm)	Male	2.810	0.305
	Female	2.619	0.202
Spinous process angle (˚)	Male	40.590	13.560
	Female	42.870	11.310
The distance between transverse processes (cm)	Male	4.748	0.499
	Female	4.373	0.186
Anterior posterior length of the vertebral foramen (cm)	Male	1.440	0.242
	Female	1.338	0.159
Vertebral body height (cm)	Male	1.557	0.304
	Female	1.359	0.136
Vertebral body width (cm)	Male	2.656	0.254
	Female	2.440	0.157
Vertebral body thickness (cm)	Male	1.621	0.139
	Female	1.419	0.120
Spinous process length (cm)	Male	2.030	0.734
	Female	1.721	0.236

Table 4. C5 vertebrae descriptive statistics

Parameters (C5)	Sex	Mean	SD
Anterior posterior length of the vertebral body (cm)	Male	2.308	0.243
	Female	2.066	0.186
Transverse length of the vertebral body (cm)	Male	1.367	0.146
	Female	1.214	0.138
Transverse length of the vertebral foramen (cm)	Male	2.876	0.305
	Female	2.704	0.174
Spinous process angle (˚)	Male	36.780	10.810
	Female	35.230	9.420
The distance between transverse processes (cm)	Male	4.645	0.272
	Female	4.309	0.175
Anterior posterior length of the vertebral foramen (cm)	Male	1.483	0.264
	Female	1.356	0.179
Vertebral body height (cm)	Male	1.451	0.241
	Female	1.281	0.136
Vertebral body width (cm)	Male	2.753	0.210
	Female	2.548	0.175
Vertebral body thickness (cm)	Male	1.587	0.152
	Female	1.406	0.121
Spinous process length (cm)	Male	2.227	0.357
	Female	1.857	0.249

Table 5. C6 vertebrae descriptive statistics

Parameters (C6)	Sex	Mean	SD
Anterior posterior length of the vertebral body (cm)	Male	2.544	0.290
	Female	2.311	0.237
Transverse length of the vertebral body (cm)	Male	1.475	0.191
	Female	1.265	0.129
Transverse length of the vertebral foramen (cm)	Male	2.822	0.219
	Female	2.697	0.180
Spinous process angle (˚)	Male	20.935	5.232
	Female	22.891	4.515
The distance between transverse processes (cm)	Male	4.783	0.297
	Female	4.439	0.194
Anterior posterior length of the vertebral foramen (cm)	Male	1.456	0.216
	Female	1.402	0.216
Vertebral body height (cm)	Male	1.454	0.267
	Female	1.264	0.135
Vertebral body width (cm)	Male	2.932	0.261
	Female	2.699	0.204
Vertebral body thickness (cm)	Male	1.666	0.183
	Female	1.456	0.120
Spinous process length (cm)	Male	2.723	0.525
	Female	2.394	0.363

As a result of ML algorithm analysis, the highest Acc value was found in groups 3 and 5 as 0.94 with LDA and LR algorithms (Table 6).

As a result of ML algorithm analysis, the highest Mcc was found in group 3 as 0.90 with LDA and LR algorithms (Table 7).

Table 6. ML algorithms Acc table

MLA	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
DT	68.52	74.07	90.74	68.52	90.74	85.19
RF	**77.78**	85.19	92.53	**81.48**	90.74	81.48
ETC	55.56	75.93	87.04	70.37	85.19	74.07
LDA	70.37	88.89	**94.44**	77.78	**94.44**	83.33
QDA	48.15	55.56	77.78	75.93	92.59	**90.74**
LR	74.07	**90.47**	**94.44**	79.63	**94.44**	85.16

Table 7. ML algorithms Mcc table

MLA	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
DT	37.4	48.1	81.5	37.2	81.5	70.6
RF	**55.8**	70.6	85.2	**63.0**	81.5	63.2
ETC	12.5	52.3	74.1	40.9	70.4	48.4
LDA	41.4	77.7	**88.9**	55.5	**89.5**	66.7
QDA	00.7	27.3	62.5	52.3	85.4	**82.0**
LR	48.9	**81.5**	**88.9**	59.2	**89.5**	70.3

As a result of ML algorithm analysis, the highest Spe value was found in groups 3 and 5 as 0.95 with LDA and LR algorithms (Table 8).

As a result of ML algorithm analysis, the highest Sen value was found in groups 3 and 5 as 0.94 with LDA and LR algorithms (Table 9).

Table 8. ML algorithms Spe table

MLA	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
DT	68.9	74.1	90.8	69.0	90.8	85.4
RF	**78.0**	85.4	92.6	**81.6**	90.8	81.7
ETC	56.6	76.3	87.1	70.6	85.3	74.3
LDA	71.0	88.9	**94.5**	77.8	**95.0**	83.4
QDA	49.1	76.9	84.8	76.3	92.8	**91.3**
LR	74.8	**90.8**	**94.5**	79.6	**95.0**	85.2

Table 9. ML algorithms Sen table

MLA	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
DT	68.5	74.1	90.7	68.5	90.7	85.2
RF	**77.8**	85.2	92.6	**81.5**	90.7	81.5
ETC	55.6	75.9	87.0	70.4	85.2	74.1
LDA	70.4	88.9	**94.4**	77.8	**94.4**	83.3
QDA	48.1	55.6	77.8	75.9	92.6	**90.7**
LR	74.1	**90.7**	**94.4**	79.6	**94.4**	85.2

Confusion Matrix table was included for LDA and LR algorithms of group 3 (C3-C6) and group 5 (C4-C6) which had the highest accuracy rate. For group 3, 26 of C3 vertebrae were predicted correctly, while 2 were predicted incorrectly and 25 of C6 vertebrae were predicted correctly, while 2 were predicted incorrectly (Figure 3).

For group 5, 25 of C4 vertebrae were predicted correctly, while 3 were predicted incorrectly and all of C6 vertebrae were predicted correctly (Figure 4).

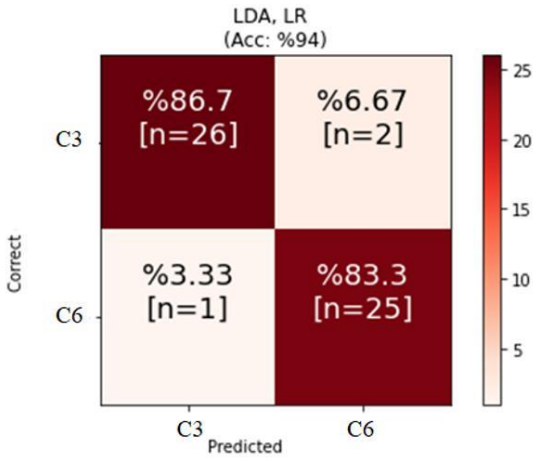

Figure 3. Group 3 Confusion Matrix table

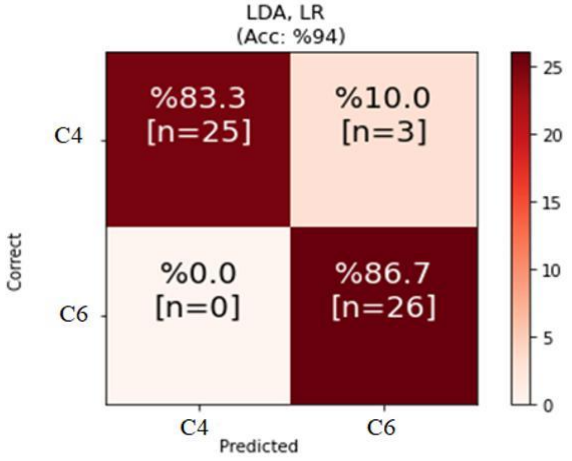

Figure 4. Group 5 Confusion Matrix table

In addition, in our study, the SHAP analyzer of the RF algorithm was applied to group 3 to reveal the contribution of the parameters to the algorithm. This group was preferred because group 3 had the highest Acc rate with the RF algorithm. As a result of the SHAP analyzer, it was found that the spinous process angle parameter provided the highest contribution (Figure 5).

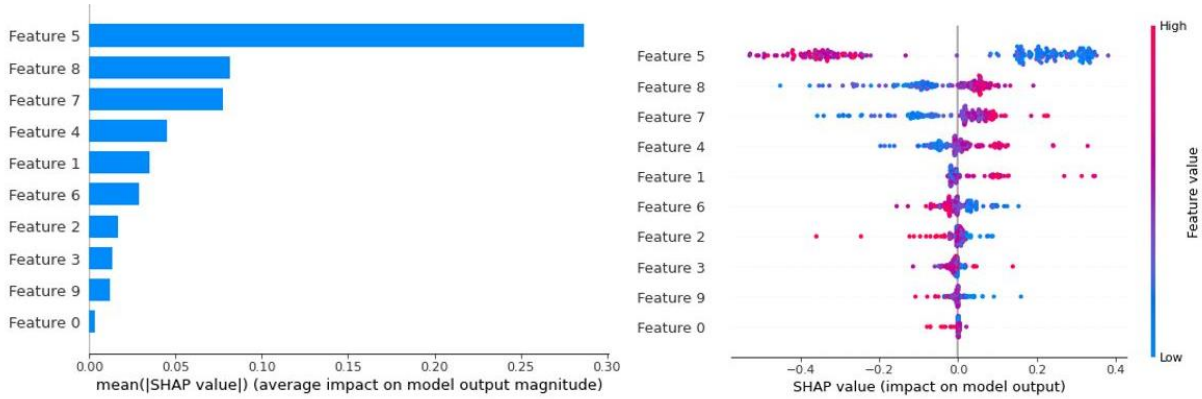

Figure 5: SHAP explanatory of RF algorithm (Feature 5: Spinous process angle, Feature 8: Spinous process length measurement, Feature 7: Vertebral body width; on sagittal image, Feautre 4: Transverse length of the vertebral foramen, Feature 1: Transverse length of the vertebral body, Feature 6: Certebral body height; on sagittal image, Feature 2: The distance between transverse processes, Feature 3: Anterior posterior length of the vertebral foramen, Feature 9: Vertebral body thickness, Feature 0: Anterior posterior length of the vertebral body)

DISCUSSION

The aim of this study was to analyze typical cervical vertebrae by using morphometric measurements taken from CT images and to distinguish typically known cervical vertebrae from one another. As a result of the study, the highest Acc rate was found as 0.94 with LDA and LR algorithm in group 3 (C3-C6) and group 5 (C4-C6); the highest Spe value was found as 0.95 with LDA and LR algorithm in group 5, the highest Mcc value was found as 0.90 with LDA and LR algorithm in group 5 (C4-C6) and the highest Sen value was found as 0.94 with LDA and LR algorithm in groups 3 (C3-C6) and 5 (C4-C6).

Lack of micro level anatomical and radio-anatomical studies defining cervical vertebrae anatomy may be the main reason why many clinicians are concerned about the application of the transpedicular screw fixation technique in subaxial cervical shoulder area (8, 28, 29). Due to its unique structure and important neural relationships, cervical vertebrae orientation and accurate correct anatomical knowledge are important to safely perform surgeries of this area (30, 31). For this reason, it can be seen that a large number of studies have been conducted to increase the level of anatomical knowledge of the cervical area in literature.

It is known that cervical vertebrae morphology is examined in detail with analyses made from cadaver and by using dry bone and computed tomography images (10-15).

However, the relationship between these osteometric measurements could not be fully demonstrated and it can be seen that there is no consensus in the results. CT is a radiological tool that can show all tissues and especially bone tissue with sharp boundaries and thus due to being less affected by orientation in length and angle

measurements, it is superior to conventional osteometric measurements (17, 18, 26).

In typical cervical vertebrae measurements they conducted with dry bones, Pramela et al. (32) found mean length of the vertebral body as 10.92±1.35 mm, mean anterior posterior length of the vertebral foramen as 12.33±1.68 mm, mean transverse length of the vertebral body as 23.22±2.16 mm, and mean anterior posterior length of the vertebral body as 14.79±1.96 mm. In the present study, we found vertebral body height as 1.640±0.298 cm in male and 1.445±0.191 cm in female on coronal image of C3 vertebrae; as 1.557±0.304 cm in male and 1.359±0.136 cm in female on C4 vertebrae; as 1.451±0.241 cm in male and 1.281±0.136 cm in female on C5 vertebrae and as 1.454±0.267 cm in male and 1.264±0.135 cm in female on C6 vertebrae. Studies have evaluated morphometric characteristics of typical cervical vertebrae and these results support our results. However, the main purpose of our study is to focus on micro-anatomical differences between typical cervical vertebrae besides their morphometric characteristics and to be a guide to physicians who carry out surgical interventions in the field.

In their study conducted with CT images of dry bones, Gupta et al. (33) found transverse length of the vertebral foramen as 20.89±1.65 mm on C3, as 21.94±1.48 mm on C4, as 21.96±1.52 mm on C5 and as 22.31±1.78 mm on C6. Pramela et al. (32) found transverse length of the vertebral foramen as 21.98±1.82 mm, while Kayalıoğlu et al. (11) found as 18.5 mm and 25.7 mm. In the radiological study they conducted with adults, Çevirgen et al. (34) found transverse length of the vertebral foramen as 25.4±1.6 mm in male and 26±2.4 mm in female for C3, as 26.1±2.1 mm in male and 26.4±2 mm in female for C4, as 26±4.5 mm in male and 26.5±1.2 mm in female for C5 and as 27.2±1.9 mm in male and 27.2±1.9 mm in female for C6. In the present study, on axial image we found transverse length of the vertebral foramen as 2.565±0.202 cm in male and 2.417±0.101 cm in female for C3 vertebrae, as 2.810±0.305 cm in male and 2.619±0.202 cm in female for C4 vertebrae, as 2.876±0.305 cm in male and 2.704±0.174 cm in female for C5 vertebrae and as 2.822±0.219 cm in male and 2.697±0.180 cm in female for C6 vertebrae. Results obtained with CT images of dry bones support the results of our study.

In their study conducted on cadaver, Uğur et al. (35) found transverse length of the vertebral foramen as 21.86 mm for C3, as 21.1 mm for C4, as 21.2 mm for C5 and as 22.3 mm for C6. The results for transverse length of the vertebral foramen were similar in the present study.

On CT images Evangelopoulos et al. (36) found anterior posterior length of the vertebral foramen as 13.31±1.71 mm in male and as 12.94±1.32 mm in female for C3, as 13.05±1.01 mm in male and as 12.49±1.49 mm in female for C4, as 13.43±1.22 mm in male and as 12.66±1.68 mm in female for C5 and as 13.28±1.85 mm in male and as 12.52±1.76 mm in female for C6. In the radiological study they conducted on adults, Çevirgen et al. (34) found anterior posterior length of the vertebral foramen as 15.9±1.7 mm in male and 16±1.5 mm in female for C3, as 15.5±1.8 mm in male and 16±1 mm in female for C4, as 16±2.1 mm in male and 16.3±1.3 mm in female for C5 and as 16.5±2.3 mm in male and 16.7±1.5 mm in female for C6. In our study, on axial images, anterior posterior length of the vertebral foramen was found as 1.456±0.188 cm in male and 1.411±0.138 cm in female for C3 vertebrae, as 1.440±0.242 cm in male and 1.338±0.159 cm in female for C4 vertebrae, as 1.483±0.264 cm in male and 1.356±0.179 cm in female for C5 vertebrae and as 1.456±0.216 cm in male and 1.402±0.216 cm in female for C6 vertebrae.

In a radiological study they conducted with CT in Poland, Ludwisiak et al. (37) measured spinous process angle as 27.8˚ for C3, as 30.3˚ for C4, as 29˚ for C5 and as 26˚ for C6. They also evaluated spinous process angle between the two ends and found as 35.590˚ in male and 38.830˚ in female for C3 vertebrae, as 40.590˚ in male and 42.870˚ in female for C4 vertebrae, as 36.780˚ in male and 35.230˚ in female for C5 vertebrae and as 20.935˚ in male and 22.891˚ in female for C6 vertebrae on axial image. We believe that the differences in angle measurements are due to differences in populations.

In our study, CT imaging technology was preferred as it provides three dimensional imaging, reconstruction and a large database in addition to classical osteometric methods. In addition, the biggest difference that distinguishes our study from the others is the ML algorithms used and the result that morphometric features of cervical vertebrae which are considered as typical can be distinguished from each other.

CONCLUSION

To the best of our knowledge, this is the first study that can distinguish typical cervical vertebrae from one another by using ML algorithms and CT imaging technology together. For this reason, we believe that our study will provide important contributions to literature, anatomists and surgeons.

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RESEARCH ARTICLE

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The Validity and Reliability Study of Mental Health Literacy in Young Adults (MHLq)

ABSTRACT

Objective: The validity and reliability of the Turkish version of the Mental Health Literacy Scale (MHLq) in young adults were examined in this study.

Methods: This methodological investigation was carried out throughout the 2018–2019 academic year at a public university. The MHLq, created by Dias et al. in 2018, and a sociodemographic data form were used to gather the data. 350 students between the ages of 18 and 25 participated in the study.

Results: A pilot study was done to translate the scale into Turkish once it had been translated from its original language and reviewed by experts. The scale validity as well as its construct validity, internal consistency, and time invariance were tested using the content validity index, confirmatory factor analysis, item analyses, reliability, Cronbach's alpha analysis, and test-retest scores. The scale is four-dimensional, as was found. Confirmatory factor analysis revealed that the scale's item loads varied between 0.40 and 0.73 while its content validity was 0.98. Its 0.91 Cronbach's alpha value was discovered. The participants' average mental health literacy scores were 84.45±7.80.

Conclusions: The analyses made showed that the MHLq could be safely used as a measurement tool for young adults' mental health literacy.

Keywords: Young Adult, Mental Health, Mental Health Literacy, Validity, Reliability.

Genç Yetişkinlerde Ruh Sağlığı Okuryazarlığının Geçerlilik ve Güvenilirlik Çalışması (MHLq)

ÖZET

Amaç: Bu çalışma, Ruh Sağlığı Okuryazarlığı Ölçeği'nin (MHLq) genç erişkinlerde Türkçe geçerlilik ve güvenilirlik çalışması üzerine yapılmıştır.

Gereç ve Yöntem: Bu metodolojik araştırma, 2018–2019 akademik yılı boyunca bir devlet üniversitesinde gerçekleştirildi. Dias ve diğerleri tarafından oluşturulan MHLq 2018 yılında veri toplama aracı olarak sosyodemografik veri formu kullanılmıştır. Çalışmaya 18-25 yaş arası 350 öğrenci katılmıştır.

Bulgular: Ölçek orijinal dilinden Türkçe'ye çevrilmiş, profesyonel görüş alınmış ve Türkçe'ye çevrilmesi için pilot çalışma yapılmıştır. Ölçeğin geçerliliği, yapı geçerliliği, iç tutarlılığı ve zamanla değişmezliği test etmek için içerik geçerlik indeksi, doğrulayıcı faktör analizi, madde analizleri, güvenilirlik, Cronbach alfa analizi ve test-tekrar test puanları kullanılmıştır. Ölçek görüldüğü gibi dört boyutludur. Doğrulayıcı faktör analizi, ölçeğin madde yüklerinin 0.40 ile 0.73 arasında değiştiğini ve kapsam geçerliliğinin 0.98 olduğunu ortaya koymuştur. 0.91 Cronbach alfa değeri keşfedildi. Katılımcıların ortalama ruh sağlığı okuryazarlığı puanları 84,45±7,80'dir.

Sonuç: Yapılan analizler, MHLq'nin genç yetişkinlerin ruh sağlığı okuryazarlığı için bir ölçüm aracı olarak güvenle kullanılabileceğini göstermiştir.

Anahtar Kelimeler: Genç Yetişkin, Ruh Sağlığı, Ruh Sağlığı Okuryazarlığı, Geçerlilik, Güvenilirlik.

INTRODUCTION

Understanding the concept of mental health, which cannot be characterized solely by the absence of psychopathology, requires examining the beliefs that influence and safeguard mental health (1). One of these is mental health literacy (MHL), a crucial idea. The development of MHL, which falls under the category of preventive mental health care and is viewed as a tool to support positive mental health, lessen harms brought on by mental illness, and improve mental health, is a focus in many countries and a study topic (2,3). The initial definition of mental health literacy, according to Jorm and colleagues, was "Knowledge and beliefs surrounding mental disorders that aid in their recognition, management, or prevention" (4). The low rates of help-seeking or help-to-receive behaviors for mental illnesses provide people with serious challenges to realize the problems that are related to their mental disorders and take action to find solutions for their problems, cause delays in seeking and receiving professional help, incomplete treatment, and an increase in the rates of hospitalization and the use of emergency care services (4-7). Individuals can only become aware of mental disorders and take action to address their issues if they are well-informed about the issue and have a high level of mental health literacy (5). In addition, it is stated that high-level mental health literacy (MHL) approaches and developed tools that comprehensively cover concepts related to mental health problems make a significant contribution to improving mental health and well-being worldwide (8). In this context, the World Health Organization (WHO) has developed a comprehensive definition of mental health literacy (4).

Before the definition developed by WHO, mental health literacy, knowledge and attitude (9,10), knowledge about mental disorders and stigma related to mental health. Various measuring instruments have been developed within the framework of (5,11-15). However, the majority of these tools have been developed for certain dimensions of mental health literacy or certain mental disorders, and their scope has been limited (3,10,16). The MHLq-young adult form, on the other hand, is a scale that surpasses the limited structure of other scales and evaluates it from a broader perspective. It is also a more up-to-date form that examines the concept of mental health literacy from the perspective of the WHO. Besides few scales were adapted to Turkish, most of which measured the MHL level of young people (3,10).

Individuals can only become aware of mental disorders and take action to address their issues if they are well-informed about the issue and have a high level of mental health literacy (5).

Young people are among the risk groups for mental disorders and constitute a significant part of the disease burden globally (17,18). (In addition, young people who do not receive therapy have poor levels of understanding about mental health and low rates of seeking treatment for mental diseases, not knowing the institutions or professionals they can apply to, and delays in seeking professional help (1,5,7,8,16,20). In this consideration, it is necessary to address MHL in the young population to discuss mental health needs and improve mental health (16). Mental Health Literacy Scale (MHLq) MHLq evaluates mental health literacy among young adults from a broader perspective. We think it's crucial to determine the scale's psychometric characteristics and adapt it to Turkish. This study incorporated self-reports of young adults' mental health literacy on a wider conceptual foundation and attempted to conduct a Turkish adaptation of the MHLq in young adults, which was established by Dias et al. in 2018 (8).

MATERIAL AND METHODS

This study used a systematic approach to conduct a Turkish validity and reliability study of the Mental Health Literacy Scale (MHLq) in young adults.

Sample Size and Study Design: This methodological study aims to develop the MHLq for usage in Turkey by conducting a validity and reliability analysis of the instrument. The sample size in methodological investigations is determined in a variety of ways. Comrey and Lee (1992) assigned the sample size ratings of 50 (very poor), 100 (weak), 200 (moderate), 300 (excellent), 500 (very good), and 1000 (amazing) for their scale validity and reliability research (21). Şencan (2005), on the other hand, considered the sample below 100 to be very low, the sample between 100 and 200 to be low, the sample between 200 and 300 to be medium, the sample between 300 and 500 to be good, the sample between 500 and 1000 to be very good, and the sample above 1000 to be excellent has accomplished (22). In this study, 350 people who were considered good to very good sample size were included in the study between April and June 2019 (23). The participants were verbally briefed about the goal of the study in their classroom before being handed written informed consent forms to sign. The data collection materials were given to the students who signed the consent form and consented to participate. It took roughly 13 minutes to complete the research forms. Ordu University ethics committee gave its clearance for this study (25/04/2019-KAEK-58-2019-68) and and permission was obtained from the Ordu University (No:17/04/2019-81515450-663.08).

The scale's responsible author, Pedro Dias, who created it via email, gave his consent in writing before it could be translated into Turkish. The participants gave their written agreement after being informed of the study's objectives and that participation was completely optional. Following a thorough examination of the forms and the exclusion of any that were incomplete or wrongly

completed, 350 forms were utilized to gauge the tool's validity and reliability. Participants in the study ranged in age from 18 to 25 and were voluntarily enrolled and did not have any communication problems.

Data Collection Tools*:* The data was gathered using the MHL and a two-part personal information form. Age, gender, income status, department, and class level were sociodemographic factors covered in the first section. Disease information covered in the second section included the presence of diseases and educational status for mental health issues.

MHLq in Young Adults Scale: This scale was developed by Dias et al. in 2018 and contains 29 items using a 5-point Likert scale (1 = severely disagree, 2 = disagree, 3 = neither agree nor disagree, 4 = agree, and 5 = strongly agree). It is broken down into 4 dimensions: understanding of mental health issues (11 items; = 0.74), false beliefs/stereotypes (8 items; = 0.72), and first aid and help-seeking abilities (6 items). The total score range for the MHLq was 29 to 145. Overall, Cronbach's alpha was estimated to be 0.84. (4)

Process

Adaptation of MHLq to Turkish and Content Validity: In this study, the adaptation of MHLq-young adult into Turkish, its validity and reliability process was structured by taking ISIPOR as a guide (24). Two Turkish language experts who work at the school of foreign languages at a public university's basic English department initially translated the scale's original items into Turkish. The items were then evaluated by nine academics who work in the young adult field using the Turkish version of the scale. The original scale was judged to be appropriate after the experts evaluated the scale components' suitability for translation to their original form and the intended audience. The scale's elements were reorganized after taking the experts' comments into account. One point was given for "strongly disagree," two for "disagree," three for "neither agree nor disagree," four for "agree," and five for "strongly agree" in the evaluation of each item's comprehensibility. To assure correctness and language scope, three professors translated the Turkish version into English in the next step. Additionally, a lecturer of Turkish language and literature examined the final scale items that were translated into Turkish before they were finalized for use. A preliminary application was submitted to a group of 15 students to test the scale's Turkish readability once all of its checks were finished. The data obtained from the preliminary application group were not included in the Turkish validity and reliability study (Figure 1).

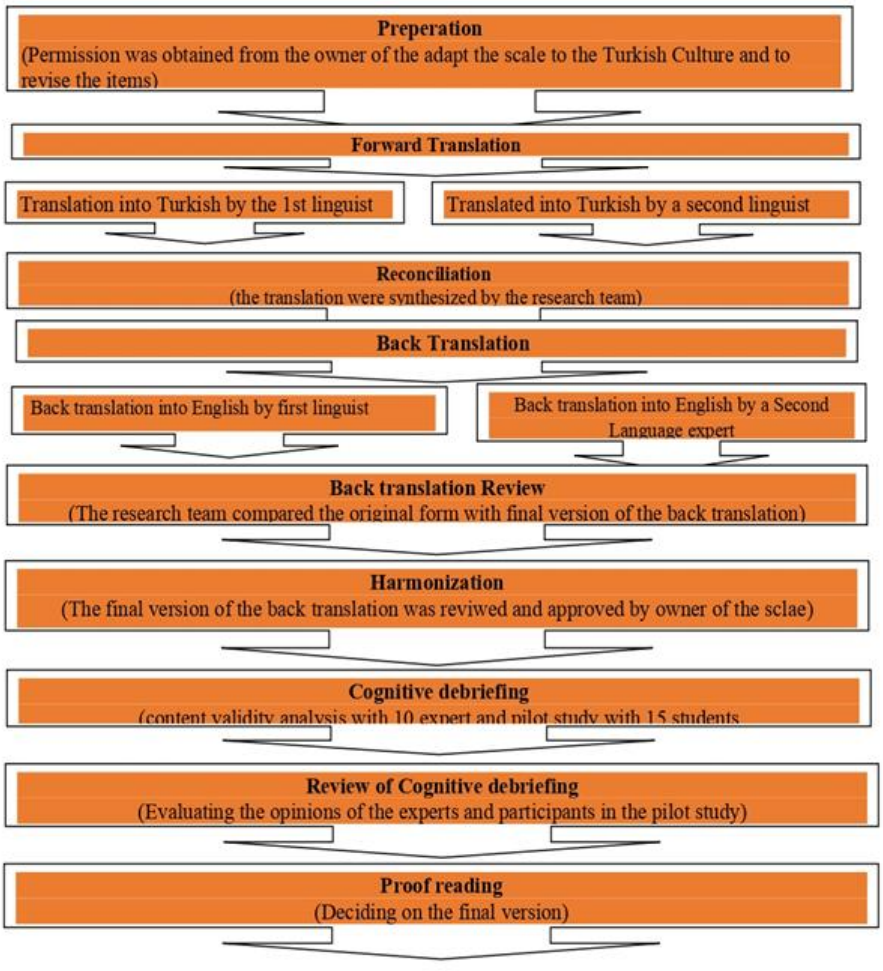

Figure 1. According to ISIPOR, the process of adapting the MHLq-young adult scale to Turkish culture.

Data Analysis: The data was analyzed using the programs SPSS (Statistical Package for Social Sciences) 21 and AMOS 23. The descriptive statistics of the scale scores and participant characteristics were calculated using the variables number, percentage, mean, and standard deviation. To determine whether the factor analysis was appropriate for the sample size and concept validity, the KMO (Kaiser-Meyer-Olkin) and Barlett chi-square tests were utilized. The Bartlett Test of Sphericity was determined to be 2=3365.776 (p0.05), while the KMO sample adequacy criterion was found to be 0.921. The scale's internal consistency and reliability were assessed using test retesting and Cronbach's alpha, and item-total score correlation analysis. Construct validity was used to assess the measure's validity. An expert reviewed the Confirmatory Factor Analysis (CFA), which was used to test the concept validity. The scale/sub-dimension scores obtained after CFA were examined using the Kolmogorov-Smirnov test to see if they had a normal distribution. Because the data were not normally distributed, the Mann-Whitney U test was used to compare the mean scale scores and descriptive features. The significance level was set at 0.05.

RESULTS

Participants' Distribution Based On Demographic Characteristics: Participants in the study ranged in age from 18 to 25, with a mean age of 20.51±1.98. . Male participants made up 50.9% of the group, and 97.1% were by themselves. Of them, 23.7% were enrolled in technical sciences, 19.4% were nursing students and almost half of them (47.1%) were first-grade students. There was no chronic disease in 92.9% of them, no physical disorder in 96%, and no mental disorder in 94.9%. In general, the students scored their general health status between 1 and 10 and the standard deviation of the general health mean score was 7.85±1.79. Of the students, 43.7% knew someone with mental disorders. Considering the degree of proximity, almost half of them (45.2%) knew someone with a mental disorder, 24.9% had a friend with a mental disorder and 19% had a relative with a mental disorder (Table 1).

Validity Analysis Explanatory and Confirmatory Factor Analyses: The validity of the scale was analyzed through construct validity.

Content Validity: Turkish-speaking experts in the relevant field translated the MHLq. For content validity, nine experts' opinions were gathered. The scoring and text both received the appropriate modifications from the experts. The scale's content validity index was discovered to be 0.98.

Construct Validity: The suitability of the scale for the sample size and construct validity was tested using KMO and Barlett Sphericity test. The KMO sample adequacy criterion was found to be 0.921 and the Bartlett Test of Sphericity was χ^2=3365.776 (p<0.05).

Table 1. Descriptive Information of the Participants

	Min-Max	**Mean±SD**
Age	18-28	20.51±1.98
General health status	1-10	7.85±1.79
Attributes		
Gender	**n**	**%**
Female	172	49.1
Male	178	50.9
Marital status		
Married	10	2.9
Single	340	97.1
Department		
Technical sciences	83	23.7
Faculty of health sciences-Nursing	68	19.4
Faculty of medicine	63	18.0
Faculty of science and literature	15	4.4
Education faculty	61	17.4
Faculty of theology	60	17.1
Grade		
1st grade	165	47.1
2nd grade	119	34.0
3rd grade	12	3.5
4th grade	54	15.4
Chronic disease		
Yes	25	7.1
No	325	92.9
Physical disease		
Yes	14	4.0
No	336	96.0
Mental illness		
Yes	18	5.1
No	332	94.9
Knowing someone with mental disorder		
Yes	153	43.7
No	129	36.9
Not sure	68	19.4
Total	350	100.0
Degree of proximity of the individual with mental disorder		
Self	24	10.9
A friend	55	24.9
A relative	42	19.0
A simple acquainted	100	45.2
Total	221	100.0

To test the four-dimensional validity of the MHLq, CFA was conducted. Thus, the significance of the scale model was tested using CFA. Seven items (4th, 10th, 11th, 18th, 21st, 23rd, and 27th items) were excluded from the scale because they did not have adequate coherence. Repeated CFA revealed that the four-dimensional scale's fit indices were within acceptable bounds (Table 2). Dimension 1: Knowledge of mental health issues (10 items), Dimension 2: False Beliefs/Stereotypes (4 items), Dimension 3: Help-Seeking and First Aid Skills (4 things), and Dimension 4: Self-Help Strategies (4 items).

The MHLq had 22 components and four sub-dimensions at the conclusion of CFA. The "knowledge of mental health problems" sub-dimension had 10 items (2, 3, 8, 9, 13, 16, 17, 18, 19, and 21), four items (5 (reverse), ten (reverse), eleven, and twelve (reverse), four items for "help-seeking and first aid skills," four items for "self-help strategies," and four items for "erroneous beliefs/stereotypes" (1, 6, 15, and 20). The range of the scale's possible scores is 22 to 110. The range of possible results for each sub-dimension is as follows: awareness of mental health issues (10–50), false assumptions/stereotypes (4–20), help-seeking, first aid, and self-help strategies (4–20). (4-20). The CFA standards are given in Table 2.

The results of the MHLq chi-square model test were (2=427.955; p=0.000); 2/df=2.15). These figures demonstrate the significance of CFA. Tucker-Lewis index (TLI) = 0.92, normed fit index (NFI) = 0.88, adjusted goodness of fit index (AGFI) = 0.88, comparative goodness of fit index (CFI) = 0.93, root mean square error of approximation (RMSEA) = 0.05, and root mean square error (RMR) = 0.05 were found to be the fit indices. The model is congruent with the data, and the MHLq

Table 2. CFA Fit Indices of the MHLq

Fit Indices	Values	Acceptable Fit Values
χ^2 /df	2.15	≤5
RMSEA	0.05	≤0.08
RMR	0.05	≤0.08
CFI	0.93	≥0.90
GFI	0.91	≥0.90
AGFI	0.88	≥0.90
NFI	0.88	≥0.90
IFI	0.93	≥0.90
TLI	0.92	≥0.90

The coherence of the model with the PATH diagram was tested according to CFA and the four-dimensional structure was found to have adequate coherence (Figure 2).

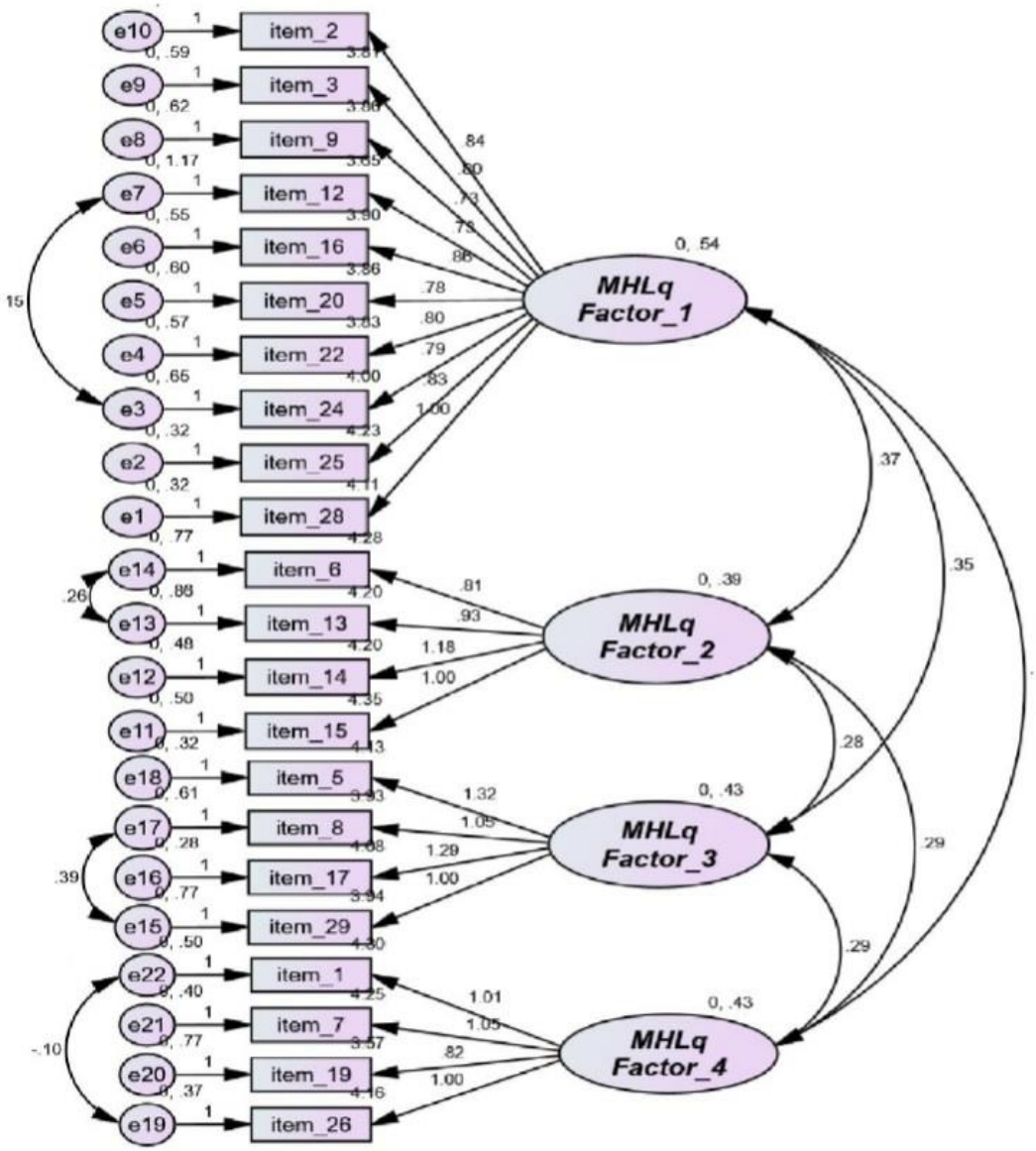

Figure 2. Path diagram for the MHLq scale Turkish version.

Distribution Properties and Reliability Analysis of the Scale*:* Using test-retest reliability studies, Cronbach's alpha internal consistency coefficient, and total item correlation, the MHLq's reliability was investigated. The range of item correlations was 0.402 to 0.738 overall. For the entire scale, 0.919 was the Cronbach's alpha internal consistency coefficient. The internal consistency coefficients of the sub-dimensions for Factors 1, 2, 3, and 4 are, respectively, 0.885, 0.744, 0.852, and 0.746 (Table 3).

Table 3. The correlation of MHLq scale/sub-dimensions and total scale scores and the Cronbach's alpha reliability coefficients

MHLq and its sub-dimensions	Mean±SD	Sub-dimension/Scale total correlation coefficients		Cronbach's alpha
		r	p	
F1: Knowledge of mental health problems	39.36±6.51	0.933	< .01	0.855
F2: Erroneous beliefs/stereotypes	17.03±3.06	0.730	< .01	0.744
F3: Help-seeking and first aid skills	16.08±3.46	0.771	< .01	0.852
F4: Self-help strategies	16.28±2.90	0.819	< .01	0.746
MHL Scale (Total)	88.75±13.37	-	-	0.919

Test-retest: 86 participants underwent test-retest procedures two weeks apart to ascertain whether the MHLq was time-invariant. The pre-and post-test measurements had a significant positive and sluggish linear association (r=0.384, p0.001). Furthermore, other dimensions of the scale except for the first sub-dimension and the total mean scores did not differ between the first and second applications (p>0.05) (Table 4).

Table 4. Comparison of the test-retest mean scores of the MHLq and its sub-dimensions

MHLq and its sub-dimensions	Pre-test Mean±SD	Post-test Mean±SD	t	p
F1: Knowledge of mental health problems	42.29±3.68	41.23±5.09	2.088	0.040
F2: Erroneous beliefs/stereotypes	9.02±1.82	9.34±1.93	-1.234	0.221
F3: Help-seeking and first aid skills	17.18±2.59	16.88±2.64	1.083	0.282
F4: Self-help strategies	17.51±1.87	16.98±2.28	1.955	0.054
MHLq Scale (Total)	86.03±6.73	84.45±7.80	1.807	0.074

The Kolmogorov-Smirnov test indicated that the scale and its sub-dimensions did not have a normal distribution, so the Mann-Whitney U test was used in its place. Scores on the scale and its subdimensions were compared by gender. Scores on the scale/sub-dimension did not significantly differ based on gender (p 0.05). The scale/sub-dimension results showed that women fared better (Table 5). Chronic, physical, or mental diseases were not statistically significantly associated with the scale/sub-dimension scores (p>0.05).

Table 5. Comparison of MHLq scale/sub-dimensions scores according to gender and departments

MHLq and its sub-dimensions	Number	Mean±SD	Median	Min	Max	Order	Test	p
F1: Knowledge of mental health problems								
Female	172	40.51±5.84	41	13	50	194.51	- 3.462	0.001
Male	178	38.24±6.93	39	10	50	157.13		
F2:Erroneous beliefs/stereotype								
Female	172	17.56±2.75	18	4	20	192.24	-3.090	0.002
Male	178	16.51±3.26	17	4	20	159.33		
F3: Help-seeking and first aid skills								
Female	172	16.77±3.00	17	4	20	195.79	-3.727	0.000
Male	178	15.41±3.75	16	4	20	155.90		
F4: Self-help strategies								
Female	172	16.89±2.57	17	4	20	197.05	-3.950	0.000
Male	178	15.68±3.09	16	4	20	154.68		
MHLq Scale (Total)								
Female	172	91.75±12.10	92	26	110	201.23	-4.678	0.000
Male	178	85.86±13.92	88	34	110	150.64		
Total	350							

DISCUSSION

Although MHLq is an important topic in the literature, it is known that scale-based measurements of MHLq are insufficient and limited psychometrically and methodologically (6). In this study, MHLq was adapted to the Turkish community. It was discovered that MHLq is a viable and accurate measurement method to assess mental health literacy.

Validity and Reliability Discussion Findings from MHLq

Constructional Accuracy: The construct validity of the MHLq was investigated using CFA, and the findings revealed that the scale contained four dimensions and 22 items. It was discovered that the sub-dimensions resembled the original scale (7). According to CFA findings, the scale's chi-square fit score was 2.15, which is within the acceptable range for the goodness of fit. The KMO (0.921) and Barlett test results (2=3365.776 and p=0.000) were used to assess whether the data. The data are regarded as perfect when the KMO value is at least 0.90, and as having a normal distribution when the Pearson Chi-square test is significant (p0.05) (25). Our study's findings are supported by other developmental studies for MHLq in the literature (3,5,26). The model obtained from the CFA analysis performed for the construct validity of the scale below 5, the 2/df value of the model acquired from the CFA analysis, and the RMSEA and RMR less than 0.08 show that the model is compatible with the CFA data. The CFI, GFI, IFI, and TLI values are over 0.90. The AGFI and NFI values are close to 0.90. (27). If the RMSEA and RMSR scores are less than five and the GFI, NFI, RFI, CFI, and IFI indices are 0.95 and higher, a match is said to be perfect (9,27,28). There were found to be the following fit indices: normed fit index (NFI) = 0.88, goodness of fit index (GFI) = 0.91, adjusted goodness of fit index (AGFI) = 0.88, comparative goodness of fit index (CFI) = 0.93, and root mean square error of approximation (RMSEA) = 0.05 and root mean square error (RMR)=0.05. This outcome is consistent with the original scale by Dias et al (4). Additionally, we can state that the scale is well-coherent with existing research on the MHLq scale (3,5,26).

Discussion of Reliability Results: The scale item score correlations in this study ranged from 0.402 to 0.738. This demonstrates that the correlation coefficients between the scale items and the overall and subscale scores are suitable and reliable. Item correlations as a whole must be higher than 0.30. (22,25).

Cronbach's alpha reliability coefficient was found to be 0.919 for the complete scale. The scale is regarded as very reliable when its Cronbach's alpha coefficient exceeds 0.80. (29). Cronbach's alpha for the initial scale was 0.84. (4). These results show that the scale's Cronbach's alpha coefficient is higher than that of previous MHLq studies and comparable to other scales (3,7,8,30).

86 participants underwent test-retest procedures two weeks apart to ascertain whether the MHLq was time-invariant. The pre-and post-test measurements had a significant positive and sluggish linear association (r=0.384, p0.001). It was also found that other dimensions of the scale except for the first sub-dimension and the total mean scores did not differ between the first and second applications (p>0.05). This result shows that the scale is consistent and reliable (31).

The MHLq level of the participants (*Total scale score:* 88.75±13.37) was found to be similar to other studies (3,10). The study results are similar and can be attributed to their similarity due to including Turkish samples and the similar cultural characteristics of the individuals included in the sample. MHLq levels of the students were found to be lower in this study compared to the original scale and other studies (4,5,32). Mental health literacy (MHLq) includes knowing how to achieve and maintain good mental health, comprehending mental diseases and their treatments, reducing stigma associated with mental disorders, and developing help-seeking behavior for mental disorders when necessary (1). Additionally, it plays a significant role in the development of behaviors that involve requesting assistance for oneself and others when necessary, as well as positive attitudes toward people with mental health conditions (10). The greatest barriers regarding mental problems in young people are knowing the symptoms, preference for self-confidence, perceived stigma, and shame (33). Therefore, young adults have difficulty taking action regarding mental health problems and they mostly may ignore these problems (34). (People are more equipped to seek assistance and receive treatment for their issues when they are knowledgeable about mental health and mental health illnesses (35).

Discussion of MHLq and Sociodemographic Attributes: The MHLq score depends on gender in all sub-dimensions. Female students were found to have greater MHLq levels than male students. The original scale and other studies support our study results (4,32,36). The reasons that women have higher MHLq levels than men can be attributed to women’s positive attitudes towards solving their mental problems, their help-seeking behaviors to solve their problems, and their use of counseling services more than the opposite sex (37). However, several investigations came to different conclusions. Males are more likely to commit suicide than women are, according to research by Eisenberg et al. Mackenzie et al. found that men were more likely to seek mental health treatment as they aged and as their education level grew (36).

The research scale was administered to university students. The results from this study and other studies conducted with similar sample groups show parallelism. This may have resulted from the participants being in their young adulthood period. In addition, we can say that the fear of being stigmatized is a major problem in seeking help, and mental problems are not recognized or are concealed by individuals. The fear of families about mental problems can prevent the appearance of mental problems, which may be regarded as a huge embarrassment.

CONCLUSION

The high prevalence of mental disorders, the inadequacy of mental health professionals, the insufficient number of health professionals to provide low quality mental health services, and the stigma associated with mental disorders make it difficult to deal with mental health problems effectively. The concept of mental health literacy defined by Jorms et al. (1997) and the scales developed accordingly, (a) the ability to recognize and distinguish various mental illnesses and disorders; (b) knowledge of how and where to seek information about risk factors, intervention strategies and professional help; and (c) attitudes and beliefs that affect a person's ability to identify their mental illness and seek appropriate help. On the other hand, the World Health Organization (WHO) states that, in line with the health literacy framework, this structure should be developed to include skills and strategies, emphasizing its essential nature for promotion, prevention and care, and demonstrating the importance of its impact on improving outcomes at both the individual and population level. This scale, which was adapted into Turkish, was developed to measure the level of skills and helping strategies to prevent or reduce mental disorders, as well as knowledge about mental health issues, within the framework of this definition of the World Health Organization (WHO). It is of great importance that the concept of mental health literacy be developed comprehensively as handled by WHO and addressed in the young population, which is one of the at-risk groups. With these features, it is a scale that cares about the individual's potential to improve mental health. It saves time for mental health professionals and allows them to recognize the patient faster and intervene more quickly.

This study provided psychometric characteristics of the MHLq. The results have shown that MHLq levels of Turkish young adults are at a moderate level. Eight experts determined that the scale's content validity index was 0.98. The MHLq's dependability coefficient according to Cronbach's alpha was 0.91. This result shows how extremely dependable the scale is. Based on the results, it is safe to use the MHLq to estimate the mental health literacy levels of the Turkish population. Additionally, lower MHLq levels among pupils indicate that these need to be raised. So, within the context of multidisciplinary collaboration, intervention programs should be developed, and these programs should be disseminated.

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Declarations

Conflict of Interest: The authors report no conflicts of interest..

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RESEARCH ARTICLE

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Multidrug-Resistant Gram-Negative Bacteria Rate and Risk Factors in the Neonatal Intensive Care Unit: A Single-Center Ten-Year Experience

ABSTRACT

Objective: Multidrug resistance (MDR) in gram-negative neonatal infections is difficult to manage, and the risk factors differ among different studies. Therefore, we aim to investigate the demographics, mortality, MDR status of gram-negative isolates, and risk factors for MDR gram-negative infections.

Methods: We conducted a retrospective single-center study about MDR gram-negative infections in neonates between January 2012-January 2022 at Duzce University Hospital in Turkey. This study evaluates the risk factors and clinical features of neonates with MDR gram-negative infections. All analyses were performed using IBM SPSS V23. In addition, univariate analyses and multivariate logistic regression models were studied to determine MDR's risk factors.

Results: Of 107 gram-negative bacteria, 41 (38.3%) accounted for *Enterobacter*, 30 (28%) for *Klebsiella pneumonia*, and 22 (20.6%) for *Escherichia coli*. Additionally, 61 (56.5%) were MDR microorganisms. Among the susceptibility tests performed for selected isolates, 41 (77.4%) had resistance to piperacillin, 57 (75%) showed resistance to amoxiclav, and 16 (72.7%) had cefoxitin resistance. In addition, carbapenemase resistance was found in 24 (43.6%) and meropenem resistance in 13 (36.1%). Colistin, aztreonam, and tigecycline resistances were the least frequent. In addition, the following dependent risk factors increased the multidrug resistance risk in gram-negative infections; late-onset sepsis 3.547 fold (p=0.005), use of mechanical ventilation 3.143 fold (p=0.007), blood culture positivity 3.587-fold (p=0.013), bronchopulmonary dysplasia 6.702 fold, (p= 0.015) and total parenteral nutrition 5.591 fold (p=0.001), lower gestational age 1.122 (1/0.891) fold (p=0.026), and birth weight 1.001 (1/0.999) fold, (p=0.013). Similarly, anti-biotherapy duration was significantly higher in the MDR group than in the non-MDR group.

Conclusions: The reported risk factors for MDR in gram-negative neonatal infections are all dependent risk factors. Hence clinicians must be alert to all potential risk factors.

Keywords: Gram-Negative Bacterial Infections, Neonates, Multidrug Resistance.

Yenidoğan Yoğun Bakım Ünitesinde Çok İlaca Dirençli Gram-Negatif Bakteri Oranı ve Risk Faktörleri: Tek Merkezli On Yıllık Deneyim

ÖZET

Amaç: Gram-negatif yenidoğan enfeksiyonlarında çoklu ilaç direncinin (ÇİD) yönetimi zordur ve risk faktörleri farklı çalışmalar arasında farklılık göstermektedir. Bu çalışmanın amacı, gram-negatif izolatların demografik özelliklerini, mortalitesini, ÇİD durumunu ve ÇİD gram-negatif enfeksiyonlar için risk faktörlerini araştırmaktır.

Gereç ve Yöntem: Düzce Üniversitesi Hastanesi'nde Ocak 2012-Ocak 2022 tarihleri arasında yenidoğanlarda ÇİD gram-negatif enfeksiyonlarla ilgili retrospektif tek merkezli bir çalışma yapıldı. Bu çalışmada ÇİD gram-negatif enfeksiyonu olan yenidoğanların risk faktörleri ve klinik özellikleri değerlendirildi. Tüm analizler IBM SPSS V23 kullanılarak gerçekleştirildi. Ayrıca, ÇİD risk faktörlerini belirlemek için tek değişkenli analizler ve çok değişkenli lojistik regresyon modelleri incelenmiştir.

Bulgular: Yüzyedi gram-negatif bakterinin 41'ini (%38,3) *Enterobacter*, 30'unu (%28) *Klebsiella pneumonia* ve 22'sini (%20,6) *Escherichia coli* oluşturmuştur. Ayrıca, 61'i (%56,5) ÇİD mikroorganizmalardır. Seçilen izolatlar için yapılan duyarlılık testleri sonucunda 41'inde (%77,4) piperasilin, 57'sinde (%75) amoksiklav ve 16'sında (%72,7) sefoksitin direnci tespit edilmiştir. Ayrıca, 24'ünde (%43,6) karbapenemaz direnci ve 13'ünde (%36,1) meropenem direnci tespit edilmiştir. Kolistin, aztreonam ve tigesiklin dirençleri en az görülen dirençlerdi. Aşağıdaki bağımlı risk faktörleri gram-negatif enfeksiyonlarda çoklu ilaç direnci riskini arttırmıştır; geç başlangıçlı sepsis 3. 547 kat (p=0. 005), mekanik ventilasyon kullanımı 3. 143 kat (p=0. 007), kan kültürü pozitifliği 3. 587 kat (p=0. 013), bronkopulmoner displazi 6. 702 kat, (p=0. 015) ve total parenteral beslenme 5. 591 kat (p=0. 001), düşük gebelik yaşı 1. 122 (1/0. 891) kat (p=0. 026) ve doğum ağırlığı 1. 001 (1/0. 999) kat, (p=0. 013). Benzer şekilde, antibiyoterapi süresi ÇİD grubunda ÇİD olmayan gruba göre anlamlı derecede daha yüksekti.

Sonuç: Gram-negatif yenidoğan enfeksiyonlarında ÇİD için bildirilen risk faktörlerinin tümü bağımlı risk faktörleridir. Bu nedenle klinisyenler tüm potansiyel risk faktörleri çoklu ilaç direncini öngörmekte önem taşımaktadır.

Anahtar Kelimeler: Gram Negatif Bakteriyel Enfeksiyonlar, Yenidoğanlar, Çoklu İlaç Direnci.

INTRODUCTION

Two-thirds of the isolates in neonatal sepsis are gram-negative. The most common organisms of sepsis in neonates are *Acinetobacter baumannii (A. baumannii), Klebsiella pneumonia (K. pneumonia), Staphylococcus aureus (S. Aureus), and Escherichia coli (E.coli).* Multidrug resistance (MDR), defined as resistance to any three of five antibiotic classes, is detected in 20% of gram-negative infections in neonates (1). In the multicenter research from China and Brazil, more than half of the late-onset conditions (after the three days of life) are caused by gram-negative microorganisms, *Enterobacterales*. In sub-Saharan Africa and India, gram negatives are the isolates in 40% of neonatal infections(2).

Antibiotic resistance, a rising problem, has different mechanisms in *Enterobacterales. E.coli, K. Pneumonia, and Proteus mirabilis* have *Extended-spectrum ß lactamases (ESBL)* genes that inactive cephalosporins, aztreonam, and penicillin. *Carbapenem-resistant Enterobacterales (CRE)* have two main resistance mechanisms; carbapenemase or having poor membrane permeability with the production of an ESBL or AmpC *ß lactamases*. *K. Pneumonia* is the most common carbapenemase-producing bacteria. Independent risk factors for gram-negative microorganisms are gestational age ≤37 weeks, very low birth weight (<1500 grams), and prolonged hospitalization (more than 15 days). The inconsistent risk factors for gram-negative infections are mechanical ventilation, central venous catheters, parenteral nutrition, renal diseases, and cytopenias. Prolonged antibiotic administrations or prior cephalosporin exposures are also associated with MDR gram-negative infections (2). There is a debate on risk factors for MDR in neonatal sepsis. In one study, Gestational age, neurologic sequelae, and aminoglycoside were found to be essential risk factors (3). In another study, except for the variables of gestational age (>2500 g), cesarian labor, cytopenias, maternal infection, early onset sepsis, and antibiotic exposure were risk factors for MDR (4).

MDR gram-negative infections in neonates may be mortal, and the risk factors are contradictory. Therefore, this study aimed to represent the demographics of the neonates with gram-negative infections and determine the independent risk factors for MDR gram-negative infections and the mortality of MDR gram-negative infections.

MATERIAL AND METHODS

We conducted a retrospective single-center study about MDR gram-negative infections in neonates at Duzce University Hospital in Turkey. Demographic and bacteriological data were obtained from electronic records among neonates hospitalized in the neonatal intensive care unit between January 2012-January 2022; newborns infected with gram-negative microorganisms were included in the study. In addition, positive gram-negative cultures (blood, urinary, conjunctival, deep tracheal aspiration, catheter, tissue biopsy) were recorded. Exclusion criteria were the positive blood cultures inconsistent with the clinical manifestations or suspected to be contaminated bacteria.

Samples were inoculated on 5% sheep blood agar, chocolate agar, and eosin methylene blue agar (EMB) (Oxoid, UK) and incubated at 35°C for 18-24 hours in an aerobic environment. The microorganisms grown were identified by conventional microbiological methods (carbohydrate fermentation, citrate utilization, presence of urease, indole positivity, movement test) or automated system (VITEK 2, bioMérieux, France, BD Phoenix). In addition, antibiotic susceptibilities were performed by the Kirby-Bauer disk diffusion method and determined according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria.

This study evaluates the risk factors and clinical features of neonates with MDR gram-negative infections. Patients infected with gram-negative bacteria were divided into; the MDR and the non-MDR groups. An MDR gram-negative organism was defined as an isolate that was non-susceptible to at least one agent in at least three antimicrobial classes. All antibiotic classes included penicillins, penicillins + ß lactamase inhibitors, non-extended spectrum cephalosporins; 1st and 2nd generation cephalosporins, extended-spectrum cephalosporins; 3rd and 4th generation cephalosporins, fluoroquinolones, carbapenemase, cephamycins, glycylcyclines, folate pathway inhibitors, monobactam, polymyxin (1).

All analyses were performed using IBM SPSS V23. Univariate analyses were performed for each of the variables. The multivariate logistic regression model studied all the variables with a P value of ≤0.05 in the univariate analyses. The strength of the associations was shown by the odds ratio (OR) and 95% confidence interval (CI)—Fisher's Exact test calculated mortality rates in MDR gram-negative infections. Statistical significance was defined with a P value of <0. 05. Duzce University Ethics Committee approved the study on 20.06.2022 with approval number 2022/120.

RESULTS

The number of gram-negative infections was 105 between January 1, 2012, to January 1, 2022. For neonates, 61 (58.1%) of the patients were males, and 82 (75.9%) were born with a cesarian section. Fifteen newborns (14.4%) developed early-

onset sepsis, and 53 (51%) developed late-onset sepsis. Thirty-six had gram-negative infections without sepsis. Of 105 infants, the median gestational age was 35 weeks, and the birth weight was 2503 grams. The cumulative mortality rate was 4.7% (n=5) (Table 1).

Table 1. Demographics and prognosis of neonates with gram-negative infections

	n	%
Sex		
Male	61	58.1
Female	44	41.9
Type of delivery		
Vaginal	26	24.1
Caesarian Section	82	75.9
Onset of sepsis		
None	36	34.6
Early-onset sepsis	15	14.4
Late-onset sepsis	53	51
Death		
Survivor	101	95.3
Exitus	5	4.7
	Mean ± standard deviation	Median (minimum-maximum)
Birth weight (gram)	2503.35 ± 940.15	2645 (730 - 5580)

Most patients (n=101) (98.1%) with gram-negative sepsis were afebrile, and the majority (n=69) (65.7%) of them received combination antibiotic therapy. Transfusion rates were 25%, and total parenteral nutrition was administered to 33 (30.8%) neonates. Table 2 includes laboratory abnormality rates and prognosis. Thrombocytopenia occurred in 16 (15.2%) and neutropenia in 9 (8.5%) (Table 2).

Table 2. Clinical features and laboratory abnormalities

	n	%
Period of pyrexia (days)		
0	101	98.1
1	2	1.9
Antibiotic Treatment		
One drug	36	34.3
Combination	69	65.7
Transfusion		
Absent	81	75
Present	27	25
Total parenteral nutrition		
Absent	74	69.2
Present	33	30.8
Surgery		
Absent	103	95.4
Present	5	4.6
Mechanical ventilation		
Absent	61	58.1
Present	44	42
Neutropenia		
Absent	97	91.5
Present	9	8.5
Thrombocytopenia		
Absent	89	84.8
Present	16	15.2
Acidosis in blood gas		
Absent	65	78.3
Present	18	21.7
Bronchopulmoner dysplasia		
Absent	92	85.2
Present	16	14.8
Prognosis	Mean ± standard deviation	Median (minimum-maximum)
The Day of positive culture	11.99 ± 12.18	8 (0 - 60)
Duration of antibiotic use (Day)	12.95 ± 15.1	7 (1 - 90)
Duration of antibiotic use before positive culture (Day)	9.11 ± 13.61	4 (0 - 78)
Length of hospital stay before positive culture	12.33 ± 16.39	5 (0 - 70)
Length of hospital stay (Day)	22.63 ± 25.65	10 (0 - 100)
Mean-time for culture negativation (Day)	9.94 ± 13.59	7 (0 - 60)

Before culture positivity, the median duration of antibiotic use was 4 (0 - 78) days, and the median length of hospital stay was 5 (0 - 70) days (Table 2). Additionally, 64 (59.3%) had positive urinary cultures, and 30 (27.8%) had positive blood cultures.

Of 107 gram-negative bacteria, 41 (38.3%) accounted for *Enterobacter*, 30 (28%) for *Klebsiella pneumonia*, and 22 (20.6%) for *Escherichia coli*. Additionally, 61 (56.5%) were MDR microorganisms. Therefore, the gram-negative isolates were mainly (n=71) (66.4%) studied between 2017-2022 (Table 3). Mortality rates were similar between the MDR (n=2) (4.3%) and non-MDR groups (n=3)(5%) (p=1).

Table 3. Microbiological findings

	n	%
Isolated site		
Missing	2	1.9
Blood	30	27.8
Urine	64	59.3
Conjunctival	1	0.9
Deep tracheal aspiration	4	3.7
Catheter	4	3.7
Tissue	2	1.9
MDR (multidrug resistance)		
Absent	47	43.5
Present	61	56.5
Period of cultural positivities		
2012-2016	36	33.6
2017-2021	71	66.4
Prevalence of gram-negative bacterial species		
Enterobacteria	41	38.3
Klebsiella pneumonia	30	28
Escherichia coli	22	20.6
Acinetobacter baumannii	6	5.6
Pseudomonas auroginosa	5	4.7
Stenotrophomonas maltophilia	1	0.9
Shigomonas paucimobilis	1	0.9
Serratia marsencens	1	0.9

Among the susceptibility tests performed for selected isolates, 41 (77.4%) had resistance to piperacillin, 57 (75%) showed resistance to amoxiclav, and 16 (72.7%) had cefoxitin resistance. In addition, carbapenemase resistance was found in 24 (43.6%) and meropenem resistance in 13 (36.1%). Colistin, aztreonam, and tigecycline resistances were the least frequent (Table 4).

Tablo 4. Antibiotic resistance among the gram-negative isolates

	Susceptible		Resistant	
	n	%	n	%
Antibiotic resistance	6	5.6	101	94.4
Penicillins				
Piperasilin	12	22.6	41	77.4
Penicillins + ß lactamase inhibitors				
Amoxilav	19	25	57	75
Antipseudomonal penicillins + ß-lactamase inhibitors				
Piperasilin/tazobaktam	23	39	36	61
Aminoglycosides				
Gentamicin	47	58	34	42
Amikacin	35	55.6	28	44.4
Non-extended spectrum cephalosporins; 1st and 2nd generation cephalosporins				
Cefuroksime, Cefazolin	24	35.8	43	64.2
Extended-spectrum cephalosporins; 3rd and 4th generation cephalosporins				
Ceftazidime	15	34.1	29	65.9
Cefotaxim	17	32.1	36	67.9
Extended-spectrum cephalosporins; 3rd cephalosporin + ß-lactamase inhibitors				
Cefaperazone/sulbactam	9	69.2	4	30.8
Fluoroquinolones				
Ciprofloksasin	22	68.8	10	31.3
Carbapenemase	31	56.4	24	43.6
Meropenem	23	63.9	13	36.1
Cephamycins				
Cefoxitin	6	27.3	16	72.7
Glycylcyclines				
Tigecycline	9	90	1	10
Folate pathway inhibitors				
Cotrimoxazole	34	65.4	18	34.6
Monobactam				
Aztreonam	5	62.5	3	37.5
Polymyxin				
Colistin	15	88.2	2	11.8

Overall, resistance to antibiotics among gram-negative isolates is shown in Table 4. *Klebsiella and Enterobacter*, the primary isolates, primarily resisted Penicillins (53.3%, and 34.1%, respectively), Penicillins + ß lactamase inhibitors (30%, and 68.2%, respectively), Piperacillin/tazobactam (26.7%, and 39% respectively), amikacin (5%, and 16%, respectively), and gentamicin (6%, and 17% respectively). Additionally, Enterobacter showed marked resistance to cefuroxime/cefazolin (51.2%) and ceftazidime (41.2%) while having resistance to Cotrimoxazole (26.8%) and carbapenems (22.3%). Acinetobacter demonstrated marked resistance to piperacillin-tazobactam (83.3%) and ceftazidime (83.3%). In addition, Escherichia coli showed significant resistance to commonly used antibiotics. Gentamycin (60%), amikacin (40%), and ceftazidime (60%) were the leading antibiotics to which Pseudomonas was resistant. *Stenotrophomonas maltophilia (n=1)* and *Serratia marsencens (n=1)* were susceptible to commonly used antibiotics. However, Shigomonas paucimobilis resisted ampicillin, amoxicillin, gentamicin, amikacin, cefotaxime, and trimethoprim/sulfometaxole (Table 5).

Tablo 5. Antibiotic resistance among the gram-negative isolates

Isolated gram-negative microorganisms	*Enterobacteria (n=41) (38.3%)*	*Klebsiella pneumonia (n=30) (28%)*	*Escherichia coli (n=22) (20.6%)*	*Acinetobacter baumannii (n=6)(5.6%)*	*Pseudomonas auroginosa (n=5) (4.7%)*	Others (n=3) (2.8%)
Antibiotic classes						
Penicillins						
Piperacillin	14 (34.1%)	16 (53.3%)	11 (50%)	0 (0%)	0 (0%)	1 (0%)
Penicillins + ß lactamase inhibitors						
Amoxilav	28 (68.2%)	15 (30%)	11 (50%)	1 (16%)	1 (20%)	1 (33.3%)
Antipseudomonal penicillins + ß-lactamase inhibitors						
Piperasilin/tazobactam	16 (39%)	8 (26.7%)	6 (27.2%)	5 (83.3%)	0 (0%)	1 (33.3%)
Aminoglycosides						
Gentamicin	17 (42.5%)	6 (20%)	6 (27.2%)	1 (16%)	3 (60%)	1 (33.3%)
Amikacin	16 (39%)	5 (16.7%)	3 (13.6%)	1 (16%)	2 (40%)	1 (33.3%)
Non-extended spectrum cephalosporins; 1st and 2nd generation cephalosporins						
Cefuroksime Cefazolin	22 (51.2%)	14 (43.3%)	7 (31.8%)	0 (0%)	0 (0%)	0 (0%)
Extended-spectrum cephalosporins; 3rd and 4th generation cephalosporins						
Ceftazidime	17 (%41.5)	3 (10%)	1 (4.5%)	5 (83.3%)	3 (60%)	0 (0%)
Extended-spectrum cephalosporins; 3rd cephalosporin + ß-lactamase inhibitors						
Cefaperazone/sulbactam	1 (2.4%)	2 (6.7%)	0 (0)	1 (16%)	0 (0%)	0 (0%)
Fluoroquinolones						
Ciprofloxacin	3 (7.3%)	5 (16.7%)	1 (4.5%)	1 (16%)	0 (0%)	0 (0%)
Carbapenemase	12 (22.3%)	7 (23.3%)	3 (13.6%)	1 (16%)	1 (20%)	0 (0%)
Meropenem	8 (19.5%)	4 (13.3%)	0 (0)	0 (0%)	1 (20%)	0 (0%)
Cephamycins						
Cefoxitin	6 (14.6%)	5 (16.6%)	3 (13.6%)	0 (0%)	0 (0%)	1 (33.3%)
Glycylcyclines						
Tigecycline	0 (0)	0 (0)	1 (4.5%)	0 (0%)	0 (0%)	0 (0%)
Folate pathway inhibitors						
Cotrimoxazole	11 (26.8%)	3 (10%)	2 (9%)	0 (0%)	1 (20%)	1 (33.3%)
Monobactam						
Aztreonam	2 (4.9%)	1 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Polymyxin						
Colistin	1 (2.4%)	1 (3.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Univariate and multivariate analyses analyzed risk factors associated with MDR gram-negative bacteria. Univariate analyses showed that late-onset sepsis increased the multidrug resistance risk 3.547 fold (p=0,005) than the non-sepsis group, use of mechanical ventilation increased the risk 3,143 fold (p=0,007) than the nonmechanical ventilator group. The risk of multidrug resistance was 3.587-fold higher among neonates with blood culture positivity than other culture positivities (p=0.013). Bronchopulmonary dysplasia and total parenteral nutrition increased the risk of multidrug resistance rates 6.702 fold and 5.591 fold with a p-value of 0.015 ve 0.001 than the non-BPD and non-TPN groups, respectively. In addition, lower gestational age [1.122 (1/0.891) fold, p=0,026] and birth weight [1.001 (1/0.999) fold, p=0.013) increased the multidrug resistance risk. Similarly, anti biotherapy duration was significantly higher in the MDR group than in the non-MDR group. However, multivariate analyses concluded that none of the variables were independent risk factors (Table 6).

Table 6. Risk factors for multidrug-resistant gram-negative infections

	MDR (multidrug resistance)		Univariate		Multivariate	
	Absent	Present	OR (% 95 CI)	p	OR (% 95 CI)	p
	Mean± SD	Mean± SD				
Gestational age	36.4 ± 3.3	34.5 ± 4.6	0.891 (0.805 – 0.986)	**0.026**	1.285 (0.927 – 1.78)	0.132
Birth weight	2764.4 ± 887.3	2295.4 ± 936.2	0.999 (0.999 - 1)	**0.013**	0.999 (0.998 - 1)	0.147
Antibiotic delivery time (Day)	8.2 ± 3.9	16.9 ± 19.3	1.086 (1.009 – 1.168)	**0.027**	1.043 (0,954 - 1,139)	0.355
	n (%)	n (%)				
Sex						
Female	18 (40.9)	26 (59.1)	Ref.		Ref.	
Male	27 (44.3)	34 (55.7)	0.872 (0.398 – 1.912)	0.732	1.227 (0.335 – 4.494)	0.757
Onset of sepsis						
None	21 (58.3)	15 (41.7)	Ref.		Ref.	
Early onset of sepsis	7 (46.7)	8 (53.3)	1.6 (0.476 – 5.374)	0.447	0,918 (0,136 - 6,199)	0.930
Late onset of sepsis	15 (28.3)	38 (71.7)	3.547 (1.453 – 8.657)	**0.005**	2.653 (0.531 – 13.246)	0.234
Mechanical ventilation						
Absent	33 (54.1)	28 (45.9)	Ref.		Ref.	
Present	12 (27.3)	32 (72.7)	3.143 (1.366 – 7.229)	**0.007**	1.409 (0.301 – 6.591)	0.663
Neutropenia						
Absent	42 (43.3)	55 (56.7)	Ref.		Ref.	
Present	3 (33.3)	6 (66.7)	1.527 (0.361 – 6.465)	0.565	1.019 (0.062 – 16.787)	0.990
Thrombocytopenia						
Absent	39 (43.8)	50 (56.2)	Ref.		Ref.	
Present	5 (31.2)	11 (68,8)	1.716 (0.55 – 5.35)	0.352	2.311 (0.268 – 19.904)	0.446
Acidosis						
Absent	30 (46.2)	35 (53,8)	Ref.		Ref.	
Present	4 (22.2)	14 (77,8)	0.988 (0.59 – 1.656)	0.964	3.001 (0.418 – 21.535)	0.274
Type of labor						
Vaginal	15 (57.7)	11 (42,3)	Ref.		Ref.	
Cesarian	32 (39.0)	60 (61.0)	2.131 (0.87 – 5.218)	0.098	0.793 (0.193 – 3.256)	0.747
Blood Transfusion						
Absent	41 (50.6)	40 (49.4)	Ref.		Ref.	
Present	6 (22.2)	21 (77.8)	3.587 (1.311 – 9.815)	**0.013**	0.808 (0.092 – 7.124)	0.848
Bronchopulmonary dysplasia						
Absent	45 (48.9)	47 (51.1)	Ref.		Ref.	
Present	2 (12.5)	14 (87.5)	6.702 (1.441 – 31.168)	**0.015**	---	
Surgery						
Absent	46 (44.7)	57 (55.3)	Ref.		Ref.	
Present	1 (20.0)	4 (80.0)	3.228 (0.349 – 29.885)	0.302	---	
Total parenteral nutrition						
Absent	41 (55.4)	33 (44.6)	Ref.		Ref.	
Present	6 (18.2)	27 (81.8)	5.591 (2.064 – 15.142)	**0.001**	3.53 (0.304 – 40.979)	0.313

DISCUSSION

In the present study, the most common three gram-negative organisms for infections were *Enterobacterium, Klebsiella pneumonia,* and *Escherichia coli,* respectively, similar to the findings of previous studies(5,6,7,8). In contrast, Solomon showed that the most prevalent gram-negative bacterial species were *Klebsiella spp, Escherichia coli, and Acinetobacter baumannii* (9). *Klebsiella pneumonia and Acinetobacter baumanii* predominance were reported in previous studies (3,9). In contrast to our research, studies by Pokhrel et al. demonstrated *Klebsiella* and *Enterobacter* as the most common organisms (11).

Fifteen newborns in our study (14.4%) developed early-onset sepsis, and 53 (51%) developed late-onset sepsis. The overall mortality rates of gram-negative infections and MDR isolates were 4.7% vs. 4.3%, respectively, consistent with the report of Liu et al. (4.4% for hospital-acquired late-onset sepsis, 7.4% for early sepsis) (8).

In our study, gram-negative organisms showed high susceptibility to colistin (88.2%) and tigecycline (90%), followed by carbapenem (63.9%), which is consistent with the findings of Pokhrel et al. (11).

Our research showed that most gram-negative microorganisms resisted the frequently used antibiotics ampicillin, amoxiclav, cephalosporins, and colymixins. Our study is consistent with studies from China and Ethiopia and showed high resistance rates to commonly used antibiotics (9). Solomon et al. showed higher resistance rates to 3th and 4th generation cephalosporins (88% vs. 65.9%), amoxiclav (92% vs. 75%), gentamicin (85% vs. 42%) compared with our study. However, the rates of carbapenemases (43.6%) were markedly higher in our neonatal population than those reported in Solomon's study (1%) (12).

We report that *Enterobacteria*, the primary gram-negative isolate, showed significant resistance (more than >50%) to amoxiclav, 1st and 2nd generation cephalosporins, and carbapenemase rates of 22.3%. A recently published review about neonates recommended colistin, high-dose meropenem., and ceftazidime-avibactam in carbapenem-resistant enterobacteria (13). However, higher Carbapenemase rates were reported in several countries; Brazil, Egypt, Ghana, Greece, Japan, Poland, Taiwan (100%), and Turkey (72.6%) among toddlers, infants, and neonates, much more than our center (14).

Our study's second most typical organism of gram-negative infections, *Klebsiella pneumonia*, showed high resistance toward piperacillin. However, in another study, *Klebsiella pneumonia* demonstrated resistance to third-generation cephalosporins, aztreonam, beta-lactam, gentamycin, and tobramycin (15).

Our findings also showed that *E. coli* had high resistance to piperacillin and amoxiclav, showing susceptibility towards colistin and tigecycline, consistent with the meta-analysis results (14).

The emergence of infections with MDR bacteria neonates remains a significant challenge (16). The MDR rate in our study was 56.5%, similar to the survey from New Delhi (17).

MDRGN has been mainly reported in preterm newborn infants. Underlying disease, extended length of stay, surgery, prior use of antibiotics, invasive procedures, line central venous catheter and urinary catheter, BPD, and cytopenias, prolonged antibiotic use were the most commonly associated conditions.

Our work showed that lower gestational age, low birth weight, late onset of sepsis, use of mechanical ventilation, blood transfusions, bronchopulmonary dysplasia, and total parenteral nutrition were significantly associated with multidrug resistance. However, none were independent risk factors for MDR gram-negative infections, unlike Solomon et al., who found that low birth weight and late-onset sepsis were significantly associated with MDR resistance in sepsis (12). Zou et al. demonstrated that late-onset sepsis and antibiotic exposure were risk factors for MDR infection (9). Prior antibiotic exposure, underlying disease, invasive procedures, medical devices, and demographics were dominant risk factors for CRE infection (18,19,20).

The limitations are the retrospective and single-centered setting, small populations, and limited yield of some pathogens.

CONCLUSIONS

It is worth mentioning that important GNB pathogens, such as Enterobacteria, *Klebsiella*, and *E.coli*. Acinetobacter, and *Pseudomonas auroginosa*, were less reported. Risk factors should be avoided, despite their dependence on other variables. Hence clinicians must be alert to all potential risk factors.

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RESEARCH ARTICLE

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Dysphagia Frequency and Associated Risk Factors in Geriatric Patients Receiving Home Care

ABSTRACT

Objective: In our study, it was aimed to determine dysphagia frequency in patients 65 years of age and older who were received home care and to assess factors associated with dysphagia.

Methods: This cross-sectional, descriptive study was conducted in patients who were registered to Home Care Services of Samsun Training and Research Hospital between December 1, 2021, and March 1, 2022. In all patients, demographic data, level of dependence, nutrition methods, use of enteral nutrition supplement, body mass index (BMI), and comorbidity were assessed by Charlson Comorbidity Index (CCI) while dysphagia symptoms were assessed by Eating Assessment Tool (EAT-10) and nutritional status was assessed by Nutritional Risk Screening-2002 (NRS) using face-to-face interview method.

Results: A total of 413 patients were included in our study, of which 62.5% (n=258) were female. Dysphagia symptoms were present in 44.6% (n=184). The dysphagia frequency was significantly high in male patients (p=0.025), in patients aged ≥85 years (p=0.001), in those with high CCI score (p<0.001), in those with cerebrovascular disease (p<0.001), dementia (p<0.001), and hemiplegia (p=0.001), and in bedridden patients (p<0.001). Similarly, dysphagia frequency was higher in patient with nutritional risk and those using enteral nutrition supplement (p<0.001). In multivariate logistic regression analysis, it was found that dementia and increased nutritional risk were independent risk factors for presence of dysphagia symptoms (p<0.001).

Conclusions: Our study showed a high rate of dysphagia symptoms in the geriatric patient population receiving home care. It has been determined that the rate of dysphagia is increased in patients with older age, nutritional risk, dementia, cerebrovascular disease, and multiple comorbidities.

Keywords: Home Care Services, Deglutition Disorders, Aged, Comorbidity.

Evde Bakım Hizmeti Alan Geriatrik Hastalarda Disfaji Sıklığı Ve İlişkili Risk Faktörleri

ÖZET

Amaç: Çalışmamızda evde bakım hizmeti alan 65 yaş ve üstü hastalarda disfaji sıklığının belirlenmesi ve disfaji ile ilişkili faktörlerin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Araştırmamız kesitsel tanımlayıcı bir çalışma olup 1 Aralık 2021 ile 1 Mart 2022 tarihleri arasında Samsun Eğitim ve Araştırma Hastanesi Evde Sağlık Hizmetlerine kayıtlı hastalar ile gerçekleştirildi. Katılımcıların demografik özellikleri, yatağa bağımlılık durumu, beslenme yöntemleri, enteral beslenme ürün kullanımı, beden kitle indeksi (BKİ) verileri ile eşlik eden kronik hastalıklarının belirlenmesi amacı ile Charlson Komorbidite İndeksi (CCI), disfaji belirtileri açısından Yeme Değerlendirme Aracı (EAT-10), beslenme durumunun değerlendirilmesi için Nütrisyonel Risk Tarama-2002 (NRS) yüz yüze uygulanarak veriler kaydedildi.

Bulgular: Çalışmaya %62,5'i (n=258) kadın olmak üzere toplam 413 hasta dahil edildi. %44,6'sında (n=184) disfaji semptomları mevcuttu. Erkeklerde (p=0,025), 85 yaş ve üzeri kişilerde (p=0,001), CCI puanı yüksek olanlarda (p<0,001), serebrovasküler hastalık (p<0,001), demans (p<0,001), hemipleji tanısı olanlarda (p=0,001), yatağa tam bağımlı kişilerde (p<0,001) disfaji oranı yüksekti. Benzer şekilde beslenme riski mevcut bireylerde ve enteral beslenme ürünü kullananlarda disfaji oranı anlamlı derecede yüksek saptandı (p<0,001). Multivaryat lojistik regresyonda demansın ve artmış beslenme riskinin disfaji semptomlarının varlığında bağımsız risk faktörleri olduğu tespit edildi (p<0,001).

Sonuç: Çalışmamız evde bakım hizmeti alan geriatrik hastalarda yüksek oranda disfaji semptomlarının varlığını göstermiştir. İleri yaş, artmış beslenme riski, demans, serebrovasküler hastalık ve çoklu komorbiditesi olan hastalarda disfaji oranının arttığı belirlenmiştir.

Anahtar Kelimeler: Evde Bakım Hizmetleri, Yutma Bozuklukları, Yaşlı, Komorbidite.

INTRODUCTION

Dysphagia is a clinical syndrome defined as difficulty moving intraoral content from mouth to esophagus safely or irregular swallowing (1, 2). Dysphagia is associated with malnutrition, dehydration, respiratory tract infections, mortality, increased hospitalization rate and healthcare costs (3-6). Dysphagia is defined secondary to stroke, head and neck cancer, or neurodegenerative disorders; however, it is generally specified as a geriatric syndrome which is highly common among elder individuals (7-10). The dysphagia frequency has been reported as 10-33% among elder individuals while it is estimated as 26.2-56.7% in hospitalized geriatric patients (3, 11-13).

Owing to advances in the methods for early diagnosis and treatment, the disease-related mortality has been decreased and the life expectancy has been prolonged, resulting in increased number of individuals requiring lifelong treatment and care. It can be sometimes challenging to visit outpatient clinics for elder individuals who require management for chronic diseases, particularly if they experience somewhat dependency in daily living activities (14). Home health services is an important step to provide solution in this problem and it is defined as provision of physical examination, laboratory tests, treatment, and rehabilitation in home settings by a professional medical team to the patients who experience difficulty accessing to healthcare facilities for several chronic or malignant diseases or postoperative care (15). By increasing prevalence of chronic diseases, a tendency towards reduction in swallowing function has been observed in many patients using home health services. Dysphagia worsens nutritional status and decreases food consumption, resulting in malnutrition and weight loss. This leads physical weakness, resulting in being vulnerable to acute diseases such as infections, heart diseases or dehydration (3-5). Such conditions may cause unscheduled hospitalizations in patients requiring health home services. It was found that the dysphagia was a predictor for poor prognosis in patients using health home services (14). In a study by Melgaard et al., it was found that there was a significant increase in length of hospital stay and mortality in hospitalized geriatric patients with dysphagia when compared to those without (12). In a systematic review by Attrill et al., it was reported that dysphagia increased healthcare costs by 40.4% (6).

Therapeutic interventions for dysphagia include dietary modification, swallowing maneuvers, postural adjustments, and rehabilitative swallowing exercises. In cases with severe swallowing dysfunction, nasogastric feeding tube or percutaneous endoscopic gastrostomy can be used to maintain adequate nutrition (16). These therapeutic interventions are planned or performed in the context of home healthcare services. The prevention of clinical outcomes resulting from dysphagia may improve patient outcomes and contribute reducing healthcare costs (1). In addition, the estimation of dysphagia frequency by early screening in patients receiving home healthcare services will provide knowledge about scope of potential efforts and benefits.

In our study, it was aimed to determine dysphagia frequency in patients 65 years of age and older who were received home care and to assess factors associated with dysphagia.

MATERIAL AND METHODS

Study Population and Design: This cross-sectional, descriptive study was conducted in patients who were registered to Home Care Services of Samsun Training and Research Hospital between December 1, 2021, and March 1, 2022. The study included patients 65 years of age and older and not in the terminal phase after obtaining informed consent from patients and/or primary caregivers (in patients with cognitive disorder). Patients under the age of 65, who refused to participate in the study, and who were in the terminal phase were excluded from the study. In all patients, demographic data, level of dependence, nutrition methods, use of enteral nutrition supplement, body mass index (BMI), and comorbidity were assessed by Charlson Comorbidity Index (CCI) while dysphagia symptoms were assessed by Eating Assessment Tool (EAT-10) and nutritional status was assessed by Nutritional Risk Screening-2002 (NRS) using face-to-face interview method.

Nutritional Risk Screening-2002 (NRS): The NRS is used to assess nutritional risk (17). The validity study of Turkish version was performed by Bolayır et al. (18). It incorporates a pre-screening test. In pre-screening tests, the patient was asked whether BMI of his/her is <20.5 kg/m2; whether he/she lost weight in the past 3 months; whether his/her food intake was reduced in the past week; and whether the patient is critically ill. If yes to one of these questions, primary screening is performed; however, if no for all answers, the patient should be re-screened regularly using pre-screening test. The primary screening measures disorders in nutritional status and disease severity. The points from items in the primary screening are added; an additional point is added if the patient is above 70 years of age. Total score ranges from 0 to 7. The scores ≥3 points indicate increased nutritional risk and need for nutritional support (17).

Eating Assessment Tool (EAT-10): The EAT-10 is a questionnaire including 10 items, which is used to screen dysphagia (19). It is proven

to be a reliable screening tool in patients at risk for dysphagia and aspiration. Although the EAT-10 is a symptom checklist, it can predict objective evidence for swallowing difficulty. Each item represents one dysphagia symptom, which is rated by 0-4 points based on presence and severity of specific symptom. The validity study of Turkish version was performed by Demir et al. (20).

Ethical Approval: Ethics committee approval was obtained with the Ethics Committee decision no. 2021/19/6 of Samsun University Samsun Training and Research Hospital Clinical Research Ethical Committee.

Data Analysis: Descriptive statistics are presented with mean and standard deviation values for continuous data; they are presented with numbers and percentages for categorical data. The compliance of continuous data with a normal distribution was evaluated by Kolmogorov-Smirnov test. Independent groups t-test was used to compare two independent groups with parametric characteristics, and the Mann-Whitney U test was used to compare two non-parametric independent groups. Finally, a multivariate logistic regression model was created to identify risk factors associated with signs of dysphagia. For statistical significance, p values in the confidence interval of 95% and below 0.05 were considered significant. The program International Business Machines Corporation Statistical Package for the Social Sciences (IBM SPSS) version 26.0 was used in the statistical analysis of data.

RESULTS

A total of 413 patients were included in our study, of which 62.5% (n=258) were female. Mean age was 80.19±9.25 years (range: 65-103 years) and 38.7% (n=160) of patients were aged ≥85 years. Of the patients 57.1% (n=236) were bedridden while 35.6% (n=147) were semi-dependent. There was dementia in 42.9%, cerebrovascular disease in 34.1%, diabetes mellitus in 32.7% and heart failure in 28.3% of the patient. Of the patients, 12 were fed by nasogastric tube and 23 by percutaneous endoscopic gastrostomy while 28.1% (n=116) were using enteral nutrition products. Of the patients, 37.8% (n=156) had normal weight while 47.5% (n=196) were overweight and 26.2% (n=106) had increased nutritional risk. Dysphagia symptoms were present in 44.6% (n=184) (Table 1).

The dysphagia frequency was significantly high in male patients (p=0.025); in patients aged ≥85 years (p=0.001); in those with high CCI score (p<0.001); in those with cerebrovascular disease (p<0.001), dementia (p<0.001) and hemiplegia (p=0.001); and in bedridden patients (p<0.001). Similarly, dysphagia frequency was significantly higher in patient with nutritional risk and those using enteral nutrition products (p<0.001). Dysphagia frequency was lower in obese and overweight patients compared to remaining groups (p<0.001) (Table 2).

Table 1. Demographic and clinical characteristics of the patients (n=413)

Variables	n	%
Gender		
Female	258	62.5
Male	155	37.5
Age		
65-74	123	29.8
75-84	130	31.5
≥ 85	160	38.7
Level of dependence		
Independent	30	7.3
Semi-dependent	147	35.6
Bedridden	236	57.1
Chronic diseases[a]		
Myocardial infarction	34	8.2
Heart failure	117	28.3
Peripheral vascular disease	50	12.1
Cerebrovascular disease	141	34.1
Dementia	177	42.9
Rheumatological disease	33	8.0
Peptic ulcer	40	9.7
Chronic pulmonary disease	65	15.7
Diabetes	135	32.7
Hemiplegia	57	13.8
Renal disease	39	9.4
Cancer	29	7.0
Use of enteral nutrition supplement		
Present	116	28.1
Absent	297	71.9
Feeding method		
Oral	378	91.5
Nasogastric tube (NG)	12	2.9
Percutaneous endoscopic gastrostomy (PEG)	23	5.6
Nutritional risk[b]		
Absent	305	73.8
Present	106	26.2
BMI category[c]		
Underweight	1	0.2
Normal weight	156	37.8
Overweight	196	47.5
Obese	60	14.5
Dysphagia[d]		
Absent	229	55.4
Present	184	44.6

[a] Charlson Comorbidity Index (CCI)
[b] Nutritional Risk Screening-2002 (NRS), Nutritional risk (NRS ≥ 3)
[c] BMI (Body Mass Index) category: <18.5 = underweight, 18.5-24.9 = normal weight, 25.0-29.9 = overweight, and ≥30 = obese
[d] Dysphagia (Eating Assessment Tool (EAT-10) ≥ 3)

A binary logistic regression model was established to determine the factors affecting the dysphagia dependent variable with the independent variables. In multivariate logistic regression analysis, it was found that dementia (OR=2.352, 95% CI 1.635-3.384, p<0.001) and increased nutritional risk (OR=41.368, 95% CI 13.329-

128.394, p<0.001) were independent risk factors for presence of dysphagia symptoms. The model's goodness of fit was statistically significant (p<0.01). It was determined that the general fit of the logistic model was good (Cox-Snell R2=0.537, Nagelkerke R2=0.718). When the model was examined by the Hosmer-Lemeshow test, the model was found adequate to predict dysphagia risk factors ($\chi 2$ =10.374, p>0.05) (Table 3).

Table 2. Evaluation of dysphagia according to demographic and clinical characteristics of the patients

Variables	Dysphagia		p value
	Absent	Present	
Gender			
Female	154 (59.6%)	104 (40.4%)	**0.025**[a]
Male	75 (48.4%)	80 (51.6%)	
Age			
65-74	84 (68.3%)	39 (31.7%)	
75-84	71 (54.6%)	59 (45.4%)	**0.001**[a]
≥ 85	74 (46.3%)	86 (53.7%)	
CCI (points)	2.61±1.96	3.52±2.46	**<0.001**[b]
Chronic diseases			
Myocardial infarction	20 (58.8%)	14 (41.2%)	0.554[a]
Heart failure	64 (54.7%)	53 (45.3%)	0.848[a]
Peripheral vascular disease	30 (60.0%)	20 (40.0%)	0.490[a]
Cerebrovascular disease	60 (42.5%)	81 (57.5%)	**<0.001**[a]
Dementia	56 (31.6%)	121 (68.4%)	**<0.001**[a]
Chronic pulmonary disease	31 (47.7%)	34 (52.3%)	0.171[a]
Rheumatological disease	18 (54.5%)	15 (45.5%)	0.913[a]
Peptic ulcer	21 (52.5%)	19 (47.5%)	0.693[a]
Diabetes	86 (63.7%)	49 (36.3)	0.112[a]
Hemiplegia	20 (35.1%)	37 (64.9%)	**0.001**[a]
Renal disease	22 (56.4%)	17 (43.6%)	0.899[a]
Cancer	12 (41.4%)	17 (58.6%)	0.114[a]
Level of dependence			
Independent	25 (83.3%)	5 (16.7%)	
Semi-dependent	104 (70.7%)	43 (29.3%)	**<0.001**[a]
Bedridden	100 (42.4%)	136 (57.6%)	
Use of enteral nutrition supplement			
Present	9 (7.7%)	107 (92.3%)	**<0.001**[a]
Absent	220 (74.1%)	77 (25.9)	
BMI category[c]			
Underweight	0 (0.0%)	1 (100.0%)	
Normal weight	54 (34.6%)	102 (65.4%)	**<0.001**[a]
Overweight	124 (63.3%)	72 (36.7)	
Obese	51 (85.0%)	9 (15.0%)	
Nutritional risk[d]			
Absent	224 (73.4%)	81(26.6%)	**<0.001**[a]
Present	5 (4.6%)	103 (95.4%)	

Abbreviations: CCI, Charlson Comorbidity Index; BMI, Body Mass Index.
[a] Pearson Chi-square test. Bold values define the statistical significance of p <0.05.
[b] Mann-Whitney U test. Bold values define the statistical significance of p <0.05.
[c] BMI (Body Mass Index) category: <18.5 = underweight, 18.5-24.9 = normal weight, 25.0-29.9 = overweight, and ≥30 = obese
[d] Nutritional Risk Screening-2002 (NRS), Nutritional risk (NRS ≥ 3)

Table 3. Multivariate logistic regression analysis of variables[a]

Variables	OR*	95% CI	p
Gender	1.302	0.587-2.885	0.516
Age	1.301	0.841-2.015	0.238
Cerebrovascular disease	1.383	0.928-2.061	0.111
Dementia	2.352	1.635-3.384	**<0.001**
Bedridden	0.960	0.477-1.933	0.909
Nutritional risk	41.368	13.329-128.394	**<0.001**
BMI category	0.818	0.461-1.449	0.491

- Abbreviations: OR, Odds Ratio; CI, Confidence interval; BMI, Body Mass Index.
[a]Constant p=0.030, model p<0.01.
Cox-Snell R^2=0.537, Nagelkerke R^2=0.718.
Hosmer-Lemeshow test ($\chi 2$ =10.374, p>0.05).

DISCUSSION

This cross-sectional study showed that frequency of dysphagia symptoms was high in patients aged ≥65 years who were registered to Home Care Services of Samsun Teaching and Research Hospital between December 1, 2021, and March 1, 2022. The dysphagia frequency was determined as 44.6% among 413 patients assessed. It was found that dysphagia was high in male patients; in patients aged≥85 years; in those with high comorbidity score; in those with cerebrovascular disease, dementia, and hemiplegia; and in bedridden patients. The dementia and increased nutritional risk were identified as independent risk factors for presence of dysphagia symptoms.

In our study, dysphagia frequency in elder individuals was consistent with literature. In studies including hospitalized patients aged ≥65 years, dysphagia frequency was reported as 43.1% and 42% (1, 13). In Denmark, it was found that dysphagia symptoms were present in 50% of elder individuals admitted to geriatrics department (12). In Japan, there was increased symptoms of dysphagia in 78.7% of elder individuals given home care services (14). Lin et al. found dysphagia frequency of >60% in elder individuals residing in nursing facilities (21).

In our study, dysphagia frequency was significantly increased in patients aged ≥85 years; however, age was not an independent factor for dysphagia in multivariate logistic regression analysis. In a study by Olesen et al., it was found that patients with dysphagia symptoms were significantly older than those with normal swallowing capacity (1). In Spain, dysphagia frequency was found to be 82.4% in elder individuals (≥80 years; mean age: 93.5) presented to acute geriatrics unit of an academic center (2).

In our study, frequency of dysphagia symptoms was significantly higher in patients with cerebrovascular disease and dementia. The dementia was identified as an independent risk factor for presence of dysphagia symptoms in multivariate logistic regression analysis in our study. Baijens et al. reported that frequency of swallowing difficulties could reach up to 93% in patients with dementia (9). Dysphagia rate was reported as 45% in patients with dementia living in nursing facilities (22). In the literature, there is a well-defined relationship between dysphagia and cerebrovascular disease. In a systematic review by Takizawa et al., it has been reported that dysphagia frequency estimations ranged from 8.1% to 80% in stroke patients (7). Güçmen et al. detected dysphagia symptoms in 23.4% of stroke patients (23). In general, patients with stroke recover motor functions partially or near-completely within few months after stroke. It was predicted that only 11-13% of patients with dysphagia after stroke had persistent dysphagia after 6 months (24). In home care settings, frequency of neurological disease is higher in elder individuals at risk for dysphagia. Watanabe et al. found that there was history of stroke in 44.7% and 27.9% of elder individuals with or without dysphagia in home care settings, respectively (14).

In our study, it was found that CCI score was significantly higher in patients with dysphagia. Similarly, in a study Olesen et al., high CCI scores were linked to dysphagia symptoms (1). These results indicate that presence of dysphagia symptoms based on CCI scoring system can be associated to multi-morbidity and severe comorbidities. Carrion et al. reached similar conclusion by assessing dysphagia symptoms and CCI scores in acute geriatric patients while Melgaard et al. found no significant association (3, 12). In elder individuals, muscle atrophy is common particularly in the presence of multiple morbidities. This leads further impairment in swallowing function (10).

In our study, it was found that nutritional risk was significantly correlated with dysphagia symptoms. In an acute geriatric patient group, Olesen et al. found similar outcomes using EAT-10 and NRS to detect dysphagia and nutritional risk (1). Güçmen et al. found higher malnutrition rate in stroke patients with dysphagia using EAT-10 and Geriatric Nutrition Risk Index (GNRI) (23). Carrion et al. found a significant correlation between malnutrition and dysphagia using V-VST and Mini Nutritional Assessment (MNA) (3). Dysphagia may increase risk for insufficient food intake and nutrition by leading challenging, painful, anxious, and socially disturbing mealtimes. On the other hand, malnutrition can cause sarcopenia, neuromuscular dysfunction and other comorbidities which may lead impaired swallowing activity (1, 25, 26). In cancer patients, dysphagia is generally associated with cachexia (27). Dysphagia results in anorexia in elder individuals and subsequent weight loss may exacerbate dysphagia (10).

It should be noted that the current study was limited to investigating the symptom of dysphagia. Again, no dysphagia diagnosis was made, or no gold standard tools such as point-of-care screening, Video Fluoroscopic Swallowing Study (VFSS) or Fiberoptic Endoscopic Evaluation of Swallowing (FEES) were used in the study. This study has some strengths such as prospective design and inclusion of elder individual with progressive physical and/or cognitive regression.

CONCLUSION

Our results showed that dysphagia frequency was higher among geriatric patient population receiving home care services. The results indicate increased dysphagia rate in individuals with nutritional risk, dementia, cerebrovascular disease, or multiple comorbidities. In elder individual, early recognition of dysphagia risk is important to

prevent dysphagia-related complications as well as morbidity and mortality in home care settings. Specific exercises and rehabilitations programs are available to enhance muscles involved swallowing. In order to promote early intervention in patients at risk for dysphagia, it is recommended that healthcare professionals involved in the management of geriatric patients should recognize early symptoms and that an objective swallowing assessment should be routinely performed during provision of home healthcare services.

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RESEARCH ARTICLE

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Assessment of the Effect of Psoriasis and Methotrexate Treatment on Liver Stiffness by ARFI Imaging

ABSTRACT

Objective: To investigate whether psoriasis and methotrexate used in its treatment cause liver fibrosis and eventually to evaluate the safety of methotrexate in treatment.

Methods: 44 cases were included in the study. Methotrexate-using (group 1, n=14) and methotrexate-not-using (group 2, n=13) psoriasis patients were compared retrospectively with a healthy control group (group 3, n=17) according to mean shear wave rates obtained from sonoelastographic examinations with Acoustic Radiation Force Impulse (ARFI) technique.

Results: Mean shear wave velocities were calculated as 2.57 ± 1.13 m/sec in the patients using methotrexate, 2.31 ± 1.16 m/sec in the patients who did not use methotrexate, and 1.56 ± 0.62 m/sec in the healthy control group. While the average shear wave velocity of the 3rd group was found to be significantly lower than that of the 1st and 2nd groups (p=0.032; p=0.012), no significant difference was observed between the 1st and 2nd groups (p=0.755).

Conclusions: Shear wave imaging with ARFI quantification findings revealed no evidence that methotrexate therapy is associated with liver fibrosis in psoriasis patients and we think that the increase in liver tissue stiffness in patients using methotrexate for psoriasis is secondary to the inflammatory process caused by psoriasis itself rather than methotrexate.

Keywords: ARFI, Methotrexate, Psoriasis, Shear Wave Elastography.

Psöriazis ve Metotreksat Tedavisinin Karaciğer Sertliğine Etkisinin ARFI Görüntüleme ile Değerlendirilmesi

ÖZET

Amaç: Psöriazisin ve tedavisinde kullanılan metotreksatın karaciğer fibrozisine neden olup olmadığını araştırmak ve böylelikle metotreksatın tedavideki güvenilirliğini değerlendirmektir.

Gereç ve Yöntem: Çalışmaya 44 olgu dahil edildi. Psöriasis tanılı olup metotreksat kullanan (grup 1, n=4) ve metotreksat kullanmayan (grup 2, n=13) hastalar ile sağlıklı kontrol grubunun (grup 3, n=17) Akustik Radyasyon Kuvveti İmpulsu (ARFI) tekniği ile yapılmış sonoelastografik incelemelerinde shear wave hız ortalamaları retrospektif olarak karşılaştırılmıştır.

Bulgular: Ortalama shear wave hızları metotreksat kullanan hastalarda 2,57 ± 1,13 m/sn, metotreksat kullanmayan hasta grubunda 2,31 ± 1,16 m/sn, sağlıklı kontrol grubunda ise 1,56 ± 0,62 m/sn olarak hesaplanmış olup 3. grubun shear wave hız ortalaması 1 ve 2. gruptan anlamlı derecede düşük bulunurken (p=0,032; p=0,012), 1 ve 2. gruplar arasında anlamlı farklılık gözlenmemiştir (p=0,755).

Sonuç: ARFI kuantifikasyon ile yapılan shear wave görüntüleme bulguları psöriasis hastalarında metotreksat tedavisinin karaciğer fibrozu ile ilişkili olmadığını ve psöriazis nedeniyle metotreksat kullanan hastalarda ortaya çıkan karaciğer doku sertliği artışının, metotreksattan ziyade, psöriazisin neden olduğu inflamatuar sürece sekonder olduğunu düşündürmüştür.

Anahtar Kelimeler: ARFI, Metotreksat, Psöriazis, Shear Wave Elastografi.

INTRODUCTION

Psoriasis is chronic skin disease which is characterized with an autoimmune inflammation and it affects 1-3% of the population. This disease is associated with an increase in local and systemic proinflammatory cytokines (1). It has been shown that proinflammatory cytokines can cause insulin resistance and as a result metabolic syndrome through various biochemical pathways (2, 3).

Metabolic syndrome, which is a multisystemic and multifactorial disease, is an important risk factor for non-alcoholic fatty liver disease (4). There are studies stating that psoriasis, which is a systemic disease, is associated with fatty liver disease and liver fibrosis through proinflammatory cytokines (5, 6).

Methotrexate is used as a first-line therapy in the treatment of psoriasis worldwide (7). However, there are also studies present indicating that the use of methotrexate in long-term treatment may lead to an important side effect of liver fibrosis (8, 9).

Methods such as radiological imaging methods, biochemical data and histopathological examination are used in the evaluation of liver fibrosis. The gold standard method is accepted as histopathological evaluation with liver biopsy (10, 11). However, albeit low, liver biopsy poses a risk of morbidity and mortality (12). This situation has led to the need for new methods for the evaluation of liver fibrosis.

Shear wave elastography (SWE) method is a relatively new and is increasingly used, non-invasive imaging method that allows the measurement of elasticity and stiffness in tissues (13, 14). SWE is used to evaluate pathologies such as thyroid nodules, breast lesions, intra-abdominal solid organ tumors and liver fibrosis. Although the gold standard method for the evaluation of liver fibrosis is liver biopsy, it is stated that SWE may be an alternative method in terms of distinguishing normal from fibrotic liver (15).

The aim of this study was to investigate whether psoriasis and methotrexate used in its treatment cause liver fibrosis and thus to evaluate the safety of methotrexate in the treatment in terms of this side effect.

MATERIAL AND METHODS

Patients: The study was conducted after the approval of the Ethics Committee of Duzce University and written informed consent was obtained.

Between January 2018 and September 2020, those who had a history of psoriasis for at least 10 years and who received methotrexate therapy due to moderate-to-severe involvement according to the Psoriasis Area Severity Index (PASI) score (A PASI score higher than 5 indicates moderate psoriasis.) (Group 1, n=14), during this period patients with a history of psoriasis and moderate-to-severe involvement who received systemic therapy other than methotrexate (Group 2, n=13) were included in the study. Mean shear wave velocity results from ARFI sonoelastographic examinations performed together with liver ultrasonographic examination, which was requested during routine follow-ups, were examined retrospectively.

A detailed medical history was obtained from medical history archive. Patients with history of alcohol consumption, abnormal liver function tests, chronic liver disease, diabetes, obesity, patients with grade 3 hepatosteatosis on sonographic examination, patients exposed to hepatotoxic agents were excluded from the study. No patient had any clinical sign of hepatic decompensation, such as hepatic encephalopathy, ascites, or variceal bleeding.

Control Group: Seventeen healthy adult volunteers (nine men, eight women) who did not have a history of metabolic syndrome or liver disease were examined with ARFI sonoelastography constituted the control group in which median shear wave velocity measurements were performed. These individuals did not consume any medication, drug and alcohol just before the ARFI imaging.

ARFI Sonoelastography: ARFI sonoelastography was performed by using a Siemens Acuson S2000 US System (Siemens Medical System, Tokyo, Japan). In all patients, ARFI sonoelastography was performed with a curved array US probe at 4 MHz for B-mode imaging. The right lobe of the liver was examined through the intercostal space with the patient lying in left lateral decubitus. A minimal scanning pressure was applied by the operator, while the patients were asked to stop breathing for a moment, in order to minimize the breathing motion. A measurement depth of 2 cm below the liver capsule was chosen to standardize the examination. Care was taken not to include any blood vessels or billiary structures. Ten successful measurements were performed in each patient, and the median values were calculated, the results were expressed in meters/second (m/s). In all patients, ARFI imaging was performed by one physician (D.G., 10 years of experience in sonography) who was blinded to the clinical data.

Statistical Analysis: Descriptive statistics of categorical variables were given as numbers and percentages, and descriptive statistics of numerical variables were given as mean, median, standard deviation, minimum and maximum.

The conformity of the numerical variables to the normal distribution was examined with Shapiro-Wilk test.

Relationships between categorical variables were examined with Pearson chi-square test. Mann-Whitney U test was used to compare two independent group means. One-way analysis of variance (ANOVA) and Kruskall-Wallis test were used to compare more than two independent group means. Dunn's test was used as a post hoc test in pairwise comparison of the groups for the variables found to be significant as a result of the Kruskal-Wallis test. The statistical significance level was taken as 0.05 and the SPSS (version 28) package program was used in the calculations.

RESULTS

The total sample of the present study was n = 44 patients. Among them, there were 14 patients (31.8 %) receiving ongoing methotrexate therapy and 13 patients (29.5 %) who were not using methotrexate. The mean age was 49.21 ± 10.68 years in group 1, 45.07 ± 11.51 years in group 2, and 41.94 ± 7.33 years in group 3. No significant difference was observed between the groups in terms of gender, age and BMI distributions, and it is presented in Table 1 (p>0.05).

Table 1. Gender, age and BMI distributions between groups

		1. Group (n=14)	2. Group (n=13)	3. Group (n=17)	p
Age (years)	Mean ± SD	49.21±10.68	45.07±11.51	41.94±7.33	0.133
Gender	Male (n (%))	7 (50)	9 (69.2)	8 (47.1)	0.442
	Female (n (%))	7 (50)	4 (30.8)	9 (52.9)	
BMI	Mean ± SD	25.92±1.41	26.92±2.71	25.55±3.37	0.383

*One way ANOVA, **Pearson chi square test was used.

No hepatosteatosis was detected sonographically in 21.4 % (n=3) in group 1, 46.2 % (n=6) in group 2, and 64.7 % (n=11) in group 3. While 50 % (n=7) in group 1 had hepatosteatosis grade 1, 23.1 % (n=3) in group 2 had grade 1, and 35.3 % (n=6) in group 3 had grade 1. In addition, while 28.6 % (n=4) in group 1 had hepatosteatosis grade 2, 30.8 % (n=4) in group 2 had grade 2, and there was no grade 2 hepatosteatosis in group 3. Shear wave measurement could not be performed in patients with Grade 3 hepatosteatosis in sonographic examination, so they were excluded from the study. A significant difference was observed between the groups in terms of shear wave velocity averages (p=0.022). When the differences were examined in detail, the average shear wave velocity of the 3rd group (mean: 1.56 ± 0.62 m/sec) was compared to the 1st and 2nd group (mean: 2.57 ± 1.13 m/sec, 2.31 ± 1 .16 m/sec) was found to be significantly lower (p=0.032; p=0.012), while no significant difference was observed between the 1st and 2nd groups (p=0.755) (Table 2).

Table 2. Shear wave mean velocity and comparison of psoriasis patients using methotrexate (group 1) and non-methotrexate (group 2) and healthy control group (group 3)

Group	n	Mean	Median	Std. Deviation	Minimum	Maximum	p
1	14	2.57	2.44	1.13	0.797	3.956	0.022
2	13	2.31	1.66	1.16	1.221	4.352	
3	17	1.56	1.24	0.62	0.897	3.190	

*Kruskall Wallis and Dunn test was used.

In the statistical analysis between the psoriasis patient group, which was formed by combining the 1st and 2nd groups, and the control group, the average shear wave velocity of the 1st group (mean: 2.45 ± 1.13 m/sec) was compared to the 2nd group (mean: 1.56). ± 0.63 m/sec) was found to be significantly higher (p=0.006) (Table 3).

Table 3. Average shear wave velocity and comparison of psoriasis patient group (group 1) and healthy control groups (group 2)

Group	n	Mean	Median	Std. Deviation	Minimum	Maximum	p
1	27	2.45	2.07	1.13	0.797	4.352	0.006
2	17	1.56	1.24	0.63	0.897	3.190	

*Mann Whitney U test was used

DISCUSSION

Methotrexate is a long-term used drug given in low dose in the treatment of many rheumatological diseases. In addition to its side effects such as nausea, mucositis, and pneumonitis, there are studies stating that it develops liver fibrosis (8, 16). There are also studies showing that the use of methotrexate has no effect on liver fibrosis (17, 18). Considering this information, the relationship between long-term methotrexate use and liver fibrosis is a process that has not been fully elucidated.

Although biopsy is the gold standard in the evaluation of liver fibrosis, it carries a risk of morbidity and mortality since it is an invasive method. The ARFI method is a SWE method, in which a specific ROI area can be evaluated without applying external pressure (15). There are many studies in the literature showing that the ARFI technique can be used in the detection of liver fibrosis (15, 19). In this study, it was investigated whether long-term methotrexate use due to psoriasis has an effect on the development of liver fibrosis by using SWE as a non-invasive method.

Feuchtenberger et al. investigated the development of liver fibrosis in patients using methotrexate for rheumatoid arthritis. In this study, in which 119 patients were evaluated with the ARFI method, it was shown that there was no relationship between long-term methotrexate use and the development of liver fibrosis (17). In another study conducted by Erre et al. with the 2D shear wave method, it was found that the use of methotrexate for rheumatoid arthritis did not pose a risk in terms of liver fibrosis (18). In this study, it was shown that the risk of developing liver fibrosis is higher in patients with rheumatoid arthritis compared to healthy population.The current study, like the previous two, found no evidence that methotrexate increased liver stiffness.. In another study, Conway et al. states that the use of methotrexate leads to elevation in transaminase levels, but that this is not a risk factor for fibrosis (20).

Horster et al. reported in their study on healthy volunteers that liver tissue stiffness was 1.19 ± 0.18 m/sec in measurements made with the ARFI method (21). In another investigation, Goertz et al. categorized the patients into five groups and set cut-off values based on the degree of liver fibrosis. (22). In our study, liver tissue stiffness was found in the healthy volunteer group at similar intervals obtained from these studies. Regardless of methotrexate use, liver stiffness values in the group of patients with psoriasis were found significantly higher than the normal cut-off values from the other study, compared to healthy volunteers. These findings show that the increase in liver tissue stiffness in the psoriasis patients group is in correlation with the data from the literature.

It is stated that psoriasis is associated with liver fibrosis due to metabolic and systemic disorders (23). Pongpit et al. reported in their study that 11% of patients with psoriasis had increased liver tissue stiffness or significant liver fibrosis. In this study, it is emphasized that the risk of liver fibrosis increases significantly in patients with increased waist circumference and diabetes. They stated that the cumulative methotrexate dose was not a risk factor for fibrosis (24). In our study, it was observed that liver stiffness increased in the psoriasis patient group compared to healthy individuals. We observed no significant differences in liver stiffness in the measurements made with ARFI between patients using methotrexate and the group of patients not using methotrexate. With these findings, it can be interpreted that the increase in liver tissue stiffness in patients using methotrexate for psoriasis is secondary to the inflammatory process caused by psoriasis itself rather than methotrexate.

Psoriasis can cause central obesity and metabolic syndrome with the pro-inflammatory processes it creates. As a result of this process, it increases the risk of non-alcoholic fatty liver disease (6, 23). In our study, we found that fatty liver was significantly more common in the psoriasis patient group than in the normal control group, as expected. However, similar to the study of Motosugi et al. (25), we found that hepatosteatosis grades and BMI did not cause an increase in liver tissue stiffness. In the light of these findings, it can be concluded that hepatosteatosis developing secondary to metabolic syndrome in the psoriasis patient group did not cause an increase in liver tissue stiffness and that patients with increased tissue stiffness should be evaluated in terms of the fibrosis process.

In conclusion, psoriasis is a chronic inflammatory disease and can affect the liver through proinflammatory cytokines. SWE, which is a noninvasive method, is a useful method in evaluating liver involvement. As a result of our study, it was concluded that long-term methotrexate use due to psoriasis has no effect on the development of liver fibrosis.

The main limitation of our study is the small number of patients. Another limitation is that the patients could not be histopathologically confirmed by liver biopsy, which is the gold standard method. Studies with larger patient series will shed light on the literature.

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RESEARCH ARTICLE

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Evaluation of Biochemical Parameters of COVID 19 Patients as Biomarkers

ABSTRACT

Objective: Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) has caused a global pandemic with more than 664 million confirmed cases and more than 6.7 million deaths worldwide. In pandemic, several studies have been done about the relationship of some biochemical and hematological parameters with COVID 19 in order to assist diagnosis and treatment. However, a lot of information is not completely complete and there are contradictions in the data. In the present study, it was focused to compare the biochemical parameters of patients and healthy individuals due to COVID 19 by investigating the relationship between age and gender.

Methods: The 317 individuals who consulted to the Pandemic Outpatient Clinic with the suspicion of COVID 19 between February 2022 and November 2022 were evaluated by laboratory tests. In present study, biochemical parameter values of individuals with positive and negative COVID 19 test outcomes were used as material. These biochemical parameters were compared statistically based on different age ranges and gender groups.

Results: It was ascertained that the values such as urea (UREA), creatine (KREA), ferritin (FER), aspartate transaminase (AST), alanine transaminase (ALT), high sensitivity troponin I (HSTI), creatine kinase (CK) and C reactive protein (CRP) in male patients with COVID 19 were higher than female patients with COVID 19. Moreover, it was detected that there was a statistically significant increase in parameters such as GLU, FER, AST, lactate dehydrogenase (LDH), HSTI, CK and CRP in COVID 19 patients aged 18-65 years.

Conclusions: Many biomarkers of prognostic importance are expensive, ordinary and pricey-effective biomarkers such as FER, AST, LDH, HSTI, CK and CRP can be used to monitor disease in patients with COVID 19 infection.

Keywords: Biochemical Parameters, Biomarkers, COVID 19, Laboratory Diagnosis, SARS-CoV-2.

COVID 19 Hastalarının Biyokimyasal Parametrelerinin Biyobelirteç Olarak Değerlendirilmesi

ÖZET

Amaç: Şiddetli Akut Solunum Sendromu-Coronavirus-2 (SARS-CoV-2), Dünya çapında 664 milyondan fazla doğrulanmış vaka ve 6,7 milyondan fazla ölümle küresel bir pandemiye neden olmuştur. Pandemide tanı ve tedaviye yardımcı olmak amacıyla bazı biyokimyasal ve hematolojik parametrelerin COVID 19 ile ilişkisi üzerine birçok çalışma yapılmıştır. Ancak pek çok bilgi tam değildir ve verilerde çelişkiler vardır. Bu çalışmada yaş ve cinsiyet ilişkisi araştırılarak COVID 19 nedeniyle hasta ve sağlıklı bireylerin biyokimyasal parametrelerinin karşılaştırılması amaçlanmıştır.

Gereç ve Yöntem: Şubat 2022-Kasım 2022 tarihleri arasında Pandemi Polikliniği'ne COVID 19 şüphesiyle başvuran 317 kişi laboratuvar testleri ile değerlendirilmiştir. Bu çalışmada materyal olarak, COVID 19 test sonuçları negatif ve pozitif olan bireylerin biyokimyasal parameter değerleri kullanılmıştır. Bu biyokimyasal parametreler farklı yaş aralıkları ve cinsiyet grupları baz alınarak istatistiksel olarak karşılaştırılmıştır.

Bulgular: COVID 19 erkek hastalarda ÜRE, kreatin (KREA), ferritin (FER), aspartat transaminaz (AST), alanin transaminaz (ALT), Yüksek Hassasiyetli Troponin I (HSTI), kreatin kinaz (CK), C reaktif protein (CRP) gibi değerlerin COVID 19 kadın hastalara göre daha yüksek olduğu belirlenmiştir. Ayrıca 18-65 yaş arası COVID 19 hastalarında GLU, FER, AST, laktat dehidrogenaz (LDH), HSTI, CK ve CRP gibi parametrelerde görülen yükselmenin istatistiksel olarak anlamlı olduğu tespit edilmiştir.

Sonuç: Prognostik öneme sahip birçok biyobelirteçlerin pahalı olmasına karşı COVID 19 enfeksiyonu olan hastalarda hastalığın izlenmesi amacıyla basit ve uygun maliyetli FER, AST, LDH, HSTI, CK ve CRP gibi biyokimyasal parametrelerin biyobelirteç olarak kullanımı söz konusudur.

Anahtar Kelimeler: Biyokimyasal parametreler, Biyobelirteç COVID 19, laboratuvar tanısı, SARS-CoV-2.

INTRODUCTION

Coronaviruses can cause ailments ranging from the common cold to severe acute respiratory diseases in humans (1). Viruses such as Severe Acute Respiratory Syndrome-Coronavirus (SARS-CoV) that cause SARS, Middle East Respiratory Syndrome-Coronavirus (MERS-CoV) that cause MERS, and, Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) that cause COVID 19, classified in the beta-coronavirus family, are named separately due to some differences (1). SARS-CoV first appeared in southern China in 2002 and subsequently affected approximately 8,000 people in 26 countries (2). MERS-CoV first emerged in Saudi Arabia in 2012 and infected 2494 people (3). SARS-CoV-2 expanded all over the world, causing the pandemic (4, 5).

SARS-CoV-2 is recognized as a novel species of the Coronoviridae family due to its high contagiousness (6). Accordingly, the World Health Organization, 203 countries have been affected by the virus. However, there were more than 664 million verified occurrence and more than 6.7 million deaths worldwide, according to data released on January 22, 2023 (7). Considering both the number of viruses affected and the number of cases resulting in death, SARS-CoV-2 has been appeared to be more pathogenic and deadly than previous coronaviruses (SARS-CoV and MERS-CoV) (8). Because the contagion and infection rate of SARS-CoV-2 is quite high (8). Sequence analyzes show that SARS-Cov-2 shows 79% and 50% homology with SARS-CoV and MERS-CoV, respectively. (9).

The lack of information and information pollution experienced at the beginning of the pandemic has been tried to be eliminated by research. Thanks to many recent studies, valuable information has been obtained in terms of both laboratory and clinical findings of hospitalized patients with COVID 19 (10, 11). However, much information was not fully completed, and conflicts were found in the available data (11). The ongoing pandemic and the rapid rise in the number of cases, especially in the last months, need to clearly demonstrate the correlation between both laboratory and clinical findings of COVID 19 patients. More than 11 million cases and more than 55,000 new deaths were recorded in the world in 28 days (26 December 2022 - 22 January 2023) (7).

It is seen that the pandemic continues, and the death rates are increasing rapidly. In this regard, there is a necessity for investigations that can help define critical determinants and provide early appropriate clinical intervention by analyzing the biochemical parameters of COVID 19 patients (12). There are many studies on the relationship of some blood parameters with COVID 19 (4,11,13,14). Each study contains very important data in terms of strategies to be developed in the fight against the disease. Some biochemical and hematological parameters reveal the mortality relationship of COVID 19 patients and can also help the treatment process (13,14).

In this study designed for this purpose, biochemical parameters such as Glucose (GLU), Urea (URE), Creatine (KRE), Ferritin (FER), Lactate Dehydrogenase (LDH), Aspartate Transaminase (AST), Alanine Transaminase (ALT), Sodium (Na), Calcium (Ca), Potassium (K), Hs-Troponin I (HSTI), Creatine Kinase Myocardial Band (CK-MB), Creatine Kinase (CK), Magnesium (Mg), and C-Reactive Protein (CRP) in blood samples taken from COVID 19 positive and negative patients were examined and the changes in these parameters depending on age and gender were examined.

MATERIAL AND METHODS

Ethical Consideration: The study was accomplished with the permission of Düzce Atatürk State Hospital and Düzce University Non-Interventional Health Research Ethics Committee dated 25.04.2022 and numbered 2022-19.

Study Design: In this study, some biochemical data of 317 individuals who applied to Düzce Atatürk State Hospital COVID 19 Pandemic Outpatient Clinic between February 2022 and November 2022 were evaluated. Biochemistry laboratory results and demographic (age and gender) findings of patients and healthy individuals were analyzed retrospectively. Patients with (+) and (-) PCR tests were included in the study. Patients with non-reference values due to malignant and chronic diseases were excluded from the study.

Data Collection: First, oropharyngeal-nasopharyngeal swab samples taken from patients who were have symptoms of COVID 19 were analyzed with a Real-Time PCR device (BioRad® CFX96 Touch C1000, Real Time PCR). A total of 268 people (Female: 171, Male: 97) with positive PCR test and 49 people (Female: 25, Male: 24) with negative PCR test (as control group) were included in the study. Then, the blood samples of 317 individuals taken into gel tubes were centrifuged (Nüve® NF 1200R) and used in the analysis of serum biochemical parameters. GLU, URE, KRE, FER, AST, ALT, LDH, Ca, Na, K, CK-MB, HSTI, CK, Mg and CRP biochemical parameters were analyzed with Alinity® Abbott Autoanalyzer Biochemistry Instrument (Shenzhen, China). The individuals included in the research were divided into four groups according to their age ranges (Group-1: 0-17years old; Group-2: 18-65years old; Group-3: 66-79years old; Group-4: 80-99years old).

Statistical Analysis: Statistical analysis was implemented using IBM SPSS 20.0 (SPSS for

Windows, SPSS Inc., Chicago, IL, USA). In descriptive statistics, numerical variables were given as mean and standard deviation. In addition, Kolmogorow – Smirnov test was used in the analysis of numerical data not suitable for normal distribution. p values <0.05 were approved statistically significant.

RESULTS

In our study, it was detected that the age of COVID 19 negative individuals (n=49) was between 1–83, and the age of COVID 19 positive individuals (n=268) was between 1–92.

In this study, there were 51% female (n=25) and 49% male (n=24) individuals in the COVID 19 negative control group, and 64% female (n=171) and 36% male (n=97) individuals in the COVID 19 positive patient group (Figure 1). In total, it was determined that 61.83% and 38.17% were female (n=196) and male (n=121) of all individuals, respectively.

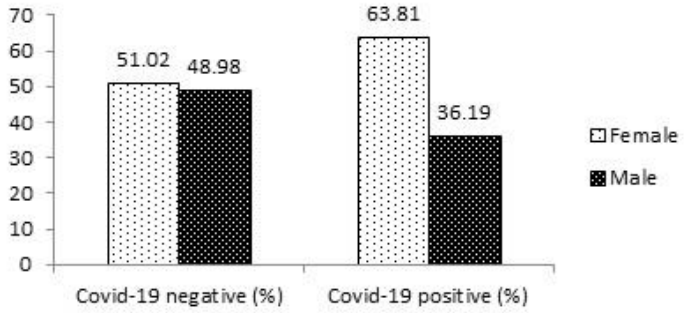

Figure 1. Distribution rates of Covid-19 positive and negative patients by gender

In our study, the age distribution among the control group and the patient study group is also shown in Figure 2 for 4 different age ranges: 0-17, 18-65, 66-79 and 80-99 age ranges. According to the data here, the 18-65 age range has the highest number of individuals in both COVID 19 negative and COVID 19 positive patients, and it is seen that the number of women is higher. The age range of 80-99 has the lowest number of individuals and the number of women is found to be higher.

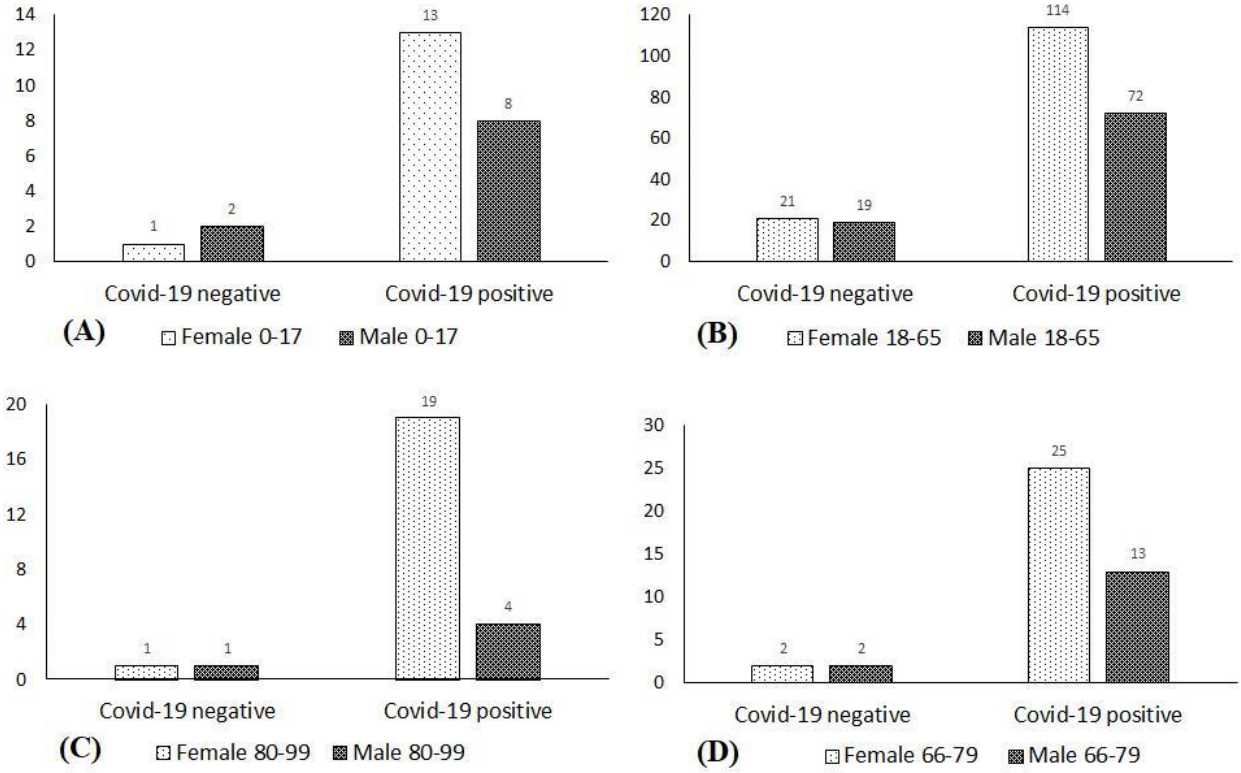

Figure 2. Distribution of Covid-19 negative and positive patients according to gender and age ranges.

The comparison of the biochemical parameter results of the COVID 19 negative (control) groups and the COVID 19 positive (patient) groups is shown in Table 1 separately for women and men. When the results obtained from biochemical parameters were investigated whether

Table 1. Evaluation of the biochemical parameter values of the individuals between the control group and the patient study group according to gender.

Test Parameters	Reference Ranges	Control Groups (N=25)	Patient Groups (N= 171)	Significance Level (P)	Control Groups (N=24)	Patient Groups (N= 97)	Significance Level (P)
		Female			Male		
GLU (mg/dL)	70-105	**98.08 ± 9.82**	**131.57 ± 64.99**	**0.002****	101.04 ± 11.40	124.74 ± 60.96	0.127
URE (mg/dL)	15-45	24.52 ± 6.64	27.04 ± 13.22	0.641	26.91 ± 8.69	34.93 ± 18.32	0.109
KREA (mg/dL)	0.5-1.1	0.85 ± 0.23	0.85 ± 0.41	0.510	**0.84 ± 0.14**	**1.09 ± 1.01**	**0.003****
FER (ng/mL)	10-204	91.52 ± 55.25	141.09 ± 241.07	0.354	**92.48 ± 45.08**	**366.62 ± 422.55**	**0.000*****
AST (U/L)	5-34	24.64 ± 8.00	27.40 ± 14.25	0.431	**22.41 ± 6.06**	**36.86 ± 20.90**	**0.004****
ALT (U/L)	0-55	25.68 ± 7.20	24.08 ± 13.25	0.122	**24.58 ± 7.63**	**36.82 ± 28.23**	**0.024***
LDH (U/L)	125-220	**188.72 ± 36.51**	**247.97 ± 86.23**	**0.001*****	**180.40 ± 26.90**	**292.73 ± 159.88**	**0.000*****
Ca (mg/dL**)**	8.4-10.2	8.74 ± 0.45	10.41 ± 22.51	0.899	8.85 ± 0.50	9.17 ± 4.93	0.237
Na (mol/L)	135-145	139.20 ± 3.87	138.96 ± 10.59	0.873	139.91 ± 2.22	138.27 ± 13.74	0.882
K (mol/L)	3.5-5.1	4.19 ± 0.38	4.92 ± 10.32	0.680	4.12 ± 0.39	5.62 ± 14.09	0.837
CK-MB(ng/mL)	0-7.2	0.63 ± 0.56	0.84 ± 0.96	0.375	0.55 ± 0.39	1.26 ± 1.99	0.286
HSTI (pg/mL)	0-33	**0.90 ± 0.95**	**50.67 ± 129.78**	**0.000*****	**0.86 ± 0.90**	**175.37 ± 541.14**	**0.000*****
CK (U/L)	30-200	**51.28 ± 25.07**	**48.22 ± 62.65**	**0.002****	**56.29 ± 21.56**	**83.73 ± 126.56**	**0.001*****
Mg (mg/dL)	1.6-2.6	1.88 ± 0.19	4.45 ± 33.11	0.388	1.89 ± 0.25	1.92 ± 0.28	0.984
CRP (mg/dL)	0-0.5	**0.62 ± 0.70**	**2.49 ± 4.35**	**0.048***	**0.67 ± 0.80**	**4.48 ± 5.53**	**0.001*****

* For the test parameter values with $p<0.05$, the difference between the groups was found to be significant. Calculated considering the Mean ± Standard Deviation.

Table 2. Evaluation of the biochemical parameter values of the individuals in the control group and the patient study group according to gender.

Test Parameters	Reference Ranges	Control Groups		Significance Level (P)	Patient Groups		Significance Level (P)
		Female	Male		Female	Male	
GLU (mg/dL)	70-105	98.08 ± 9.82	101.04 ± 11.40	0.356	131.57 ± 64.99	124.74 ± 60.96	0.529
URE (mg/dL)	15-45	24.52 ± 6.64	26.91 ± 8.69	0.759	27.04 ± 13.22	34.93 ± 18.32	**0.001*** **
KREA (mg/dL)	0.5-1.1	0.85 ± 0.23	0.84 ± 0.14	0.740	0.85 ± 0.41	1.09 ± 1.01	**0.000*** **
FER (ng/mL)	10-204	91.52 ± 55.25	92.48 ± 45.08	0.536	141.09 ± 241.07	366.62 ± 422.55	**0.000*** **
AST (U/L)	5-34	24.64 ± 8.00	22.41 ± 6.06	0.105	27.40 ± 14.25	36.86 ± 20.90	**0.001*** **
ALT (U/L)	0-55	25.68 ± 7.20	24.58 ± 7.63	0.955	24.08 ± 13.25	36.82 ± 28.23	**0.001*** **
LDH (U/L)	125-220	188.72 ± 36.51	180.40 ± 26.90	0.185	247.97 ± 86.23	292.73 ± 159.88	0.054
Ca (mg/dL)	8.4-10.2	8.74 ± 0.45	8.85 ± 0.50	0.364	10.41 ± 22.51	9.17 ± 4.93	0.992
Na (mol/L)	135-145	139.20 ± 3.87	139.91 ± 2.22	0.740	138.96 ± 10.59	138.27 ± 13.74	0.913
K (mol/L)	3.5-5.1	4.19 ± 0.38	4.12 ± 0.39	0.778	4.92 ± 10.32	5.62 ± 14.09	0.974
CK-MB(ng/mL)	0-7.2	0.63 ± 0.56	0.55 ± 0.39	0.814	0.84 ± 0.96	1.26 ± 1.99	0.173
HSTI (pg/mL)	0-33	0.90 ± 0.95	0.86 ± 0.90	1.000	50.67 ± 129.78	175.37 ± 541.14	**0.009*** **
CK (U/L)	30-200	51.28 ± 25.07	56.29 ± 21.56	0.527	48.22 ± 62.65	83.73 ± 126.56	**0.017*** **
Mg (mg/dL)	1.6-2.6	1.88 ± 0.19	1.89 ± 0.25	0.778	4.45 ± 33.11	1.92 ± 0.28	0.514
CRP (mg/dL)	0-0.5	0.62 ± 0.70	0.67 ± 0.80	1.000	2.49 ± 4.35	4.48 ± 5.53	**0.003*** **

* For the test parameter values with $p<0.05$, the difference between the groups was found to be significant. Calculated considering the Mean ± Standard Deviation.

Table 3. Comparison of the biochemical parameters of the individuals in the control and patient groups according to different age ranges

Test Parameters	0-17 age range			18-65 age range			66-79 age range			80-99 age range		
	Control Groups (N=3)	Patient Groups (N= 21)	p	Control Groups (N=40)	Patient Groups (N= 186)	p	Control Groups (N=4)	Patient Groups (N= 38)	p	Control Groups (N=2)	Patient Groups (N= 23)	p
GLU(mg/dL)	94.00 ± 11.13	136.38 ± 83.04	0.932	98.72 ± 9.36	123.74 ± 57.37	**0.000*** **	106.50 ± 19.07	139.86 ± 67.31	0.710	110.00 ± 11.31	147.95 ± 80.94	0.979
URE(mg/dL)	30.66 ± 18.90	27.80 ± 16.92	1.000	23.92 ± 5.36	28.91 ± 15.86	0.141	37.00 ± 4.69	33.52 ± 13.90	0.391	31.00 ± 14.14	36.69 ± 15.12	0.963
KREA(mg/dL)	0.76± 0.12	0.80 ± 0.22	0.983	0.83 ± 0.20	0.94 ± 0.77	0.305	0.87 ± 0.60	1.02 ± 0.73	0.464	1.11 ± 0.02	0.91 ± 0.19	0.162
FER (ng/mL)	40.23 ± 38.22	157.44 ± 257.87	0.721	96.63 ± 48.30	225.22 ± 339.12	**0.001*** **	96.84 ± 68.17	278.23 ± 424.41	0.828	67.05 ± 44.18	170.35 ± 168.86	0.503
AST (U/L)	19.33 ± 10.59	33.00 ± 22.27	0.591	23.22 ± 6.71	31.00 ± 17.67	**0.021***	28.50 ± 9.53	31.10 ± 16.92	0.997	26.50 ± 3.53	27.00 ± 12.20	0.794
ALT (U/L)	17.00 ± 8.71	28.57 ± 24.43	0.841	25.72 ± 6.65	29.34 ± 22.22	0.110	28.75 ± 11.05	27.21 ± 14.64	0.668	18.50 ± 2.12	26.00 ± 14.85	0.599
LDH (U/L)	154.86 ± 18.83	279.28 ± 263.72	0.095	184.55 ± 33.26	261.02 ± 105.33	**0.000*** **	206.50 ± 17.63	277.57 ± 108.95	0.141	187.50 ± 10.60	262.91 ± 82.30	0.210
Ca (mg/dL)	8.60 ± 1.11	8.71 ± 0.46	0.983	8.82 ± 0.42	10.30 ± 21.58	0.501	8.95 0.44	8.55 ± 0.67	0.326	8.30 ± 0.42	8.56 ± 0.50	0.941
Na (mol/L)	139.66 ± 1.52	139.23 ± 4.03	0.983	140.07 ± 2.95	139.10 ± 10.02	0.985	135.25 ±3.50	139.47 ± 5.45	0.326	137.50 ± 2.12	139.65 ± 2.75	0.794
K (mol/L)	4.46 ± 0.41	4.06 ± 0.41	0.467	4.13 ± 0.39	4.86 ± 9.89	0.999	4.30 ± 0.24	4.28 ± 0.45	0.997	3.95 ± 0.07	4.17 ± 0.30	0.414
CK-MB(ng/mL)	0.83 ± 0.75	1.62 ± 3.33	0.932	0.58 ± 0.44	0.79 ± 0.97	0.890	0.35 ± 0.10	1.28 ± 1.30	0.141	0.90 ± 1.27	1.39 ± 1.64	0.747
HSTI (pg/mL)	0.53 ± 0.46	70.15 ± 102.38	0.095	0.89 ± 0.99	103.33 ± 407.73	**0.000*** **	1.05 ± 0.17	87.58 ± 135.08	**0.006** **	1.00 ± 0.98	71.94 ± 108.46	0.124
CK (U/L)	39.33 ± 10.69	49.32 ± 68.78	0.467	55.85 ± 24.67	60.97 ± 87.26	**0.000*** **	45.25 ± 11.67	65.72 ± 124.92	0.219	50.00 ± 24.04	64.90 ± 94.90	0.698
Mg (mg/dL)	2.01 ± 0.25	1.90 ± 0.24	0.591	1.89 ± 0.22	1.93 ± 0.25	0.890	1.80 ± 0.08	13.31 ± 70.25	0.296	1.62 ± 0.26	1.86 ± 0.24	0.414
CRP (mg/dL)	0.30 ± 0.30	2.15 ± 5.62	0.983	0.61 ± 0.71	3.22 ± 4.94	**0.000*** **	1.32 ± 1.22	4.00 ± 5.13	0.710	0.55 ± 0.21	2.79 ± 3.19	0.698

* For the test parameter values with $p<0.05$, the difference between the groups was found to be significant. Calculated considering the Mean ± Standard Deviation.

there was a difference between individuals of the same sex, statistical significance was found between GLU, LDH, HSTI, CK and CRP values in women. In males, statistical significance was found between CREA, FER, AST, ALT, LDH, HSTI, CK and CRP levels**.**

The data of COVID 19 negative women were contrasted with that of COVID 19 negative men; the data of COVID 19 positive women were compared with that of COVID 19 positive men in Table 2. According to the results obtained, it is seen that the gender difference among individuals who are negative for COVID 19 is not statistically significant. However, it has been determined that UREA, CREA, FER, AST, ALT, HSTI, CK, CRP values are higher in patients with COVID 19 positive patients and this increase is statistically significant.

Considering the age distributions between COVID 19 negative and positive groups; Statistical data of biochemical factors determined for the age ranges of 0-17, 18-65, 66-79, 80-99 for both groups are shown in Table 3. Accordingly, for the COVID 19 negative (control) group; it has been determined that K and Mg values are highest in the 0-17 age range, Na and CK values are the highest in the 18-65 age range. Furthermore, it was detected that UREA, FER, AST, ALT, LDH, Ca, CK-MB, HSTI and CRP levels are the highest in the 66-79 age range and, GLU, KREA and CK-MB levels are the highest in 80-99 age range. For the patient group who are positive for COVID 19; AST, LDH and CK-MB in the 0-17 age range; ALT, Ca, K and HSTI in the 18-65 age group; KREA, FER, CK and Mg in the age range of 66-79; GLU, UREA and Na values were found to be the highest in the age range of 80-99 years.

In our study, the biochemical parameters of individuals in different age ranges in the control group and individuals in different age ranges in the patient group were compared (Table 3). According to this; There was no statistically significant difference between the control group and the patient group in the 0-17 age range When the data of the control and patient groups for the 18-65 age range were compared; GLU, FER, AST, LDH, HSTI, CK and CRP values were statistically significant; for the 66-79 age range, only the HSTI value was statistically significant between the control and patient groups. For the 80-99 age range, there was no statistically significant difference between the control and patient groups.

DISCUSSION

In our study, regardless of age, considering gender; It has been determined that UREA, CREA, FER, AST, ALT, HSTI, CK, CRP values are higher in men who are positive for COVID 19 than in women. Similarly, Atici et al. (2022) investigated the changes in hematological and inflammatory parameters according to age and gender in patients with COVID 19 positive at Lokman Hekim University Ankara Hospital (15). When the correlations of these parameters with age were examined, CRP, LDH and FER values displayed a unextreme correlation; when evaluated according to gender, they determined that it was higher in male patients. It is thought that these differences between men and women may be due to the sex hormones that change with age, and therefore the cause of the different severity of COVID 19 in men and women (16).

In present study, it was detected that there was a statistically significant increase in all of the GLU, FER, AST, LDH, HSTI, CK and CRP values in COVID 19 positive patients aged 18-65, regardless of gender. For the patient group between the ages of 66-79, it was found that there was only a statistically significant increase in the HSTI value. Similarly, there are many studies about biochemical parameters. Kar et al. (2022) examined the impacts of COVID 19 on biochemical and hematological parameters in individuals who applied to Eskisehir City Hospital, they found that ALT, AST, CRP, Ferritin, Creatinine, LDH and Troponin levels were high in patients with positive (17). Guneysu et al. (2021) reported that there was a statistically significant difference in terms of CRP, ferritin and LDH values in COVID 19 patients (18). Harbalioglu et al. (2021) found that LDH, CRP, ferritin values were statistically significant in inpatients, but there was no change in GLU, CREA, ALT and AST values (19).

In the study of Balcı et al. (2021), in which they evaluated full blood count and biochemical parameters in the all groups admitted to Mersin University Hospital, it was determined that the CRP value was higher in the patient groups. There is no significant difference in other biochemical parameters (CREA, ALT and AST) (20).

However, as can be seen, while GLU, CREA, AST, and ALT had significantly higher values in some studies, no significant difference was observed in some studies. Unfortunately, the contradictions between the results still persist. In this context, other factors that trigger changes in these parameters should also be taken into account. For example, Sarhan et al. (2021), in their study at Al-Hussein Teaching Hospital (Thi-Qar Province, Iraq) to investigate the interaction between some clinical features (non-smokers, non-diabetic, etc.) and biochemical parameters, they determined several potential biochemical indices and whether certain comorbidities and clinical features affect these markers (21).

In our study, GLU, FER, AST, LDH, HSTI, CK and CRP levels, which are routine biochemistry tests, were found to be high regardless of gender, when age is taken into account. There are studies emphasizing a direct relationship between glycemic control and COVID 19, and the relationship between glucose levels and disease severity (22,23).

Although high ferritin values are observed in

bacterial rather than viral infection, in the context of COVID 19, high ferritin levels may have pointed out violent secondary bacterial infection. Therefore, it is used as a marker for poor prognosis. In addition, it has been shown that higher serum ferritin value is correlated with acute respiratory distress syndrome, mortality, and severe COVID 19 (24).

Abnormalities in liver function tests can be used as a predictor to monitor disease severity. AST is one of them. It has shown that the probability of progression in violent COVID 19 is significantly higher. There are also researches showing that the use of therapeutic antiviral drugs increases the likelihood of liver damage fourfold. (25). Since the primary area affected by SARS-CoV-2 is the lower respiratory tract and LDH is an important indicator of lung damage, it is thought that LDH levels are high in patients with COVID 19 positive.

HSTI and CK are important biomarkers, so an increase in HSTI (in myocardium) and CK (in skeletal muscle, heart muscle and brain) levels indicates that damage may occur in the relevant regions. As one of the mechanisms in the occurrence of myocardial damage, plaques may break off due to the increase in oxygen demand and cause sudden occlusions (26).

Although CRP levels, which are one of the other biochemical parameters, are seen to increase in bacterial infections contrasted to viral infections, many studies have reported that CRP levels are high in COVID 19 patients (27). IFCC guidelines recommended the inclusion of CRP as one of the markers for assessment of infection severity, prognosis, and therapeutic monitoring (28).

CONCLUSION

In conclusion, evaluation of biochemical parameters is one of the cornerstones of laboratory medicine. Because many biomarkers of prognostic importance are expensive, ordinary and pricey-effective biomarkers such as FER, AST, LDH, HSTI, CK and CRP can be used to monitor disease in patients with COVID 19 infection.

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RESEARCH ARTICLE

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Clinical Record Keeping Education Needs in a Medical School and the Quality of Clinical Documentations

ABSTRACT

Objective: In relation to clinic record keeping, we aimed to determine the need in the undergraduate education at our university and propose a program recommendation regarding the content of the training program to be implemented based on the needs analysis.

Methods: Qualitative descriptive research method was used. To determine clinical record keeping education needs, interviews were conducted with 10 faculty members working at the Faculty of Medicine in the 2022-2023 academic year, using a semi-structured form. In addition, a 17-question survey was administered to elicit the needs of the students attending the Faculty of Medicine.

Results: A total of 102 students participated in the study. Eighty-two (80.4%) students reported not having received any education on clinical record keeping. For the questions scored on a seven-point Likert scale, related to "how sufficient do you consider the clinical records you keep?" and "how comfortable do you feel when writing patient notes?", the mean scores were calculated to be 3.89±1.66 and 3.55±1.74, respectively. Ninety-two (90.2%) students considered it necessary to take a course on how to keep clinical records. Ten faculty members participated in the interviews conducted using a semi-structured form. During these interviews, emerging themes concerning the quality of clinical records were the comprehensiveness and usefulness of these records, and the use of appropriate language. When questioning the reasons for deficiencies in clinic record keeping, issues within the education system and, predominantly, a lack of training have come to the forefront. Our main guiding topics that could serve as references for the training programs to be conducted are the format, content, writing, and legal responsibilities arising from the records.

Conclusions: We identified the deficiencies and needs related to clinical record keeping in our faculty. Based on our results, we consider that the implementation of appropriate curricula and activities will increase the quality of clinical records.

Keywords: Medical Documentation, Clinical Records, Needs Analysis, Medical Education.

Bir Tıp Fakültesinde Klinik Kayıt Tutma Eğitimindeki İhtiyacın Belirlenmesi ve Klinik Kayıtların Niteliği Üzerine Bir Çalışma

ÖZET

Amaç: Klinik kayıt tutma ile ilgili olarak üniversitemizde lisans eğitimindeki ihtiyacı belirlemeyi ve ihtiyaç analizi sonucuna göre uygulanacak eğitim programının içeriğinde hangi konuların yer alması gerektiğine dair bir program önerisi sunmayı amaçladık.

Gereç ve Yöntem: Çalışmamız nitel araştırma türünde olup betimsel araştırma yöntemi kullanılmıştır. Klinik kayıt tutma eğitimi ihtiyacını belirlemek için 2022-2023 eğitim öğretim yılında Tıp Fakültesinde görevli 10 öğretim üyesi ile yarı-yapılandırılmış form aracılığıyla görüşmeler gerçekleştirilmiştir. Ayrıca Tıp Fakültesi öğrencilerinin ihtiyaçlarını belirlemek için 17 soruluk anket formu kullanılmıştır.

Bulgular: Çalışmaya 102 öğrenci katıldı. Katılımcıların 82'si (%80,4) klinik kayıt tutma ile ilgili eğitim almadığını belirtti. 7'li Likert tipi ölçekle değerlendirilen "tuttuğunuz kayıtları ne kadar yeterli görüyorsunuz" ve "hasta notu yazarken kendinizi ne kadar rahat hissediyorsunuz" sorularına verilen cevapların puanları ise sırasıyla 3.89±1.66 ve 3.55±1.74 olarak hesaplandı. Öğrencilerin 92 (%90,2)'si klinik kayıt tutmanın nasıl olması gerektiği ile ilgili ders almanın gerekli olduğunu düşünmekteydi. Yarı-yapılandırılmış formla yaptığımız görüşmelere 10 öğretim üyesi katıldı. Görüşmelerde klinik kayıtların niteliği ile ilgili olarak klinik kayıtların kapsamlı olması, kullanışlı olması, uygun dil kullanılması gibi temalar ön plana çıkmıştır. Klinik kayıt tutma açısından eksikliklerin sebepleri sorgulandığında eğitim sistemi sorunları ve yoğunlukla birlikte eğitim eksikliği ön plana çıkmıştır. Yapılacak eğitimler için birer yol gösterici olabilecek başlıklarımız kayıtların formatı, içeriği, yazımı ve kayıtlardan doğan hukuki sorumluluk olarak çalışmamızda öne çıkmıştır.

Sonuç: Fakültemizde klinik kayıtlar konusundaki eksiklik ve ihtiyaçları belirlediğimizi, ilerde buna uygun eğitim öğretim faaliyetlerinin gerçekleştirilmesinin klinik kayıtların niteliğini artıracağını düşünmekteyiz.

Anahtar Kelimeler: Tıbbi Dokümantasyon, Klinik Kayıt, İhtiyaç Analizi, Tıp Eğitimi.

INTRODUCTION

Medical records and clinical documentation can generally be defined as note taking by physicians and other health professionals in relation to the patient's symptoms, history, laboratory and imaging findings, or treatments. Clinical record keeping forms the basis of many activities in healthcare delivery and research (1). High-quality medical records play a critical role in effective and timely communication and coordination between the in-hospital team and healthcare personnel in other institutions, thus laying the foundation for safe and efficient patient care (2). In addition, keeping medical documentation up-to-date and of high quality positively supports clinical and quality audits that aim to improve the delivery of healthcare services and patient outcomes (3). From another perspective, clinical records constitute a legal proof since they provide important evidence in cases related to health presentations that may be encountered (4,5). It is also important to keep accurate clinical records for financial reasons. Comprehensive and timely clinical documentation allows healthcare institutions to code and bill for transactions (6). Finally, in the literature, it has been stated that accurate clinical records support the reasoning and thought processes of physicians during diagnosis, examination, and treatment, and serve as a cognitive assistant (1).

In parallel with the importance of clinical record keeping, the literature indicates that young healthcare workers spend a significant part of their time keeping records (4). In a study conducted in Australia, young workers were reported to allocate 10% of their weekly work to the preparation of epicrises and 13% to the preparation of other documents (7). Similarly, in a study conducted in the USA, it was stated that resident physicians spent 32% of their time on paperwork, and in another study, 67% of resident physicians were reported to spend more than four hours on clinical record keeping (8,9). In addition, in a study conducted with the deans of American and Canadian medical schools, more than 90% of the deans stated that the records kept by students should also be evaluated as part of medical records, since the exclusion of student records from medical clinical records would have a negative impact on the health system (10). In Turkey, these good medical practices are listed under the title "record keeping, reporting, and notification" in the undergraduate core education curriculum, and expected competence levels are specified as "performs [the task] in uncomplicated or common situations/cases" and "performs [the task] in complex situations/cases" (11).

When evaluated from all these aspects, a significant amount of clinical record keeping is undertaken in medical education during both the undergraduate education period and the postgraduate education period, and this affects the health system. Despite the important points emphasized in the literature and educational outcomes targeted throughout Turkey, to the best of our knowledge, there is no study on clinical record keeping in undergraduate medical education in our country. Therefore, in the current study, we aimed to determine the needs of clinical record keeping education in undergraduate programs at our university and present a proposal on subjects to be included in the content of such curricula according to the results of the needs analysis.

MATERIAL AND METHODS

This study was approved by the Ethics Committee of Gazi University (Date: 26.10.2022, Number: E.484093) and designed with a qualitative descriptive research method. Data were collected in compliance with Helsinki Declaration. Purposive sampling was used for sample selection. To determine the clinical record keeping education needs, interviews were conducted with 10 faculty members working at the Faculty of Medicine in the 2022-2023 academic year, using a semi-structured form. In addition, survey created using Google Forms was administered to the students attending undergraduate programs at the Faculty of Medicine to explore their needs related to clinical record keeping.

The survey was designed by three investigators (EE, ÖC, IIB) and comprised a total of 26 questions. The survey was delivered to the six grade-final year students (282 Turkish medical program and 89 English medical program) at of the Faculty of Medicine our university online via social media and e-mail. All students in the medical faculty's final year were targeted for our study. Because they had finished all of their internship training in both theoretical and clinical aspects. Only the students who provided consent were included in the study. The survey contained three questions on demographic characteristics, seven questions on the history of clinical record keeping education, four questions on consultation request/response notes, and three questions on the students' general needs related to clinical record keeping education. Lastly, how comfortable the students felt while keeping clinical records/writing consultation notes and how competent they considered themselves to be in this area were questioned using a seven-point Likert scale (7-very competent/comfortable, 1-very incompetent/uncomfortable).

Experts in medical education were consulted on the extent to which the semi-structured interview form served the purpose of the study and its clarity

and applicability. Interviews were held with faculty members working at the Faculty of Medicine for at least one year. In light of the literature, faculty members were selected from the departments of the faculty where most consultation/examination requests were made (12,13). A voice recorder was used during the interviews, and then the interviews were transcribed. Two team members (EE, ÖC) independently reviewed and coded the faculty members reflections using the open-coding immersion-crystallization method (14). The team then decided on categories of codes within the data and matched the nomenclature for the codes. These categories were then organized into primary themes.

Statistical Analysis: Statistical analysis was performed using SPSS version 22.0 (IBM, Chicago, IL, USA). Descriptive statistics were applied to demographic and questionnaire data. The results were explained as the mean±standard deviation (SD) for continuous variables and percentage for categorical variables. SPSS was used for all statistical analyses.

RESULTS

Student Survey: In this survey study, we reached a total of 105 students, of whom three were excluded because they did not provide consent for participation in the study. The survey was administered to the remaining 102 students, constituting 78 (27.7%) Turkish medical program and 24 (27%) students attending the English medical program of the Faculty of Medicine of Gazi University. Of the students participating in the study, 50 (49%) were male and 52 were female (51%).

Only 20 (19.6%) of the participants stated that they had previously received clinical record keeping education. Of these students, five had taken courses on clinical record keeping for "less than one lesson hour", eight for "one to three lesson hours", and seven for "more than three lesson hours". When these students were asked when they had received this education, one (0.98%) student responded as "second grade", 14 (13.73%) students "fourth grade", and three (2.94%) students "fifth grade". Furthermore, six (5.88%) students reported that they had received clinical record keeping education during their internal medicine internship, two (1.96%) during their pediatrics internship, one (0.98%) during the problem-based teaching session, and three (2.94%) during their internships in different clinical branches, while the remaining two (1.96%) students did not remember it. Table 1 presents the detailed data on where the students learned to keep clinical records. For the questions scored on a seven-point Likert scale, related to how competent the students considered themselves in keeping clinical records and how comfortable they felt while writing patient notes, the mean scores were calculated to be 3.89 ± 1.66 and 3.55 ± 1.74, respectively.

Table 1. Sources specified by students for learning how to write clinical records and consultation notes

Sources	Clinical records		Consultation/examination request notes	
	n	%	n	%
Theoretical lectures at faculty	10	9.80	0	0
Bedside teaching/patient visits at faculty	32	31.37	4	3.92
Training programs/courses outside faculty	0	0	8	7.84
Faculty members/their notes	9	8.82	94	92.16
Assistant physicians/their notes physicians	84	82.35	22	21.57
Peers at faculty	47	46.08	3	2.94
None (did not learn)	1	0.98	0	0.00

Table 1 summarizes the data on how the students learned to write consultation notes. Sixty-seven (65.69%) of the students who participated in the survey stated that they wrote the consultation notes themselves. The mean scores of the seven-point Likert responses to the questions on how competent the students considered themselves in writing consultation/examination request notes and how comfortable they felt while writing these notes were determined to be 4.54 ± 1.37 and 4.43 ± 1.7, respectively. Ninety-two (90.2%) of the students thought that it was necessary to take courses on how to keep clinical records and write consultation/examination request notes. Concerning the question on how these courses should be planned, for which the participants were allowed to choose more than one option, 67 (65.69%) responded as "small group sessions", 46 (45.1%) "bedside lessons", 17 (16.67%) "small group theoretical lessons", and five (4.9%) "lectures and online lessons".

The survey also included an open-ended question to elicit the students' general views on clinical record keeping. Of the 14 participants who responded to this question, 12 had positive and two had negative opinions in relation to receiving education on clinical record keeping. Some of the student responses are given below.

S1: "I think clinical record keeping is very important, especially for internships. I believe that

it would be very beneficial to organize an applied/theoretical lesson on this subject at the end of the fifth term or at the beginning of the internship."
S2: "I think that instructions on record keeping and the points that are considered important can be gathered in a single document as a guideline and distributed to the students."
S3: "I don't feel comfortable examining the patient and keeping records. I think this is because we were not sufficiently involved in clinical settings during our medical education. I think this problem can be resolved by assigning small [student] groups to clinical units from the first years of medical education."
S4: "I don't think [clinical record keeping] education is necessary because we sufficiently engage in processes such as anamnesis and consultation during both the internship and the traineeship. We learn from both our instructors and assistants how these processes are and should be."

Views of Faculty Members: A total of 10 faculty members, four men and six women, from the departments of internal medicine, chest diseases, neurosurgery, emergency medicine, general surgery, gynecology and obstetrics, neurology, cardiology, ophthalmology, and radiology participated in the interviews conducted with a semi-structured form. When the faculty members were asked whether they had received any education on clinical record keeping during their education, only one had received practical education during undergraduate studies, while two had received only practical education and one both theoretical and practical education during residency. Concerning whether clinical record keeping was included in the current curriculum of their faculties, it was determined that the internal diseases department offered a theoretical course and bedside practices, while practical education was offered by the emergency medicine department for senior students and the general surgery department for fourth-year students. However, the faculty members noted that this education was not fully structured or formal. The remaining seven departments did not provide any education on clinical record keeping.

Quality of Clinical Records: The faculty members were asked what they thought was important to achieve high-quality clinical records by taking their own records into account. Table 2 summarizes the data on the related responses. In relation to this subject, the most prominent themes were the records being "useful" and "short and concise". Some participants' views on these themes are given below.

Table 2. Views of faculty members concerning the quality of clinical records

The quality of clinical records	Views
Organized	Should be in a specific format
Short and concise	Should not include any unnecessary details
	Should be of reasonable length
	Should focus on the patient's problem
Comprehensible	Should be clear for someone else that reads it
	Should be written in accordance with the knowledge level of other medical branches
Written in appropriate language	Should be written like an official document
	Medical terminology should be used
Useful	Should be useful for the relevant person
	Should contribute to the clinical process
	Should be written for purpose
Comprehensive	Should include all procedures that have been undertaken
	Should include the patient's consent for the procedures performed

FM2: "I think that my notes serve the purpose. They must provide the basic necessary information, rather than overwhelming [the reader] with superfluous information that is not related to the main disease."
FM5: "I don't keep long notes, but they are definitely enough. I think nobody reads long notes. When I look at my own notes years later, I can easily access the information I want, but it is not unnecessarily detailed or long."

Deficiencies in Clinical Records Kept by Colleagues: The faculty members were also asked about the deficiencies of the clinical records/consultation notes kept by their colleagues in the hospital. Below are some excerpts from their responses.
FM1: "Sometimes the drugs used by the patient are not written down, or there is no information in the file concerning the side effects or toxicity of drugs used by the patient."
FM4: "When we check the clinical follow-up of the residents, there are times we only see 'today was good' in their notes. Today is good! No record of any information on the clinical case."
FM5: "Although grammar doesn't seem very important, the way they [colleagues] write has poor readability. They use strange abbreviations in a way

that no one can understand. This is simply a waste of time."

FM6: "They [notes] are very short and not detailed, and some information is missing. For example, the ultrasound report does not include all details; they prefer to write shorter reports. We love to talk; we communicate more by talking."

As revealed by these views, most faculty members considered the major problem related to clinical records to be the lack of comprehensiveness, which was addressed under a few sub-themes. In addition, other prominent themes that emerged were grammatical deficiencies and disorganized notes (Table 3).

Table 3. Views of faculty members concerning the deficiencies of clinical records kept by colleagues and students

Deficiencies of clinical records	Views
Non-comprehensive	Does not adequately explain clinical findings
	Does not include the patient's medical history
	Does not include drugs taken by the patient
	Does not include information on the side effects or toxicity of drugs taken by the patient
	Not detailed enough
Not short and concise	Full of unnecessary information
Grammar deficiencies	Does not follow spelling rules
	Includes uncommon abbreviations
Disorganized	Does not present information in appropriate order
Incomprehensible	Not written in appropriate clinical language
	Includes uncommon abbreviations
Not useful	Consultation responses do not solve the problem
	Records are kept only out of obligation

Reasons for Deficiencies in Clinical Records: In the analysis of deficiencies in clinical records, five themes emerged: lack of education, problems in the education system, busy schedules, not keeping/inability to keep records timely, and defensive medicine. The prominent themes in this regard were busy schedules, problems in the education system, and lack of education (Table 4). Some of the related comments of the faculty members are given below.

Table 4. Views of faculty members concerning the causes of deficiencies in clinical records

Causes of deficiencies	Views
Lack of education	No training on how to keep clinical records
	No training on how to write consultation notes
Education system problems	Lack of student motivation
	Too many students
	Students wanting to prepare for the medical specialty examination
Busy schedule	Too many patients
	Heavy workload
	Not enough time to take notes
	Short patient examination times
Not taking/inability to take clinical records timely	Urgent tasks shorten note-taking time
	Notes can be collectively entered into the electronic record system at a later time
Defensive medicine	Unnecessary details given to avoid responsibility

FM4: "Even if you know the importance of clinical records, I think the working conditions are not suitable for this. For example, sometimes I can't even write any notes on the clinical course in an emergency situation because I have to urgently request medicine for the patient from the system or someone comes to me for consultation. Unfortunately, in our working system, neither assistants nor attending physicians have any time frame allocated for note-taking."

FM5: "Students do not get involved; some stand behind. Today, the number of students in practice groups is naturally high. It is even difficult for everyone to see the computer screen at once. Moreover, senior students have an additional preoccupation: the medical specialty examination. They think that whatever you try to teach is useless; you can see how they think: 'I could have solved two more test questions instead of being here and listening to you'."

Harms of Poor-Quality Clinical Records: The faculty members were asked what harm poor-quality clinical records could cause. According to their responses, the major problem was that poor-quality clinical records led to a waste of time and could cause medical errors (Table 5). Below are some examples.

Table 5. Views of faculty members concerning the results of poor-quality clinical records

The results of poor-quality clinical records	Views
Waste of time	Same information needs to be obtained repeatedly due to the non-comprehensive nature of notes
	Patient loses time due to repeated procedures
	It is necessary to work overtime to correct notes
Medical errors	Treatment changes are overlooked
	Contraindicated situations can be overlooked
	Missing or incorrect notes cause misdiagnoses
Communication problems	Incomprehensible notes cause disagreement
	Illegible handwriting can result in misunderstanding.
Workload	Examinations are repeated at each healthcare institution
	Patient admissions increase
	Repeated consultations may be needed
Delayed diagnosis	Patient follow-up is delayed
	Information is forgotten if not comprehensive.

FM1: **"**Every time a patient visits, I take his anamnesis again. But I see that he visited many other doctors before, if not me. If proper clinical records were kept, it would not be necessary to question patients' medical history all over again."
FM4: "For example, when there is a patient with bleeding diathesis, we need to be careful, but if proper clinical records are not kept, necessary pre-operative information can be overlooked. Or, as another example, treatment may be changed in the medical order but other records may not be updated accordingly, which causes problems both during intra-departmental transfers and in consultations between branches."

Contribution of Student Notes to Routine Clinical Practice: Concerning whether the clinical records kept by the students could contribute to routine clinical practice, five of the faculty members had positive views and four had negative views, while one participant stated that this could have both positive and negative effects. The sub-themes that emerged from the positive views of the faculty members were as follows: "benefits student learning", "facilitates routine clinical practice", "saves time", "reduces workload", and "reveals overlooked details". Among the sub-themes related to negative views were "difficult to supervise them under the current conditions", "absence of students' legal responsibilities", and "the high probability of errors". Another view was as follows: "Students should receive education and take clinical notes, but we should not take them into account during routine clinical practice."

Education Subjects: The faculty members were asked which subjects should be included in a possible education program on clinical record keeping. Under this heading, the prominent themes were "legal responsibility" and "the content of records" (Table 6).

Table 6. Views of faculty members concerning educational issues

Educational issues	Views
Legal responsibility	Obligation to keep records
	Malpractice concept
	Documents of legal/official nature
Format of records	Order of information presented in records
Content of records	Information to be included in records
	Information to inquire about
	Justification of what has been included in records
	Inclusion of diagnoses and indications of possible diagnoses
Writing style	Grammar
	Comprehensibility

FM1: "They are official documents, so one must be very careful. They have evidential value, but there is no awareness of it."
FM2: "All the test results should be included, but considering that they can also be used as legal documents in the registration system, diagnostic methods and justifications for the treatments applied should also be explained."
FM5: "All kinds of information are listed one after another. These documents should have specific a format, as in an essay with an introduction, a body, and a conclusion. You cannot simply begin a subject in the middle and present information in an illogical order. Education should be given on this subject."

When asked which academic terms such

education should be planned for, three faculty members responded as “residency and preclinical period”, three “residency and clinical period”, two “residency alone”, and two “preclinical period alone”. Five faculty members stated that practical education should be provided in the form of small group lessons. Five participants who considered that education should be offered for assistants stated that this should be in the form of theoretical and practical education integrated into orientation at the beginning of the assistantship.

DISCUSSION

In this study, we aimed to determine the need for clinical record keeping education by reaching the students and faculty members of Gazi University Faculty of Medicine. One of the most striking findings of our study was that both the students and faculty members stated that the medical faculty did not provide adequate education in clinical record keeping.

In this survey study, 80.39% of the students stated that they had not received any clinical record keeping training, and 4.9% had only attended a single class for less than one lesson hour. In the interviews conducted with the faculty members, only three stated that clinical record keeping education was offered by their departments, albeit not fully structured. However, despite all these educational difficulties, every medical school graduate is obliged to keep clinical records and somehow learns to keep records. This leads to the emergence of many incomplete and inaccurate records. In the literature, there are also other studies reporting that clinical record keeping education is lacking. In a study conducted with third- and fourth-year medical students, Lai et al. reported that 30% of the students had not received any formal clinical record keeping education, and 36% had received less than 30 minutes of this education (15). In addition, according to the literature, the post-graduate programs of many departments do not provide sufficient education on clinical record keeping (16,17).

When we inquired about how the students learned to keep clinical records and write consultation notes using a question allowing for the selection of more than one option, 82.35% of the students stated that they had learned how to keep clinical records by observing their assistants and 46.08% by observing their peers at the faculty, and these rates were 92.16% and 21.57%, respectively for writing consultation notes. In the core education program of Turkey, this competence is referred to as “record keeping, reporting, and notification” under the title “good medical practices”. This title contains the following headings: “clarification and obtaining consent”, “preparing epicrisis”, “preparing patient files”, and “preparing prescriptions”. The levels of these headings were expressed as “4”, which represents the highest level and indicates that the student “performs [the task] in complex situations/cases” (11). However, despite the importance attached to clinical record keeping in the core education program, the students in the current study had mean scores of only 3.89 ± 1.66 and 3.55 ± 1.74 for feeling competent and comfortable in keeping clinical records, respectively. These mean scores and the fact that the majority of the students stated that they had learned how to keep clinical records by observing their assistants and peers show that the real situation is far from the educational target.

During the interviews with faculty members, themes such as the quality of clinical records, their comprehensiveness and usefulness, and the use of appropriate language came to the fore. In addition, the participants referred to the lack of comprehensiveness, incomprehensibility, and lack of usefulness as the main deficiencies encountered in this practice. Here, the key deficiency appears to be the notes not being comprehensive or containing incomplete information. These issues have also been addressed in the literature (18). In a previous study, it was reported that 27.4% of the students did not indicate the symptoms objectively, 90.5% did not state the diagnosis, and 98.72% did not include the plan in their notes (4).

When the reasons for the deficiencies in clinical record keeping were questioned, in addition to the lack of education, problems in the education system and busy schedules were prominent. Themes other than the lack of education can be considered national problems in Turkey. When evaluated from this perspective, education is the only area where we can intervene to improve the quality of clinical records. The majority (90.2%) of the students in this study stated that it was necessary for them to take courses on clinical registration and writing consultation and examination request notes. In the literature, as reasons for incomplete clinical records, similar themes and sub-themes have been described, including the overcrowded nature of hospitals, a lack of sense of responsibility in students, the absence of punishment-reward systems, and, most importantly, a lack of education (18). In many studies conducted, training programs were implemented to improve the quality of records. Some of these programs were in specific sub-specialties, such as emergency department and the oncology department (15,19,20), while others focused on the record keeping of medical students in general (21,22). Although these settings had different curricula, content, and practices, they commonly reported an increase in the quality of record keeping as a result of the implementation of such programs (19-22). In the current study, we found that the format, content, and writing style of clinical records and the legal responsibility arising from these records are important subjects that can guide future training programs in this area.

Another finding of our study concerned how

the use of clinical notes taken by students in clinical records would contribute to the process. The faculty members had positive and negative views on this issue, which also seems to be a controversial topic in the literature. In one study, while some people in charge of education argued that the duration of education would decrease due to students being expected to write notes within clinical records, others stated that not allowing such documentation might be a problem in the integration of student participation into patient care (23). In another publication, it was stated that medical students should document their patient records as a part of clinical education, but this could only be achieved through the strict supervision and evaluation of student records (24).

The first limitation of our study concerns its descriptive design. Second, the results we obtained are significant only for our institution and cannot be generalized to the entire medical student population. Third, students' self-evaluation was based on subjective criteria. Quantitative studies on student proficiency can further elucidate this issue. Lastly, the number of faculty members we interviewed was relatively low. Future studies can aim to reach more participants from a larger number of departments.

CONCLUSION

In this study, we aimed to reveal the deficiencies in clinical record keeping in our faculty by eliciting the views of students and faculty members. In the survey conducted with the students, it was determined that the education provided in the faculty was significantly lacking. Similarly, according to the interviews with the faculty members, a lack of education was the leading cause of deficiencies in the quality of clinical records. By further exploring the expected quality of clinical records and current deficiencies, we were able to identify subject areas that require improvement, which will be useful for future researchers planning training programs for clinical record keeping. We consider that the deficiencies and needs we identified concerning clinical record keeping in our faculty will facilitate the implementation of appropriate educational activities in the future, thereby improving the quality of clinical records.

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RESEARCH ARTICLE

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Investigation of Subcarinal Angle and Tracheobronchial Morphology in Patients with COVID 19: A Retrospective Computed Tomography Study

ABSTRACT

Objective: Morphological features of the trachea are very important in choosing the correct endotracheal tube size for intubation. In this study, it was proposed to reveal the effect of SARS-CoV-2 on tracheobronchial morphology and subcarinal angle.

Methods: 56 (26 female, 30 male) COVID-19 and 48 (24 female, 24 male) healthy individuals aged 40 and over were included in the study. The mean age of female patients with COVID-19 was 51.30±12.78 years, while the women in the control group were 45.00±11.89 years. The mean age of male patients with COVID-19 was 48.73±13.99 years, while the mean age of men in the control group was 43.76±8.45 years. The trachea length (TL), proximal, middle and distal levels anteroposterior (AP) and transverse (TR) trachea diameters (TD), subcarinal angle (SA), proximal right main bronchus (RMB) and left main bronchus (LMB) diameters were also measured on computed tomography (CT) images.

Results: The RMB angle was higher in men with COVID-19 than in the control group (p=0.005). TL was lower in women with COVID-19 than in the control group (p=0.030). Proximal AP-TD was higher in men with COVID-19 than in the control group (p=0.006). Proximal TR-TD was lower in men with COVID-19 than in the control group (p=0.029). TL, proximal, middle, and distal levels of AP and TR-TD, SA, RMB, and LMB angles, and proximal RMB and LMB diameters were found to be lower in women with COVID-19 than in men with COVID-19 (p=0.001).

Conclusions: It was deduced that tracheobronchial morphology might change in patients infected with SARS-CoV-2. It is clinically important that this situation should not be overlooked, especially in the indication of endotracheal intubation.

Keywords: Bronchi, COVID 19, CT, Morphology, SARS-CoV-2, Subcarinal Angle, Trachea.

COVID 19'lu Hastalarda Subkarinal Açı ve Trakeobronşiyal Morfolojinin İncelenmesi: Retrospektif Bilgisayarlı Tomografi Çalışması

ÖZET

Amaç: Trakeanın morfolojik özellikleri, entübasyonda doğru endotrakeal tüp boyutunu seçmede oldukça önemlidir. Çalışmada SARS-CoV-2'nin trakeobronşiyal morfolojiye ve subkarinal açıya olan etkisinin ortaya konulması amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya 40 yaş ve üstü 56 (26 kadın, 30 erkek) COVID-19 ve 48 (24 kadın, 24 erkek) sağlıklı birey dahil edilmiştir. COVID-19'lu kadın hastaların yaş ortalaması 51,30±12,78 yıl iken, kontrol grubundaki kadınların yaş ortalaması 45,00±11,89 yıldır. COVID-19'lu erkek hastaların yaş ortalaması 48,73±13,99 yıl iken, kontrol grubundaki erkeklerin yaş ortalaması 43,76±8,45 yıldır. Bilgisayarlı tomografi (BT) görüntüleri üzerinde trakea uzunluğu (TU), proximal, orta ve distal seviyelerde anteroposterior (AP) ve transvers (TR) trakea çapları (TÇ), subkarinal açı (SA), proximalden bronkus prinsipalis dekster (BPD) ve sinister (BPS) çapları ayrıca açıları da ölçülmüştür.

Bulgular: Çalışmaya katılan hasta ve kontrol grupları arasında her iki cinsiyette de yaş farkı istatistiksel olarak anlamlı değildi (kadınlarda p=0,051, erkeklerde p=0,126). BPD açısı COVID-19'lu erkeklerde kontrol grubuna göre daha yüksekti (p=0,005). TU COVID-19'lu kadınlarda kontrol grubuna göre daha düşüktü (p=0,030). Proksimal AP-TÇ COVID-19'lu erkeklerde kontrol grubuna göre daha yüksekti (p=0,006). Proksimal TR-TÇ COVID-19'lu erkeklerde kontrol grubuna göre daha düşüktü (p=0,029). TU, proksimal, orta ve distal seviyelerde AP ve TR-TÇ, SA, BPD ve BPS açıları, proksimalden ölçülen BPD ve BPS çapları COVID-19'lu kadınlarda COVID-19'lu erkeklerden daha düşük bulunmuştur (p=0,001).

Sonuç: SARS-CoV-2 ile enfekte olan hastalarda trakeabronşiyal morfolojinin değişebileceği sonucuna varılmıştır. Özellikle endotrakeal entübasyon endikasyonunda bu durumun gözardı edilmemesi klinik olarak önemlidir.

Anahtar Kelimeler: Bronkus, COVID 19, CT, Morfoloji, SARS-CoV-2, Subkarinal Açı, Trakea.

INTRODUCTION

The trachea is a channel that ensures the connection between the outside world and the parenchyma of the lungs. The trachea, which plays a major role in respiration, has a cartilaginous tubular structure, which is connected to the main bronches below and with the larynx above (1). Recent studies show that tracheobronchial morphology may be associated with chronic diseases (2). Tracheobronchial angles can vary according to age, race, and person, as well as affect the results of angle measurement (3). In a study using computed tomography (CT) in the Asian population, it was reported that the right main bronchus (RMB) angle was 35° and the left main bronchus (LMB) angle was 43° (4). It is known that the tracheal bifurcation angle can expand due to cardiac diseases and mediastinal abnormalities (3,5). It is also affected by the patient's age, gender, body structure, and the size of the chest cavity (6).

COVID-19 droplet infection can be transmitted by direct contact or fecal-oral way and be examined in three different phases, the first 2-14 days of clinical course asymptomatic phase, then the upper and lower airway response lasting for a few days, followed by hypoxia, frosted glass opacities in the lung, acute respiratory distress syndrome (ARDS) (7). SARS-CoV-2 enters the cell with ACE-2 receptors. ACE-2 receptors are expressed in the airway epithelium, especially in the lung, distal airways, glottis and supraglottic space, and trachea (8). In COVID-19, type 2 pneumocytes are activated, diffuse alveolar damage, hyaline membrane formation, and fibrin storage occur (9). Respiratory system uptake is correlated with type 2 pneumocytes uptake. In lung uptake cough, shortness of breath, and fever are typically seen. Radiologically, bilateral peripheral ground-glass areas and consolidation are seen (10). When analyzed histopathologically, interstitial mononuclear infiltrates dominated by lymphocytes and multinucleated and overgrown pneumocytes in intra-alveolar areas can be seen. Pulmonary edema, diffuse alveolar damage, and hyaline membrane formation can be observed (11).

The SARS-CoV-2 target receptor ACE-2 is most commonly found in the lungs, and small intestine and is expressed in endothelial cells and smooth muscle cells of vital organs. Endotheliitis occurs in virus-infected cells (12). Lymphocytic endotheliitis was observed in liver, kidney, heart, and lung examinations of patients who decedent from COVID-19 (13). For this reason, there is not only respiratory system involvement but also the central nervous system, circulatory system, and gastrointestinal system involvement (14). Although the findings related to COVID-19 are generally related to the respiratory system, the cardiovascular features of the disease started to be taken into consideration after a significant part of the patients showed signs of cardiac damage (15). It is a fact that has come up over time that the group most affected by the epidemic and with the highest mortality rate is the elderly with known cardiovascular diseases. Due to cardiac damage, tracheobronchial angles may also be affected. The conducive virus of COVID-19 causes serious consequences because it affects the trachea and tracheobronchial structures by first causing respiratory system involvement devastation.

Computed tomography (CT) is a non-invasive imaging method that is frequently preferred in the anatomical evaluation of the tracheobronchial tree, in determining the location of pathological changes and in monitoring the treatment process (16,17).

In our literature research, there are not enough studies indicating the effect of COVID-19 on the morphology of the subcarinal angle (SA) and other tracheal structures. This study aimed to propound the morphological changes caused by COVID-19 in the SA, trachea, and bronchi.

MATERIAL AND METHODS

Study Design and Patients: Ethics committee approval was obtained from the ethics committee of Malatya Hasan Çalık State Hospital with protocol number 2021/29 in this cross-sectional descriptive study. The study was implemented retrospectively in a total of 104 patients (56 COVID-19 and 48 control groups) aged 40 years and older, who were diagnosed with COVID-19 and had computed tomography (CT) scans taken at the Radiology Department of Malatya Hasan Çalık State Hospital. The measurements were performed in a single center in the relevant institution by an expert radiologist with 12 years of experience in thoracic and neuroradiology.

CT Scanning: Radiological images of patients treated for COVID-19 in our hospital were examined through the PACS system between March 2019 and December 2021. 56 patients diagnosed with COVID-19 who underwent thoracic CT were included in the study. The other group was generated from 48 patients who underwent thoracic CT for different reasons but did not have a history of COVID-19. After age and sex were recorded in both groups, (from three levels: proximal, middle and distal) transverse (TR) and anteroposterior (AP) tracheal diameter (TD), SA, tracheal length (TL), RMB and LMB diameters and angles were measured. Besides, the group with COVID-19 was evaluated in terms of the number of lobes retained in the lung. In both groups, those with lung masses and lung surgery were excluded from the study.

Moreover, those with a diagnosis of Chronic Obstructive Pulmonary Disease (COPD) were excluded from the study, as it may change the measurements in the non-COPD-19 group.

Measurement: SA was measured at the tracheal bifurcation level on coronal reformatted CT images (Fig 1a). The tracheobronchial angle was acquired by measuring the angle on coronal reformatted CT images where a perpendicular line to the RMB axis intersects a perpendicular line to the tracheal lumen (Fig 1b). The same method was used in the LMB (Fig 1c).

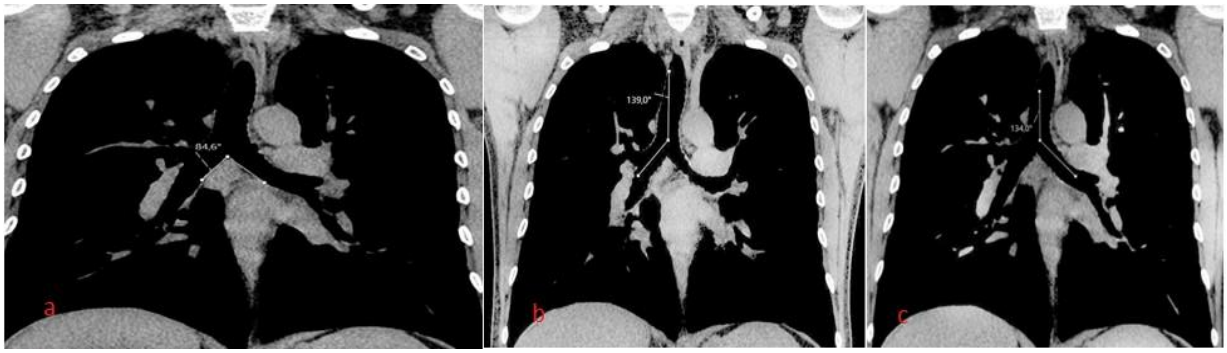

Figure 1. a-Left tracheobronchial angle measurement from CT images in coronal plane (Left main bronchus angle), b- Subcarinal angle measurement from CT images in the coronal plane, c- Right tracheobronchial angle measurement from CT images in coronal plane (Right main bronchus angle).

By examining the TL multiplanar reformat images, the proximal and distal trachea were designated, and measurements were made from the sagittal plane. The proximal trachea was determined as the lower level of the cricoid cartilage, and the distal trachea was specified as the carina level, and the distance was measured (Fig 2).

TD was measured as TR diameter and AP diameter in the axial plane from the proximal, distal, and mid-level (Fig 3a). RMB and LMB diameter measurements were measured in the most distal axial plane (Fig 3b).

Statistical Analysis: For statistical analysis of the data, IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) package program was used. The conformity of the data to the normal distribution was tested with Kolmogorov Smirnov test. Mean and standard deviation were used for numerical data, number and percentage values were used for categorical data, and independent t test and Mann Whitney U test was used for group comparisons. In evaluating the level of significance in the analysis, a p-value equal to and less than 0.05 was considered statistically significant.

Figure 2. Trachea length measurement in sagittal plane by determining proximal and distal trachea from multiplanar reformat images.

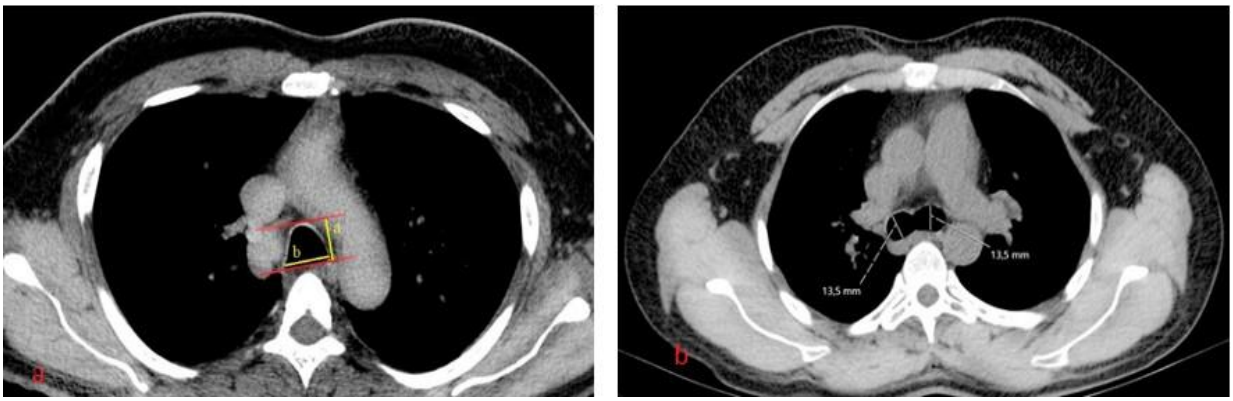

Figure 3. a- Anteroposterior (a) and transverse (b) trachea diameter measurements in the distal trachea from the axial plane CT image, b- Diameter measurements of right main bronchus and left main bronchus from CT image in axial plane.

RESULTS

46.4% were female and 53.6% were male of the 56 COVID-19 patients included in the study. The mean age of women in the COVID-19 group was 51.30±12.78 years, while the mean age of men was 48.73±13.99 years, and the difference was not statistically significant (p=0.478). A statistically significant difference was found between men and women in the diameters of RMB, and LMB, proximal, distal, and intermediate levels of AP and TR-TD, TL in patients with COVID-19 (p<0.05). The results of tracheobronchial morphological measurements acquired from COVID-19 patients are given in Table 1.

Table 1. Distribution of tracheobronchial morphological measurements of COVID-19 patients by gender.

	COVID-19 Groups		
Parameters	**Female**	**Male**	**p**
Age	51.30±12.78	48.73±13.99	0.478
SA	91.92±14.60	87.33±14.08	0.194
RMB angle	139.42±8.06	137.68±6.86	0.132
LMB angle	126.03±7.49	125.89±8.64	0.928
TL	82.09±7.32	93.37±10.17	0.001
Proximal AP-TD	16.19±2.34	21.13±2.90	0.001
Proximal TR-TD	14.18±1.68	17.07±2.26	0.001
Middle AP-TD	14.73±1.98	19.62±2.54	0.001
Middle TR-TD	14.69±1.33	17.48±2.12	0.001
Distal AP-TD	15.28±1.81	18.88±2.65	0.001
Distal TR-TD	16.95±2.66	20.58±2.37	0.001
RMB diameter	12.23±1.49	14.84±1.84	0.001
LMB diameter	11.52±1.41	13.58±1.50	0.001

SA: Subcarinal angle, RMB angle: Right main bronchus angle, LMB angle: Left main bronchus angle, TL:Trachea length, Proximal AP-TD:Proximal anteroposterior trachea diameter, Proximal TR-TD:Proximal tranverse trachea diameter, Middle AP-TD: Middle anteroposterior trachea diameter, Middle TR-TD: Middle tranverse trachea diameter, Distal AP-TD:Distal anteroposterior trachea diameter, Distal TR-TD: Distal tranverse trachea diameter, RMB diameter: Right main bronchus diameter, LMB diameter: Left main bronchus diameter.

The mean age of female patients with COVID-19 was 51.30±12.78 years, while the women in the control group were 45.00±11.89 years, and there was no statistically significant difference between them (p=0.051). The mean age of male patients with COVID-19 was 48.73±13.99 years, while the mean age of men in the control group was 43.76±8.45 years, and the difference was not statistically significant (p=0.126). TL was statistically lower in female patients with COVID-19 according to females in the control group (p<0.05). It was determined that the RMB angle and the TR-TD measured from the proximal level were statistically significantly lower in men with COVID-19 than in the control group (p<0.05). AP-TD measured from the proximal in male patients with COVID-19 was found to be significantly higher than those in the control group (p<0.05) (Table 2).

Table 2. Comparison of tracheabronchial morphometric measurements of COVID19 and control groups by gender

Parameters	***Female***			***Male***		
	COVID 19 Group	**Control Group**	**p**	**COVID 19 Group**	**Control Group**	**p**
Age	51.30±12.78	45.00±11.89	0.051	48.73±13.99	43.76±8.45	0.126
SA	91.92±14.60	88.20±9.57	0.509	87.33±14.08	85.18±12.76	0.754
RMB angle	139.42±8.06	142.48±6.33	0.238	137.68±6.86	142.24±5.10	0.005
LMB angle	126.03±7.49	128.28±7.19	0.455	125.89±8.64	127.48±5.22	0.520
TL	82.09±7.32	87.12±8.67	0.030	93.37±10.17	95.95±12.68	0.407
Proximal AP-TD	16.19±2.34	15.34±1.87	0.159	21.13±2.90	19.06±2.39	0.006
Proximal TR-TD	14.18±1.68	14.02±1.51	.0924	17.07±2.26	18.05.1.68	0.029
Middle AP-TD	14.73±1.98	14.54±2.08	0.740	19.62±2.54	18.81±2.98	0.286
Middle TR-TD	14.69±1.33	15.40±1.50	0.95	17.48. ±2.12	22.18±26.37	0.866
Distal AP-TD	15.28±1.81	14.82±1.54	0.289	18.88±2.65	17.83±1.92	0.168
Distal TR-TD	16.95±2.66	16.96±2.17	0.988	20.58±2.37	20.11±2.48	0.477
RMB diameter	12.23±1.49	12.90±1.39	0.061	14.84±1.84	15.08±1.95	0.594
LMB diameter	11.52±1.41	11.69±1.22	0.713	13.58±1.50	13.91±1.76	0.493

SA: Subcarinal angle, RMB angle: Right main bronchus angle, LMB angle: Left main bronchus angle, TL:Trachea length, Proximal AP-TD:Proximal anteroposterior trachea diameter, Proximal TR-TD:Proximal tranverse trachea diameter, Middle AP-TD: Middle anteroposterior trachea diameter, Middle TR-TD: Middle tranverse trachea diameter, Distal AP-TD:Distal anteroposterior trachea diameter, Distal TR-TD: Distal tranverse trachea diameter, RMB diameter: Right main bronchus diameter, LMB diameter: Left main bronchus diameter.

When we look at the lung lobe involvements in patients with COVID-19, it was observed that the upper lobe of the right lung 65.4%, middle lobe of the right lung 92.3%, lower lobe of the right lung 100% and lower lobe of the left lung 100% in women. In the case of men, upper lobe of the right lung 76.7%, middle lobe of the right lung 86.7%, lower lobe of the right lung 96.7%, and upper lobe of the left lung 80%, lower lobe of the left lung 100%.

DISCUSSION

The effect of COVID-19 pneumonia caused by the SARS-CoV-2 virus, which was declared a pandemic by the (World Health Organization) WHO, is now better known on the lung parenchyma and vascular structures (18). It is seen that conditions such as diffuse alveolar damage and related acute respiratory distress syndrome, ventilation/perfusion mismatch, thrombosis formation, and consequently raised risk of pulmonary embolism lend to existing hypoxia in patients. In patients with a high degree of hypoxia, it is frequently ventilated mechanically by endotracheal intubation. Here in, the decision is made by considering gas exchange and hemodynamic parameters. In these patients, surgical interventions such as endotracheal intubation and tracheostomy cause an increased risk of complications in the trachea and main bronchi. For this reason, respiratory tract morphology and morphometry are important in COVID-19 patients (19).

It was determined that TL was statistically higher in men with COVID-19 than in women in our study. In the study of Kamel et al., it was observed that the TL was 105.1 mm in men and 98.3 mm in women, and the difference was statistically significant (20). In the study conducted by Mi et al., on the Chinese population, the TL was found to be 107.8±13.2 mm in men and 101.4±12.8 mm in women, and the difference was statistically significant (4). It was reported in another study, that it was 116.21 mm in men and 105.67 mm in women (21). The findings of our study support the literature. However, although there is no data to state that the Sars-CoV-2 virus causes the difference, we can only say that it is due to the gender difference. In our study, while there was no difference in TL in men with COVID-19 according to the healthy group, it was found that it was lower in women with COVID-19 than in the healthy group. With ciliary activity in respiration, the particles descending into the lower respiratory tract are cleared from the trachea and bronchi through the epithelium. Within this process, some of the immunological reactions and some inhaled particles can cause inflammation (22). If there is a discomposed immune system, immune cells are piled in the lung and a large amount of pro-inflammatory substance cytokine is released (23). Cytokines normally regulate immunity, inflammation, and hematopoiesis. But, in some patients, excessive cytokine secretion can lead to a cytokine storm and lead to capillary leakage, tissue damage, thrombus formation, and even organ failure (24). The uncontrolled and increased cytokine release caused by COVID-19 is called a cytokine storm (23). As a result of cytokine storm and damage directly caused by the virus, widespread alveolar damage, hyaline membrane formation, and pulmonary edema take place (25), and multi-organ damage occurs. Because of the chronic inflammation that occurs, the tracheal cartilages can change and the patient becomes more prone to tracheomalacia (26). This may explain the TL change in the COVID-19 group.

In the current study, proximal AP-TD was found to be higher in men with COVID-19 compared to the control group. In a study, it was procured that the AP-TD length was 22.3 mm in patients with COPD and 19.4 mm in the control group, and the difference was statistically significant (2). In a study committed on patients with COVID-19, patients were divided into four groups upon lung involvement, and they found that the mean AP-TR diameter at the thyroid level was statistically higher in the fourth group, where the disease was most severe, compared to other groups. They indicated that severe inflammation may cause edema in the trachea, and as a result, this would set forward an increase in tracheal diameter (27). The findings of our study were found to be compatible with the literature. Taking into account the involvement of both lungs in our patient group, it is obvious that especially the upper lobes are more involved in men than in women, but we consider that the inflammation may cause edema in the trachea and lead to an increase in the AP-TD measured at the level of the thyroid gland.

It was defined in our study, that the proximal, middle and distal TR-TD was statistically significantly longer in men with COVID-19 than in women. In another study, it was established that there was no statistical difference in TR-TD between COPD patients and the control group (2). Similar to this study, it was determined in our study that TR-TD measured in the middle and distal segments was not different between the COVID-19 and control groups in both genders. However, it was determined that there was a reduction in the proximal TR-TD measured at the thyroid level in men with COVID-19 according to the control group. In a study, it was shown that this diameter increased in patients with COVID-19, who were divided into four groups, in contrast to our results, especially in the severe group compared to other groups (27). In a study (28), hard and inflammatory tissues in the paratracheal region were notified as well as areas containing coagulation necrosis during airway reconstruction to correct tracheal stenosis caused by COVID-19. These findings support the inflammation and edema process in the trachea. Edema and inflammation in the trachea engender an increase in the diameter of the trachea and narrowing of the tracheal lumen, that is, stenosis may also occur (27). We believe that cartilage tissue inflammation that may develop due to the symptoms of the disease in severe and long-term multisystemic infections such as COVID-19 may cause changes in tracheal diameters.

The SA was found to be lower in women than in men in a study executed on patients who applied to the hospital with various complaints and had thoracic CT scans (6). Kamel et al., determined that SA did not differ between men and women in their study of adult healthy individuals (20). In another study that was conducted on COPD patients, it was observed that there was no difference in intrabronchial angle measurement compared to the control group (2). Similar to previous studies, in the present study, no difference was found in the measurement of SA in both genders, both between male and female patients with COVID-19 and between the patient and control groups. Consequently, SA has an extensive range in normal individuals, and essential measurements of SA have little diagnostic value. At the same time, the patient's gender, body habits, and left atrium dimensions are also affected by the position of the carina (6).

In a study committed to patients with COPD, no significant difference was found between the right and left tracheobronchial angle values when evaluated according to the control group (2). In the current study, there was no difference between the COVID-19 and control group in terms of LMB, but it was found that the RMB angle was lower in men with COVID-19 compared to the control group. Studies have shown that edema and inflammation caused by COVID-19 in the tracheobronchial lumen can cause narrowing of the lumen and changes in diameter (27).

CONCLUSION

COVID-19 is a multisystem disease that can affect all systems in the body. Conceiving that it is transmitted through the respiratory tract, it is also very important to exhibit the situations in which the respiratory system organs are affected. Changes in tracheal morphology caused by COVID-19 were revealed in our study. It is significant for clinicians to consider these changes, especially in patients with endotracheal intubation indication, in the follow-up of patients with COVID-19 in clinics or intensive care units. The most important limitation of our study is that we cannot follow up whether our findings have changed or not, since the patients did not have long-term follow-up tomography. Comprehensive studies with larger series on the subject are needed.

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CASE REPORT

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A Rare Cause of Unexplained Left Flank Pain: Nutcracker Syndrome

ABSTRACT

Nutcracker syndrome refers to the compression of the left renal vein, usually between the aorta and the superior mesenteric artery. Flank pain is the most common complaint and hematuria can be seen among the laboratory findings. This syndrome, which is more common in women with low body mass index, can be difficult to diagnose.

A 41-year-old female patient with persistent left flank pain was admitted to our family medicine outpatient clinic. Despite many polyclinic applications, there was no finding that could explain the pain in the patient, who did not have any features in her history. Computed tomography requested in our family medicine outpatient clinic revealed that the left renal vein was compressed between the aorta and the superior mesenteric artery, and the patient was diagnosed with nutcracker syndrome.

Nutcracker syndrome is difficult to diagnose and is a diagnosis of exclusion to be considered in patients presenting with atypical left flank pain. A wide variety of methods are used in the treatment, from conservative treatment to the endovascular stent and surgical treatment, depending on the severity of the symptoms.

Keywords: Nutcracker Syndrome, Pain, Family Medicine

Sol Yan ağrısının Açıklanamayan Nadir Bir Sebebi: Nutcracker Sendromu

ÖZET

Nutcracker sendromu, genellikle aort ve superior mezenterik arter arasında, sol renal venin sıkışmasını ifade eder. Yan ağrısı en sık yakınmadır ve laboratuvar bulguları arasında hematüri görülebilir. Vücut kitle indeksi düşük olan kadınlarda daha sık görülen bu sendromun teşhisi zor olabilir.

41 yaşında kadın hasta kalıcı sol yan ağrısı şikâyeti ile aile hekimliği polikliniğimize başvurdu. Özgeçmişinde herhangi bir özellik bulunmayan hastada birçok poliklinik başvurusuna rağmen ağrıyı açıklayacak bir tanı konulamadı. Aile hekimliği polikliniğimizde istenen bilgisayarlı tomografide sol renal venin aorta ile süperior mezenterik arter arasında sıkıştığı saptandı ve hastaya Nutcracker sendromu tanısı konuldu.

Nutcracker sendromunun tanısı zordur ve atipik sol yan ağrısı ile başvuran hastalarda düşünülmesi gereken bir ekartasyon tanısıdır. Tedavide semptomların şiddetine göre konservatif tedaviden endovasküler stent ve cerrahi tedaviye kadar çok çeşitli yöntemler uygulanmaktadır.

Anahtar Kelimeler: Nutcracker Sendromu, Ağrı, Aile Hekimliği

INTRODUCTION

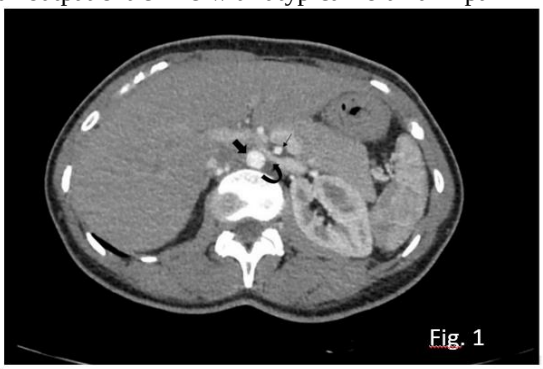
The nutcracker phenomenon (NF) was first described in 1950 as compression of the left renal vein (1). The left renal vein usually passes between the aorta and the superior mesenteric artery and joins the Vena Cava Inferior (VCI). During this transition, the left renal vein can become compressed between the aorta and the superior mesenteric artery (SMA), and this is called NF. More rarely, the renal vein has a retro-aortic or circumaortic course and is compressed between the aorta and the vertebral body (2). Distal dilatation and venous HT occur as a result of renal vein compression. The combination of NF with clinical complaints was defined as Nutcracker Syndrome (NS). While NS can progress asymptomatically, it also produces severe and persistent symptoms (3). Flank pain is the most common complaint and the most common finding is microscopic hematuria. The prevalence of NS has not been revealed yet, but it is known that it is slightly more common in women. Most symptomatic patients are female patients in their second or third decades with a low body mass index. NS, of which diagnostic and therapeutic criteria have not yet been sufficiently defined, is a disease that is usually diagnosed late and with difficulty (4).

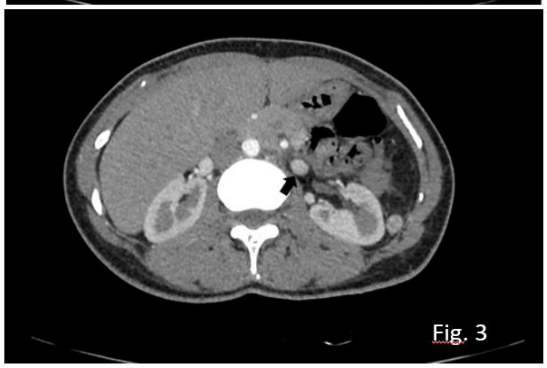
In this case, we aimed to present our patient who presented with complaints of long-term flank pain and chest pain in the lower left side, which are common complaints in our family medicine units.

CASE REPORT

A 41-year-old female patient was admitted to our outpatient clinic with atypical left flank pain that had been present for a long time but had been exacerbated recently. The patient had a body mass index of 17.4 and did not have any chronic disease. The pain, which did not change with breathing and had no difference between day and night, was exacerbated by physical activity and radiated to the left leg. There were multiple emergency service and polyclinic applications with this pain complaint, which did not impair his daily functionality, but significantly reduced his quality of life. There was no finding that could explain the pain in the patient who applied to cardiology, neurosurgery, chest diseases, physical therapy and rehabilitation, psychiatry outpatient clinics. The patient, who regularly used Selectra 50 mg and NSAIDs, applied to our family medicine outpatient clinic because his complaints continued and increased recently. There were no pathologic findings in laboratory parameters. Contrast-enhanced thorax computed tomography (CT) and abdominal ultrasonography were requested by us.

The obtained CT noted significant compression of the left renal vein as it passes between the aorta and the SMA. (Fig. 1) In the angle measurement, the aortomesenteric angle was found to be 24.1 degrees. (Fig. 2) A significant enlargement of the ovarian vein was observed secondary to this compression. (Fig. 3) In the ultrasonography performed later, the left renal vein was again shown to be compressed between the aorta and the SMA. The left ovarian vein was measured at 8 mm. When all imaging findings were combined with clinical data, the patient was diagnosed with NS.





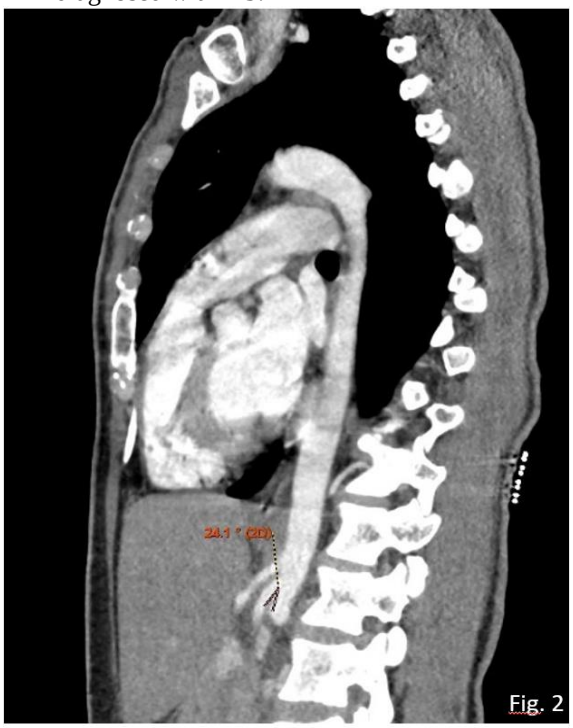


Fig 1. Compression of the left renal vein (↷) as it passes between the aorta (➡) and the SMA (➞) **Fig2.** Aortomesenteric angle; 24.1 degrees **Fig 3.** Enlargement ovarian vein (➡).

DISCUSSION

Patient-centered clinical management is one of the main features that make family medicine a discipline. According to the principle of a comprehensive approach, which is one of the basic competencies of Family Medicine, it should include systematic evaluation in detail and have a holistic perspective. As in our case, the patient's advocacy and ability to make the necessary coordination in solving medical problems is an important part of the Family Medicine discipline.

The nutcracker phenomenon, also known as left renal vein impingement syndrome, was first reported in 1950, and De Schepper, a Belgian radiologist, named it nutcracker syndrome for the first time in 1972. Although NF and NS are often used interchangeably, NS refers to the disease with typical signs and symptoms. There are two main types of NS. In anterior NS, which is the more common type, the left renal vein is compressed between the aorta and the SMA, and the Retro aortic or circumaortic renal vein compression between the aorta and the vertebral body is called posterior NS. It's much rarer causes include pancreatic neoplasms, para-aortic lymphadenopathy, retroperitoneal masses, abdominal aortic aneurysm, and lumbar lordosis. Although the exact prevalence is not known, it is more common in young women with asthenic structures (5).

NS can be asymptomatic or cause severe and permanent complaints. The most common complaints are atypical left flank and lower rib pains that increase with physical activity. These pains, which sometimes radiate to the left posteromedial thigh and hip, are also exacerbated by standing and increasing lumbar lordosis. Hematuria is the most common finding and microscopic hematuria is frequently seen. This is explained by the increase in venous pressure secondary to the distal stasis with the compression of the renal vein and rupture of the capillary veins into the collecting system. Rarely, macroscopic hematuria may also be seen, which may require a blood transfusion (6). In approximately half of the cases, pelvic congestion syndrome and varicocele occur, respectively, due to enlargement of the ovarian vein or testicular vein draining into the left renal vein.

NS should be considered in the presence of atypical left flank pain and hematuria, which is a diagnosis of exclusion and the cause of which cannot be found (7). Diagnosis should be confirmed by ultrasonography, computed tomography, or magnetic resonance imaging. Imaging findings include a left renal vein diameter with a hilar/aortomesenteric ratio ≥4.9, the 'beak sign' defined as severe narrowing of the SRV in the aortomesenteric segment, and the angle between the aorta and SMA <41°. When all these findings are detected, the sensitivity increases considerably (8).

In the treatment, depending on the severity of the symptoms, a wide range of methods are applied, from conservative treatment to endovascular stenting and surgical treatment (9). Since most of the patients under the age of 18 have spontaneous regression, only conservative treatment is chosen. While symptomatic treatment is preferred in mild microscopic hematuria, surgical treatment should be considered in cases that do not respond adequately to the treatment for 24 months, and who develop severe pain and renal failure (10,11).

CONCLUSION

NS is an important cause of morbidity that should be considered in patients presenting with atypical left flank pain, which is difficult to diagnose and is diagnosed by evaluating clinical suspicion and imaging findings together. This clinical picture, which has many treatment options from symptomatic treatment to surgical methods, should be considered in the differential diagnosis.

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