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ORIGINAL ARTICLE

Investigation of the Relationship Between Upper Middle Arm Circumference Measurement and the Gomez, Waterlow and World Health Organization Classifications Used in the Diagnosis of Malnutrition in Turkish Children Aged 1-5

Üst Orta Kol Çevresi Ölçümünün 1-5 Yaş Arası Türk Çocuklarda Malnütrisyon Tanısında Kullanılan Gomez, Waterlow ve Dünya Sağlık Örgütü Sınıflandırmaları ile Bağlantısının Araştırılması

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ABSTRACT

Aim: Waterlow, Gomez, and WHO Classification are used all over the world as reliable methods in the evaluation of malnutrition in children's age group. In our study, the purpose was to evaluate the usability of Upper Middle Arm Circumference measurement in malnutrition diagnosis between the ages of 1-5 in the children of our country by investigating the relation with the other three methods.
Material and Methods: A total of 1500 children, who were between the ages of 1 and 5, and admitted to the clinics of Selçuk University, Faculty of Medicine, Department of Child Health and Diseases were included in the study. Anthropometric measurements that consisted of height, weight, and Upper Middle Arm Circumference were made for all children who participated in the study.
Results: Among the 1.500 children, who were included in the study, a total of 704 were girls (46.93%), and 796 (53.07%) were boys. Upper Middle Arm Circumference measurement values were similar in girls and in boys. It has been determined in our study that Upper Middle Arm Circumference has better compatibility with Gomez classification in respect of sensitivity and specificity. When the cut-off point value of the compatibility of Upper Middle Arm Circumference with other malnutrition classifications was accepted as 11.5 cm in respect of sensitivity, specificity, positive predictive values, and negative predictive values in severe diagnosis of malnutrition, it was seen that it produced better results than 11.0 cm.
Conclusion: Early recognition of an important public health problem such as malnutrition is very important for taking precautions and identifying treatment modalities. Although the Upper Middle Arm Circumference cut-off point differs among countries and regions for the diagnosis of severe malnutrition, our study showed that it would be appropriate to prefer 11.5 cm for our country.

Keywords: Children, Malnutrition, Mid-upper arm circumference, Malnutrition classification

ÖZ

Amaç: Çocuk yaş grubunda malnütrisyonun değerlendirilmesinde tüm dünyada güvenilir yöntemler olarak Waterlow, Gomez ve WHO Sınıflandırması kullanılmaktadır. Çalışmamızda ülkemizdeki çocuklarda 1-5 yaş arası malnütrisyon tanısında Üst Orta Kol Çevresi ölçümünün diğer üç yöntemle ilişkisi araştırılarak kullanılabilirliğinin değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntemler: Çalışmaya Selçuk Üniversitesi Tıp Fakültesi Çocuk Sağlığı ve Hastalıkları Anabilim Dalı polikliniğine başvuran 1-5 yaş arası toplam 1500 çocuk dahil edildi. Çalışmaya katılan tüm çocukların boy, kilo ve Üst Orta Kol Çevresi ölçümünden oluşan antropometrik ölçümler yapıldı.
Bulgular: Araştırmaya dahil edilen 1500 çocuğun 704'ü (%46,93) kız, 796'sı (%53,07) erkekti. Üst Orta Kol Çevresi ölçüm değerleri kızlarda ve erkeklerde benzerdi. Çalışmamızda duyarlılık ve özgüllük açısından Üst Orta Kol Çevresi ölçümünün Gomez sınıflamasına daha iyi uyum gösterdiği saptanmıştır. Ciddi malnütrisyon tanısında Üst Orta Kol Çevresi ölçümünün diğer malnütrisyon sınıflamaları ile uyumluluğunun duyarlılık, özgüllük, pozitif prediktif değerler ve negatif prediktif değerler açısından 11,5 cm olarak kesme noktası değeri kabul edildiğinde, 11,0 cm'den daha iyi sonuçlar verdiği görülmüştür.
Sonuç: Malnütrisyon gibi önemli bir halk sağlığı sorununun erken tanınması, önlem alınması ve tedavi yöntemlerinin belirlenmesi açısından oldukça önemlidir. Ağır malnütrisyon tanısı için Üst Orta Kol Çevresi kesme noktası ülkeler ve bölgeler arasında farklılık gösterse de çalışmamız ülkemiz için 11,5 cm'nin tercih edilmesinin uygun olacağını göstermiştir.

Anahtar Kelimeler: Çocuklar, Malnütrisyon, Orta-üst kol çevresi; Malnütrisyon sınıflandırması

Introduction

Malnutrition is a complex pathological condition with structural deficiencies in tissues and dysfunctions in organs occurring as a result of insufficient, unbalanced or excessive intake of macro and micronutrients, which are necessary for the continuity of the functions of the body tissues and organs. World Health Organization (WHO) defines malnutrition as an imbalance in the intake of nutrients and energy, which are required by an individual to grow, survive, and perform some special functions (1). Nutrition problems are often found in preschool and school-age children of mothers who work in cities and rural areas because of the inability

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to eat regularly, eat well, and have good care and follow-up. The most frequently affected age group is the children who are between the ages of 6 months and 5 years. Early diagnosis, proper treatment, and careful follow-up are important elements in preventing and treating malnutrition (2).

The prevalence of malnutrition varies according to different societies that live in different parts of the world. Many factors, such as local and private beliefs, traditions, economic status, social characteristics, breastfeeding habits, and the age of breastfeeding affect the social prevalence and clinical characteristics. It is more prevalent especially in children from broken families that have low socioeconomic status, and cannot benefit from education and health services. Malnutrition is frequent in rural areas of developing countries because an important part of the society is poor and feed heavily on grain. According to the data released by the WHO, the rate of children that have malnutrition in developing countries decreased from 29% to 18% between 1990 and 2010, and the related mortality rate under the age of 5 decreased at a rate of 35%. Among the approximately 500 million children who are under the age of 5 on a worldly scale, nearly 100 million have malnutrition, and the number of children with severe and acute malnutrition is predictive to be around 20 million (3).

Waterlow, Gomez, and WHO Classification are used all over the world as reliable methods in the evaluation of malnutrition in children's age group. However, trained medical personnel is required for all these three methods to be used successfully. It is recommended in various publications that Upper Middle Arm Circumference (UMAC) measurement should be used as a simple and practical alternative method in the evaluation of malnutrition (4,5). Although UMAC increases at significant levels in the first year of life, it is like an absolute value between the ages of 1 and 5 in children, and changes very little. It was argued that arm circumference was a good marker in the evaluation of the nutritional status in children (6).

According to UMAC measurement, different values are accepted as limits for severe malnutrition in the evaluation of malnutrition in different countries. In our study, the purpose was to evaluate the usability of UMAC measurement in malnutrition diagnosis between the ages of 1-5 in the children of our country by investigating the relation with the other three methods.

Material and Methods

A total of 1500 children, who were between the ages of 1 and 5 (12-60 months), and admitted to the clinics of Selçuk University, Faculty of Medicine, Department of Child Health and Diseases between June 1, 2014 and September 30, 2014, were included in the study.

Anthropometric measurements that consisted of height, weight and UMAC were made for all children who participated in the study. All anthropometric measurements were made by the same person (an experienced pediatric health and diseases junior doctor) by using the same measurement tools. Stature measurement was made without shoes with a wall-mounted 0.1 cm-sensitive stadiometer (Holtain Limited, Crymych, Dyfed, Made in Britain) for children who could stand upright. The height measurements of the children who could not stand upright were made with a special height measuring tape with a measuring band on its edge and a moving part applied to the child's feet. Body weight measurements were made with 100-gram precision scales (Oncomed Electronic body scale SC-105 and Charder model MS3500, made in China) with thin clothes on children who could stand upright, and the measurements of the children who could not stand upright were made in lying position. UMAC was measured with a non-flexible but curling measurement tape by taking the left arm to 90 degrees of flection from the elbow. The arm was placed in neutral position after the exact midpoint of the distance between the acromion and olecranon protrusions was marked, and the arm circumference was measured from this point with the measuring tape. The weight-for-age (WFA), height-for-age (HFA) and weight for height (WFH) percentages were calculated by using the body weight and stature reference values in Turkish Children reported in the study conducted by Neyzi et al. in the Journal of Child Health and Diseases in 2008 (7). The Z-scores for height and weight (SS score) were determined by using the SS data for height and weight based on the study conducted by Neyzi et al (7).

Malnutrition degrees were determined according to Gomez, Waterlow, and WHO Classifications. The YGA percentage in Gomez class was calculated with the following formula: (Child's Weight/50th percentile value of the same age and gender) X 100; and between 110 and 90 percent were evaluated as normal, 89 to 75 percent moderate (1st degree), 74 to 60 percent moderate (2nd degree), and below 60 percent as severe (3rd degree) malnutrition.

The YGB Percentage in Waterlow classification was calculated with the following formula: (Child's Height/50th percentile value in the same age and gender) X 100; and 95 percent and above was evaluated as normal, between 94 and 90 percent moderate, 89 percent and 85 moderate, and 85 percent and below as severe malnutrition.

The BGA percentage, which is the other parameter of Waterlow Classification, was calculated with the following formula: (Child's Weight/The Weight of the Child corresponding to the 50th Percentile Value) X 100; and 90-110 percent were considered to be normal, 89-80 percent were considered mild, 79 to 70 percent moderate, 70 percent and below severe malnutrition. Weight and Height Z-scores (SSS) were calculated as WHO Classification. SSR scores were defined as normal if between -2 and +2, moderate if between -2 and -3, and -3 and below were defined as severe malnutrition.

The limit of 12.5 cm was taken as the limit value for the diagnosis of malnutrition in the evaluation of UMAC.

Since two values were reported in the literature for severe malnutrition diagnosis, the limit values of 11.5 cm and 11.0 cm were used (8-10). In our study, in terms of malnutrition diagnosis of children, UMAC cut-off values were determined separately with ROC analysis for Gomez (WFA), Waterlow (HFA, WFH), and WHO Classifications.

The specificity, sensitivity, positive and negative predictive values were determined for Gomez (WFA), Waterlow (HFA, WFH), and WHO Classifications of UMAC measurement for malnutrition diagnosis. Linear Regression Analyses were made to examine the relations between UMAC and the other three classifications.

Statistical Analysis

The SPSS 20.0 Package Program was used in statistical analyses. Frequency and percentage distributions of the data were determined. As a result of the normality test, the Mann Whitney U-Test was used for the variables that were not normally distributed in binary groups when the differences between the groups were examined. The Kruskal Wallis H-Test with Bonferroni Correction was used in more than two groups for the variables that were not normally distributed. The inter-variable relations were investigated with the Chi-Square Test. P<0.05 was taken as the level of significance.

Results

Among the 1.500 children, who were included in the study, a total of 704 were girls (46.93%), and 796 (53.07%) were boys. The mean age was 35.28±14.82 months in girls (median 36 months; age range 12-60 months), and the mean age was 34.77±14.72 months in boys (median 35 months; age range 12-60 months). UMAC measurement values were similar in girls (mean 15.18±1.97 cm, median value 15 cm, range 10-24 cm) and in boys (mean 15.26±1.8 cm, median 15.3 cm, range 10.4-21.1 cm) (p:0.328). However, the mean values of both genders in 48-60-month age group were higher compared to in other age groups (p:0.001). The distribution of upper middle arm circumference measurements according to age groups is shown in Table 1.

In the evaluation that was made by using the Gomez (WFA) Malnutrition Classification it was found that 623 out of 1.500 children had normal (41.53%), 438 (29.20%) mild, 147 (9.8%) moderate, and 34 (2.27%) had severe malnutrition. The WFA values were above the normal values in 258 children (17.20%). In Gomez Classification, it was seen that the frequency of malnutrition was similar in both genders (p:0.147). The gender distribution of the cases according to the Gomez, Waterlow (HFA, WFH), WHO (Weight, Height) Classifications is shown in Table 2. When malnutrition levels and age groups of the Gomez Classification were compared, decreases were detected in the frequency in all malnutrition levels as age increased (p:<0.001). The distributions of Gomez, Waterlow (HFA, WFH), WHO (Weight, Height) Classifications according to age groups are shown in Table 3.

Table 1: The distribution of upper middle arm circumference measurements according to age groups

Gender	Age (Month)	n	Median	Min	Max	p
Female	12-23	191	13.90	10.00	17.60	<0.001
	24-35	153	15.00	10.00	19.50	
	36-47	166	15.40	12.00	19.40	
	48-60	194	16.50	12.50	24.00	
Male	12-23	216	14.50	10.40	20.50	<0.001
	24-35	191	15.30	11.00	19.50	
	36-47	178	15.50	12.00	21.10	
	48-60	211	16.00	12.70	21.00	
Total	12-23	407	14.00	10.00	20.50	<0.001
	24-35	344	15.20	10.00	19.50	
	36-47	344	15.50	12.00	21.10	
	48-60	405	16.00	12.50	24.00	

When the degrees of malnutrition and UMAC measurements of Gomez classification were compared, it was found that UMAC values decreased as malnutrition degrees increased in both genders (p:<0.001). The comparison of Gomez, Waterlow (HFA, WFH), WHO (Weight, Height) Classification and UMAC measurements is given in Table 4. When the degrees of malnutrition obtained based on the HFA parameter of Waterlow Classification and UMAC measurements were compared, it was seen that UMAC values decreased as the malnutrition degree increased in both genders (p:<0.001). When the degrees of malnutrition obtained based on the WFH parameter of Waterlow Classification and UMAC measurement were compared, it was determined that UMAC values decreased as malnutrition degrees increased in both genders (p:<0.001). When the malnutrition degrees obtained based on the weight parameter of WHO Classification and UMAC measurement were compared, it was observed that UMAC values decreased as malnutrition degrees increased in both genders (p:<0.001). When the malnutrition degrees obtained on the basis of the height parameter of WHO Classification and UMAC measurement were compared, it was found that UMAC values decreased as malnutrition degrees increased in both genders (p:0.001).

The relations between UMAC measurement and WFA, HFA, WFH and WHO Classification was investigated. Also, sensitivity, specificity, and positive and negative predictor values of UMAC were determined. When the cut-off point of the UMAC measurement was taken as 11.0 cm for severe malnutrition, the sensitivity was 17.6% compared to Gomez (WFA) Classification; however, the specificity was 98.9%. The positive predictive value was 28.5%, and the negative predictive value was 98.1%. The comparison of Gomez, Waterlow (HFA, WFH) and WHO (Weight, Height) Classification and UMAC measurements is shown in Table 5. When the cut-off point of UMAC measurement was taken 11.5 cm for severe malnutrition, the sensitivity was found as 52.9%, and the specificity was 98.1% compared to

Table 2: The gender distribution of the cases according to the Gomez, Waterlow (HFA, WFH), WHO (Weight) and WHO (Height) Classifications

n		Female		Male		Total			
		%	n	%	n	%	Ki-Kare	p	
GOMEZ (WFA)	Normal	307	43.61	316	39.7	623	41.53	6.792	0.147
	Mild (1.)	202	28.69	236	29.65	438	29.20		
	Moderate (2.)	56	7.95	91	11.43	147	9.80		
	Severe (3.)	14	1.99	20	2.51	34	2.27		
	Above-Normal	125	17.76	133	16.71	258	17.20		
	Total	704	100	796	100	1500	100.00		
WATERLOW (HFA)	Normal	453	64.35	505	63.44	958	63.87	5.956	0.202
	Mild (1.)	167	23.72	179	22.49	346	23.07		
	Moderate (2.)	42	5.97	72	9.05	114	7.60		
	Severe (3.)	31	4.4	27	3.39	58	3.87		
	Above-Normal	11	1.56	13	1.63	24	1.60		
	Total	704	100	796	100	1500	100.00		
WATERLOW (WFH)	Normal	395	56.11	456	57.29	851	56.73	9.017	0.061
	Mild (1.)	146	20.74	160	20.1	306	20.4		
	Moderate (2.)	39	5.54	37	4.65	76	5.07		
	Severe (3.)	1	0.14	12	1.51	13	0.87		
	Above-Normal	123	17.47	131	16.46	254	16.93		
	Total	704	100	796	100	1500	100		
WHO (Weight)	Normal	601	85.37	661	83.04	1262	84.13	4.373	0.358
	Moderate	48	6.82	61	7.66	109	7.27		
	Severe	18	2.56	35	4.4	53	3.53		
	Above-Normal	37	5.26	39	4.9	76	5.07		
	Total	704	100	796	100	1500	100		
WHO (Height)	Normal	575	81.68	614	77.14	1189	79.27	12.764	0.012
	Moderate	64	9.09	88	11.06	152	10.13		
	Severe	50	7.1	69	8.67	119	7.93		
	Above-Normal	15	2.13	25	3.14	40	2.67		
	Total	704	100	796	100	1500	100		

Table 3: The age groups distribution of the cases according to the Gomez, Waterlow (HFA, WFH), WHO (Weight) and WHO (Height) Classifications

	Age Groups (Month)											
	12-23		24-35		36-47		48-60		Total		Ki-Kare	p	
	n	%	n	%	n	%	n	%	n	%			
WFA	Normal	147	36.12	155	45.06	135	39.24	186	45.93	623	41.53	70.088	<0.001
	Mild (1.)	143	35.14	101	29.36	102	29.65	92	22.72	438	29.20		
	Moderate (2.)	60	14.74	20	5.81	28	8.14	39	9.63	147	9.80		
	Severe (3.)	18	4.42	6	1.74	9	2.62	1	0.25	34	2.27		
	Above-Normal	39	9.58	62	18.02	70	20.35	87	21.48	258	17.20		
HFA	Normal	218	53.56	230	66.86	231	67.15	279	68.89	958	63.87	43.914	<0.001
	Mild (1.)	106	26.04	79	22.97	72	20.93	89	21.98	346	23.07		
	Moderate (2.)	46	11.30	18	5.23	22	6.40	28	6.91	114	7.60		
	Severe (3.)	27	6.63	13	3.78	15	4.36	3	0.74	58	3.87		
	Above-Normal	10	2.46	4	1.16	4	1.16	6	1.48	24	1.60		
WFH	Normal	222	54.55	200	58.14	203	59.01	226	55.80	851	56.73	19.502	<0.001
	Mild (1.)	77	18.92	51	14.83	72	20.93	106	26.17	306	20.40		
	Moderate (2.)	20	4.91	18	5.23	18	5.23	20	4.94	76	5.07		
	Severe (3.)	3	0.74	0	0.00	9	2.62	1	0.25	13	0.87		
	Above-Normal	85	20.88	75	21.80	42	12.21	52	12.84	254	16.93		
WHO (Weight)	Normal	321	78.87	287	83.43	289	84.01	365	90.12	1262	84.13	50.451	<0.001
	Moderate	45	11.06	26	7.56	23	6.69	15	3.70	109	7.27		
	Severe	27	6.63	11	3.20	15	4.36	0	0.00	53	3.53		
	Above-Normal	14	3.44	20	5.82	17	4.94	25	6.17	76	5.07		
WHO (Height)	Normal	269	66.09	280	81.40	292	84.88	348	85.93	1189	79.27	62.184	<0.001
	Moderate	55	13.51	36	10.47	26	7.56	35	8.64	152	10.13		
	Severe	63	15.48	22	6.40	21	6.10	13	3.21	119	7.93		
	Above-Normal	20	4.92	6	1.74	5	1.45	9	2.22	40	2.67		

Table 4: The comparison of Gomez, Waterlow (HFA, WFH), WHO (Weight), and WHO (Height) Classification and UMAC measurements

				Upper Middle Arm Circumference				
n								
Median				Min	Max	p		
Gomez (WFA)	Female	Normal	307	15.50	11.00	19.50		<0.001
		Mild (1st degree)	202	14.00	10.00	20.00		
		Moderate (2nd degree)	56	12.95	10.10	15.00		
		Severe (3rd degree)	14	11.20	10.00	15.00		
		Above-Normal	125		17.00	13.00	24.00	
	Male	Normal	316	15.65	13.00	19.00		<0.001
		Mild (1st degree)	236	14.50	11.50	17.50		
		Moderate (2nd degree)	91	12.90	10.40	17.00		
		Severe (3rd degree)	20	12.05	10.50	13.40		
		Above-Normal	133	17.50	14.50	21.10		
Waterlow (HFA)	Female	Normal	453	15.80	10.00	23.00		<0.001
		Mild (1st degree)	167	14.20	10.50	19.50		
		Moderate (2nd degree)	42	14.00	10.80	18.00		
		Severe (3rd degree)	31	11.40	10.00	16.50		
		Above-Normal	11	16.10	11.00	24.00		
	Male	Normal	505	15.70	10.40	21.10		<0.001
		Mild (1st degree)	179	14.80	10.50	20.00		
		Moderate (2nd degree)	72	13.70	10.40	17.50		
		Severe (3rd degree)	27	12.10	11.00	15.20		
		Above-Normal	13	17.00	14.00	21.00		
Waterlow (WFH)	Female	Normal	395	15.50	10.10	19.50		<0.001
		Mild (1st degree)	146	14.00	10.00	20.00		
		Moderate (2nd degree)	39	13.40	10.00	17.80		
		Severe (3rd degree)	1	14.50	14.50	14.50		
		Above-Normal	123	16.50	10.40	24.00		
	Male	Normal	456	15.50	11.50	20.00		<0.001
		Mild (1st degree)	160	14.50	10.40	19.00		
		Moderate (2nd degree)	37	14.30	10.40	17.00		
		Severe (3rd degree)	12	12.20	10.50	14.00		
		Above-Normal	131	17.20	13.50	21.10		
WHO (Weight)	Female	Normal	601	15.20	10.00	20.00		<0.001
		Moderate	48	13.00	10.10	15.00		
		Severe	18	11.25	10.00	13.80		
		Overweight	24	17.80	14.00	22.50		
		Above-Normal	13	20.00	16.00	24.00		
	Male	Normal	661	15.50	11.50	20.00		<0.001
		Moderate	61	13.00	10.40	17.00		
		Severe	35	11.90	10.80	13.20		
		Overweight	24	18.00	15.00	21.00		
		Above-Normal	15	19.40	18.00	21.10		
WHO (Height)	Female	Normal	575	15.40	10.00	23.00		<0.001
		Moderate	64	14.00	11.00	19.50		
		Severe	50	12.55	10.00	18.00		
		Lengthy	6	16.80	15.00	24.00		
		Above-Normal	9	16.10	11.00	20.00		
	Male	Normal	614	15.50	10.40	21.10		<0.001
		Moderate	88	14.30	10.40	19.00		
		Severe	69	12.90	11.00	16.20		
		Lengthy	21	17.00	13.50	21.00		
		Above-Normal	4	15.75	15.50	19.00		

Table 5: The comparison of Gomez, Waterlow (HFA, WFH), WHO (Weight) and WHO (Height) Classification and UMAC measurements

	UMAC	Present*	Absent*	TOTAL	Sensitivity	Specificity	PPV**	NPV***
GOMEZ	<11.0 cm	6	15	21				
	>11.0 cm	28	1451	1479	17.60%	98.90%	28.50%	98.10%
	TOTAL	34	1466	1500				
	<11.5 cm	18	27	45				
	>11.5 cm	16	1439	1455	52.90%	98.10%	40.00%	98.90%
	TOTAL	34	1466	1500				
	≤ 12.5 cm	125	2	127				
	> 12.5 cm	494	879	1373	20.20%	99.70%	98.40%	64.00%
	TOTAL	619	881	1500				
	≤14.95 cm	396	223	619				
	>14.95 cm	136	745	881	74.00%	77.00%	64.00%	84.60%
	TOTAL	532	968	1500				
Waterlow (HFA)	<11.0 cm	9	12	21				
	>11.0 cm	49	1430	1479	15.50%	99.10%	42.80%	96.60%
	TOTAL	58	1442	1500				
	<11.5 cm	9	12	21				
	>11.5 cm	49	1430	1479	36.20%	98.30%	46.60%	97.40%
	TOTAL	58	1442	1500				
	≤ 12.5 cm	95	32	127				
	> 12.5 cm	423	950	1373	18.00%	96.70%	74.80%	69.10%
	TOTAL	518	982	1500				
	≤14.95 cm	324	136	460				
	>14.95 cm	295	745	1040	70.40%	71.60%	52.30%	84.60%
	TOTAL	619	881	1500				
Waterlow , (WFH)	<11.0 cm	1	20	21				
	>11.0 cm	12	1467	1479	7.60%	98.60%	4.70%	99.10%
	TOTAL	13	1487	1500				
	<11.5 cm	3	42	44				
	>11.5 cm	10	1445	1455	23.10%	97.10%	6.60%	97.10%
	TOTAL	13	1487	1500				
	≤ 12.5 cm	82	45	127				
	> 12.5 cm	313	1060	1373	20.70%	95.90%	64.50%	77.20%
	TOTAL	395	1105	1500				
	≤14.95 cm	324	295	619				
	>14.95 cm	136	745	881	68.00%	67.20%	40.00%	86.80%
	TOTAL	460	1040	1500				
WHO (Weight)	<11.0 cm	7	14	21				
	>11.0 cm	46	1433	1479	13.20%	99.00%	33.30%	96.80%
	TOTAL	53	1447	1500				
	<11.5 cm	19	26	45				
	>11.5 cm	34	1421	1455	35.84%	98.20%	42.20%	97.60%
	TOTAL	53	1447	1500				
	≤ 12.5 cm	79	48	127				
	> 12.5 cm	83	1290	1373	48.70%	96.40%	62.20%	93.90%
	TOTAL	162	1338	1500				
	≤13.95 cm	105	213	318				
	>13.95 cm	22	1160	1182	82.60%	84.40%	33.00%	98.10%
	TOTAL	127	1373	1500				
WHO (Height)	<11.0 cm	10	11	21				
	>11.0 cm	109	1370	1479	8.40%	99.20%	47.60%	92.60%
	TOTAL	119	1381	1500				
	<11.5 cm	28	17	45				
	>11.5 cm	91	1364	1455	23.50%	98.70%	62.20%	93.70%
	TOTAL	119	1381	1500				
	≤ 12.5 cm	74	53	127				
	> 12.5 cm	197	1176	1373	27.30%	95.60%	58.20%	85.60%
	TOTAL	271	1229	1500				
	≤14.55 cm	178	362	540				
	>14.55 cm	56	904	960	76.00%	71.40%	33.00%	94.10%
	TOTAL	234	1266	1500				
All Classifications	≤15.15 cm	554	191	745				
	>15.15 cm	183	572	755	75.20%	75.10%	74.40%	75.80%
	TOTAL	737	763	1500				

*Malnutrition; ** PPV: Positive Predictor Values; *** NPV: Negative Predictor Values

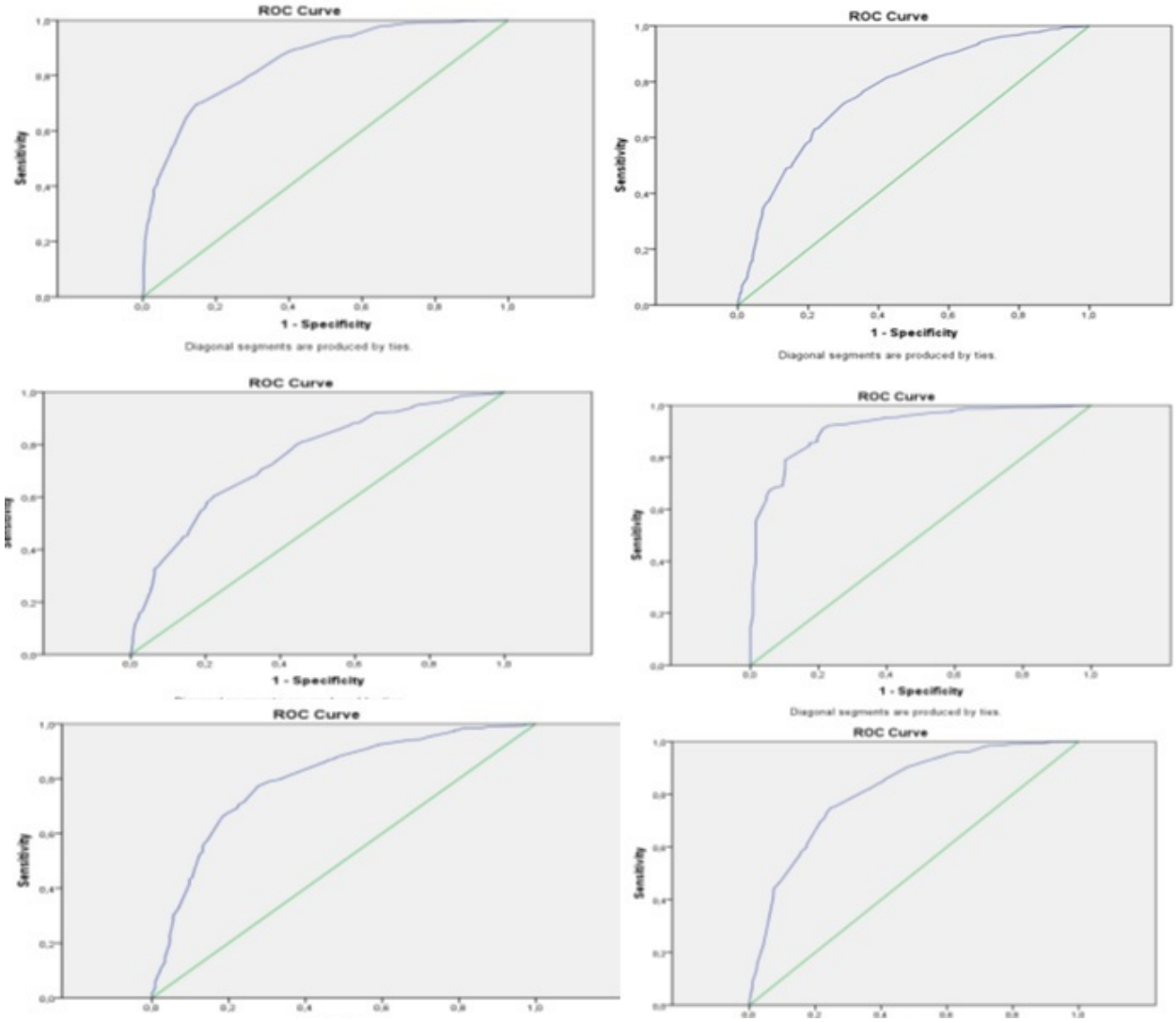

Figure 1: UMAC cut-off values in respect of malnutrition were found for Gomez, Waterlow and WHO classifications by the means of ROC analysis.

Gomez (WFA) Classification. The positive predictive value was 40%, and the negative predictive value was 98.9%.

Regression Test was made to investigate the relation between UMAC and WFA, HFA, WFH and WHO Classifications. The variable that had the highest agreement with the arm circumference was identified as Gomez (WFA) Classification (p:<0.001).

The cut-off value of UMAC was 14.95 cm in children who were found to have malnutrition according to Gomez (WFA) Classification. The sensitivity was 74%, and the specificity was 77%. The positive predictive value was determined as 64%, and the negative predictive value was 84.6%. The specificity and sensitivity of the cut-off value detected for Gomez, Waterlow (HFA, WFH), WHO (Weight, Height) are given in Figure 1. The cut-off value of UMAC was 14.95 cm in children with malnutrition according to Waterlow (HFA) Classification. The sensitivity was 70.4% and specificity was 71.6%.

Discussion

Since any situation, which affects child health adversely, might also affect the growth process adversely, each child should be monitored and evaluated with regular intervals after birth (11). Monitoring growth by using standard growth curves is necessary to take precautions without any adverse conditions in the child with early detection of deviations from normal growth pattern. The method that will be used in such a growth monitoring should be proven in terms of validity, have high sensitivity, yield results in a short time, and have low economic cost. All the methods employed to monitor growth are based on anthropometric measurements (12). The main anthropometric criteria used in this respect are body weight, stature, head circumference, arm span, sitting height, neck and waist circumference, upper middle arm circumference, skin fold thickness, and Body Mass Index.

From anthropometric measurements, UMAC is frequently used in epidemiological studies. The reason

why it is especially preferred in field studies is that the measurement is easy, does not require special expertise, and can be interpreted without the need to evaluate with percentile curves.

In our present day, the cut-off values of 125 mm (malnutrition) and 110 mm (severe malnutrition) were used in children who were under 5 years of age (10). With the common use of WHO growth standards, the NOCD cut-off point was changed to 115 mm in the diagnosis of severe acute malnutrition according to the results of the study from African countries (13). It was questioned in a study conducted in India with 1879 children who were aged 0-6 from the Madhya Pradesh Region whether the upper middle arm circumference could be a simple method for acute serious malnutrition screening in the society. It was emphasized in this study that the 115 mm cut-off point value recommended as the upper middle arm circumference for the diagnosis of severe acute malnutrition in line with the studies from African countries had low sensitivity (17.5%) and low positive prediction value (30.4%); and this measurement value should be questioned again (14).

In a study conducted in Senegal, a total of 5751 children under the age of 5 who had malnutrition were compared with UMAC and WHO's WFH Z-score to predict severe malnutrition. According to the height, the specificity of those who were under the weight of -3 SS and under 115 mm was 99% in terms of severe malnutrition, but the sensitivity was found as 5.9%. The specificity was 96.9% in those with weight below -3 SS or under UMAC 115 mm according to the height, but the sensitivity was 13.2%. In the present study, it was emphasized that the UMAC measurement that was lower than 115 mm and/or the WFH Z-score lower than -3 SS was not a useful result in defining severe malnutrition, and only UMAC measurement was more valuable in severe malnutrition diagnosis (15).

UMAC was measured along with the heights and weights of the children in a study conducted with 205 children in the Hanoi Region in Vietnam, and these children were monitored at regular intervals. The measurements of children who were between 0-12 months were followed-up monthly, the measurements of children between 12-36 months were followed-up every 3 months, the measurements of children between 36-72 months were followed-up every 6 months, and children over 72 months were followed-up yearly. The purpose of the study was to monitor the increase in UMAC in children. The increase in UMAC between the ages of 1-5 was 1 cm in girls, and 1 cm in boys. Only when the cut-off point value was taken as 13.5 cm in malnutrition definition in children 6-12 months of age, it yielded high specificity and sensitivity; 14 cm in 13-24 months, 14.5 cm at 25-36 months, and 15 cm in 37-60 months. It was emphasized in the study that if 13.5 cm was not accepted as the UMAC cut-off value for malnutrition screening in children under 5 years of age, the cut-off point value would increase with age (16). In a study conducted with 24.792 children at a center that applied a treating feeding program in Burkina Faso, it was concluded that UMAC was more effective than WFH Z-score as a criterion for admission and discharge to/from the center (17). In a study conducted with 1.166 children in Kenya, when the UMAC's WHO's WFH Z-scores were compared by considering the visible severe weight loss for severe acute malnutrition identification, the diagnostic performance was reported to be better in terms of specificity and sensitivity (18).

In a study conducted with 319 children who were aged between 12 and 59 months in Nigeria, when the cut-off point value of UMAC was taken as 13.5 cm for malnutrition, sensitivity was 20% and specificity was 95.3%; and when it was taken as 15.5 cm, the sensitivity increased to 80%; however, the specificity decreased to 53.5%, and the cut-off point value should be increased to a further value to increase sensitivity7. In another study, UMAC, triceps skin fold thickness and arm and whole body fat mass were compared in the UK. In this study, which included 110 healthy children and 49 children with cystic fibrosis, UMAC measurement results and triceps skin fold thickness had a good correlation level with all body fat mass results (19).

Very few studies were conducted in Turkiye on the upper middle arm circumference, which is one of the anthropometric investigation topics. The first studies were conducted in children who were between the ages of 0-3 in Istanbul, and the results of the study showed low values compared to British and Swedish standards (20).

Two studies have been conducted in recent years regarding UMAC in our country in Kayseri Region. A total of 5553 children and adolescents who were aged 6-17 years were included in the first study, and left UMAC, triceps skin fold thickness, and arm fat circumference reference values were determined. Regarding the upper middle arm circumference, the 50th percentile were 17 cm at age 6 and 23.6 at age 17 in boys, and 15.6 cm at age 6 and 20.9 cm at age 17 in girls (2). In the second study, the role of left UMAC measurements in addition to waist circumference was investigated to define obesity; and was conducted with 2.621 boys and 2.737 girls who were aged 6-17; and it was speculated that the left UMAC threshold values, which show obesity, could be used as an additional parameter in the diagnosis of obesity in PEM diagnosis used so far (21).

A study was conducted in Çankırı City Center to evaluate the nutritional status with anthropometric measurements for 12-48-month-old children; and 258 children were included in the study. The age groups were classified as 12-24 months, 24-36 months, and 36-48 months. The mean UMAC value of boys was 20±0.14 cm, and 20±0.13 cm in girls (9).

No studies were detected in the literature showing the data of our country on the relations of UMAC with Gomez, Waterlow, and WHO Classifications used in malnutrition diagnosis.

In our study, it was also found that UMAC measurement

values were similar in girls (mean 15.18±1.97 cm, median value 15 cm, range 10-24 cm) and in boys (mean 15.26±1.8 cm, median 15.3 cm, range 10.4-21.1 cm). It was seen that the UMAC measurement values decreased as the malnutrition degree increased in all classifications.

In the present study of ours, it was determined that UMAC's compliance with other malnutrition Classifications in terms of sensitivity, specificity, positive prediction value, and negative prediction value in severe malnutrition diagnosis for children who are between the ages of 1-5 yielded better results than 11.0 cm when the cut-off point value was taken as 11.5 cm.

The agreement between UMAC and Gomez (WFA) Classification was found better than other classifications in terms of sensitivity and specificity. The relation of UMAC with all classification groups in terms of negative predictive value was high, which suggests that children aged 1-5 years who are UMAC 11.0 cm and 11.5 cm and above may move away from severe malnutrition. It was noteworthy in terms of positive predictor value of UMAC that Waterlow (WFH) was the least associated classification. When the cut-off point of UMAC was 11.0 cm and 11.5 cm for severe malnutrition diagnosis, its specificity was high. The best agreement was with Gomez Classification when the cut-off point was 11.5 cm in terms of the sensitivity of UMAC in severe malnutrition detection. It was noted that the sensitivity increased 3-fold when the cut-off point was increased to 11.5 cm from 11.0 cm. When the sensitivity of UMAC in detecting severe malnutrition was increased to 11.5 cm from 11.0 cm, its compliance with Waterlow (HFA, WFH) and WHO (WFA, HFA) Classification increased at a rate of 2.3, 3, 2.71, and 2.8-fold.

When the 12.5 cm and below cut-off values of UMAC were considered as the criterion for malnutrition diagnosis, it was found that the highest compliance was with WHO's YGA classification in terms of sensitivity, and the compliance with all classification methods was good in terms of specificity. It is worth noting that the highest compliance was with Gomez (WFA) Classification in terms of positive predictor value; and the compliance in terms of negative predictive value was with WHO's WFA and HFA.

According to the results of our study, considering the previously reported studies showing that the sensitivity and specificity increased when the limit value increased in diagnosing malnutrition with UMAC, the cut-off points of UMAC were determined for each classification. The cut-off point was 14.95 cm for Gomez and Waterlow (HFA and WFH) Classifications of UMAC for malnutrition diagnosis in children aged 1-5 years, 13.95 cm for WHO WFA, 14.55 cm for WHO HFA, and 15.15 cm for all classifications. It is noteworthy that the sensitivity and negative predictive value increased when UMAC cut-off point value was increased to the values detected in our study for classifications; however, specificity and positive predictive value decreased. This suggests that it would be more appropriate to use the cut-off point values that were found in our study in terms of the sensitivity of UMAC for not to overlook malnutrition cases in children between the ages of 1 and 5 in our country.

It was found in our study that UMAC showed the best correlation with Gomez (WFA) Classification among the other three classifications (Gomez, Waterlow, and WHO) (R2=0.631, p:0.001).

Conclusion

Early recognition of an important public health problem, such as malnutrition is very important for taking precautions and identifying treatment modalities. Although the UMAC cut-off point differs among countries and regions for the diagnosis of severe malnutrition, our study showed that it would be appropriate to prefer 11.5 cm for our country. Similarly, it was concluded that the sensitivity would increase if the cut-off point values defined in our study were used instead of 12.5 cm cut-off point value that is used for the diagnosis of malnutrition with UMAC. It was also found that UMAC was most compatible with Gomez (WFA) among the other three classification methods. It was also concluded that UMAC measurement alone would not be adequate for malnutrition diagnosis, and that it would be more appropriate to evaluate it together with Gomez, Waterlow, and WHO Classifications by making other anthropometric measurements in physical examinations. Multi-centered studies are required in our country to determine UMAC malnutrition and severe malnutrition limit values to prevent delayed diagnosis and treatment of children with malnutrition between the ages of 1 and 5.

Ethical Approval: The study was conducted with the approval of the Local Ethics Committee of the Ethics Committee of Selçuk University, Faculty of Medicine (No: 10.06.2014 and 2014/12).

Author Contributions: Conceptualization, HHE and MSÖ.; Methodology, HHE, MSÖ and ME.; Formal analysis, HHE, MSÖ and ME.; Investigation, HHE and MSÖ.; Resources, MSÖ, ME, FK. and AY; Writing—original draft preparation, MSÖ and AY.; Writing—review and editing, HHE, MSÖ and AY. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: This study was performed according to the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the Institutional Review Board at Selçuk University Medical Center (no:2021/6).

Conflicts of Interest: There are no financial and non-financial conflicts of interest for any of the authors regarding specific financial interests that are relevant to the work conducted or reported in this manuscript.

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ORIGINAL ARTICLE

Factors Affecting COVID-19 Vaccine Confidence and Prevalence of Post-COVID Syndrome

COVID-19 Aşılarına Yönelik Güven Durumlarını Etkileyen Faktörler ve Post COVID Sendromu Prevalansı

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ABSTRACT

Background/Aims: Determining the attitudes and confidence levels of society towards vaccines is important even after administering vaccinations. The aims of this study are: to determine the prevalence of post-COVID syndrome, the side effects after COVID-19 vaccinations, and the factors affecting COVID-19 vaccine confidence in individuals aged eighteen years old and over.
Methods: The population of this cross-sectional study consisted of people aged eighteen years old and above living in the city center of Amasya. In total, 762 people were reached. Data collection was carried out between August 15 – September 15, 2022 by applying the questionnaire form prepared by the researchers face-to-face in rural areas and face-to-face or online in urban areas.
Results: The number of people having chronic COVID disease was 55 (20.0%). Three hundred nine people (43.2%) developed side effects after at least one dose of the vaccine. The rate of trusting all the vaccines was higher among those who did not develop side effects after vaccination, who did not use social media as a source of information, who were aged 65 and over, who resided in rural areas, who had secondary school education and below, who did not work and who were housewives (p<0.001).
Conclusions: One in five people who have had the disease developed chronic COVID syndrome and almost half of respondents trusted all types of COVID-19 vaccines. For vaccines to be accepted by the society, the ways in which media such as social media reduce the trust in the vaccine should be examined and the reasons for the lack of confidence in the vaccine should be determined, especially in people with a high education level.

Keywords: COVID-19, Vaccine, Side effect, Confidence, Attitude

ÖZ

Amaç: Toplumun aşılara yönelik tutum ve güven düzeylerinin belirlenmesi, aşı uygulaması sonrası da oldukça önem taşımaktadır. Bu çalışmanın amaçları Amasya il merkezinde yaşayan on sekiz yaş ve üstü bireylerde; post COVID prevalansını, COVID-19 aşıları sonrası görülen yan etkileri ve COVID-19 aşılarına yönelik güven durumunu etkileyen faktörleri belirlemektir.
Yöntem: Kesitsel tipteki çalışmanın evrenini Amasya il merkezinde yaşayan on sekiz yaş ve üzeri kişiler oluşturdu. Toplamda 762 kişiye ulaşıldı. Veri toplama işlemi araştırmacılar tarafından hazırlanan anket formunun kırsal kesimde yüz yüze, kentsel bölgede ise yüz yüz veya çevrimiçi uygulanmasıyla 15/08/2022 - 15/09/2022 tarihleri arasında gerçekleştirildi.
Bulgular: Kronik COVID tanımına uyan kişi sayısı 55 (%20,0) olarak tespit edildi. Üç yüz dokuz kişide (%43,2) en az bir doz aşı sonrası yan etki geliştiği bulundu. Aşıların tümüne güvenme oranı aşı sonrası yan etki gelişmeyenlerde, bilgi kaynağı olarak sosyal medya kullanmayanlarda, 65 yaş ve üzeri grupta, köylerde ikamet edenlerde, öğrenim durumu ortaokul ve altı olan bireylerde ve çalışmayanlar ile ev hanımlarında daha yüksekti (p<0,001).
Sonuç: Hastalığı geçiren her beş kişiden birinde kronik COVID sendromu geliştiği ve katılımcıların neredeyse yarısının tüm COVID-19 aşı tiplerine güvendiği tespit edilmiştir. Aşıların toplum tarafından kabul edilmesi için sosyal medya gibi mecraların aşıya olan güveni hangi yollarla azalttığı incelenmeli ve yapılacak çalışmalarla özellikle eğitim düzeyi yüksek olan kişilerde aşıya olan güvensizliğin nedenleri belirlenmelidir.

Anahtar Kelimeler: COVID-19, Aşı, Yan etki, Güven, Tutum

Introduction

As of February 12, 2023, more than 755 million confirmed cases and more than 6.8 million deaths have been reported worldwide (1). The epidemic still affects certain parts of the world, and it is always possible for the number of cases and deaths to rise again due to the potential mutations creating new variants of the SARS-CoV-2 virus. Another feature of the disease is that some symptoms can be seen weeks or months later, depending on the prolongation of the expected recovery period. This condition, called long COVID or Post-COVID syndrome, can be divided into two stages depending on the duration of symptoms: post-acute COVID, at which symptoms exceed three weeks but less than 12 weeks, and chronic COVID, at which symptoms exceed 12 weeks (2). Currently, vaccination is still seen as the most effective method of prevention. While the number of vaccines approved for emergency use worldwide is 50, the World Health Organization (WHO) has approved 11 vaccines(3). In Türkiye, the first vaccine application was started with CoronaVac produced by Sinovac company on January 14, 2021. Following the approval of Comirnaty (BNT162b2) produced by Pfizer/BionTech company, and Turkovac (ERUCOV-VAC) produced as a result of cooperation between TÜSEB-Erciyes University; three vaccines continue to be administered based on the

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person's choice. While CoronaVac and Turkovac are inactive, Comirnaty vaccine is an mRNA vaccine. After mRNA vaccines are administered, mRNA enables the production of spike protein, which uses this code in the cell before it reaches the cell nucleus (4).

WHO recommends that 70% of the population should be vaccinated for the formation of herd immunity(5). In Türkiye, people who have received two doses of vaccine constitute of 62.3% of the population, but booster doses are required at regular intervals for effective protection(6). Before the introduction of COVID-19 vaccines, various studies were conducted to determine the attitude and confidence level towards vaccines in many regions. It has been found that the rate of people who have a positive attitude about COVID-19 vaccines in the world varies between 27.7% and 93.3%, depending on countries and the various sociodemographic characteristics of individuals (7). Determining the attitudes and confidence levels of society towards vaccines is also important after vaccination. In the literature review, it was observed that no study was conducted on the general population regarding the trust in vaccines in the process following the administration of vaccines. Mass vaccination programs will be more effective if the reasons for possible mistrust of vaccines and the target population to which various interventions such as education and information can be applied to overcome this mistrust can be identified. The aims of this study are to determine: (i) the prevalence of post-COVID and its symptoms, (ii) the side effects seen after COVID-19 vaccinations, (iii) the factors affecting the state of trust and attitude towards COVID-19 vaccines in individuals aged eighteen and over living in Amasya city center, Türkiye.

Material and Methods

This is a cross-sectional study. In the population of 108,712 people aged eighteen and older living in the city center of Amasya, the minimum sample size was calculated as 196, considering the COVID-19 vaccine confidence as 50% and the deviation rate as 10%, with 80% power and 5% type-1 error. With the calculation of the design effect, it was aimed to reach 392 people. The sample obtained was stratified according to (i) settlement (rural/urban areas), (ii) gender, and (iii) age groups (18-64 years/65 years and above). In determining the factors affecting the trust and attitude towards vaccines, the independent variables were determined as the development of side effects after vaccination, information sources about the vaccine and sociodemographic characteristics. Following the approval from ..... Non-Interventional Research Ethics Committee numbered 2022/76, the data collection was carried out between August 15 – September 15, 2022. A questionnaire form prepared by the researchers was used as the data collection method. While the first part of the questionnaire included 9 items on sociodemographic characteristics, the second part included 12 items on the history of the COVID-19 disease and COVID-19 vaccines. To determine the state of confidence in vaccines, the participants were asked "Which of the following options reflects your opinion on COVID-19 vaccines?". The participants were expected to choose among these three options: "I trust all", "I trust some" and "I trust none". The study was conducted in two main strata, rural and urban areas, with different sampling methods. For the sample in the rural areas, considering the education status of the participants, the data was collected through a face-to-face survey. Through a one-stage random selection method five villages were selected, each as a cluster. The information of the people who were at home during the visiting hours was obtained from the community leader and they were interviewed in their homes. The questionnaire was applied to all those aged 18 and over in the relevant households who agreed to participate in the study. In the urban area, both online and face-to-face surveys were conducted using the non-probabilistic sampling method. In both regions, the face-to-face questionnaire was administered by the researchers in this project. The data collection process started after obtaining informed consent from the participants. Within the scope of post-COVID, people whose complaints continued for 12 weeks or more were categorized as chronic COVID (2).

After the data were coded, they were transferred to the SPSS (Version 22 for Windows, SPSS Inc, Chicago, IL, USA) package program and analyzed. In statistical analyses, the conformity of the numerical variables to the normal distribution was evaluated with the Kolmogorov-Smirnov test. Since the continuous numerical variables did not fit the normal distribution, their median (interquartile range) values were presented. The categorical data were presented as numbers and percentages. Chi-square test was used to compare categorical variables. Statistical significance level was accepted as $p<0.05$ for all tests.

Results

The median age of the 762 people participated in the study was 41 (IQR 23) years, and 385 (50.5%) were women. Of the participants, 537 (70.5%) resided in urban areas; 396 (52.2%) had associate degrees or higher education level; and 494 (64.8%) worked in an income generating job (Table 1). Of the participants, 276 individuals (36.3%) had a self-reported diagnosis of COVID-19 with a PCR test; 77 (28.0%) of the participants who had the disease stated that they had symptoms that started with COVID-19 and still continued. While the median period between the diagnosis of the disease and the time the data were collected was 7 (IQR 12) months, the median of this period was 6 (IQR 10) months in people who stated that they had symptoms that started with the disease and still continued. The number of people who were diagnosed with chronic COVID (whose complaints continued for at least 12 weeks) was 55 (20.0%). The most common symptom among these individuals was weakness and easy fatigue (25.5%) (Table 2).

It was found that 721 (94.6%) of the participants had at least one dose of the COVID-19 vaccine. Among

the answers given to the reasons for not being vaccinated, the most frequent reason was "I do not trust the vaccines" (90.2%). It was found that the most administered vaccine was Comirnaty (89.2%), 293 people (41.5%) had 3 doses of vaccines, and 309 people (43.2%) developed side effects after at least one dose of the vaccine. The rate of developing a side effect after the Comirnaty vaccine was 45.3%. The most common side effect in all three vaccine types was arm pain at the injection site.

Table 1. Distribution of participants' sociodemographic characteristics

Sociodemographic characteristic	n	%
Age group (years) (n=762)		
18-25	115	15.1
26-50	388	50.9
51-64	161	21.1
65 and over	98	12.9
Gender (n=762)		
Male	377	49.5
Female	385	50.5
Place of residence (n=762)		
Urban area	537	70.5
Rural area	225	29.5
Educational status (n=758)		
Illiterate	29	3.8
Primary school	182	24.0
Middle school	34	4.5
High school	117	15.4
Associate's degree and above	396	52.2
Working status (n=762)		
Working	494	64.8
Unemployed/housewife	117	15.4
Retired	79	10.4
Student	72	9.4

Table 2. Distribution of the Characteristics of the Participants Regarding the COVID-19 Disease

COVID-19 Disease (n=761)	n	%
Diagnosed	276	36.3
Undiagnosed	485	63.7
Ongoing Symptom After Disease (n=275)		
Yes	77	28.0
No	198	72.0
Chronic COVID Symptoms (n=55)*		
Weakness/fatigue	14	25.5
Shortness of breath	8	14.5
General muscle/joint pain	7	12.7
Brain fog/drowsiness/forgetfulness	6	10.9
Loss of taste/smell	5	9.1
Lower back pain	4	7.3
Psychiatric symptoms	4	7.3
Cough	3	5.5
Back pain	3	5.5
Hoarseness	2	3.6
Hypertension	2	3.6
Dizziness	2	3.6
Vision loss/impairment	2	3.6
Other†	6	10.9

*Multi-choice

†Angina, palpitations/arrhythmia, sore mouth, headache, insomnia, knee pain

Table 3. Distribution of Confidence in Vaccines by Sociodemographic Characteristics

	COVID-19 Vaccine confidence				
Sociodemographic Characteristics	Trusting all		Not trusting at least one		
Age Group (Year) (n=754)	n	%*	n	%*	p
18-25	34	29.6	81	70.4	<0.001
26-50	131	34.4	250	65.6	
51-64	119	74.4	41	25.6	
65 and over†	80	81.6	18	18.4	
Gender (n=754)					
Male	185	49.6	188	50.4	0.47
Female	179	47.0	202	53.0	
Place of residence (n=754)					
Urban area	174	32.9	355	67.1	<0.001
Rural area	190	84.4	35	15.6	
Educational status (n=750)					
Middle school and below	213	86.9	32	13.1	<0.001
High school and above	149	29.5	356	70.5	
Working status (n=754)					
Working	214	44.0	272	56.0	<0.001
Unemployed/housewife†	77	65.8	40	34.2	
Retired	49	62.0	30	38.0	
Student	24	33.3	48	66.7	

*Row percentage

†The subgroup from which the difference originates

Table 4. Attitudes and Confidence Towards Vaccines According to Post-Vaccination Side Effects Development

	Post Vaccine Side Effect				
	Developed		Not developed		
Vaccine Confidence Status*	n	%†	n	%†	p
Trusting all	128	42.1	224	55.6	<0.001
Not trusting at least one	176	57.9	179	44.4	
Reminder Dose*	n	%†	n	%†	p
Considering	163	53.1	228	56.2	0.41
Not considering/indecisive	144	46.9	178	43.8	

*Due to missing answers, the numbers in the eyes do not give the total.

†Column percentage

Of the 754 people who answered the question "Which of the following options reflects your thinking about COVID-19 vaccines?", 364 (48.3%) stated that they trusted all the vaccines, 281 (37.3%) trusted some of them, and 109 (14.5%) did not trust any of them. Of those who declared that they trusted some of the vaccines, 217 (77.2%) stated that they trust the Comirnaty vaccine. Of the participants, 402 (52.9%) stated that they were considering the reminder doses. It was found that the most preferred vaccine for the reminder dose was Comirnaty (78.8%). Regarding the source of information, written and visual media (63.7%) were the most commonly used source about COVID-19 vaccines.

The rate of 'confidence in all the vaccines' was higher in the 65-year-old and above group, in those residing in rural areas, in individuals with secondary school education and below, and in those who do not work or are housewives (p<0.001) (Table 3). When looked at separately for the vaccine types, it was determined

that individuals with a secondary education level and below were more likely to trust each vaccine type too ($p<0.001$). Of the 253 participants who declared that they use social media platforms as one of the sources of information about vaccines, 70 (27.7%) stated that they trusted all the vaccines. Of the 501 people who stated that they did not use social media as a source of vaccine information, 294 (58.7%) stated that they trusted all the vaccines ($p<0.001$).

While the level of confidence in all vaccines was lower in the participants who stated that they developed side effects after any vaccine dose ($p<0.001$), it was seen that the development of side effects did not affect the thoughts of the individuals about the reminder dose ($p>0.05$) (Table 4).

Discussion

The number of people whose symptoms continued for 12 weeks, defined as chronic COVID, constituted 20% of those who had the disease. In two studies conducted in England, this rate was 65% and 74% in patients hospitalized with the diagnosis of COVID-19 (8, 9). As a result of the more severe course of the disease in hospitalized patients, a higher rate of chronic COVID-19 cases can be expected. In the literature, the two most frequent symptoms in chronic COVID cases are fatigue and shortness of breath (8, 9). In this study, the most common symptoms in chronic COVID cases were similarly weakness/fatigue and shortness of breath. In the study conducted in Türkiye, the most common symptoms among patients admitted to the COVID-19 outpatient clinic of a hospital were fatigue, musculoskeletal pain, cough, joint pain and exertional dyspnea (10). Studies show that sporadic necrosis, general atrophy of muscle fibers, focal infiltration of muscle fibers and neuronal demyelination contribute to this condition (11). The other most reported symptoms reported in previous studies are general muscle-joint pain, brain fog/drowsiness/forgetfulness, and loss of taste-smell (2).

The most preferred type of vaccine by the participants was Comirnaty, followed by CoronaVac and Turkovac vaccines, respectively. It is worth noting that, Coronavac was the first vaccine administered in Türkiye, to healthcare workers and individuals over 65 years of age, without the possibility of making a choice. Despite this, it is thought that the preference of the Comirnaty vaccine is due to the higher protection rate of the vaccine (12). In another study in which dentists and dentistry students participated, it was also seen that the Comirnaty was the more preferred vaccine (13).

Of the people vaccinated, 43% had a side effect after at least one dose of vaccination. The incidence of developing a side effect was higher in the Comirnaty vaccine compared to the other two vaccines (45%). The most common side effects after this vaccine were pain, weakness, and fever at the injection site. In a review, the average rate of side effects seen after the first and second dose of the Comirnaty vaccine was 79% and 89% respectively, which is higher than the rates in this study. In terms of the type of side effects, injection site pain and fatigue were the most common symptoms similar to this study (14). Side effects associated with vaccines are mostly attributed to the production of type-I interferon, a cytokine that plays a vital role in enhancing the early stages of the immune response. The fatigue and headache seen after COVID-19 vaccines have suggestively been attributed to effective immune response as a result of adequate release of type-I interferon (15). The incidence of side effects in any dose of CoronaVac vaccine was 26%, and the most common types of side effects were pain at the injection site, weakness, and muscle/joint pain. In another study conducted among healthcare professionals in Türkiye, the incidence of side effects after any CoronaVac dose was 62%, and the most common types of side effects were fatigue and pain at the injection site similar to this study. In brief, several studies show that pain at the injection site and fatigue are the most common symptoms after COVID-19 vaccines. We think that the most probable reason for the lower incidence of side effects after vaccination in our study compared to the literature is the memory factor.

Of the individuals in this study, 48% stated that they trusted all of the COVID-19 vaccines. In one of the few studies conducted after the introduction of vaccines in Türkiye, 42% of the participants from a health sciences faculty stated that they found COVID-19 vaccines safe (16). In a study in which students from the Faculty of Medicine participated, 40% of the participants stated that they trusted the COVID-19 vaccines, and 41% stated that this situation might vary according to the type of vaccine (17). The most striking finding in our study was that the rate of trusting all vaccines was higher in those residing in rural areas, those with a secondary education level and below, those who were not working, housewives, and those over the age of 65. It is indicated that education level is the main determinant of vaccine confidence in these subgroups. It is interesting that while the rate of trusting all vaccines is 86%, among those with a secondary education level and below, this rate is 29% for those with a high school or higher education level. In fact, it has been shown in the literature that higher education level is a protective factor against COVID-19 vaccine refusals. In a review of fifteen studies, it was observed that the level of acceptance of COVID-19 vaccines increased as the level of education increased, and only two of these studies had similar results to our study (18). In studies conducted in Türkiye on this subject, it was observed that parents with a high level of education had a more negative attitude towards COVID-19 vaccines (19). In another study, it was observed that education level did not affect the attitude towards COVID-19 vaccines in individuals aged 18 and over (20). In this case, the first explanation that comes to mind is that those with a high level of education responded according to the protection rates of the vaccines. As such, it is expected that the Comirnaty vaccine will be more reliable in people with a higher education level. However, although the Comirnaty vaccine is seen as

the most trusted vaccine in the entire sample, the rate of confidence in vaccines was lower in individuals with higher education levels for each vaccine. The high level of education for vaccines in general is known as a factor that positively affects vaccine acceptance (21). However, it is thought that the most likely reason for the emergence of contradictory results in the case of COVID-19 vaccines is the spread of scientifically invalid information, especially through social media. As a matter of fact, the findings of our study support this. People who use social media as a source of vaccine information have a lower rate of trust in COVID-19 vaccines. This situation makes us think that health literacy is independent of education level and that there is a need for community-oriented studies on this issue. In a study conducted with the employees of the organized industrial site in Aydın province, Türkiye which examined the effect of education status on the knowledge of COVID-19 vaccines and the reason for preference was, it was determined that the average score of high school graduates was significantly higher than other education groups, including university graduates (22).

In previous studies it is seen that the most important determinants of vaccine hesitancy are the side effects that can be experienced after vaccination (23, 24). It is known that serious side effects such as anaphylaxis occur at rates as low as 5 per million vaccine doses (25). It was observed that such a situation did not develop in any of the participants in this study, and the expected mild side effects negatively affected the level of confidence in vaccines. To prevent this situation, it is suggested that health professionals should clearly explain what side effects are expected and how long after vaccination.

A parallel situation with the level of confidence in COVID-19 vaccines is also seen in reminder doses. More than half of the individuals in the study consider taking the reminder dose. It was observed that the most preferred vaccine for reminder doses was Comirnaty vaccine, followed by Turkovac and CoronoVac, respectively. In a study conducted in industrial field workers in Türkiye, it was seen that the Comirnaty vaccine was preferred over CoronaVac (22). Although it is a new type of vaccine, the high level of protection shown for the Comirnaty vaccine in many scientific studies, and its high preference by developed countries has made the Comirnaty vaccine the most reliable and preferred vaccine (26).

The most important limitations of this study are that the samples in rural and urban areas do not represent their general population due to the sampling method used, and that the confidence in vaccines is measured with a single question. In addition, the effect of vaccination on COVID-19 disease could not be determined well, since the majority of the participants did not have precise information about whether they were first vaccinated or contracted the disease.

Conclusion

It has been determined that one out of every five people who have had COVID-19 disease develop symptoms lasting for more than 12 weeks; nearly half of the participants trust all COVID-19 vaccine types. Nearly half of people reported developing side effects after any dose of COVID-19 vaccines and the side effects occurred most commonly after the Comirnaty vaccine. It was determined that the most common side effects after vaccination were local pain at the injection site and fatigue. The level of trust in vaccines was lower in those with a high level of education, those who reported side effects after vaccination, and those who used social media as a source of information. For the vaccines to be accepted by society, the ways in which media -such as social media- reduce the trust in the vaccine should be examined. Also, particularly among people with a high education level, the reasons for the lack of confidence in the vaccine should be determined. Another important precaution is that healthcare professionals clearly explain what side effects are expected after the vaccination and that they are temporary.

Compliance with Ethics Guidelines

Approval number 2022/76 was obtained from the Amasya University Non-Interventional Research Ethics Committee. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Informed Consent

Informed consent was obtained from all of the participants included in the study.

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Conflict of Interests

The authors have no conflicts of interest to declare.

Author Contributions

Conception: B.T., Design: B.T., Supervision: B.T., Resource: B.T., M.Ç., A.M., Z.K., Materials: B.T., M.Ç., A.M., Z.K., Data Collection and/or Processing: B.T., A.M., Z.K., Analysis and/or Interpretation: B.T., Literature Review: B.T., A.M., Z.K., Writer: B.T., M.Ç., A.M., Z.K., Critical Review: B.T., M.Ç., A.M., Z.K.

Main Points

- One out of every five people who have had COVID-19 disease develop symptoms lasting for more than 12 weeks.
- Nearly half of the participants trust all COVID-19 vaccine types.
- The rate of people who stated that they developed side effects after any dose of COVID-19 vaccines was 43%.

• The level of trust in vaccines was found lower in those with a high level of education, those who reported side effects after vaccination, and those who used social media as a source of information.

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ORIGINAL ARTICLE

The Effect of Montelukast Treatment on Elderly Patients Diagnosed with COVID-19

COVID-19 Tanısı Konan Yaşlı Hastalarda Montelukast Tedavisinin Etkisi

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ABSTRACT

Objective: The clinical course in COVID-19 patients can vary from asymptomatic cases to acute respiratory distress syndrome (ARDS), multi-organ dysfunction and respiratory failure. Clinical progression is thought to be mainly due to the release of proinflammatory cytokines. The most common symptoms are shortness of breath, fever, malaise, and cough. Montelukast, which is used in the treatment of seasonal allergic rhinitis and asthma, started to be used in Covid-19 infection due to its anti-inflammatory and cytokine release-reducing effect. There are studies in the literature showing that montelukast treatment is beneficial in the treatment of COVID-19. However, there are not enough studies evaluating the efficacy of montelukast treatment in elderly patients.
The aim of our study is to evaluate the clinical and laboratory efficacy of montelukast treatment in patients aged 60 and over in COVID-19 disease, and to indicate the differences from the studies in the literature.
Method: Our research was planned as a retrospective, single-center, observational study. The medical records of 75 COVID-19 patients aged 60 and over who were hospitalized in the internal medicine clinic of Ankara Bilkent City Hospital between September 2021 and December 2022 were included.
Results: Clinical findings and results were compared between the patients who received montelukast and the control group. There was no statistically significant difference between two groups in terms of cough, dyspnea, gastroenteritis and oxygen theraphy requirement. There wa no significant difference between the groups in terms of the need for intensive care unit admission and mortality. The length of hospital stay was compared in both groups, it was 10.88±7.24 days in the control group and 10.51±5.44 days in the montelukast group, and there was no statistically significant difference between the groups. The laboratory parameters of the patients in both groups were compared. The neutrophil count and leukocyte count measured before hospitalization were found significantly lower in the patient group receiving montelukast ($p<0.05$). No significant difference was found in other laboratory parameters.
Conclusion: Although montelukast treatment has positive effects on prognosis in COVID 19 disease in the literature, a similar effect was not observed in the population aged 60 and over in our study. We did not find a beneficial effect of short-term montelukast use on prognosis in COVID-19 patients aged 60 and over. We thought that this was due to the low efficacy of montelukast in the elderly population. Our study is a rare study in that it examines montelukast treatment in the geriatric population with COVID-19.

Keywords: Montelukast, COVID-19, Elderly, Geriatrics, SARS-CoV-2

ÖZ

Amaç: COVİD-19 hastalarında klinik seyir asemptomatik vakalardan akut solunum sıkıntısı sendromuna (ARDS), solunum yetmezliğine ve çoklu organ fonksiyon bozukluğuna kadar değişebilmektedir. Klinik ilerlemenin temel olarak proinflamatuar sitokinlerin salınımına bağlı olduğu düşünülmektedir. En sık görülen semptomlar ateş, öksürük, halsizlik ve nefes darlığıdır. Mevsimsel alerjik rinit ve astım tedavisinde kullanılan montelukast, antiinflamatuar ve sitokin salgısını azaltıcı etkisi nedeniyle COVİD-19 enfeksiyonunda da kullanımını gündeme getirmiştir. Literatürde montelukast tedavisinin COVİD-19'un prognozu ve mortalitesi üzerine olumlu etkisi olduğunu gösteren pek çok çalışma bulunmaktadır. Ancak yaşlı hastalarda montelukast tedavisinin etkinliğini değerlendiren yeterli çalışma bulunmamaktadır.
Çalışmamızın amacı, COVİD-19 hastalığında 60 yaş ve üzeri hastalarda montelukast tedavisinin klinik ve laboratuvar etkinliğini değerlendirmek ve literatürdeki çalışmalardan farklılıklarını ortaya koymaktır.
Metod: Araştırmamız retrospektif, tek merkezli, gözlemsel bir çalışma olarak planlandı. Eylül 2021 ile Aralık 2022 tarihleri arasında Ankara Bilkent Şehir Hastanesi dahiliye kliniğinde yatarak tedavi gören 60 yaş ve üzeri 75 COVİD-19 hastasının tıbbi kayıtları dahil edildi.
Bulgular: Montelukast alan hastalar ile kontrol grubu arasında klinik bulgular ve sonuçlar karşılaştırıldı. Öksürük, dispne, gastroenterit ve oksijen tedavisi gereksinimi açısından gruplar arasında istatistiksel olarak anlamlı fark saptanmadı. Yoğun bakıma yatış ihtiyacı ve mortalite değerlendirildiğinde gruplar arasında anlamlı fark yoktu. Hastanede kalış süreleri her iki grupta karşılaştırıldığında kontrol grubunda 10,88±7,24 gün, montelukast grubunda 10,51±5,44 gün olup gruplar arasında istatistiksel olarak anlamlı fark saptanmadı. Her iki gruptaki hastaların laboratuvar parametreleri karşılaştırıldı. Montelukast alan hasta grubunda hastaneye yatmadan önce ölçülen nötrofil sayısı ve lökosit sayısı anlamlı olarak düşük bulundu ($p<0,05$). Diğer laboratuvar parametrelerinde anlamlı bir fark bulunamadı.
Sonuç: Literatürde montelukast tedavisinin COVİD-19 hastalığında prognoza olumlu etkileri olmasına rağmen çalışmamızda 60 yaş ve üzeri popülasyonda benzer bir etki gözlenmedi. Kısa süreli montelukast tedavisinin COVİD-19 nedeniyle hastaneye yatırılan 60 yaş ve üzeri hastaların prognozlarına olumlu etkisini bulamadık. Bunun yaşlı popülasyonda montelukastın etkinliğinin düşük olmasından kaynaklandığını düşündük. Çalışmamız, COVID-19'lu geriatrik popülasyonda montelukast tedavisini inceleyen ilk çalışmalardan biridir.

Anahtar Kelimeler: COVID-19, Montelukast, Yaşlı, Geriatri, SARS-CoV-2

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Introduction

Coronavirus disease 2019 (COVID-19) is a pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which broke out in 2019. At the onset of the disease, the use of various treatment regimens such as remdesivir and hydroxychloroquine was recommended, but there were conflicting reports in the literature about the effects of these agents. Therefore, studies on the use of effective agents for the treatment have continued (1, 2).

The clinical course in patients can vary from asymptomatic cases to acute respiratory distress syndrome (ARDS). The most common symptoms are cough, fever, malaise, shortness of breath and phlegm. Clinical progression is thought to be mainly due to the release of proinflammatory cytokines (3-5).

Interleukins (IL-6, IL-2, IL-10), procalcitonin (PRC), tumor necrosis factor alpha (TNF- a) and C-Reactive Protein (CRP) levels were detected high in COVID-19 patients (6). In addition, in severe COVID-19; cytokine release syndrome and ARDS, characterized by the uncontrolled release of proinflammatory cytokines, may develop (7). ARDS is the clinical definition of acute injury due to inflammation of the lungs, which is frequently observed in severe COVID-19 infection but not clearly understood due to its complex pathogenesis. The production of interleukins (IL-1/6/8) and TNF released in the early phase and the production of other proinflammatory cytokines in the late phase stimulate leukocyte migration to the infected tissue. Reactive oxygen radicals and proteases released from accumulated and activated leukocytes damage capillary endothelial tissue and alveolar epithelium (8, 9). Due to the increased release of inflammatory cytokines in COVID-19, the use of various anti-inflammatory agents in the treatment has come to the fore.

In the suppression of the proinflammatory process resulting from the damage of in-vitro astrocytes, decreased IL-6 levels were observed in the culture treated with curcumin and piperine compared to the control group (10). Additionally, it has been experimentally shown that the use of montelukast in an in vitro eosinophilic upper respiratory tract inflammation model has a significant inhibitory effect on the production of granulocyte macrophage colony stimulating factor (GM-CSF) and interleukins (IL-6/8) (11).

Coronovirus disrupts the gas exchange balance in alveolar cells with its cytotoxic effect (12). COVID-19 causes pneumonia by reaching alveolar angiotensin converting enzyme-2 (ACE-2) receptors (8, 9). Increased bradykinin level as a result of ACE inhibition may cause increased airway sensitivity and bronchoconstriction. Montelukast, as a selective Leukotriene D4 (LTD4) antagonist, reduces these effects of bradykinin accumulation with an unknown mechanism (13, 14). Montelukast, which is used in the treatment of seasonal allergic rhinitis and asthma, has brought its use in COVID-19 infection due to its previously mentioned eosinophilic anti-inflammatory and cytokine secretion-reducing effect (15, 16).

There are studies suggesting that montelukast can be used in the treatment of COVID-19 (1, 17-19). However, the number of studies evaluating the efficacy of montelukast treatment on elderly patients in COVID-19 is insufficient. The efficacy of montelukast treatment in elderly asthma patients differs from adult asthma patients (20). The aim of our study is to evaluate the clinical and laboratory efficacy of montelukast therapy in patients aged 60 and over in COVID-19 disease.

Material and Method

Our research was planned as a retrospective, single-center, observational study. In this study, the medical records of 75 COVID-19 patients aged 60 and over who were hospitalized in the internal medicine clinic of Ankara Bilkent City Hospital between September 2021 and December 2022 were included. Diagnosis of COVID-19 was confirmed with a reverse transcription polymerase chain reaction (RT-PCR) test from nasopharyngeal swab. Thirty-five patients who were treated with montelukast before hospitalization for COVID-19 were defined as the montelukast treatment group. 40 patients who had never received montelukast treatment were determined as the control group.

The definition of montelukast use was defined as patients using a therapeutic dose of 10 mg once daily in addition to standard treatment during their hospitalization. Patients aged 60 years and older hospitalized for COVID-19 were randomized from the system in both groups.

The patients were not followed up after discharge. Age, gender, prognosis, patient clinic, laboratory parameters, mortality, length of hospital stay and the need for intensive care were examined. Clinical findings and symptoms were evaluated during the hospitalization period. Laboratory findings were evaluated as the hospitalization day of the patients and the parameters checked at discharge. In our hospital, the need for ICU is determined as patients with a MODS (multiple organ dysfunction score) of 1 and above. Mortality was evaluated during the hospitalization period.

Statistical analysis

Statistical analyzes were performed using the SPSS 25.0 program. The conformity of the variables to the normal distribution was evaluated with histogram graphs and Kolmogorov-Smirnov test. While descriptive analysis are presented; mean, standard deviation, median min-max values were used. Categorical variables were compared with the Chi-Square Test. The Mann Whitney U Test was used when evaluating non-normally distributed (non-parametric) variables between two groups. While the change in measured values was evaluated between groups, Repeated Measures Analysis was used. P-values below 0.05 were considered as statistically significant results.

Results

Clinical findings and outcomes were compared between the montelukast group and the control group. There was no statistically significant difference between the groups in terms of cough, dyspnea, gastroenteritis and oxygen demand. There was no significant difference between two groups in terms of intensive care admission and mortality. The data are summarized in Table 1.

Table 1. Clinical findings and outcomes

	Montelukast				
	No		Yes		p
	n	%	n	%	
Female	19	(47.50)	16	(45.71)	0.877
Male	21	(52.50)	19	(54.29)	
O2 demant	22	(55.00)	19	(54.29)	0.951
Dyspnea	22	(55.00)	19	(54.29)	0.951
Cough	28	(70.00)	21	(60.00)	0.364
Gastroenteritis	28	(70.00)	21	(60.00)	0.364
Mortality	4	(10.00)	3	(8.57)	0.832
ICU admission	3	(7.50)	5	(14.29)	0.342

Chi-Square Test
p: Statistical difference between the groups

The length of hospital stay was compared in both groups, with an average of 10.88±7.24 days in the control group, and 10.51±5.44 days in the group receiving montelukast, and no statistically significant difference was found between the groups. When the groups were compared, no significant difference was found in terms of age. The data are summarized in Table 2.

The laboratory parameters of the patients in both groups were compared. The neutrophil count and white blood cell count measured before treatment were significantly lower in the montelukast treatment group. (p=0.022, p=0.016). No significant difference was found in other laboratory parameters. When the p^2 values were compared, there was no difference between the groups. The data are summarized in Table 3.

Table 3. Comparison of laboratory parameters between two groups

	Montelukast			
	No	Yes	p^1	p^2
	Mean±s.s.	Mean±s.s.		
Neutrophil 1 (x10^9/L)	6.38±3.28	4.66±3.05	0.022	0.525
Neutrophil 2 (x10^9/L)	7.06±3.99	6±3.34	0.220	
Lymphocyt 1 (x10^9/L)	1.01±0.53	1.16±0.57	0.252	0.496
Lymphocyt 2 (x10^9/L)	1.62±1.17	1.96±1.34	0.244	
Procalcitonin 1 (mg/dl)	0.16±0.18	0.21±0.41	0.485	0.342
Procalcitonin 2 (mg/dl)	0.39±1.89	0.13±0.27	0.433	
Fibrinogen 1 (mg/dl)	4.23±1.54	4.38±1.63	0.681	0.280
Fibrinogen 2 (mg/dl)	3.44±1.26	4.04±1.38	0.052	
NLR1	6.86±6.62	6.87±6.7	0.577	0.496
NLR2	7.27±9.44	5.77±5.86	0.953	
Eosinophil 1 (x10^9/L)	0.05±0.06	0.05±0.06	0.800	0.589
Eosinophil 2 (x10^9/L)	0.09±0.13	0.08±0.09	0.957	
WBC 1 (x10^9/L)	8.07±3.26	6.29±3.69	0.016	0.757
WBC 2 (x10^9/L)	9.43±4.09	7.98±4.5	0.104	
CRP 1 1 (mg/dl)	34.83±58.74	30.7±65.32	0.823	0.773
CRP 2 (mg/dl)	8.85±21.43	0.71±2.12	0.709	
Ferritin 1 (mg/dl)	316.91±336.99	280.57±297.41	0.592	0.862
Ferritin 2 (mg/dl)	356.74±655.06	307.34±400.24	0.603	
D-Dimer 1 (mg/dl)	2.62±6.63	0.9±0.61	0.811	0.738
D-Dimer 2 (mg/dl)	2.94±7.44	0.74±0.63	0.224	

[1]Independent T-Test
[2]Repeat Measurements Analysis
p^1: Statistical difference between the groups in terms of laboratory values
p^2: Statistical value showing the relationship between pre- and post-treatment laboratory parameters in the groups
1: Parameter before Covid-19 standard treatment
2: Parameter after Covid-19 standard treatment

Table 2. Comparison of age and length of hospital stay between groups

	Montelukast				p
	No		Yes		
	Mean±s.s.	Median (Min-Max)	Ort±s.s.	Median (Min-Max)	
Lenght of Hospital Stay (day)	10.88±7.24	9 (2-32)	10.51±5.44	9 (3-28)	0.810
Age (year)	65.35±4.31	64 (60-75)	66.14±5.04	64 (60-75)	0.465

İndependent t test
p: Statistical difference between the groups

Discussion

There are studies suggesting that leukotriene antagonists can be used in the treatment of COVID-19 disease (1, 17-19, 21-22). There is no study in the literature evaluating the efficacy of montelukast treatment in elderly COVID-19 patients. There are studies in the literature showing that the effectiveness of montelukast treatment in asthma patients differs between adults and the elderly (20,23). In our study, we examined whether this difference exists in the treatment of elderly COVID-19 patients.

In our study, there was no significant difference in prognosis, mortality and laboratory parameters after montelukast treatment in patients over the age of 60 who were diagnosed with COVID-19 compared to the control group. Many studies in the literature stated that treatment had positive effects on prognosis, laboratory and mortality (1,17-19, 21-22). In the study of Schihilone et al., it was emphasized that further studies should be conducted on the long-term use of montelukast in elderly asthma patients. They noted that available data on the role of montelukast in the treatment of elderly asthmatics in the study do not indicate a specific role for this drug in this age group. (24). We thought that the lack of a similar effect of montelukast treatment in our study may be due to the low efficiency of the treatment in elderly patients.

It has been shown in the literature that these drugs have protective effects after cerebral ischemia and reperfusion (25). We suggest examining the effects of these drugs on elderly patients in Covid 19-induced cerebral ischemia.

Gastroenteritis has been reported as a side effect of montelukast treatment in the literature (26). However, in our study, inconsistent with the literature, we could not detect a significant difference between the treatment group and the control group. In the study of Scichilone et al., elderly patients had the highest incidence of headache, abdominal pain, nausea and diarrhea (24). We recommend studying the effect of montelukast treatment in geriatric patients with diarrhea in large patient groups. Because elderly patients are more sensitive to electrolyte disturbances due to Covid 19-related nausea, vomiting and diarrhea.

Kerget et al. reported that patients receiving montelukast treatment had significantly lower levels of lactate dehydrogenase, D-dimer(18). However, no significant difference was found in our study. In addition, we did not detect any significant change in these values before treatment and before discharge.

Limitations

There were some limitations in our study. Our study includes symptoms at the time of hospitalization. We could not examine the effect of montelukast treatment on these symptoms. In addition, the small number of patients was our limitation. The patients in our study had no lung disease diagnosed. However, we thought that there may be patients with previously undiagnosed lung disease. In addition, the fact that the mean age of our patient groups matched the early geriatric population was a limitation of our study. We recommend that different studies should be conducted on elderly geriatric patients.

Conclusion

In conclusion, many side effects of montelukast treatment are similar to the symptoms detected in COVID-19. We recommend conducting large-scale studies investigating the effects of montelukast treatment on these symptoms in elderly patients. Although montelukast treatment has positive effects on clinical and prognosis on many COVID-19 cases in the literature, we did not detect this efficacy in the population over 60 years of age in our study. In the study of Sánchez et al. montelukast treatment was found effective in long-term use in elderly patients, unlike younger patients (27). Therefore, we recommend using montelukast therapy for a longer period of time in patients with COVID-19 and further comprehensive studies should be conducted in this regard.

Our study is one of the first to examine montelukast therapy in the geriatric population with COVID-19. Unlike studies involving all age groups, we did not find a positive effect on the prognosis and clinic in patients over 60 years of age.

Ethical Approval

Ethical approval for the study was granted by the Ethics Committee of Ankara City Hospital (Date: 12/04/2023, Number: E2-23-3911).

Authorship Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

Conflict of Interests

The authors have no conflicts of interest to declare.

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ORIGINAL ARTICLE

The Effect of Electromagnetic Field Exposure on Fetal Development

Elektromanyetik Alan Maruziyetinin Fetal Gelişime Etkisi

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ABSTRACT

Aims: The aim of our study is to evaluate the effect of electromagnetic field exposure during pregnancy on fetal anthropometric measurements by means of ultrasonography.
Methods: This is a cross sectional study. The study was conducted among 261 pregnant women who applied to the Obstetrics and Gynecology outpatient clinic. A face-to-face questionnaire was applied to 261 volunteer pregnant women and fetal anthropometric measurements (head circumference (HC), abdominal circumference (AC), femur length (FL), biparietal diameter (BPD)) were performed by transabdominal ultrasound.
Results: The mean age of the pregnant women in this study was 29.65 ± 6. Of the pregnant women 140 (53.6%) were between the ages of 25-34, 260 (99.6%) were married, 85 (32.6%) were high school graduates and 184 (70.5%) were housewives. The income of 116 (44.4%) pregnant women was equal to their expenses. The frequency of those exposed to electromagnetic fields at home is 98.5%. There was no difference between FL, AC, HC and BPD values and electromagnetic field exposure at home, exposure to x-ray or tomography (p>0.05). It was observed that FL, HC, BPD ultrasonographic measurement values were significantly lower in people exposed to electromagnetic field at work compared to those not exposed to electromagnetic field at work.
Conclusion: It was observed that FL, HC, BPD ultrasonographic measurement values were significantly lower in people exposed to electromagnetic field at work. There are studies that show the negative effects of electromagnetic field on the fetus, especially during pregnancy, although there is no definitive evidence. Studies to be carried out on this subject can be a guide for protection from the negative effects of electromagnetic field.

Keywords: electromagnetic field, radiation, fetal development, fetal growth, maternal exposure, environmental health

ÖZ

Amaç: Çalışmamızın amacı gebelikte elektromanyetik alan maruziyetinin fetal antropometrik ölçümler üzerine etkisini ultrasonografi yardımıyla değerlendirmektir.
Yöntemler: Bu kesitsel bir çalışmadır. Araştırma Kadın Hastalıkları ve Doğum polikliniğine başvuran 261 gebe ile gerçekleştirildi. 261 gönüllü gebeye yüz yüze anket uygulandı ve transabdominal ultrason ile fetal antropometrik ölçümler (baş çevresi (HC), karın çevresi (AC), femur uzunluğu (FL), bipariyetal çap (BPD)) yapıldı.
Bulgular: Araştırmaya katılan gebelerin yaş ortalaması 29,65±6,140 idi. Gebelerin 140'ı (%53,6) 25-34 yaş aralığında, 260'ı (%99,6) evli, 85'i (%32,6) lise mezunuydu. 184'ü (%70,5) ev hanımıydı. 116 (%44,4) gebenin geliri harcamalarına eşitti. Evde elektromanyetik alanlara maruz kalanların sıklığı %98,5'ti. FL, AC, HC ve BPD değerleri ile evde elektromanyetik alan maruziyeti, röntgen veya tomografiye maruz kalma arasında fark bulunamadı (p>0,05). İş yerinde elektromanyetik alana maruz kalan kişilerde FL, HC, BPD ultrasonografik ölçüm değerlerinin iş yerinde elektromanyetik alana maruz kalmayanlara göre anlamlı derecede düşük olduğu görüldü.
Sonuç: İş yerinde elektromanyetik alana maruz kalan kişilerde FL, HC, BPD ultrasonografik ölçüm değerlerinin anlamlı derecede düşük olduğu görüldü. Kesin bir kanıt bulunmamakla birlikte, özellikle hamilelik döneminde elektromanyetik alanın fetüs üzerindeki olumsuz etkilerini gösteren çalışmalar bulunmaktadır. Bu konuda yapılacak çalışmalar elektromanyetik alanın olumsuz etkilerinden korunmak için yol gösterici olabilir.

Anahtar Kelimeler: elektromanyetik alan, radyasyon, fetal gelişim, fetal büyüme, maternal maruziyet, çevre sağlığı

Introduction

A person is both affected by the environment he lives in and can affect the environment. People are exposed to electromagnetic field (EMF) from basic radio, electrical and telecommunications stations, as well as direct radiation from individuals, such as cell phones. Each person will potentially be exposed to several EMF sources simultaneously(1). As a result of the development of technology over the years, the concept of electromagnetic field, which is included in our lives in many fields, has gained considerable importance. Radiation can be grouped into non-ionizing radiation, which is considered less harmful, and ionizing radiation, which is potentially harmful to cells and DNA. Ionizing radiations are more harmful because they cause DNA damage by breaking chemical bonds. Ionizing radiation causes mutagen, carcinogenic or teratogenic effects, cataracts, infertility problems, premature aging and skin problems in humans. The risk of exposure is greatest in the 'in utero' period (2–4). Non-ionizing radiations, on the other hand, lack the energy needed to break chemical bonds. Examples of this type of radiation are visible light, ultraviolet light, infrared light, radio waves and microwaves. Non-ionizing radiation can have harmful effects on the body(2,3). In 2011, an expert working group of the International Agency for Research on Cancer (IARC) classified

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radiofrequency radiation emitted by mobile phones and other wireless devices as a Group 2B ("probable") human carcinogen(5). There are studies showing that the electromagnetic field increases the risk of cancer (6,7).

Pregnancy, infancy and childhood are critical periods of vulnerability, especially for the rapidly developing brain(8). Although few studies have been conducted on human exposure to non-ionizing electromagnetic fields in utero, there are numerous negative effects on pregnancy and the health of offspring who are regularly exposed to electromagnetic field (9). While some studies have not found a relationship between radiation exposure during pregnancy and the weight of newborn babies (10,11), some studies have found a relationship between the exposure of pregnant women to EMF during pregnancy and problems such as the risk of miscarriage and fetal development disorders (12–14). The risk of miscarriage, stillbirth, and birth defects was not significantly higher among pregnant women who lived near electromagnetic fields compared to the control group(15).

Examples of common sources of electromagnetic fields are radio and TV broadcast antennas, Wi-Fi access points, routers and clients (e.g. smartphones, tablets), wireless and mobile devices, base stations (16). Researches on the relationship between cell phone use and pregnancy has shown conflicting results. In a study conducted in Turkiye, the pregnancy period was found shorter in mothers using mobile phones and computers(17). In a study conducted with four birth cohorts, a relationship was shown between mobile phone use and premature birth and shortening of the pregnancy period, but no relationship was found with fetal growth(18). In a cohort conducted in Norway, no relationship was found between the mother's pre-pregnancy exposure to mobile phones and pregnancy outcomes such as premature birth and low birth weight(19). A study conducted in Turkiye showed that watching TV, mobile phone usage and living near a base station during pregnancy may have negative effect on the anthropometric measurements of the newborn (20).

In a review that collected studies examining the effects of electromagnetic field emitted by mobile phones and other wireless devices, symptoms related to learning, memory, attention and behavior problems and diseases such as autism, attention deficit movement disorder were associated(21).

This study is different in that it evaluates the effects of electromagnetic field exposure on the fetus during the prenatal period. The aim of our study is to evaluate the effect of electromagnetic field exposure during pregnancy on fetal anthropometric measurements by means of ultrasonography.

Material and Methods

This is a cross-sectional study. The study was conducted among pregnant women who applied to the Obstetrics and Gynecology outpatient clinic of Adıyaman Training and Research Hospital.

The questionnaire form was prepared by reviewing the necessary literature. The applied questionnaire consists of 27 questions. In addition to the questions about sociodemographic information, there are questions about the sources of electromagnetic fields to which exposure at home and, if they work, exposure at work. Inclusion criteria in the study group are pregnant women aged 18 and over admitted to the obstetrics clinic.

The people included in the study were women who applied consecutively and accepted the study as of 15/04/2022. The formula $n= Nt^2pq/ d^2 (N-1)+t^2pq$ was used to determine the number of people to be sampled, and the number of people to be sampled was calculated as 273 people with a 95% confidence interval and 5% deviation. Necessary permission was obtained from Adıyaman University Non-Interventional Clinical Research Ethics Committee (decision dated 15.03.2022 and numbered 2022/3-21). Starting on the first working day after the permission was granted, 95.6% (261) of the targeted number of people has been reached. A face-to-face questionnaire was applied to 261 pregnant women on voluntary basis and fetal anthropometric measurements (head circumference (HC), abdominal circumference (AC), femur length (FL), biparietal diameter (BPD)) were performed by transabdominal ultrasound.

Statistical package (SPSS 12.00) program was used in the evaluation of the data. Descriptive variables were provided as numbers and percentages. Chi-Square and Fischer's exact Chi-Square tests were used to explore the correlations between the variables in the categorical structure. The means were compared using one-way ANOVA and the t test. Means were provided with standard deviation. The results were evaluated at 95% confidence interval and $p<0.05$ was accepted as significant.

Results

The mean age of the pregnant women is 29.65 ± 6. Of the pregnant women 140(53.6%) were between the ages of 25-34, 260 (99.6%) were married, 85 (32.6%) were high school graduates and 184 (70.5%) were housewives. The income of 116 (44.4%) pregnant women was equal to their expenses (Table 1).

The mean number of pregnancies was 3.0 ± 2.0, and the number of births was 1.7 ± 1.5. Of the pregnant women 106 (40.6%) had miscarriage before. 70 (26.8%) of the pregnant women had a chronic disease before pregnancy.

The frequency of those exposed to electromagnetic fields at home is 98.5%. 252 (96.9%) of the pregnant women were using the phone. 249 (95.8%) of the pregnant women had a TV at home, 148 (56.9%) had a hair dryer, 148 (56.9%) had a wi-fi modem, 95 (36%, 5) stated that they had air conditioning, 81 (31.2%) had a computer and 63 (24.2%) had a microwave oven. The houses of 39 (14.9%) of the pregnant women were close to the base station and the houses of 38 (14.6%)

Table 1. Certain sociodemographic characteristics of pregnant women.

	n, %
Age	
<24 years	57 (21.8)
25-34 years	140 (53.6)
≥35 years	64 (24.5)
Marital Status	
Married	260 (99.6)
Divorced	1 (0.4)
Educational Status	
Illiterate	22 (8.4)
Primary School Graduate	44 (16.9)
Secondary School Graduate	41 (15.7)
Highschool Graduate	85 (32.6)
University Graduate	69 (26.4)
Employment Status	
Housewife	184 (70.5)
Working	77 (29.5)
Household Income	
Income more than expense	69 (26.4)
Income less than expense	76 (29.1)
Income equal to expense	116 (44.5)

difference in fetal FL, AC, HC and BPD measurement values of pregnant women who had exposure to x-ray or tomography compared to the group that had no exposure (p>0.05) (Table 2).

When the pregnant women's home was close to the high-voltage line and fetal anthropometric measurement values were examined, there was no difference between the measurement values of those who were close to the high-voltage line and those who were not (p>0.05).

155 (59.4%) of the pregnant women had a television and 56(21.5%) had a wi-fi modem in the room where they spent most of their time. 186(%74,7) of the pregnant women did not turn off the wi-fi modem at night.

There was no difference between the presence of television and modem in the room where the most time was spent and education level (p>0.05). As the education level increases, the situation of turning off the modem at night increases (p<0.05).

Discussion

Fetal effects of electromagnetic field exposure during pregnancy have been tried to be related to pediatric measurements mostly made after birth (22,23). In our study, the investigation of this relationship by means

Table 2: The effect of electromagnetic field exposure on fetal anthropometric measurements.

Electromagnetic field exposure status		FL		AC		HC		BPD	
		Mean±SD, p		**Mean±SD, p**		**Mean±SD, p**		**Mean±SD, p**	
EMF exposure at work	Yes	32.8±3.4	t= 3.72 **p<0.01**	32.3±3.9	t=1.347 p>0.05	33.5±3.3	t=3.639 **p<0.01**	33.2±3.4	t=3.478 **p<0.01**
	No	34.7±3.7		36.3±25.4		35.2±3.4		34.9±3.7	
EMF exposure at home	Yes	34.1±3.7	t=0.194 p>0.05	35.2±21.5	t=0.092 p>0.05	34.7±3.4	t=0.269 p>0.05	34.4±3.7	t=0.222 p>0.05
	No	34.5±3.0		34.2±3.4		35.2±3.5		34.0±3.4	
Exposure to X-ray or tomography	Yes	32.9±4.2	t=1.062 p>0.05	32.7±3.9	t=0.345 p>0.05	33.5±4.0	t=1.041 p>0.05	32.8±4.0	t=1.295 p>0.05
	No	34.2±3.6		35.2±21.7		34.7±3.4		34.5±3.7	

Abbreviations: EMF: Electromagnetic Field, SD: Standard Deviation, FL: Femur length, AC: Abdominal Circumference, HC: Head Circumference, BPD: Biparietal Diameter

Independent sample t test was used to analyze the data for Table 2.

were close to the high voltage line.

When fetal anthropometric measurements of pregnant women with exposure to electromagnetic fields at work were examined, FL, HC and BPD values were lower than those without exposure to electromagnetic fields at work (p<0.05) (Table 2).

When fetal anthropometric measurements of pregnant women exposed to electromagnetic field at home were examined, there was no difference in FL, AC, HC and BPD values compared to those who were not exposed to electromagnetic fields at home (p>0.05) (Table 2).

When the exposure status of pregnant women to x-ray or tomography and fetal anthropometric measurements were examined, there was no

of ultrasonography before the birth may be guiding in the study of the early effects of the electromagnetic field.

In a study conducted in 2019, the most common sources of electromagnetic fields that pregnant women were exposed to during pregnancy were listed as television (92.8%), mobile phone (91.3%), and wi-fi (52%). In the same study, while 28.7% of the participants stated that their home was near the base station, this rate was 14.9% in our study (22). In our study, pregnant women stated that they were most frequently exposed to sources such as telephone (96.9%), television (95.8%), and wi-fi modem (56.9%). Sources of electromagnetic fields exposed at home are of similar frequency.

In a study examining the data of pregnant women who

were exposed to electromagnetic fields due to high voltage line and those who were not, no significant difference was found between the two groups in terms of birth weight, height and head circumference values of the babies (24). In a study conducted in England, it was shown that maternal residence close to electromagnetic field sources is associated with inadequate fetal growth (25).

In a descriptive study examining the proximity of the houses to the high voltage lines and the presence of symptoms, the proximity to the high voltage line and the electromagnetic field values measured at the house showed a positive correlation, but no relationship was found between these values and symptoms (26).

In our study, when the pregnant women's home was close to the high voltage line and fetal anthropometric measurement values were examined, no statistically significant difference was found between those who were close to the high voltage line and those who were not ($p>0.05$). This may be due to the fact that we have done a study on the statements of individuals.

In a cohort study conducted in Norway, no evidence of adverse neurodevelopmental effects of prenatal cell phone use was reported (27).

In a different study, those who were more exposed to mobile phones had a shorter gestational period and increased risk of preterm birth compared to those who were less exposed (28). Babies of pregnant women who use more than one phone during pregnancy have lower birth weight and shorter stature than babies of pregnant women who use one phone (22).

In a study involving 138 women in China, it was stated that exposure to electromagnetic field sources such as mobile phones, televisions during the first trimester of pregnancy significantly increases the risk of embryo development arrest (29). In a cohort study, it was found that exposure to video display terminal use at home or at work during pregnancy was not associated with fetal development retardation (30). In a birth cohort conducted in China, exposure to high prenatal electromagnetic field exposure was associated with growth in baby girls but not in boys (23).

In our study, while the electromagnetic field exposure of pregnant women at home did not make a significant difference in fetal measurements, the electromagnetic field exposed by pregnant women at work caused significant changes in fetal measurements such as femur length, head circumference, and biparietal diameter.

More studies are needed to evaluate the effects of home or work-induced electromagnetic field exposure during pregnancy on fetal development and to raise awareness in pregnant women.

Conclusion

It was observed that FL, HC, BPD ultrasonographic measurement values were significantly lower in people exposed to electromagnetic field at work compared to those not exposed to electromagnetic field at work. There are studies that show the negative effects of electromagnetic field on the fetus, especially during pregnancy, although there is no definitive evidence. Studies to be carried out on this subject can be a guide for protection from the negative effects of electromagnetic field.

Ethics Committee Approval

This research complies with all the relevant national regulations, institutional policies and is in accordance the tenets of the Helsinki Declaration and has been approved by the Adıyaman University Non-Interventional Research Ethics Committee (Decision dated 15.03.2022 and numbered 2022/3-21).

Informed Consent

All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions

F.K.: Conceptualization, Methodology, Software, Validation, Formal analysis, Writing - Review & Editing. M.C.N.: Resources, Visualization, Data Curation. E.F.T.Ç.: Formal analysis, Investigation, Writing - Original Draft.

Conflict of Interest

The authors have no conflict of interest to declare.

Financial Disclosure

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Limitations

Limitations of the study are that electromagnetic field exposure was not measured objectively with a device in our study but was only questioned through a questionnaire. The fact that this study was conducted in a single center limited its generalizability to the community. The subject studied needs further research.

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ORIGINAL ARTICLE

Factors Related to Middle-Long-Term Mortality in Acute Kidney Injury

Akut Böbrek Hasarında Orta-Uzun Dönem Mortaliteyle İlişkili Faktörler

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ABSTRACT

Aim: To determine the clinical and laboratory parameters that affect the mid-long term mortality of patients hospitalized for acute kidney injury (AKI).
Material and methods: Patients hospitalized with the diagnosis of AKI in the intensive care unit and clinic of Nephrology for four years were retrospectively screened. The files of these patients were scanned. Demographic data, comorbidities, vital signs and laboratory parameters were scanned. It was determined in terms of factors affecting mortality in these patients (living and dying) over a 4-year period.
Results: The effects of the variables found significant [age, presence of hypertension and coronary artery disease (CAD), sedimentation, C-reactive protein (CRP), urea, potassium (K), magnesium (Mg), pH and CRP-albumin ratio (CAR)] on mortality was performed using multiple logistic regression analysis, which was used to identify the independent risk factors of mortality. Multiple logistic regression analysis using Stepwise selection method revealed that increasing age (IQR=1.04, 95% CI=1.01 – 1.07, p=.004), presence of CAD (IQR =2.16, 95% CI=1.16 – 4.02, p=.016), increased Mg (IQR =2.64, 95% CI=1.18 – 5.92, p=.018) and K (IQR =1.70, 95% CI=1.21 – 2.41, p=.002) were independent risk factors for mortality. The accuracy rate for the predictive performance of this prediction model in predicting mortality was 71.1%, with a sensitivity of 26.5%, a specificity of 90%, and an AUC of 0.753.
Conclusion: In our predictive model, in the medium-long term, we found old age, the presence of coronary artery disease, increased K and Mg as the independent risk factors for mortality in AKI patients.

Keywords: Acute kidney injury, Age, Comorbidity, Mortality

ÖZ

Amaç: Akut böbrek hasarı (ABH) nedeniyle hastaneye yatırılan hastaların orta-uzun dönem mortalitesini etkileyen klinik ve laboratuvar parametrelerini belirlemek.
Gereç ve yöntem: ABH tanısıyla yoğun bakım ünitesinde ve Nefroloji kliniğinde dört yıl boyunca yatan hastaların dosyaları geriye dönük olarak tarandı. Demografik veriler, komorbiditeler, vital ve laboratuvar parametreleri incelendi. Bu hastalarda 4 yıllık süreçte mortaliteyi etkileyen faktörler açısından belirlendi.
Bulgular: Tek değişkenli analiz ile anlamlı bulunan değişkenlerin (yaş, hipertansiyon ve koroner arter hastalığı (KAH) varlığı, sedimantasyon, C-reaktif protein (CRP), üre, potasyum (K), magnezyum (Mg), pH ve CRP-albümin oranı (CAR)) mortalite üzerine etkileri , mortalitenin bağımsız risk faktörlerini belirlemek için kullanılan çoklu lojistik regresyon analizi kullanılarak yapıldı. Multipl lojistik regresyon analizi sonucu artan yaş (IQR=1.04, %95 CI=1,01 – 1,07, p=0,004), KAH varlığı (IQR =2,16, 95% CI=1,16 – 4,02, p=0,016), artmış Mg (IQR =2,64, %95 CI=1,18 – 5,92, p) =0,018) ve K (IQR =1,70, 95% GA=1,21 – 2,41, p=0,002) mortalite için bağımsız risk faktörleri olarak saptandı. Bu tahmin modelinin mortaliteyi öngörmedeki prediktif değeri %71,1, sensitivitesi %26,5, sensitivitesi %90 ve AUC 0,753 idi.
Sonuç: Orta-uzun vadede ABH hastalarında ileri yaş, koroner arter hastalığı varlığı, K ve Mg artışını mortaliteyi etkileyen faktörler olarak bulduk.

Anahtar kelimeler: Akut böbrek hasarı, Yaş, Komorbidite, Mortalite

Introduction

The incidence of AKI, regardless of requiring dialysis, is increasing in the World.1 Aging of the population, high comorbidities, increased AKI awareness, increased nephrotoxic drugs and increased surgical procedures are the factors that increase the incidence.2

AKI is related to short- and long-term undesirable consequences. While it increases short-term mortality, the long-term mortality is significantly higher in those with AKI compared to those who do not have.3 Long-term mortality is generally considered as mortality after 3 months. In a review evaluating the long-term mortality of AKI patients, the mortality rate was found as 15-74%, but only around 60% when intensive care patients were included. Factors affecting mortality were determined as old age, presence of comorbidity and incomplete recovery of kidney functions.4 The fact that AKI affects not only the kidneys but also other vital organs such as the heart and lungs may be associated with a long-term increase in mortality.

In this study, we aimed to determine the factors that are effective in long-term mortality by retrospectively screening the patients hospitalized in our clinic and intensive care unit with the diagnosis of AKI between 2018-2022.

Material and Methods

After the approval of local ethics committee (2023/87), the study was started. Between January 2018 and

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December 2022, the files of the patients hospitalized in our Nephrology clinic and intensive care clinic with the AKI diagnostic code (N17 and its subfractions) were scanned. Patients that did not meet the diagnosis of AKI according to KDIGO 2012 criteria were excluded from the study. Demographic data, comorbidities (diabetes mellitus-DM, hypertension-HT, coronary artery disease-CAD, congestive heart failure-CHF, chronic obstructive pulmonary disease-COPD, chronic kidney disease-CKD, atrial fibrillation-AF), vital signs at admission, length of hospital stay, laboratory parameters at the time of hospitalization (hemogram, biochemistry, hemoglobin A1C, venous blood gas, C reactive protein, procalcitonine, sedimentation, ferritin, vitamin D level, whether there was reproduction in blood, urine, sputum or swab cultures) of the patients were recorded from their files. For the patients who died, the duration until death was recorded. Patients who died due to cancer or Covid 19 were excluded from the study.

Statistical analysis

All statistical analysis were performed with R version 4.1.2 (The R Foundation for Statistical Computing, Veinna, Austria; https://www.r-project.org) Statistical Language. Shapiro-Wilk ln normality test and Q-Q plots were used to check the normality of the data. Levene test was also used to assess the homogeneity of the variances. Numerical variables were expressed as mean ± standard deviation, median with range (min – max) or median with interquartile [25th percentile – 75th percentile], as appropriate. Categorical variables were also defined as numbers (n) and percentage (%). A Welch's t-test, Mann-Whitney U test and Independent samples t-test was utilized to determine whether there was a statistically significant difference in numerical variables according to the demographical and clinical characteristics of patients with and without survivors. Besides, a Pearson chi-square test, chi-square test Yates continuity correction and Fisher's exact test was conducted to examine if there was a significantly association between patient's groups with and without survivors in terms of categorical variables in demographical and clinical characteristics. The effects of the variables found significant (age, presence of hypertension and CAD, sedimentation, CRP, urea, K, Mg , pH and CAR) by univariate analysis on mortality was performed using multiple logistic regression analysis, which was used to identify the independent risk factors of mortality. Odds ratios were represented with 95% confidence intervals. For the diagnostic performance of the prediction model obtained by multiple logistic regression analysis in predicting of mortality, the area under the curve, accuracy, sensitivity and specificity values of this model were calculated. A two-tailed p-value less than .05 was considered as statistically significant.

Results

The mean age (75.81 ± 10.08 vs. 68.28 ± 15.63, p<.001), length of hospitalization (10 days vs. 7 days, p=.003), presence of hypertension (79.4% vs. 64.4%, p=.037) and CAD (60.3% vs. 37.5%, p=.002), sedimentation level (40 vs. 29.5, p=.028), urea (136vs. 122, p=.003), K (5.24 ± 0.91 vs. 4.66 ± 0.93, p<.001) and Mg (2.18 ± 0.35 vs. 2.04 ± 0.41, p=.020) values were significantly higher in patients who were non-survivors compared to the patients who were survivors, whereas follow-up time (12 days vs. 34 days, p<.001), saturation at admission (94 vs. 96, p=.012), CRP (26.1 vs. 63.5, p=.020) and pH (7.31 ± 0.09 vs. 7.33 ± 0.08, p=.048) levels and CAR (7.95 vs. 19.76, p=.031) values were lower.

The effects of the variables found significant (age, presence of hypertension and CAD, sedimentation, CRP, urea, K, Mg, pH and CAR) by univariate analysis on mortality was performed using multiple logistic regression analysis, which was used to identify the independent risk factors of mortality. Stepwise variable selection method was used to eliminate the variables that was not statistically significant. Multiple logistic regression analysis using stepwise selection method revealed that increasing age (p=.004), presence of CAD (p=.016), increased Mg (p=.018) and K (p=.002) were independent risk factors for mortality (Table 2). The accuracy rate for the predictive performance of this prediction model in predicting mortality was 71.1%, with a sensitivity of 26.5%, a specificity of 90%, and an AUC of 0.753 (Figure 1).

Discussion

AKI affects 13.3 million people worldwide each year, causing 1.7 million deaths.5 In a meta-analysis covering a large number of studies, the incidence was found as 22% and in a study including 33 countries, it was found as 57%. 6, 7 AKI is a factor that increases short-term (within 90 days) and long-term (after 90 days) mortality in hospital or after discharge from the hospital. In-hospital mortality reaches 40-60% in patients who develop AKI requiring dialysis in the intensive care unit. 8 In a study involving more than 5 million patients, short-term mortality was examined in those with and without AKI. Mortality was 3 times higher in patients with AKI compared to those without AKI. 9 The underlying comorbidities and infection were effective factors in short-term mortality.

Long-term mortality also increases after AKI. In a study involving over 800 patients who underwent cardiac surgery and those who did not undergo AKI after surgery were compared. Mortality was 1.6 times higher in those who had AKI compared to those who did not have.10 In a meta-analysis of 47.017 people, the relative risk of mortality was 2.5 times higher in those who had AKI.3

In this study, the mean follow-up period after discharge was 27.4 ± 16 months, and the mortality rate was 29.7%. Stevens et al. found 2-year mortality as 69% and 3-year mortality as 72% in patients with AKI associated with sepsis. However, in their study, patients were not followed up by a nephrologist.11 Mortality may be significantly higher in our study, both for this reason and because they included only patients with sepsis. In another study, mortality rates were found similar to the study of Stevens et al.12 In this study, only patients

Table 1. Demographical and clinical characteristics of the patients.

	Survivors (n=160)	Non-survivors (n=68)	p-value
Demographical characteristics			
Age (years), mean ± SD	68.28 ± 15.63	75.81 ± 10.08	<.001[1]
Gender (F/M), n (%)	83 (51.9) / 77 (48.1)	39 (57.4) / 29 (42.6)	.448[2]
Follow-up time, median (month) (range)	34 (1 – 57)	12 (1 – 58)	<.001[3]
Length of stay at hospital, median (range) (day)	7 (2 – 35)	10 (2 – 45)	.003[3]
Pneumonia, n (%)	23 (14.4)	15 (22.1)	.219[4]
Cough, n (%)	10 (6.3)	7 (10.4)	.412[4]
Sputum, n (%)	9 (5.6)	4 (5.9)	>.999[5]
Fever, n (%)	19 (11.9)	7 (10.3)	.908[4]
Shortness of breath, n (%)	40 (25)	24 (35.3)	.155[4]
Comorbidity, n (%)			
Diabetes mellitus	57 (35.6)	30 (44.1)	.227[2]
Hypertension	103 (64.4)	54 (79.4)	.037[4]
CAD	60 (37.5)	41 (60.3)	.002[2]
COPD	31 (19.4)	20 (29.4)	.136[4]
AF	20 (13)	15 (22.7)	.108[4]
CKD	46 (28.7)	24 (35.3)	.410[4]
Saturation at admission, median (range)	96 (65 – 99)	94 (60 – 99)	.012[3]
SBP at admission, mean ± SD	115.41 ± 21.39	116.97 ± 21.97	.630[6]
DBP at admission, mean ± SD	69.93 ± 12.89	70.15 ± 12.05	.906[6]
MAP at admission, mean ± SD	85.08 ± 14.93	85.76 ± 14.54	.760[6]
Pulse rate at admission, mean ± SD	87.58 ± 15.62	87.42 ± 18.92	.948[6]
Fever at admission, mean ± SD	36.75 ± 0.59	36.73 ± 0.61	.763[6]
Laboratory parameters			
WBC(K/uL), mean ± SD	11.32 ± 5.20	10.95 ± 4.49	.612[6]
Lymphocyte(K/uL), median [IQR]	1.10 [0.74 – 1.61]	1.20 [0.80 – 1.70]	.493[3]
Neutrophile(K/uL), median [IQR]	7.55 [5.58 – 11.41]	7.60 [5.33 – 10.74]	.545[3]
Monocyte(K/uL), mean ± SD	0.78 ± 0.39	0.77 ± 0.37	.844[6]
Eosinophile(K/uL), median [IQR]	0.06 [0.01 – 0.18]	0.07 [0.01 – 0.10]	.723[3]
Hemoglobin (g/dL), mean ± SD	12.07 ± 2.06	11.87 ± 2.17	.498[6]
Hemotocrit (%), mean ± SD	36.53 ± 6.27	36.89 ± 6.43	.698[6]
Platelet(K/uL), median [IQR]	239 [174.25 – 280]	261 [200.25 – 324]	.062[3]
Sedimentation(mm/h), median [IQR]	29.5 [11 – 48.5]	40 [24 – 61]	.028[3]
CRP(mg/L), median [IQR]	63.5 [11.53 – 171.25]	26.1 [6.73 – 108.5]	.020[3]
Procalcitonin(µ/L), median [IQR]	0.41 [0.16 – 3.70]	0.42 [0.19 – 1.30]	.555[3]
Glucose (mg/dL), median [IQR]	120 [97 – 179.25]	132 [101 – 174.5]	.455[3]
HgA1c, median [IQR]	7.10 [5.60 – 8.47]	7.25 [7.20 – 7.82]	.504[3]
Urea(mg/dL), median [IQR]	122 [86.75 – 161.25]	136 [107 – 207]	.003[3]
Creatine(mg/dL), median [IQR]	3.16 [2.17 – 4.74]	2.79 [2.03 – 4.15]	.172[3]
Na(mEq/L)(mmol/L), mean ± SD	135.29 ± 7.84	133.76 ± 5.98	.153[6]
K(mg/dL), mean ± SD	4.66 ± 0.93	5.24 ± 0.91	<.001[6]
Ca(mg/dL), mean ± SD	8.46 ± 0.96	8.60 ± 0.81	.293[6]
P(mg/dL), median [IQR]	4.1 [3.3 – 5.2]	4.5 [3.2 – 5.4]	.624[3]
Mg(mg/dL), mean ± SD	2.04 ± 0.41	2.18 ± 0.35	.020[6]
Uric acid(mg/dL), median [IQR]	8.6 [6.9 – 10.1]	8.7 [6.2 – 10.35]	.626[3]
Albumin(g/dL), mean ± SD	3.29 ± 0.59	3.19 ± 0.61	.245[6]
PH, mean ± SD	7.33 ± 0.08	7.31 ± 0.09	.048[6]
HCO3, mean ± SD	19.00 ± 4.76	18.72 ± 6.06	.710[6]
PCO2, mean ± SD	36.13 ± 7.52	37.71 ± 10.53	.262[1]
Ferritin(ng/mL), median [IQR]	178.85 [86.45 – 334.18]	109.35 [75.4 – 291.58]	.130[3]
Vitamin D(ng/mL), median [IQR]	7.92 [4.02 – 15.30]	10.27 [6.41 – 22.30]	.148[3]
CAR, median [IQR]	19.76 [2.90 – 57.38]	7.95 [1.81 – 36.99]	.031[3]
Culture, n (%)	48 (43.2)	32 (59.3)	.053[2]

1Welch's t-test; 2Pearson chi-square test; 3Mann-Whitney U test; 4Chi-square test with Yates continuity correction; 5Fisher's exact test;6 Independent samples t-test. *CAR; CRP-albumin ratio.*

hospitalized in the intensive care unit were included in the study. In our study, both clinical and intensive care patients were included.

Table 2. Multiple logistic regression analysis for predicting of mortality

	Adjusted Odds Ratio	95% confidence intervals	p-value
Age (years)	1.04	1.01 – 1.07	.004
CAD (presence vs. absence)	2.16	1.16 – 4.02	.016
Mg	2.64	1.18 – 5.92	.018
K	1.70	1.21 – 2.41	.002

In our study, as a result of multiple logistic regression analysis, old age remained a significant factor in mortality (OR=1.04, 95% CI=1.01 – 1.07, p=.004). Old age is a factor that increases the mortality of many diseases. In the study of Gursu et al., in which they included only patients who developed AKI in the intensive care unit and were followed up for 6 months, old age was found as an independent risk factor.13 Again, Zhou et al. found old age as a factor affecting mortality at the end of 1 year in their study in which they followed up intensive care AKI patients. 14

Coronary artery disease is the most important cause of mortality in CKD patients.15 Xi et al. showed that the presence of concomitant significant coronary artery disease in AKI patients undergoing cardiac valve surgery is a factor that increased mortality.16 In our study, the presence of CAD was a risk factor for long-term mortality in AKI patients.

Hyperkalemia is a common problem in AKI, and is one of the indications for dialysis if it is resistant to medical treatment. In a study involving AKI patients over 75 years of age in China, the 1-year mortality rate was found significantly higher in patients with hyperkalemia. Since there are many comorbidities in elderly patients, and fragility is common and tubular damage is permanent after AKI, it is considered that it may also affect long-term mortality.17 In this study, we found that hyperkalemia was an independent risk factor for mortality at longer follow-up. The fact that the mean age in our died patients' group was 75 years may suggest that the possible causes expressed in the aforementioned study may also be effective in our patient group. In a study conducted in Mexico, hyperpotassemia was significantly associated with short-term mortality in AKI patients.18

Mg is an important molecule involved in more than 300 intracellular reactions. Low or high Mg levels have been shown to be associated with undesirable results and mortality in many different patient populations.19 In a study examining more than 22 thousand intensive care patients, hypermagnesemia was found as a factor increasing mortality.20 Again, both hypomagnesemia and hypermagnesemia were associated with mortality in a large cohort of intensive care patients.21 In the present study, we found that the mean Mg level was higher in patients who died compared to those who survived. In the case of high Mg, problems such as decrease in blood pressure and pulse, respiratory failure and arrhythmias are common. Perhaps, one of these effects of Mg may have occurred in long-term mortality of our patient group.

Our study has some limitations. The shortcomings of our study are that it is single-center, retrospective and the number of patients is relatively low.

AKI is a condition with an increasing frequency in the world, leading to morbidity and mortality. In this study, among many demographic and laboratory data in AKI patients in the medium-long term, we found old age, the presence of coronary artery disease, increased K and Mg as the independent risk factors for mortality. We believe that the results of our study will contribute to the literature concerning AKI.

Ethical Approval: This study was approved by the Selcuk University Faculty of Medicine Local Ethics Committee on 31.01.2023 with decision number 2023/87.

Coflict of interest: There is no conflict of interest between the authors.

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ORIGINAL ARTICLE

The Cyberchondria Severity Scale-Short Form: A Psychometric Study

Siberkondri Ciddiyet Ölçeği-Kısa Formu: Psikometrik Bir Çalışma

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ABSTRACT

Background/Aims: This study was conducted to evaluate the psychometric properties of the Cyberchondria Severity Scale-Short Form.
Methods: This is a methodological-type study. Voluntary adult individuals, registered to three different family-health-centers located in Ankara were included in the study (n=322). The data were collected online using Google forms in July 14-August 8, 2021, via a questionnaire, the Cyberchondria Severity Scale-Short-Form (CSS-12-TR) and the Health Seeking Behavior Scale (HSBS). The data were analyzed via the IBM-SPSS 25.0 and IBM-AMOS 24.0. The Davis method for the content validity, The Explanatory and Confirmatory Factor Analysis methods for the construct validity were applied. The criterion-dependent validity was assessed via the concurrent validity method. Cronbach's alpha, the split-half and test-retest (n=32) reliability tests were used.
Results: The mean age was 31.95±12.45 (min. 18-max. 65). The content validity index of the scale was 0.93. The CSS-12-TR and the HSBS was found moderately correlated (r=0.485, p<0.001). The model-fit indexes were mostly in perfect agreement. The Cronbach's alpha coefficient of the total scale was 0.884, and between 0.751-0.822 for the sub-dimensions. The variance between the test-retest measurements was statistically insignificant (t=0.447, p=0.658) and correlated (r=0.759, p<0.001). The intraclass correlation coefficient was 0.936 (F=15.699, p<0.001).
Conclusion: The CSS-12-TR with 12 items and four sub-dimensions was found as an easy to implement, valid and reliable instrument for Turkish community-dwelling adult population. Since the cyberchondria can potentially be a problematic issue for all adult groups, its psychometric structure is recommended to be re-conducted with the Turkish older adult population.

Keywords: Anxiety, Factor analysis, Hypochondriasis, Internet, Research methodology

ÖZ

Amaç: Bu çalışma Siberkondri Ciddiyet Ölçeği-Kısa Formunun psikometrik özelliklerini değerlendirmek amacıyla yapıldı.
Yöntem: Çalışma metodolojik tipte yapıldı. Araştırmaya Ankara'da bulunan üç farklı aile sağlığı merkezine kayıtlı gönüllü yetişkin bireyler dahil edildi (n=322). Veriler, 14 Temmuz-8 Ağustos 2021 tarihlerinde çevrimiçi olarak kişisel bilgi formu, Siberkondri Ciddiyet Ölçeği-Kısa Form (SCÖ-12-TR) ve Sağlık Arama Davranışı Ölçeği (SADÖ) kullanılarak Google formlar aracığıyla çevrimiçi olarak toplandı. Veriler IBM-SPSS 25.0 ve IBM-AMOS 24.0 programları kullanılarak analiz edildi. İçerik geçerliği için Davis yöntemi, yapı geçerliği için Açımlayıcı ve Doğrulayıcı Faktör Analizi yöntemleri uygulandı. Ölçüt bağımlı geçerlikte eşzaman geçerliği yöntemi kullanıldı. Cronbach alfa, iki yarıya bölme testi ve test-tekrar test (n=32) güvenilirliği kullanıldı.
Bulgular: Katılımcıların ortalama yaşı 31.95±12.45 idi (min.18-maks.65). Ölçeğin kapsam geçerlik indeksi 0.93 olarak bulundu. SCÖ-12-TR ile SADÖ arasında orta düzeyde korelasyon olduğu belirlendi (r=0.485, p<0.001). Model uyum indeksleri çoğunlukla mükemmel uyum içerisindeydi. Cronbach alfa katsayısının ölçek toplamı için 0.884, alt boyutları için 0,751-0,822 arasında olduğu bulundu. Test-tekrar test ölçümleri arasındaki varyans istatistiksel olarak anlamsız (t=0,447, p=0,658) ve korele (r=0,759, p<0.001) idi. Sınıf içi korelasyon katsayısının 0,936 (F=15,699, p<0.001) olduğu belirlendi.
Sonuç: 12 madde ve dört alt boyuttan oluşan SCÖ-12-TR'nin, toplumda yaşayan Türk yetişkin bireyler için uygulaması kolay, geçerli ve güvenilir bir araç olduğu belirlendi. Siberkondri potansiyel olarak tüm yetişkin gruplar için sorun teşkil edebileceğinden, psikometrik yapısının Türk yaşlı yetişkin nüfusu ile yeniden yapılması önerilir.

Anahtar kelimeler: Anksiyete, Araştırma metodolojisi, Faktör analizi, Hipkondriazis, İnternet

Introduction

The internet use has been in a must-have position on a daily basis of today's world. In Turkiye, 85% of the 16-74 age group had been reported as the internet users in 2022 (1). An increasing number of individuals are known to incline into the internet to search for health-related knowledge (2). In the European Union, it has been reported that 55% of Europeans aged 16-74 search for health-related information online (3). In Türkiye, it has been reported that 68.2% of adults search for health information online (4). Nevertheless, cyberchondria term, which comes into light nowadays, is asserted as the "negative side" of the increased interest in the improving information and communication technology environment. Cyberchondria refers to excessive or repetitive health related information search on the internet associated with increased levels of health anxiety (2). Cyberchondria is stated as a process by which generally results in interruption of other daily activities and generally a physician consultation in response to increased distress or anxiety as a result of health-related knowledge search on the internet (5, 6). Cyberchondria can occur in accordance with the change in the focus of health related knowledge search on the internet within time whether between different

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individuals or even in one person (5). In a longitudinal study conducted by te Poel et al., the more the health anxiety of the individuals was stated the higher the rate of health-related information search on the internet (7). In the study of Mohammed et al., cyberchondria was reported higher in the one-thirds of individuals who searched for the health information on the internet (8). Cyberchondriacs tend to neglect their responsibilities and/or activities, or change their priorities in their living, education and working environments. This situation can also make negative impacts on their social and interpersonal interactions (5, 6).

There has been stated a potential behavioral dependence relationship between the problematic internet use and cyberchondria (5, 6, 9). In the study of Durak-Batıgün et al., health anxiety associated with cyberchondria was positively related to the internet addiction (10). In cyberchondria, excessive health-related knowledge searching on the internet causes anxiety, and this can direct the help-and-treatment-seeking behavior (5). Cyberchondria is also be associated with the increased healthcare service usage, measured by the number of visits to various health professionals (11). Additionally, in some cases, individuals may also prefer to cope with the cyberchondria-based anxiety on their own by avoiding consultation to the healthcare professionals. This can eventuate an increase in the undesirable effects and a decrease in proper healthcare service seeking. Therefore, it is stated that cyberchondria can cause highly negative impacts on health both individual and community levels from the community-health perspective (5).

The very-first tool, which measures the cyberchondria severity, was developed by McElroy and Shevlin as 33 items and five subscales with five-point Likert-type, in 2014 (12). Although scientific evidences and research related to cyberchondria has been increased gradually following this development, more studies are required to investigate the factors associated with cyberchondria and its effects in various areas (2, 5). Along with the current studies examining the cyberchondria in Turkiye (10, 13), the need for the tools which measure cyberchondria severity has been accordingly increased. Although there was a validated brief cyberchondria severity measurement tool into Turkish by Tuğtekin and Tuğtekin, the sample group in that study was comprised of university students (14). When the higher risk of gaining cyberchondria behavior among the middle-aged adult individuals living in Turkiye is considered (10), the need of a practical measurement tool, which is specific to Turkish adult population, is thought to emerge. In this context, it is thought that an acceptable, effective, valid and reliable measurement of cyberchondria severity in the Turkish adult population will facilitate future studies on the subject. Therefore, the factors associated with the cyberchondria severity among Turkish adult group could be well defined with an internationally accepted and culturally adapted measurement tool in order to motivate this group to change cyberchondria behavior.

This study was conducted to evaluate the psychometric properties of the Cyberchondria Severity Scale-Short Form with 12 items.

Methods

Study type

This methodological study was conducted to evaluate the Turkish validity and reliability of the Cyberchondria Severity Scale-Short Form (CSS-12-TR). This study was reported according to the Guidelines for Reporting Reliability and Agreement Studies (GRRAS) checklist (15).

Participants

The population was composed of adult individuals (18-65 age group) registered to three different family health centers located in the capital city of Türkiye. In the validity and reliability studies, the sample size is recommended to be at least five to 10 times larger than the number of items in the scale to be performed the factor analysis (16). Moreover, the sample size with at least 20 times larger than the number of items in the scale is also suggested in order to create a more solid structure in the scale (16). Therefore, 322 individuals, who agreed to participate in, were included in the study via using a convenience-sampling method (n=322). In test-retest reliability, the scale is recommended to be re-applied to the 10-20% of the sample within 2-6 weeks later from the first application (17). In this study, the retest of the scale was performed to the 10% of the selected sample four weeks later from the first application date (n=32).

The inclusion criteria were; a) being 18 and older age, b) being social media (the WhatsApp) user, c) having the skill and the technical opportunities of filling an online questionnaire, and d) speaking Turkish as the mother tongue. The exclusion criteria were; a) having any visual problem, b) having any neuropsychiatric disorder, c) being unable to fill the online forms independently. Because of having special and complex health needs, individuals who were older 65 years old were also excluded from the study.

Data collection tools

A questionnaire, the Cyberchondria Severity Scale-Short Form and the Health Seeking Behavior Scale (HSBS) were used to collect the data.

The questionnaire

It was prepared by the researchers as nine questions to determine the sociodemographic features and the internet usage habits of the adults, according to the related literature (5).

The Cyberchondria Severity Scale-Short Form

It was developed according to the 33-item scale prepared by McElroy and Shevlin (12) as short form with 12 items by McElroy et al (18). The Cyberchondria Severity Scale-Short Form is used to evaluate the behavior of searching for diseases on the internet about the health problems that individuals think they may have (18). It is a five-point Likert-type scale (1=never-

5=always) with four sub-dimensions (excessiveness, compulsion, reassurance, distress). Total score can be gathered from the scale is minimum 12, and maximum 60. The higher the total mean score, the higher the cyberchondria severity level. The Cronbach's alpha of the total scale was 0.90, and the Cronbach's alpha values of the sub-dimensions varied between 0.755-0.855 in the original study (18).

The Health Seeking Behavior Scale (HSBS)

It was developed by Kıraç and Öztürk in order to determine the health seeking behavior (19). The HSBS is a five-point Likert-type scale (1=strongly disagree-5=strongly agree) with 12 items and three sub-dimensions (online health seeking, professional health seeking, traditional health seeking). Total score can be gathered from the scale is minimum 12, and maximum 60. The higher the total mean score, the higher the health seeking behavior level. The Cronbach's alpha of the total scale was 0.75 in the original study (19), and it was calculated as 0.73 in this study.

Data collection process

The data were collected in July 14-August 8, 2021. The data collection tools were transformed into an online form using Google Forms because of the ongoing COVID-19 pandemic. The link of the online form was shared to the individuals who visited the related health centers between the data collection dates via the WhatsApp with the help of local authorities of the selected family health centers. The online form was designed to gather the e-mail addresses of the participants and restrict the second access by the same person. The explanation of the study aim, characteristics of the focus group of the study (i.e., age, obligations of having an e-mail address, living in the area of the selected family health centers etc.), and participant approval were presented on the first page of the form. The participants were not allowed to reach the data collection tools before approving their voluntary participation. The answers were only allowed to be changed by the participants before the submission of the form. The re-test link was sent to the participants via the WhatsApp and e-mail. It took approximately 10 minutes to be filled the data collection tools.

Cultural adaptation process of the scale

The cultural adaptation of the scale was carried out in three stages as language validity, content validity and pilot testing (17).

Language validity

Translate-back translate approach was used to ensure the language validity. Two researchers, who are experts in the field of public health nursing, and know both Turkish and English cultures and languages well, translated the scale. The translated versions were merged, discussed, and reached a consensus by the research team. Prepared Turkish form was translated back to English by an independent researcher, who is a native English speaker, also speaks Turkish fluently, and the differences of the expressions in the original scale were assessed. The Turkish translation of the scale containing the agreed statements, and the original of the scale were presented to the experts in the field for language and content validities. In line with the experts' suggestions for expression changes, the final version of the Turkish version of the scale was created (Cyberchondria Severity Scale-Short Form-Turkish [CSS-12-TR]).

Content validity

The Davis method was used to assess the content validity of the scale (20). The draft form of the CSS-12-TR was sent to 11 experts from different fields of nursing science working with the adult group and specialized in the methodological research. The experts were requested to evaluate the understandability of the scale items in a four-point Likert type (1= strongly inapplicable-4=strongly applicable) scoring sheet. The content validity ratio was accepted as ≥0.80 for the sufficiency of per item (20).

Pilot Test

Following the content validity of the CSS-12-TR, the scale was presented to 12 adults in order to assess its readability and understandability. Subsequently ensuring its readability and understandability, the scale was applied to these 12 adults. Any changes were not performed in the scale after the pilot test. Those who participated in the pilot testing were not included in the study sample.

Assessment of the psychometric properties of the CSS-12-TR

The total and the sub-dimension' mean scores of the scale, and the proportion of floor-ceiling effect were calculated to be assessed the psychometric properties of the CSS-12-TR. The floor-ceiling effect value was accepted as less than 20% in this study (17). Then, the validity and reliability analysis were performed.

Validity analysis

The construct validity of the CSS-12-TR was evaluated via Explanatory Factor Analysis (EFA) and Confirmatory Factor Analysis (CFA) methods. Before the EFA, the suitability of the data set to the factor analysis was assessed via the Bartlett's Test of Sphericity ($p<0.05$) and the Kaiser-Meyer-Olkin coefficient (KMO≥0.60) (16).

The principal component analysis and since the factors were independent from each other the Varimax rotation method were used to determine the factor loads. Factor load was accepted significant as >0.32 (16). The multicollinearity between the items and the sub-dimensions of the CSS-12-TR was tested via linear regression analysis (21).

Confirmatory Factor Analysis (CFA) was applied to examine whether the theoretical structure obtained for the scale was provided in the study sample. Maximum likelihood estimation method was used in the CFA. The Chi-Square Goodness [CMIN/df]≤5, Goodness of

Fit Index [GFI]≥0.90, Comparative Fit Index [CFI]≥0.90, Normed Fit Index [NFI]≥0.90, Tucker-Lewis Index [TLI]≥0.90, Incremental Fit Index [IFI]≥0.90, Root Mean Square Error of Approximation [RMSEA]<0.80, and Standardized Root Mean Square Residual [SRMR]<0.08 fit indexes were calculated in the CFA (22).

The criterion-dependent validity of the CSS-12-TR was assessed via the concurrent validity method. In this context, the Health Seeking Behavior Scale (HSBS) and the CSS-12-TR were applied simultaneously. The relationship between the total mean scores of these two scales, and the CSS-12-TR total score and the total score of each item in the scale were examined via the Pearson correlation coefficient. Because there has not been a standard evaluation approach, a general guideline's suggestion to correlation values were accepted: <0.30 indicates little or no agreement, a correlation between 0.30-0.40 indicates fair agreement, a correlation between 0.41-0.60 indicates moderate agreement, 0.61-0.70 indicates good agreement, a correlation between 0.71-0.75 indicates very good agreement, and a correlation >0.75 indicates excellent agreement (23).

Reliability analysis

The internal consistency of the CSS-12-TR was assessed via the Cronbach's alpha coefficient, the split-half test, and item-total correlation coefficients and the correlation between the items and the subscales of the scale. The Cronbach's a ≥0.70 was assessed as acceptable (17). In the split-half test, the Cronbach's alpha coefficients of the two halves were evaluated ≥0.60; Spearman-Brown and Guttmann Split-Half coefficients were ≥0.70 as acceptable (17). Item-total correlation coefficients were accepted to be positive and above 0.20 (17).

Test-retest method was used to test the time invariance of the CSS-12-TR. Test-retest reliability was assessed four weeks later from the first application via paired samples t-test (p>0.05), Pearson correlation coefficient and Intraclass Correlation Coefficient (ICC). ICC <0.50 was interpreted as little reliability, between 0.50-0.75 as moderate reliability, between 0.76-0.90 as good reliability, and >0.90 as excellent reliability (24).

The construct reliability of the CSS-12-TR was assessed via Composite Reliability (CR) coefficient (CR>0.70). The convergent validity between the items in the sub-dimensions of the CSS-12-TR was determined via Average Variance Extracted (AVE) value (AVE>0.50) (22). Discriminant validity of the CSS-12-TR was tested via Heterotrait-Monotrait (HTMT) ratio of correlations. HTMT value for each sub-dimensions of the scale with <0.90 was determined as adequate (25).

Data analysis

The data were analyzed via the IBM SPSS 25.0 and IBM AMOS 24.0 package programs. The normality of the data was evaluated via the Shapiro-Wilk test. The content validity ratio of per item and content validity index of the total scale were calculated using the experts' scoring. The construct validity was tested via EFA and CFA. Tukey's Test for Non-Additivity was used to evaluate the additivity of the scale. The Hotelling T2 test was used to determine whether the given responses to the items by the participants were similar. Statistical significance value was accepted as, p<0.05.

Ethical considerations

A written permission from Dr. Eoin McElroy, the developer of the scale, was gathered via e-mail. An ethical approval was obtained from the university's ethical committee (16.04.2021-73) before conducting the research. An informed consent was gathered from the participants. The informed consent, which included the aim of the study, the information about the data collection tools and the assurance of personal data protection according to the Turkish regulations, was presented on the first page of the online form. The online form was designed in such a way that individuals could see the questions after their consent was obtained.

Results

Sociodemographic characteristics are depicted on the Table 1. The mean age of the participants was 31.95±12.45 (min. 18-max. 65).

The content validity ratio of per item in the CSS-12-TR was found to vary between 0.82-1.00, and the content validity index of the scale was 0.93.

Table 1. Sociodemographic characteristics of the participants (n=322)

Sociodemographic characteristics	n	%
Gender		
Woman	242	75.2
Man	80	24.8
Marital status		
Single	181	56.3
Married	141	43.7
Graduation		
Literate-Elementary school	15	4.7
Secondary school	105	32.6
Bachelor's and above	202	62.7
Employment status		
Yes	141	43.8
No	181	56.2
Income level		
Less than expense	101	31.4
Equal to expense	179	55.6
More than expense	42	13.0
Having any co-morbidity		
Yes	85	26.4
No	237	73.6
Self-health perception		
Poor	5	1.6
Moderate	122	37.9
Good	176	54.7
Excellent	19	5.9
Daily internet usage time		
Up to 2 hours	87	27.0
3-4 hours	121	37.6
5 hours and above	114	35.4

Table 2. Suitability to the factor analysis results of the CSS-12-TR

Subscales	Items	Item score	Factor loadings after varimax rotation	Extraction values	r	Explained variance	Cumulative variance	KMO	X^2	p
		Mean (SD)				%	%			
Excessiveness	Item 1	3.15 (0.06)	0.787	0.724	0.886	44.356	71.643	0.863	1750.903	<0.001
	Item 3	3.02 (0.06)	0.849	0.796	0.822					
	Item 6	3.28 (0.07)	0.730	0.706	0.871					
Compulsion	Item 2	1.75 (0.05)	0.673	0.682	0.880	12.480				
	Item 7	1.46 (0.05)	0.838	0.808	0.807					
	Item 10	1.45 (0.05)	0.777	0.741	0.814					
Reassurance	Item 5	2.66 (0.07)	0.703	0.705	0.870	8.471				
	Item 11	1.80 (0.06)	0.621	0.605	0.901					
	Item 12	2.47 (0.07)	0.807	0.777	0.844					
Distress	Item 4	2.41 (0.06)	0.682	0.683	0.869	6.336				
	Item 8	2.26 (0.07)	0.730	0.616	0.934					
	Item 9	2.41 (0.06)	0.725	0.754	0.881					

X2: Bartlett's Test of Sphericity; KMO: Kaiser-Meyer-Olkin; r: item-total correlation

Table 3. Correlation analysis results of the CSS-12-TR

Scales and sub-scales	Mean (SD)	Multicollinearity of subscales		Total CSS-12-TR	
Total CSS-12-TR	29.19 (8.76)	Colli-nearity tolerance	Statistics VIF	r	p
Excessiveness	9.45 (2.79)	0.606	1.651	0.796	<0.001
Compulsion	4.65 (2.14)	0.702	1.425	0.691	<0.001
Reassurance	6.92 (2.75)	0.535	1.869	0.834	<0.001
Distress	7.09 (2.74)	0.476	2.099	0.860	<0.001
Total HSBS	37.81 (6.62)			0.485	<0.001
Online health seeking	16.71 (4.83)			0.527	<0.001
Professional health seeking	11.13 (2.44)			0.030	0.587
Traditional health seeking	9.96 (2.54)			0.232	<0.001

r: Pearson correlation coefficient; collinearity tolerance was accepted >0.2; VIF was accepted <10

Table 5. Convergent and discriminant validity results of the CSS-12-TR

Subscales	CR	AVE	HTMT			
			Excessi-veness	Com-pulsion	Reassu-rance	Distress
Excessive-ness	0.832	0.624				
Compulsion	0.808	0.586	0.436			
Reassu-rance	0.755	0.510	0.707	0.588		
Distress	0.755	0.511	0.721	0.694	0.823	

CR: composite reliability; AVE: Average Variance Extracted; HTMT: heterotrait-monotrait ratio of correlations

Table 4. Reliability analysis results of the CSS-12-TR

Scale and subscales	Cronbach's alpha	Items	Item-total corre-lation	Cronbach's alpha if item deleted
Excessiveness	0.822	Item 1	0.611	0.873
		Item 3	0.607	0.873
		Item 6	0.601	0.874
Compulsion	0.751	Item 2	0.459	0.881
		Item 7	0.523	0.878
		Item 10	0.491	0.880
Reassurance	0.761	Item 5	0.627	0.872
		Item 11	0.564	0.876
		Item 12	0.623	0.872
Distress	0.761	Item 4	0.667	0.870
		Item 8	0.523	0.879
		Item 9	0.714	0.867
CSS-12-TR	0.884			

Total score of the CSS-12-TR	Mean (SD)	t	p	r	p	ICC	p
First measu-rement	29.19 (8.76)	0.447	0.658	0.759	<0.000	0.936	<0.001
Second measure-ment	28.72 (8.27)						

t=paired-samples test; r=Pearson correlation coefficient; ICC: intraclass correlation coefficient

Psychometric test results

Validity analysis results

The suitability of the data set to the factor analysis results of the CSS-12-TR is shown in the Table 2. The results of the Bartlett's Test of Sphericity and the KMO coefficient indicated that the dataset was applicable to the EFA (df=66, p<0.001). The extraction values of the items were >0.30, and all the diagonal values in the Anti-image correlation matrix were >0.60 (0.807-0.934). The factor structure of the original scale was preserved in the CSS-12-TR (Figure 1.). All the four sub-dimensions of the CSS-12-TR were found the explain 71.643% of the total variance (Table 2.).

The relationship between the total mean scores of the CSS-12-TR and the HSBS and the sub-dimensions of both scales is depicted in Table 2. The CSS-12-TR and the HSBS was moderately correlated (r=0.485,

p<0.001). The correlation coefficients of the total mean score of the CSS-12-TR and its sub-dimensions were found between 0.691-0.860 (p<0.001) (Table 3.). Although it was not depicted on the table, the correlation coefficients between the total mean score of the CSS-12-TR and its items were identified between 0.551-0.774 (p<0.001).

The correlation coefficients between the total mean scores of the sub-dimensions of the CSS-12-TR were >0.30 (min=0.351; max=0.626), and there was not a multicollinearity between the sub-dimensions of the scale (Adjusted R^2=0.713, F=200.501, p<0.001). All these results showed that the scale construction was suitable to conduct the CFA (Table 3.).

The standardized coefficients of the CSS-12-TR are depicted in the path diagram (Figure 2.). The model fit indexes, which were gathered via first level CFA using maximum likelihood estimation method and conducting three modifications with 12 items and four sub-dimensions obtained following the EFA, were found to be CMIN=158.625, CMIN/df=2.993, GFI=0.927, CFI=0.938, RMSA=0.79, SRMR=0.054, NFI=0.911, TLI=0.923, and IFI=0.939.

Reliability analysis results

The scale was found to be in the additivity characteristic, according to the Tukey's Test for nonadditivity result (F=56.973; p<0.001). Moreover, there was no response bias in the scale (Hotelling T2=1033.411; F=91.020; p<0.001).

The Cronbach's alpha coefficients of the CSS-12-TR and its sub-dimensions are shown in the Table 4. The Cronbach's alpha coefficient of the total scale was 0.884, and the Cronbach's alpha coefficients of the sub-dimensions were between 0.751-0.822.

In the split-half reliability of the CSS-12-TR, the scale was separated into two parts as part-1 (items: 1-6) and part-2 (items: 7-12). Cronbach's alpha coefficient of the part-1 and the part-2 were 0.820 and 0.801, respectively. Spearman-Brown coefficient was 0.831 for each part, and Guttmann Split-Half coefficient was 0.829.

Item-total correlation values of the CSS-12-TR varied between 0.459-0.714, and all correlation values were positive (Table 4.).

The test-re-test reliability results of the CSS-12-TR are shown in the Table 4. The variance between the two measurements was statistically insignificant (t=0.447, p=0.658), and the correlation between the two measurements was found as r=0.759 (p<0.001). The intraclass correlation coefficient was 0.936 (F=15.699, p<0.001).

The convergent and discriminant validity results, which prove the construct reliability of the scale, are shown in the Table 5. The CR values of the four sub-dimensions were found between 0.755-0.832 (CR >0.70), and the AVE values were between 0.510-0.624 (AVE >0.50). HTMT correlations of the subscales were between 0.436-0.823 (Table 5.).

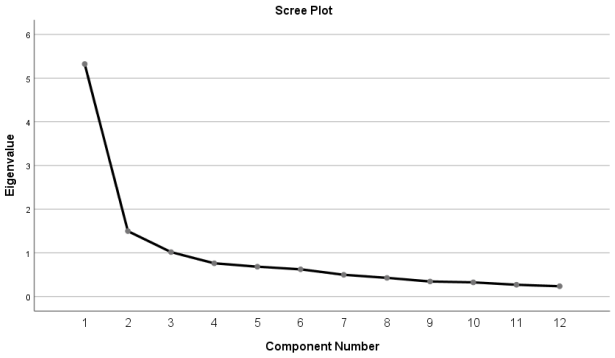

Figure 1. Scree plot chart of the factor structure

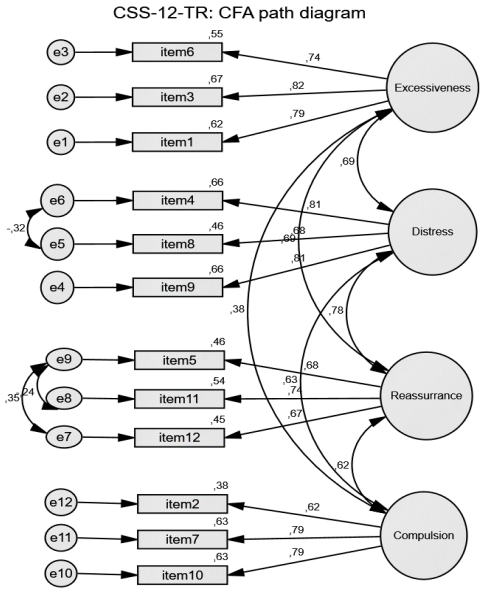

Figure 2. Path diagram of CFA

Discussion

The short form of The Cyberchondria Severity Scale with 12 items was adapted to Turkish culture (CSS-12-TR) in this study. The CSS-12-TR was found as a valid and reliable tool for the Turkish adult population in terms of psycholinguistics and psychometric validity and reliability criteria in the related literature (16, 17, 20-25).

The content validity ratio is recommended to be ≥0.80 per scale item (20). In this study, it was found that the content validity ratio per item of the CSS-12-TR ranged between 0.82-1.00, so the original structure of the scale was preserved, and no items were omitted. The sufficiency of the sample size for the factor analysis is suggested to be evaluated via accepting the Bartlett's Test of Sphericity as statistically significant (p<0.05) and the KMO coefficient as ≥0.60 in the literature (16). In this study, KMO coefficient was very above the reference value, and the result of the Bartlett's Test of Sphericity was statistically significant. Therefore, items of the CSS-12-TR were accepted as suitable to the factor analysis. The explained variance rate is recommended to be

at least 30% for one-factor structured scales and >50% for the scales with multifactorial structure (17). In this context, it was found that the four factor-structured CSS-12-TR met this recommendation with the above of 70% explained variance. CFA is performed to test the relation between the scale items, correlations between the items and described factors, whether the defined factors are freed from each other and sufficient enough to explain the model structure (22). In this study, the correlation coefficient between the items, the factors and CSS-12-TR were found mostly at moderate levels. Moreover, the results of the model fit indexes obtained via CFA were found mostly in perfect fit. These findings presented in better or excellent agreements, which were in line with the development study of the scale (18), and the other Turkish version which was conducted with the education faculty students' sample (14).

In the concurrent validity, moderate to excellent correlation values show the similarity of measured constructs, however, lower correlation coefficients indicate the difference between the measurements of the constructs (23). Similar to the original study of the scale (18), the significant correlation between the CSS-12-TR revealed moderate agreement to the Health Seeking Behavior Scale.

The internal consistency reliability in the validity and reliability studies is recommended to be tested via split-half test and inter-item correlation coefficient along with the Cronbach's alpha coefficient (17). The Cronbach's alpha internal consistency coefficient was found highly acceptable in this study, similar to its original version (18) and the other Turkish version, which was conducted with the education faculty students' sample (14). Moreover, the split-half reliability of the CSS-12-TR was found also adequate, and its item-total correlation coefficients were in between positively moderate to very good agreement. Therefore, the CSS-12-TR was stated as an internally valid instrument for the Turkish general adult population.

Test-retest application is used to determine the consistency of a scale within a certain time interval (24). The correlation coefficient between the two measurements of the CSS-12-TR was found as in excellent agreement, and the Intraclass correlation coefficient was excellently reliable. Similar to the original form (18), the CSS-12-TR was also determined as a reliable tool in terms of construct reliability, which was tested via convergent and discriminant validity (CR >0.70; AVE > 0.50; CR >AVE; HTMT <0.90). All these results revealed that the measurement via the CSS-12-TR was consistent and reliable over time, similar to the related literature (14, 18).

Strengths and limitations

The current study has several strengths. Firstly, the adaptation study of the CSS-12-TR was conducted with the 18–65-year-old adult population living in Turkiye, which is thought to increase its availability and applicability in correlational studies with wider sample groups to be mapped the cyberchondria severity degree of the Turkish general adult population. Likewise, its relatively high sample size is considered as the other strength of the current study. However, the present study is not without limitations. Initially, obtaining the data via an online questionnaire may have affected the data quality. Secondly, individuals unable to use an active e-mail and the WhatsApp could not be included. The online data collection procedure made the retesting process difficult.

Conclusion

The CSS-12-TR is an easy to implement, valid and reliable instrument for Turkish community-dwelling adult population aged between 18 and 65. The two-step factor analysis revealed consistent results to its original study (18). The scale was also highly internally and structurally reliable. Since the cyberchondria can potentially be a problematic issue for all adult groups, its psychometric structure is recommended to be re-conducted with the Turkish senior adult population aged 65+ and older. When the increase in the online health-related information seeking behavior among the younger population is considered, the validity and reliability of the CSS-12-TR is also recommended to be re-performed to measure cyberchondria severity among Turkish teenagers.

Ethics Approval

It was gathered an ethical approval from the Ankara Yıldırım Beyazıt University's Ethical Committee (16.04.2021-73) before conducting the research. The online informed consent were obtained from the participants. This research conforms to all the provisions of the Declaration of Helsinki, 2013.

Author contribution statement

HT: Conceptualization, methodology, supervision, investigation, validation, visualization, formal analysis, writing-original draft, review & editing. AA: Conceptualization, methodology, data curation, writing-original draft, review & editing. SAA: Project administration, conceptualization, methodology, supervision, investigation, visualization, writing-original draft, review & editing.

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ORIGINAL ARTICLE

MicroRNAs and Their Targets Could Have a Crucial Role in Breast Cancer Drug Resistance: A Bioinformatics Research

MikroRNA'lar ve Hedefleri Meme Kanseri İlaç Direncinde Önemli Bir Role Sahip Olabilir: Biyoinformatik Bir Araştırma

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ABSTRACT

Objective: MicroRNAs(miRNAs) have been demonstrated to contribute to cancer development by playing essential roles in processes including proliferation, migration, invasion, and metastasis. One of the most serious issues in breast cancer (BC) is drug resistance. Recent research suggests that miRNAs may play a role in drug resistance. Using diverse datasets and in silico approaches, we focused on the BC/drug resistance/miRNA link in our study.
Material and Methods: GSE73736 and GSE71142 geo datasets (for miRNAs) and GSE162187 geo dataset (for genes) were obtained from the GEO database to detect differently expressed miRNAs and genes using the R software "LIMMA" package. Potential target genes of screened differentially expressed miRNAs (DE-miRNAs) were predicted using miRMap, miRTarbase, and miRNet tools. Differently expressed genes (DE-genes) were filtered and common DE-genes were identified via TCGA data and miRNet. Afterward, Enrichr, and Funrich tools were used to perform GO annotation and KEGG pathway enrichment analysis. KMplot and GEPIA2 web tools were utilized to investigate further hub miRNAs and genes' expression and prognostic effects.
Results: 3 miRNAs that were considerably downregulated and had prognostic significance in BC were identified using the criteria defined in the investigated geo datasets. MiR-586, which is expected to be more closely linked to BC, has been found to have the ability to target 5 genes involved in BC resistance to therapy. GO, KEGG, and survival analysis showed that the probable target genes of miR-586 could be closely connected to BC.
Conclusion: In this study, a comprehensive BC-drug resistance-miRNA-gene network was established and new targets for the treatment and prognosis of BC were revealed using bioinformatics data.

Keywords: Breast Cancer, Drug Resistance, microRNA, Bioinformatics

ÖZ

Amaç: MikroRNA'ların (miRNA'ların) hücre çoğalması, göç, istila ve metastaz gibi süreçlerde önemli roller oynayarak kanser gelişimine katkıda bulunduğu gösterilmiştir. Meme kanserinde (MK) en ciddi sorunlardan biri ilaç direncidir. Son araştırmalar, miRNA'ların ilaç direncinde rol oynayabileceğini öne sürmektedir. Çalışmamızda çeşitli veri setleri ve in silico yaklaşımlar kullanılarak MK/ilaç direnci/miRNA bağlantısı araştırılmıştır.
Gereç ve Yöntem: Geo veritabanından GSE73736 ve GSE71142 veri setleri (miRNA'lar için) ve GSE162187 veri seti (genler için) indirilerek R yazılımı "LIMMA" paketi aracılığıyla farklı şekilde ifade edilen miRNA'lar ve genler tespit edilmiştir. Farklı şekilde eksprese edilen miRNA'ların (DE-miRNA'lar) potansiyel hedef genleri, miRMap, miRTarbase ve miRNet araçları kullanılarak tahmin edildi. İfade düzeyi farklı olan genler (DE-genler) filtrelenmiş olup TCGA verileri ve miRNet'te ortak olan genler belirlenmiştir. Daha sonra GO ve KEGG ilişkilendirme analizleri Enrichr ve Funrich araçlarıyla yapılmıştır. Hub miRNA ve genlerin ekspresyon düzeyleri ve prognostik etkileri KMplot ve GEPIA2 web araçları kullanılarak araştırılmıştır.
Bulgular: MK'da önemli ölçüde ifadesi azalmış ve prognostik önemi olan 3 miRNA tespit edilmiştir. MK ile daha yakından bağlantılı olabileceği düşünülen miR-586'nın, MK'nın tedaviye direncinde rol oynayan 5 geni hedefleme potansiyeline sahip olduğu görülmüştür. GO ve KEGG analizlerinde, miR-586'nın olası hedef genlerinin MK ile yakından ilişkili olabileceği gösterilmiştir.
Sonuç: Bu çalışmada kapsamlı bir MK ilaç direnci-miRNA-gen ağları araştırılmıştır. Çalışmada biyoinformatik veriler kullanılarak MK'nın tedavi ve prognozuna yönelik yeni veriler ortaya çıkarılmıştır.

Anahtar kelimeler: Meme kanseri, İlaç direnci, mikroRNA, Biyoinformatik

Introduction

Breast cancer (BC) is the most frequent malignancy and the main cause of death related to cancer in women worldwide. Chemotherapy, hormonal therapy, and targeted therapy continue to be the first-line treatment options in BC. In clinical trials, some immunotherapeutic drugs showed promising efficacy (1). Nonetheless, drug resistance and the absence of biomarkers for predicting treatment response is a formidable obstacle in the treatment of BC (1). For more successful BC treatment, a deeper understanding of the probable molecular pathways underlying drug resistance is required urgently. MicroRNAs (miRNAs) are non-coding RNAs and they have 18-25 nucleotides in general (2, 3). Many studies showed that they function in a variety of critical biological processes including proliferation, differentiation, migration and metastasis (4, 5). Cross-talk between malignant cells and their surrounding environment is recognized to have a significant impact on tumor formation and resistance to cancer chemotherapy. miRNAs, which have an essential function in the etiology of human malignancies, are among the molecules involved

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in this pathological cross-talk (6). The link between miRNAs and genes is quite complicated. The addition of multiple components such as drug resistance in this intricate structure complicates this process even further. Rapid advances in bioinformatics, particularly in recent years, have made a significant contribution to the understanding of the complicated mechanisms of these biomolecules (7-10).

Using several bioinformatics approaches, this study evaluated miRNAs and genes that may be related to treatment resistance in BC. Following that, the impacts of selected miRNAs and genes on biological processes were uncovered using a variety of in silico tools and literature.

Material and Methods

Identification of Differently Expressed miRNAs Associated with Drug Resistance in Breast Cancer

GSE73736 (miRNA microarray was performed on tissue samples obtained from 10 drug-resistant BC patients and 10 drug-sensitive individuals) and GSE71142 (miRNA microarray was performed using tissue samples from 5 drug-resistant cases and tissue samples from 5 drug-sensitive cases) geo datasets have been obtained from the geo database to find miRNAs (DE-miRs) associated with BC resistance to chemotherapy. GEO2R was used for analyzing differentially expressed miRNAs.

In silico validation of the connection between DE-miRs and BC, as well as a review of the literature

The overlapping miRNAs in the two datasets (GSE73736 and GSE71142) were compared to the BC-related miRNAs in The Cancer Genome Atlas (TCGA) using KMplot (11). Furthermore, the drug resistance link of overlapping DE-miRNAs was investigated in PubMed by entering the words "relevant miRNA name drug, drug resistance, cancer, disease". Next, the kmPlot tool, which was utilized with TCGA data, was used to evaluate the link between overlapping miRNAs and BC overall survival.

Potential target genes of the chosen miRNA were identified in silico.

The selected miRNA's potential target genes were identified using the web tools miRTarbase, miRNet, and miRMap (12).

The Identification of Differently Expressed mRNAs Relevant to Drug Resistance in BC

GSE162187 (22 patients tissues, before and after chemotherapy) geo dataset was obtained from geo database and analyzed using GEO2R (https://www.ncbi.nlm.nih.gov/geo/geo2r/) to find drug resistance-related mRNAs (DE-Genes) in BC.

In silico verification of DE-Genes and BC relationship

DE-Genes in BC were identified in the TCGA database via the GEPIA2 web tool (13). Then, overlapping genes were identified between GSE162187 DE-Genes and TCGA DE-Genes with the genes shown as potential targets of the selected DE-miR in miRNet 2.0 (14), miRTarbase (15) and miRMap.

Survival analysis of selected DE-Genes

GEPIA2, which was constructed using TCGA data, was used to perform survival analysis regarding the selected genes.

KEGG ve GO analysis

Enrichr (16) and FunRich (17) performed the GO functional annotation and KEGG pathway enrichment evaluation for the selected DE-genes.

Statistical Analysis

Functional enrichment evaluations were carried out using publicly available tools (Enrichr. FunRich and GEPIA2). Overall survival was estimated using the Kaplan-Meier technique, and differences were determined using the log-rank test. P-value<0.05 was established as the statistical cut-off for overall survival evaluation and assessment of enrichment in tools.

Table 1: Overlapping miRNAs between GSE73736 and GSE71142 datasets

miRNAs	GSE73736			GSE71142		
	P-value	LogFC	Regulation	P-value	LogFC	Regulation
hsa-miR-586	0.008114	-2.393	Down	0.00209	-4.589	Down
hsa-miR-587	0.002157	-3.878	Down	0.00446	-4.952	Down
hsa-miR-2681-3p	0.014868	-2.549	Down	0.00724	-3.370	Down
hsa-miR-3927-3p	0.023943	3.732	Up	0.00726	5.449	Up
hsa-miR-4472	0.012622	-1.73	Down	0.00861	-2.294	Down
hsa-miR-4771	0.008397	3.222	Up	0.01585	3.923	Up
hsa-miR-4264	0.02729	3.337	Up	0.01684	4.030	Up
hsa-miR-4277	0.042948	2.952	Up	0.01802	3.064	Up
hsa-miR-620	0.003741	-4.752	Down	0.02168	-4.316	Down
hsa-miR-4633-3p	0.010691	3.808	Up	0.02358	4.804	Up
hsa-miR-619	0.031135	-2.701	Down	0.03378	-4.079	Down
hsa-miR-200c-3p	0.026268	1.702	Up	0.03428	2.660	Up
hsa-miR-4422	0.033616	2.961	Up	0.03776	2.160	Up
hsa-miR-15b-3p	0.04193	-2.935	Down	0.04024	-3.427	Down
hsa-miR-17-3p	0.00929	-2.99	Down	0.04694	-3.187	Down

Results

DE-miRs identification

Between the GSE73736 and GSE71142 datasets, 15 overlapping miRNAs were identified (logFC>1.5 and p<0.05). Among the 15 overlapping miRNAs in the datasets, the miRNAs miR-586, miR-4771, and miR-4422 were found to be present in the TCGA BC data (Figure 1(A) and Table 1).

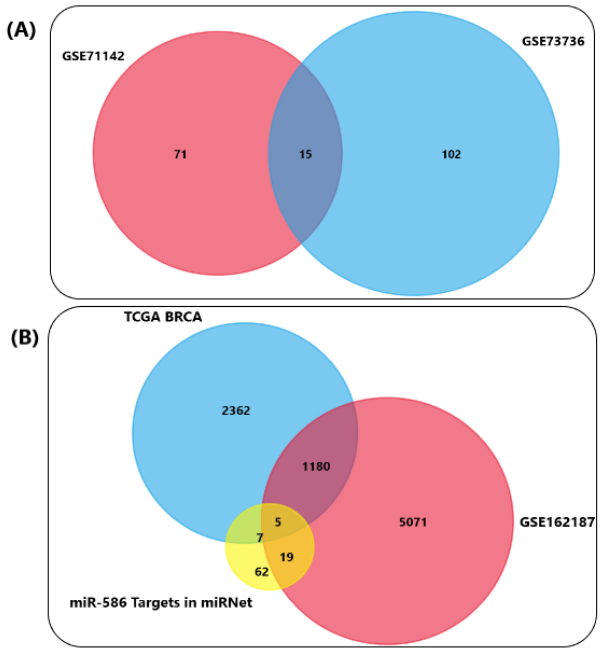

Figure 1: **(A)** Overlapping miRNAs and **(B)** overlapping genes between used datasets in the present study.

Identifying the link between DE-miRs and BC

The literature analysis revealed that there was very little knowledge available on miR-4771 and miR-4422, which are found in the GSE73736-GSE71142 datasets and the TCGA BC data. The associations of miR-587, miR-4277, miR-620, and miR-619 miRNAs with various tumors have been confirmed, and these miRNAs have been linked to drug resistance in several cancers (Table 2).

Table 2. PubMed research results of overlapping miRNAs between GSE73736-GSE71142 datasets and drug resistance relations. (Four miRNAs have been associated with drug resistance)

MiRNA	Drug	Target	Disease	Reference
hsa-miR-587	5-fluorouracil	PPP2R1B	Colorectal Ca	(36)
miR-4277	Sorafenib	CYP3A4	HCC	(37)
miR-620	Gemcitabine	DCTD	BC (TNBC)	(38)
miR-619	Cisplatin	ATXN3	OSCC	(39)

Selected miRNA and Potential Target Genes

The screening to identify the possible target genes of miR-586, one of the DE-miRs, revealed that miR-586 may target 93 genes (Figure 2).

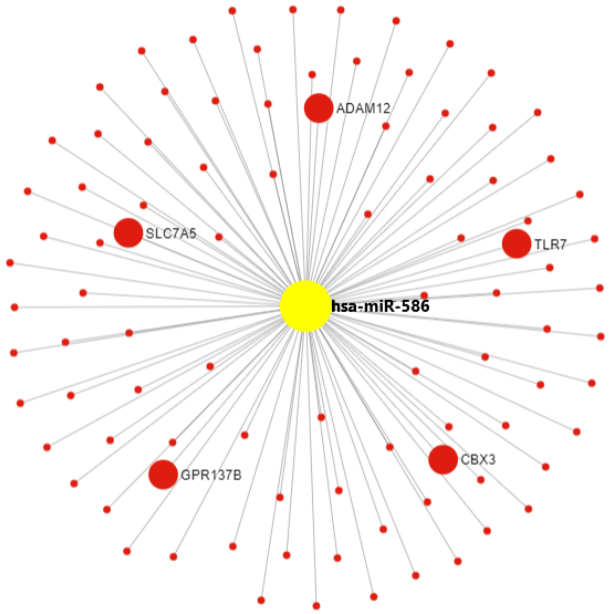

Figure 2: miR-586 and its 93 potential targets including *GPR137B, ADAM12, SLC7A5, TLR7* and *CBX3* in miRTarbase and miRNet. (Red circles represent genes and yellow circles represent miR-586)

DE-Genes Identification

In the GSE162187 geo dataset, 6275 genes matched the logFC>0.4 and p<0.05 criterion. It was found that 3554 genes in TCGA BC samples met the logFC>2 and p<0.05 criterion as seen in Figure 1(B). It was found that 12 genes overlapped between miR-586's targets and TCGA BC data. It was assumed that because miR-586 was observed to be downregulated in the GSE73736 and GSE71142 datasets, its target genes should be overexpressed in BC. As a result, because 7 of the 12 possible miR-586 target genes were downregulated in TCGA, they were eliminated from the analysis (Table 3). It was determined that there were five common genes (GPR137B, ADAM12, SLC7A5, TLR7, CBX3) among possible in silico target genes of miR-586, GSE162187 dataset, and TCGA BC data (and these five genes were overexpressed in BC). These genes are subjected to enrichment analysis (Figure 3, Figure 4).

Enrichment Analysis Results

Selected potential target genes of miR-586 were associated with many cancers, including BC (Figure 5).

Effect of Overlapping miRNAs on BC Overall Survival

Among the 15 overlapping miRNAs between GSE73736 and GSE71142 datasets, miR-586, miR-4771, and miR-4422 miRNAs were observed to affect overall survival of BC TNBC (Figure 6).

Effect of selected genes on BC overall survival

Although it was observed that GPR137B, ADAM12, TLR7, and CBX3 gene had no significant effect on BC overall survival, SLC7A5 had a significant effect on BC overall survival (Figure 7).

Table 3: Overlapping genes between the potential targets of miR-586 found miRNet and TCGA BC data

Gene name	Description	Regulation In TCGA
ACSL4	acyl-CoA synthetase long chain family member 4	Down
MYC	MYC proto-oncogene, bHLH transcription factor	Down
PLP1	proteolipid protein 1	Down
GPR137B	G protein-coupled receptor 137B	Overexp.
TNS1	Tensin 1	Down
ZFP36	ZFP36 ring finger protein	Down
ADAM12	ADAM metallopeptidase domain 12	Overexp.
SLC7A5	solute carrier family 7 member 5	Overexp.
CBX3	chromobox 3	Overexp.
TLR7	toll like receptor 7	Overexp.
ERRFI1	ERBB receptor feedback inhibitor 1	Down
ITIH5	inter-alpha-trypsin inhibitor heavy chain 5	Down

Down: Down-regulation, Overexp.: Overexpression

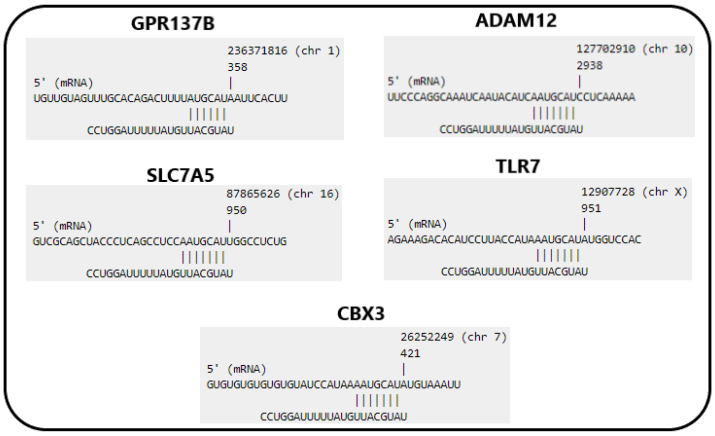

Figure 3: Sequence matching of miR-586 and selected target genes.

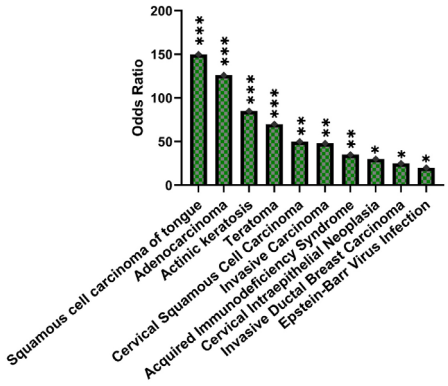

Figure 5: The relation between selected miR-586 potential targets and diseases. Selected genes have been associated with many cancers including BC (***: p<0.0001, **: p<0.001, *: p<0.01).

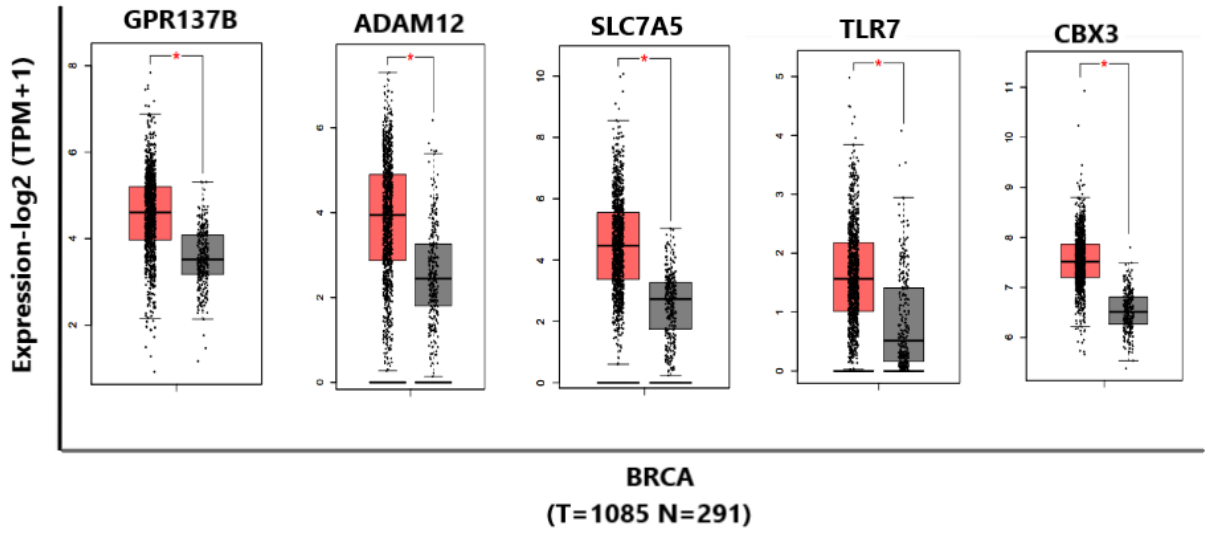

Figure 4: Expression levels of 5 selected target genes of miR-586 in TCGA BC patient samples. (T: tumor, N: Normal, TPM: Transcript Per Million)

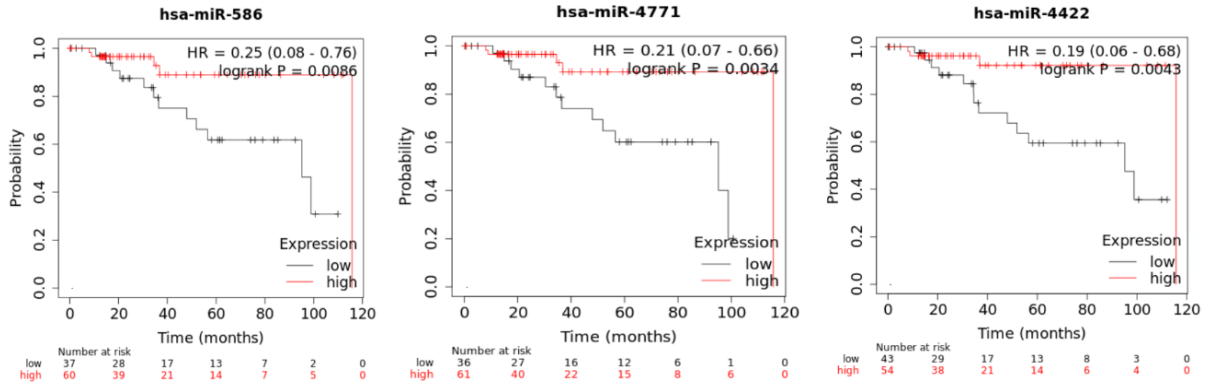

Figure 6: Survival effects of overlapping miRNAs in triple-negative breast cancer (TNBC). (based on 300 patients in TCGA) (HR: Hazard Ratio)

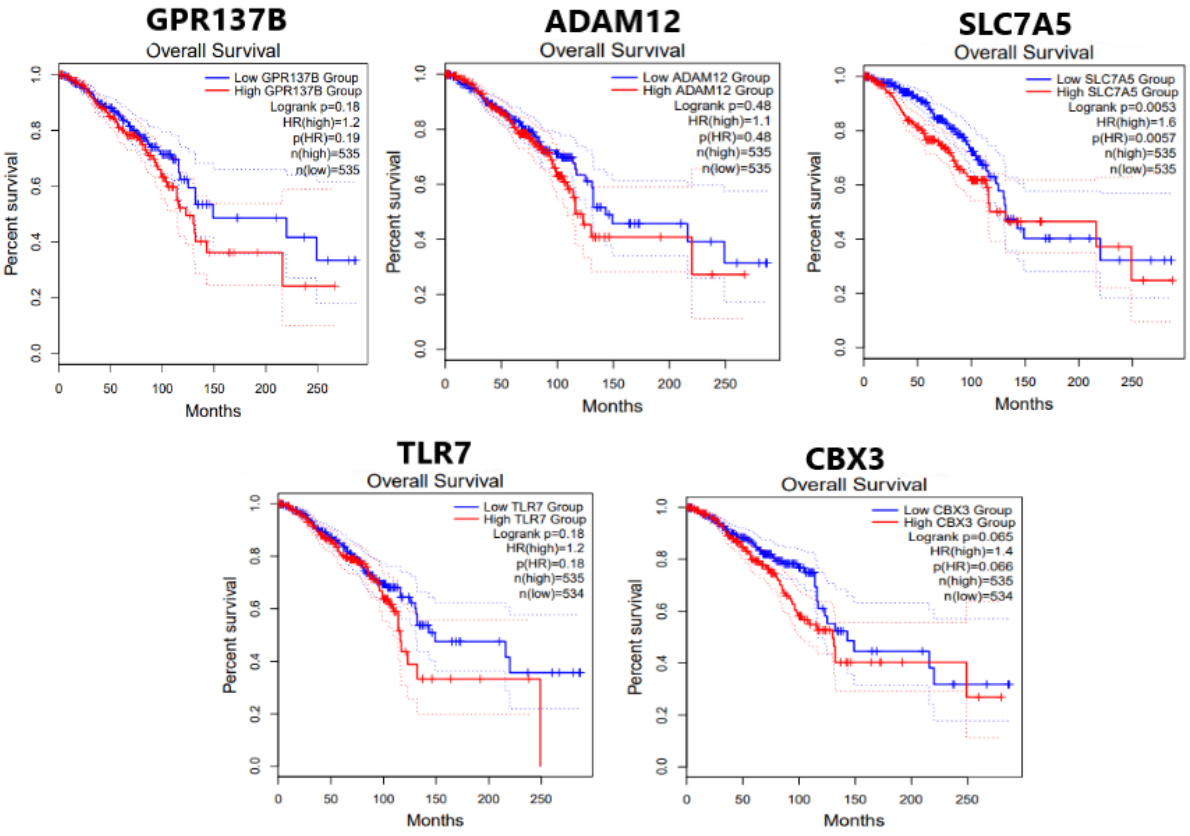

Figure 7: Overall survival analysis of selected genes according to TCGA BC data

Discussion

Cancer drug resistance is a well-known condition that occurs when cancer becomes resistant to pharmaceutical therapy. Anticancer drug resistance is caused by a range of causes, including mutations in DNA and/or epigenetic modifications and several other molecular variations. Resistance to drugs and the insufficient efficacy of therapy with drugs are the causes of up to 90% of cancer-related deaths (18). Unfortunately, many traditional chemotherapy drugs are not targeted to cancer cells and have considerable toxicity. Targeted drug therapies have contributed to great progress in the fight against cancer in recent years. However, while such drugs have impressive results during early treatment, drug resistance may pose a significant challenge in completely eliminating cancer (19). Therefore, identifying molecules related to resistance to drugs and elucidating the underlying pathways is critical.

Using bioinformatics data, this study found many miRNAs and genes that may be related to drugs resistance in BC. Among them, miR-587, miR-4277, miR-620, miR-619 have been shown as a part of the drug resistance mechanism in several cancers (Table 2). Although there is little knowledge about miR-4277 in the literature, the other three miRNAs have been

linked to a variety of malignancies, including BC. For example, miR-587 was identified as having a role in the initiation and progression of TNBC, a subtype of BC in a study using a bioinformatics approach by A et al. (20). MiR-620 has been observed to promote tumor radioresistance by targeting HPGD (21). Tumor-derived exosomal miR-619 has been reported to promote tumor angiogenesis and metastasis via RCAN1.4 (22).

According to the present study findings, another miRNA that we consider to be associated with drug resistance in BC is miR-586. The miRNAs miR-586, miR-4771, and miR-4422 were found effective in the overall survival of TNBC patients in survival analysis (Figure 6). To our knowledge, there is only one study in PubMed regarding the relationship between miR-4771 and cancer. In the relevant study, it was shown that the rs3737589 polymorphism in the TP73-AS1 gene may be associated with the colorectal cancer process by affecting the binding of miR-4771 (23). miR-586 has been reported to be implicated in cancer processes via multiple genes in tumors ranging from BC to gastric cancer (24, 25). According to our results, there are five genes (GPR137B, ADAM12, SLC7A5, TLR7, and CBX3) that are distinctive in resistance to drugs in BC. These five genes, which are putative miR-586 target genes, have also been linked to a variety of malignancies, including BC: For instance, in a study it has been demonstrated that knockdown of GPR137 in HepG2 cells leads to cell cycle arrest in the G0/G1 phase and G2/M phase and induces cell apoptosis (26). The ADAM12 gene has been reported to be a prognostic factor in ER-positive BC (27). According to the study of Wang et al. (28) it was underlined that selective ADAM12-L suppression could optimize the 5-FU-based treatment of BC, hence minimizing BC recurrence in patients. The SLC7A5 gene has also been associated with BC in many studies (29, 30). For example, a study highlighted that SLC7A5 is a potential prognostic biomarker and may be a valuable therapeutic target in BC patients (31). The SLC7A5 gene has also been associated with resistance to various chemotherapeutics. For example, in Retinoblastoma, SLC7A5 has been found to increase chemosensitivity by directly inhibiting it through the tumor suppressor miR-184 (32). In a study conducted using BC patient's tissues and cell lines, it has been evaluated that the LAT1 (SLC7A5) gene plays a role in drug resistance and may be a new therapeutic target against chemotherapy resistance in luminal-type BC (33). TLR 7/8 agonists have been found to reverse oxaliplatin drug resistance in colorectal cancer by directing myeloid-derived suppressor cells to tumor-killing M1 macrophages (34). CBX3, another possible target gene of miR-586, is also one of the important genes associated with drug resistance. For instance, Sang et al. (35) showed that the CBX3 (HP1γ) gene contributes to cervical cancer cells being sensitive to cisplatin via UBE2L3.

Conclusion

In our study, many miRNAs and genes that might be associated with drug resistance in BC were identified using bioinformatics data. Prominent miRNAs are miR-587, miR-4277, miR-620, miR-619 and miR-586. Notable genes in this regard are GPR137B, ADAM12, SLC7A5, TLR7, and CBX3, among the potential target genes of miR-586. Our study results may guide new studies using in vitro and in vivo methods.

Ethics Committee Approval: Open Geo Datasets were used to conduct the study. Ethics committee approval is not necessary since these data are from bioinformatics analysis and no clinical or experimental study has been performed.

Conflict of Interest: None declared by the authors.

Financial Disclosure: None declared by the authors.

Acknowledgments: None declared by the authors.

Author Contributions: All parts of the study prepared by MK

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ORIGINAL ARTICLE

Non-Invasive Assessment of Liver Fibrosis Using Diffusion-Weighted MRI

Difüzyon Ağırlıklı MR Kullanarak Karaciğer Fibrozisinin Non-Invaziv Değerlendirilmesi

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ABSTRACT

Objective: In this study, we aimed to evaluate the stage of liver fibrosis in patients with chronic hepatitis and cirrhosis due to HBV and HCV, with DWI-MRI instead of the liver biopsy, and to investigate whether ADC values can practically replace histological fibrosis staging.
Material and methods: Forty-six patients diagnosed with chronic hepatitis who underwent biopsy with the Ishak fibrosis scoring system and 11 cases who were evaluated as normal according to radiological and clinical findings were included in the study.The ADC value of liver fibrosis patients and healthy controls was compared. The correlation of ADC value and liver fibrosis staging was analyzed. It was shown that ADC values decreased as the fibrosis stage increased.
Results: Very high statistical significance was found between the mean liver ADC values ($p<0.001$). A high level of statistical significance was found between the normalized liver ADC values ($0.001\leq p<0.01$).
Conclusion: DWI images have been among the routine sequences in many imaging centers, are being used extensively, and give good results in the staging of fibrosis. With further studies we can access to standardized values which can lead to more efficient results.

Keywords: Liver fibrosis, ADC, Diffusion MRI, Fibrosis

ÖZ

Amaç: Bu çalışmada, HBV ve HCV'ye bağlı kronik hepatit ve sirozlu hastalarda karaciğer fibrozisinin evrelerini karaciğer biyopsisi yerine DAG-MR ile değerlendirmeyi ve ADC değerlerinin histolojik fibroz evrelemesinin yerine kullanılabilirliğini araştırmayı amaçladık.
Metod: Biyopsi ile İshak fibrozis skorlama sistemi uygulanmış kronik hepatit tanılı 46 hasta ile radyolojik ve klinik bulgulara göre normal olarak değerlendirilen 11 olgu çalışmaya dahil edildi.
Bulgular: Karaciğer fibrozisi olan hastaların ve sağlıklı kontrol grubunun ADC değerleri karşılaştırıldı. ADC değeri ile karaciğer fibrozis evreleri arasındaki korelasyon analiz edildi. ADC değerlerinin fibrozis evresi arttıkça azaldığı gösterildi. Ortalama karaciğer ADC değerleri arasında çok yüksek düzeyde istatistiksel olarak anlamlı fark bulundu ($p<0.001$). Normalize edilmiş karaciğer ADC değerleri arasında yüksek düzeyde istatistiksel olarak anlamlı fark bulundu ($0.001\leq p<0.01$).
Sonuç: DWI görüntülemesi, birçok görüntüleme merkezinde rutin sekanslar arasında yer almakta, yaygın bir şekilde kullanılmakta ve fibrozis evrelemesinde iyi sonuçlar vermektedir. İleri çalışmalar ile standartlaştırılmış değerlere ulaşılabilir ve daha etkin sonuçlara ulaşmak mümkün olabilir.

Anahtar Kelimeler: Karaciğer fibrozis, Difüzyon Ağırlıklı MRG, ADC

Introduction

Fibrosis is the term used to define the over-accumulation of connective tissue in parenchymal organs. Liver fibrosis is an indicator of progressive liver disease. All of the causes causing liver injury also lead to fibrosis through inflammation and necrosis of the liver. Fibrosis, which is reversible in acute cases, can advance to portal hypertension and cirrhosis, with the course of complications of liver dysfunction and the formation of regeneration nodules and fibrous bands in the chronic injury process. Factors leading to liver fibrosis include viral hepatitis (B, C, D), metabolic causes (e.g., hemochromatosis, alpfa-1 antitrypsin deficiency, Wilson disease, galactosemia, tyrosinemia, and Type IV glycogen storage disease), hepatic venous obstruction, toxins and drugs (e.g., alcohol, amiodarone, and methotrexate), primary biliary cirrhosis, nonalcoholic steatohepatitis (NASH), autoimmune hepatitis, helminthes (schistosomiasis) and cryptogenic cirrhosis (1,2).

The fibrosis evaluation is based on whether the liver biopsy specimen is stained with collagen stains. There are several scoring systems in use, such as the histologic activity index (HAI) (3) and the Ishak score (4), which evaluate the degree of inflammation and fibrosis in liver tissue. The Ishak system uses a scale from 0 to 6 to grade the severity of fibrosis, in which 0 indicates no fibrosis and 6 indicates cirrhosis. The evaluation of fibrosis stage in cases with chronic hepatitis related to hepatitis B virus and hepatitis C virus is important regarding the determination of the prognosis and the planning of treatment. Early-stage hepatic fibrosis can be reversed with specific therapeutic agents or the removal of the cause (e.g., alcohol and hepatitis) (5-7). The gold standard for the diagnosis and staging of hepatic fibrosis is biopsy. However, biopsy is an invasive procedure that can cause pain with a rate of 40%, and major complications with a rate of 0.5% (8). In addition,

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biopsy has been found to be associated with significant sampling error (9). Therefore, a reliable, simple, and noninvasive method is required to evaluate hepatic fibrosis.

ADC (Apparent Diffusion Coefficient) values are a type of quantitative measurement obtained from diffusion-weighted magnetic resonance imaging (DW-MRI). These values reflect the degree of water diffusion in tissues, which can be affected the microstructure of tissues including the presence of fibrosis (10).

Fibrosis is a process of excessive accumulation of extracellular matrix components such as collagen in tissues. In general, fibrosis leads to a decrease in the mobility of water molecules, which results in a reduction of ADC values. This means that tissues with higher degree of fibrosis tend to show lower ADC values on DW-MRI (11).

Therefore, ADC values can be used as a potential biomarker to assess the degree of fibrosis in various tissues, including the liver, kidney, and lung. By analyzing ADC values in conjunction with other imaging or clinical parameters, radiologists and clinicians can evaluate the severity of fibrosis, monitor disease progression, and guide treatment decisions.

In our study, we aimed to evaluate the fibrosis level noninvasively using diffusion-weighted magnetic resonance imaging (DW-MRI) instead of the gold-standard biopsy and to investigate the usability of ADC values in place of the histologic evaluation of fibrosis. The hypothesis of the paper is that DW-MRI can be a reliable, simple, and non-invasive method for the evaluation of hepatic fibrosis, and that ADC values can practically replace histological fibrosis staging.

Material and Methods

The Institutional Ethics Committee of İstanbul Education and Research Hospital approved this study Year 2017, number 1114, and informed consent was obtained from all participants. Our study included 46 cases of chronic hepatitis diagnosed between January 2014 and April 2015 at İstanbul Education and Research Hospital, who underwent liver biopsy with modified Knodell and Ishak fibrosis scoring and underwent abdominal MRI examination. Additionally, 11 cases with normal liver evaluations based on radiological and clinical-laboratory assessments of abdominal MRI for various reasons (5 hemangiomas, 4 liver cysts, and 2 adrenal masses) were also included in the study.

Liver ADC studies on all of the cases were carried out using a 1.5-Tesla MRI device with a superconductor (Signa HDxt; GE Medical Systems, Milwaukee, Wisconsin, ABD), with an 8-channel body helix. DW-MRI were obtained at b values of 0 and 400 s/mm2. ADC maps were created at a separate workstation (Advantage Workstation 4.4-GE Medical Systems) using a software program. ADC values were measured on the ADC map using 80- to 100-mm2 regions of interest (ROI) on four quadrants of the liver (anterior and posterior segments in the right lobe, and medial and lateral segments on the left lobe), avoiding the focal lesions, vascular structures and artifact areas, and the mean value was calculated. Spleen ADC values were measured on slices at the same level (Figures 1 and 2). Normalized liver ADC (liver ADC/spleen ADC) values were calculated. Normalization is a technique used to reduce variability and improve the accuracy of ADC measurements. By comparing the liver ADC values to those of the spleen, it is possible to account for individual differences in patient physiology and imaging conditions that could affect the ADC measurements. This process involves calculating a ratio of the liver ADC to the spleen ADC, which provides a more standardized measure that can be more reliably compared across different patients and studies. (12)

Statistical Analysis

The Kruskal-Wallis test was performed to test the significance of the mean ADC values based on the fibrosis stage. Very high statistical significance was found between the mean liver ADC values ($p<0.001$). A high level of statistical significance was detected between the normalized ADC values ($0.001\leq p<0.01$). There were no statistically significant differences between the splenic ADC values (Tables 3-4).

The relationship between Spearman correlation analysis and the quantitative variables was calculated in the statistical evaluation. A high level of statistical significance was found between the corrected ADC (mean liver ADC value/spleen ADC value) values together with fibrosis stages and HAI –Ishak scores ($0.001\leq p<0.01$). Very high statistical significance was detected between the mean liver ADC value and fibrosis stage ($p<0.001$) (Table 5).

In the ROC analysis carried out between stages 0, 1 and 2 and stages 5 and 6 (cirrhosis), 100% specificity and sensitivity were calculated with a very high performance. The area under the curve (AUC) value was equal to 1. An unsuccessful performance was observed in the ROC analysis carried out in stage 0 (healthy subject) and stage 1 and 2 (onset of cirrhosis). The AUC value was 0.560. In the ROC analysis between stage 0 and stages 3 and 4, 100% specificity and sensitivity were calculated. The AUC was equal to 1. In the ROC analysis carried out between stages 1 and 2 and stages 3 and 4, 96% specificity and 92.3% sensitivity were calculated with a very high performance. The AUC value was equal to 0.988. In the ROC analysis carried out between stages 3 and 4 and stages 5 and 6, the specificity was calculated as 84.6%, and the sensitivity was calculated as 100% with very high performance. The AUC value was equal to 0.976. In the ROC analysis carried out between stages 4 and 6, the specificity was 85.7%, and the sensitivity was 100% with a very high performance. The AUC value was equal to 0.964. In the ROC analysis carried out between stage 5 and 6, 100% specificity and 50% sensitivity were calculated with poor performance. The AUC value was equal to 0.688.

Table 1: Distribution of the cases based on age and gender

	N	Minimum	Maximum	Mean	Std. Deviation
Age	57	26,00	80.00	49.96	13,65
Gender		n	%		
	Man	31	54.4		
	Woman	26	45.6		

Table 2: Measurements of the differences between the mean ADC values based on the fibrosis stage

	Mean liver ADC	Normalized Liver ADC	Mean Spleen ADC
Chi-Square	46.827	18.208	9.058
p	0.001	0.006	0.170

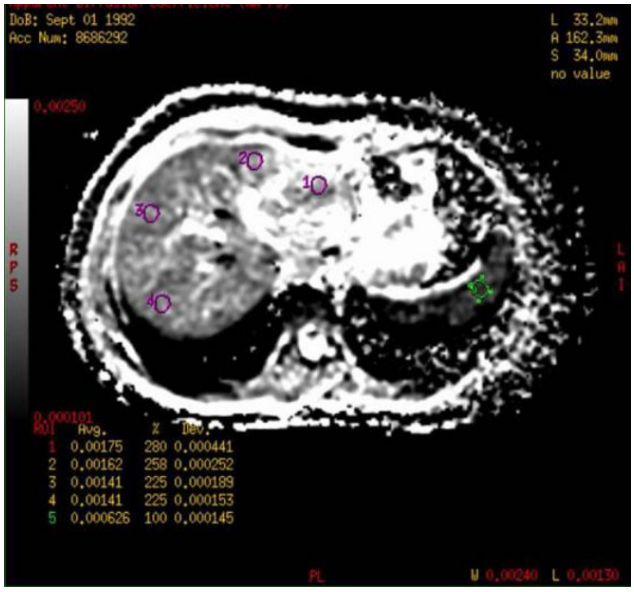

Figure 1: The ADC measurements made on the four quadrants of the liver and on the spleen in a 23-year-old man for whom the liver was evaluated as normal in radiological, clinical and laboratory studies, and fibrosis stage was determined as "0".

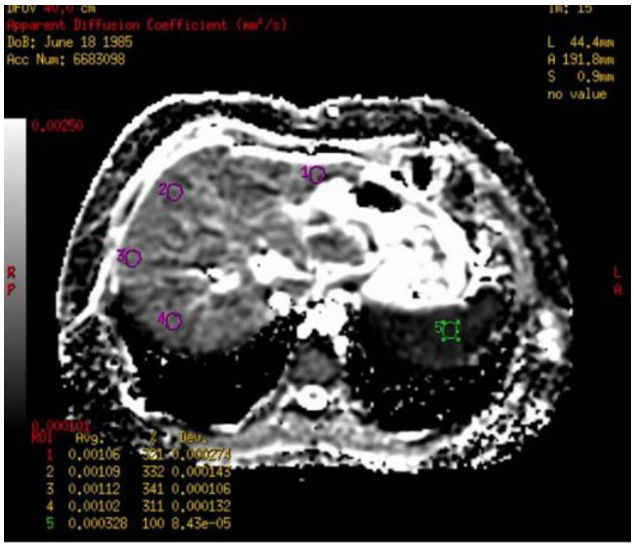

Figure 2: The ADC measurements made on the four quadrants of the liver and on the spleen in a 30-year-old man with fibrosis stage determined to be "4".

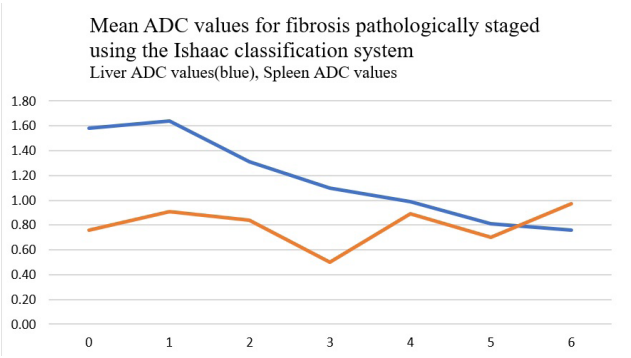

Figure 3: Mean ADC values for fibrosis staged using Ishak classification system.

Table 3: ADC values based on fibrosis stage

Fibrosis		Mean liver ADC	Normalized Liver ADC	Mean Spleen ADC
0	N	11	11	11
	Mean	0.00158	4.54481	0.00076
	Standard Deviation	0.00032	6.71658	0.00039
	Median	0.00152	1.96053	0.00076
	Minimum	0.00126	1.27593	0.00011
	Maximum	0.00245	22.43119	0.00135
1	N	16	16	16
	Mean	0.00164	1.94473	0.00091
	Standard Deviation	0.00032	0.66045	0.00027
	Median	0.00158	1.76139	0.00092
	Minimum	0.00129	1.06884	0.00052
	Maximum	0.00269	3.25000	0.00138
2	N	9	9	9
	Mean	0.00131	1.62906	0.00084
	Standard Deviation	0.00012	0.38820	0.00018
	Median	0.00132	1.71893	0.00085
	Minimum	0.00110	1.20087	0.00051
	Maximum	0.00145	2.33760	0.00110
3	N	6	6	6
	Mean	0.00110	3.74474	0.00050
	Standard Deviation	0.00008	3.98442	0.00027
	Median	0.00108	2.19924	0.00052
	Minimum	0.00102	1.34910	0.00011
	Maximum	0.00124	11.67453	0.00078
4	N	7	7	7
	Mean	0.00099	1.30522	0.00089
	Standard Deviation	0.00009	0.68037	0.00030
	Median	0.00103	1.12776	0.00095
	Minimum	0.00084	0.67200	0.00033
	Maximum	0.00107	2.75994	0.00125
5	N	4	4	4
	Mean	0.00081	1.71545	0.00070
	Standard Deviation	0.00008	1.40442	0.00039
	Median	0.00079	1.16764	0.00075
	Minimum	0.00074	0.76376	0.00020
	Maximum	0.00090	3.76276	0.00109
6	N	4	4	4
	Mean	0.00076	0.86047	0.00097
	Standard Deviation	0.00012	0.35168	0.00030
	Median	0.00075	0.89338	0.00090
	Minimum	0.00065	0.47263	0.00073
	Maximum	0.00090	1.18248	0.00137

Table 4: Spearman correlation analysis

Spearman's rho			HAI score	Fibrosis stage
	Mean liver ADC	rs (ro)	-0.748	-0.850
		p	0.000	0.000
	Normalized Liver ADC	rs (ro)	-0.349	-0.432
		p	0.008	0.001
	Mean Spleen ADC	rs (ro)	-0.013	-0.017
		p	0.923	0.900

Table 5: Comparison of sensitivity, specificity, AUC and p values between different fibrosis stages

Fibrosis stages	AUC	P value	Sensitivity	Specificity
F0,1,2 to F5,6	1.000	<0.0001	100%	100%
F0 to F1,2	0.560	0.5680	56%	72.7%
F0 to F3,4	1.000	<0.0001	100%	100%
F1,2 to F3,4	0.988	<0.0001	92.3%	96%
F3,4 to F5,6	0.976	<0.0001	100%	84.6%
F4 to F6	0.964	<0.0001	100%	85.7%
F5 to F6	0.688	0.3993	50%	100%

Results

In total, 57 cases were included in our study. The ages of the cases ranged between 26 and 80 years, and the mean age was 50 years (std: 13.65) (Table 1). Thirty-one of the cases were men, and 26 were women.

Our study included 11 cases (19%) that were radiologically and clinically evaluated as normal, 16 cases (28%) with a pathology fibrosis score of stage 1, nine cases (16%) with stage 2, six cases (11%) with stage 3, seven cases (12%) with stage 4, and 4 cases each (7% each) in stages 5 and 6, respectively (as shown in Figure 3). We measured the ADC values for the liver (Dliver mean) and spleen (Dspleen), and calculated the normalized liver ADC (D dif) values. (Table 2).

The mean ADC values were calculated according to the fibrosis stage. The fibrosis stage was inversely proportional to the mean ADC values for the measurements made on the liver. It was determined that theADC values decreased with the increasing fibrosis stage. No similar

ratio was found with a single measurement made in the liver; however, it was observed that

spleen ADC values tended to increase with increasing fibrosis levels (Figure 3).

Discussion

Liver fibrosis occurs through collagen accumulation in the extracellular matrix and chronic liver damage (13). Hepatic fibrosis was accepted previously as a passive and irreversible event because of the collapse in the hepatic parenchyma and replacement of the parenchyma with tissue rich in collagen (14, 15). We know that hepatic fibrosis is a dynamic event that can advance or regress within short periods of time such as a few months (16).

Hepatic fibrosis is related to inflammatory response and accumulation restricted in the matrix. The distribution of the fibrous material depends on the cause of liver damage. The fibrotic tissue in chronic viral hepatitis and chronic cholestatic disease can be found around the portal paths at the beginning; however, it occurs in peri-central and peri-sinusoidal paths in alcoholic liver injuries (17).

Liver biopsy is accepted as the standard reference for evaluating hepatic fibrosis (18). However, a biopsy is an invasive procedure that causes pain with a rate of 40% and major complications with a rate of 0.5% (9). Furthermore, biopsies have been found to be related to sampling errors (9). Therefore, a reliable, simple and noninvasive method is required to evaluate hepatic fibrosis.

The no-contrast MR images taken in patients with liver fibrosis in the pre-cirrhotic stage and early-stage cirrhosis are often normal or are characterized by minimal changes and heterogeneity (19). Fibrous septa, bridging, and reticulations that produce low signals in T1AG and high signals in T2AG are observed in patients with advanced age cirrhosis (11).

In their study on mice, Yi-Ping Zhao et al. (19) reported decreases in the ADC value with increasing fibrosis stage (r = -0.903 and P = 0). A similar correlation was also observed in our study regarding the ADC values.

Lower than normal ADC values have been found in many studies (20-23). It is thought that while the decrease in water diffusion in hepatic fibrosis is multi-factorial, the increase in the amount of collagen, in which the free water content is less than that in normal liver parenchyma, plays an important role (24,25).

Do et al. (25) achieved better results in their study when they normalized the liver ADC value with the splenic ADC value in the diagnosis of fibrosis and cirrhosis. In our study, a very high correlation was found in the mean liver ADC values (P=0); however, while the correlation between DWI and fibrosis was significant after normalization with the spleen, it was reduced (P=0.006). In their study, Bonekamp et al. (26) concluded that normalization with the spleen provided no diagnostic benefit. Prospective studies on larger patient groups are needed in this area.

Our study also observed a significant statistical correlation between the HAI score, showing the necro-inflammatory activity, and ADC values. We believe that this correlation is related to the increasing fibrosis level. Fujimoto et al. (27) reported significant differences between the inflammatory activity scores and mean ADC values in their study; however, since their aim was to use the ADC values in the staging of fibrosis or inflammation, they did not investigate the effects of inflammation on fibrosis. In another study, Bonekamp et al. claimed that (26), in their multiple-regression model, inflammation did not have a significant effect on the ADC values.

It is important to detect patients with fibrosis stage 3 or greater among patients with chronic viral hepatitis because the toxicity risk is high in these patients and antiviral therapy can be required; furthermore, the

effectiveness of treatment can be reduced with increasing fibrosis stage. (28)

Soylu et al. (29) concluded that, although the ADC values were smaller in cirrhotic patients, they were useless in HAI and fibrosis staging. In our study, however, the differentiation of healthy subjects and cases with stage 3 and 4 fibrosis (medium level) (AUC: 1.000, p:<0.0001) was possible with ROC analyses with 100% sensitivity and specificity. Likewise, the differentiation of early-stage fibrosis (F0, 1,2) and advanced-stage fibrosis (F5,6) (AUC:1.000, p:<0.0001) was possible with 100% sensitivity and specificity. The differentiation of early-stage fibrosis (F1, 2) and medium-level fibrosis (F3, 4) (AUC: 0.988, p:<0.0001) was possible with 92.3% sensitivity and 96% specificity. It was possible to differentiate medium-level fibrosis (F3, 4) from advanced-stage fibrosis (F5, 6) (AUC:0.976, p:<0.0001) with 100% sensitivity and 84.6% specificity.

Charatcharoenwitthaya P et al. (30) reported that DWI, particularly with spleen-normalized ADC values, could serve as a non-invasive, accurate tool for diagnosing cirrhosis. The study also discusses the impact of necroinflammation and steatosis on ADC values and proposes a diagnostic algorithm incorporating DWI and the Fibrosis-4 index to reduce the need for liver biopsies potentially.

Pan Z et al's study (31) uses of fat- and iron-corrected Apparent Diffusion Coefficient (ADC) values to assess liver fibrosis in chronic hepatitis B patients. The study aimed to improve diagnostic accuracy by accounting for the effects of hepatic steatosis and iron deposition on ADC measurements. The results indicated that correcting ADC values for fat and iron content improved the diagnostic performance for identifying significant fibrosis and cirrhosis, suggesting that fat- and iron-corrected ADC could be a more reliable, non-invasive tool for liver fibrosis assessment.

Jang, W et al.'study (32) presents a meta-analysis comparing the diagnostic performance of diffusion-weighted imaging (DWI) and magnetic resonance elastography (MRE) techniques, specifically gradient-recalled echo-based MRE (GRE-MRE) and spin-echo echo-planar imaging-based MRE (SE-EPI-MRE), in staging liver fibrosis. The study includes data from 60 studies involving 6620 patients. It concludes that both GRE-MRE and SE-EPI-MRE offer high diagnostic accuracy for liver fibrosis at all stages and could potentially replace liver biopsy. DWI, while showing moderate accuracy, is highlighted as a widely available and easily implemented alternative in routine liver MRI settings.

Jiang Y et al. (33) evaluate the clinical potential of a continuous-time random-walk diffusion model (CTRW) for staging liver fibrosis, comparing it with traditional diffusion-weighted imaging (DWI) and serum biomarkers. It involved 52 patients and used multi-b value DWI to derive various diffusion parameters. The findings demonstrate that the CTRW model, especially when combined with other parameters like ADC and LSM, can accurately stage liver fibrosis, offering a reliable, non-invasive tool for liver fibrosis evaluation.

The b value determines the amplitude and period of the diffusion gradient and greatly affects the sensitivity for selective diffusion and the image quality (34-36) High b values must be used to increase the diffusion sensitivity and to decrease the perfusion effect in diffusion-weighted sequences (31). The selected b value will change the measured ADC value; lower ADC values are obtained with increasing b values. However, some studies have shown that average values such as b=400 are more advantageous in the calculation of ADC value for fibrosis staging (35). Only the b=400 value was used in our study, and this is one of the limitations of our study.

In particular, it was not possible to obtain significant results in the differentiation of healthy cases (F0) from cases with early-stage fibrosis (F1, 2) in several studies (20, 25). Similarly, in our study, the differentiation of healthy individuals (F0) from early-stage fibrosis (F1, 2) (AUC: 0.560, p: 0.568), and differentiation of incomplete cirrhosis (F5) from complete cirrhosis (F6) (AUC: 0.688, p: 0.399) was not possible.

However, there are several limitations to this study that must be considered. Firstly, the study only utilized one b value (b=400) in the DWI-MRI examination, which may have influenced the measured ADC values and the overall sensitivity of the findings. Secondly, the study did not compare DWI-MRI to other non-invasive methods for liver fibrosis staging, such as transient elastography or blood biomarkers, which could have provided a more comprehensive understanding of the relative strengths and weaknesses of DWI-MRI. Another possible limitation is the use of a single MRI device and software program for ADC measurements, which could introduce measurement bias and limit the generalizability of the results to other imaging platforms. Additionally, our study was limited by the inability to detect pathologic fibrosis stages in cases considered healthy based on clinical and laboratory results. Furthermore, the small number of cases in stage 5 and stage 6 fibrosis groups (4 in each) is another constraint of this study.

In the light of these limitations, future research should aim to conduct larger-scale studies with a more diverse patient population to validate the findings and enhance their generalizability. Researchers should also investigate the optimal b value for liver fibrosis staging, as well as compare the performance of DWI-MRI to other non-invasive methods. Furthermore, longitudinal studies should be conducted to evaluate the ability of DWI-MRI to predict disease progression, treatment response, and patient outcomes.

Conclusion

In this study, we demonstrated that diffusion-weighted MRI (DWI-MRI) is a highly effective non-invasive tool for staging liver fibrosis. Our findings show that liver ADC values decrease with increasing fibrosis stage. The statistical analyses confirmed a high level of

significance, underscoring the reliability of DWI-MRI in differentiating between various stages of liver fibrosis.

The practical implications of our findings are significant for clinicians, as DWI-MRI offers a safer, less invasive alternative to liver biopsy, reducing patient discomfort and risk of complications. For patients, this method means a more accessible and repeatable option for monitoring liver health, potentially leading to earlier detection and treatment of liver fibrosis. These benefits reinforce the value of our research in advancing liver disease management and improving patient outcomes.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Ethics committee approval (place/date/number)

The Institutional Ethics Committee of İstanbul Education and Research Hospital approved this study Year 2017, number 1114, and informed consent was obtained from all participants.

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Authorship Contribution Statement

Conception: M.H.P., A.H.Y., Design: M.H.P., A.H.Y., Supervision: M.H.P., A.H.Y., Data Collection and/or Processing: M.H.P., A.H.Y., Analysis and/or Interpretation: M.H.P., A.H.Y., Literature Review: M.H.P., A.H.Y., Writer: M.H.P., A.H.Y., Critical Review: M.H.P., A.H.Y.

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ORIGINAL ARTICLE

Characteristics of Patients Receiving Home Care Services from A Tertiary Care Facility and Examination of Provided Medical Services

Üçüncü Basamak Bir Bakım Kuruluşundan Evde Bakım Hizmeti Alan Hastaların Özellikleri ve Sunulan Sağlık Hizmetlerinin İncelenmesi

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ABSTRACT

Aim: Understanding the patient characteristics and medical needs that drive the programming and operation of home care services is crucial. This study evaluates the descriptive characteristics of patients receiving home care services and examines the medical services provided.
Material and Methods: This cross-sectional study included 164 patients receiving home care services from Trabzon Kanuni Training and Research Hospital, Turkiye, for at least one year. Patient records from 2022 were reviewed to gather data on the number of home visits, reasons for visits and procedures performed.
Results: Of the patients, 60.4% were female, and 83.6% were aged ≥65 years. The majority (72.6%) were bedridden, 30.5% used urinary catheters, and 32.9% had pressure ulcers. A total of 2774 home visits (median=16) were conducted, with the most common procedures being blood tests and wound dressing. Risk factors identified included functional bed use and pressure ulcers for wound dressing, rural location and diabetes for blood tests, and rural location, urinary catheter use and history of pulmonary embolism for urinalysis.
Conclusion: This study highlights the intricate relationship between patient characteristics and the delivery of home care services. By identifying specific patient needs such as functional bed use, presence of pressure ulcers, rural residence, diabetes, urinary catheter use and history of pulmonary embolism, we can enhance the planning and execution of home care services. These insights are vital for shaping service delivery policies that aim to maximize resource utilization and improve overall efficiency in healthcare provision.

Keywords: Elderly population, home care services, patient care planning.

ÖZ

Amaç: Evde sağlık hizmetlerinin planlanması ve yürütülmesinde, hasta özelliklerinin ve tıbbi ihtiyaçların bilinmesi önem arz etmektedir. Bu çalışmada evde sağlık hizmeti alan hastaların tanımlayıcı özellikleri ve sunulan tıbbi hizmetler değerlendirildi.
Gereç ve Yöntem: Ocak 2023 tarihinde yürütülen bu kesitsel çalışmaya en az bir yıl boyunca üçüncü basamak bir sağlık kurumundan evde sağlık hizmeti alan hastalar dahil edildi (n=164). Hasta kayıtları incelenerek tanımlayıcı özelliklerin yanı sıra ev biriminin her hasta için son bir yılda (Ocak - Aralık 2022) yaptığı ziyaret sayısı, bu ziyaretlerin nedenleri ve yapılan işlemler kaydedildi.
Bulgular: Hastaların %60,4'ü kadın, %83,6'sı 65 yaş ve üzeriydi. Hastaların %72,6'sının yatağa tam bağımlı olduğu, %30,5'inin idrar sondası kullandığı ve %32,9'unun bası ülseri olduğu belirlendi. Toplam 2774 (ortanca=16) ev ziyareti yapıldı ve en sık uygulanan tıbbi prosedürler kan tetkiki ve yara pansumanıydı. Yara pansumanı için; fonksiyonel yatak kullanımı ve bası yarası, kan tahlili için; kırsal yerleşim ve diyabet, idrar tahlili için; kırsal yerleşim, idrar sondası kullanımı ve pulmoner emboli öyküsünün olması risk faktörleri olarak belirlendi.
Sonuç: Bu çalışma, hasta özellikleri ile evde bakım hizmetlerinin sunumu arasındaki karmaşık ilişkiyi göstermektedir. Fonksiyonel yatak kullanımı, bası yarası varlığı, kırsal yerleşim, diyabet, idrar sondası kullanımı ve pulmoner emboli öyküsü gibi durumlara özel belirli hasta ihtiyaçlarını tespit ederek, evde bakım hizmetlerinin planlanmasını ve yürütülmesini geliştirebiliriz. Bu anlayış, kaynak kullanımını en üst düzeye çıkarmayı ve sağlık hizmeti sunumunda genel verimliliği iyileştirmeyi amaçlayan hizmet sunumu politikalarını şekillendirmek için hayati önem taşımaktadır.

Anahtar Kelimeler: Evde sağlık hizmetleri, hasta bakım planı, yaşlı nüfus.

Introduction

Home care services (HCS) encompass a wide array of services and equipment provided at patients' homes to enhance comfort, function and overall health (1). Beyond medical care, HCS includes personal care, household support, and addresses social needs. In Turkiye, HCS involves comprehensive patient examination, analysis, treatment, follow-up, and rehabilitation, including social and psychological counseling within the home and family environment, primarily overseen by family physicians and hospital home health units (2).

HCS particularly benefits individuals facing mobility limitations, advanced age, or those who are bedridden and dependent on others for daily life (3,4). As evidenced by data from the Turkish Statistical Institute, Turkiye's elderly population is steadily growing due to declining fertility rates and increased life expectancy, rising by 21.4% over the past five years to nearly 9 million individuals (5). This demographic trend suggests an impending increase in the demand for HCS.

Patients requiring HCS often present with multiple comorbid conditions such as cerebrovascular diseases, cardiovascular diseases, dementia, chronic lung diseases, end-stage cancer, geriatric syndromes,

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chronic kidney failure and obesity (6). This necessitates a holistic and continuous approach to medical care, leading to the integration of additional practices in HCS such as chronic disease management, nutritional support, immunization, coagulopathy management, provision of medical devices, and post-surgical care.

While existing literature discusses the characteristics of patients receiving HCS and provides insights into their medical conditions, there remains a gap in understanding how these patient-specific factors influence the delivery of services. Understanding the medical needs and characteristics of HCS recipients is crucial for effective service management. This study aims to elucidate the descriptive characteristics of patients registered in the HCS unit of a tertiary hospital and analyze the medical services provided over a one-year period. By doing so, it aims to provide HCS providers with valuable insights for staff planning, logistical organization and time management, all critical for optimizing service delivery.

Material and Methods

Study Design and Participants

This cross-sectional study was conducted in January 2023 within the HCS unit of a tertiary care facility. The study included all patients enrolled in the unit and receiving HCS continuously for at least one year. Permission for the study was obtained from the hospital management and approved by the Trabzon Kanuni Training and Research Hospital, Clinical Research Ethics Committee with 27.06.2022 date and 2022/38 number.

The study was conducted at a center serving both rural and urban areas, providing a representative sample of the broader home health service population in the region.

Healthcare Personnel and Organization

The center employs a total of 11 healthcare personnel organized into 3 separate teams, each serving distinct geographic locations. Each team consists of a physician, nurse, and health officer responsible for conducting home visits. Additionally, there is a coordinating physician overseeing these teams and providing consultative support, along with an administrative officer handling secretarial duty.

Patient Follow-up and Visit Protocol

Each team manages a caseload ranging from 150 to 180 registered patients. Visits are scheduled and conducted by appointment, with each patient receiving at least one visit within a maximum interval of 3 months. During these visits, physicians conduct comprehensive assessments regardless of patient complaints. They evaluate the patient's condition, document relevant information in patient records, arrange treatments as necessary, and initiate consultations when indicated.

Data Collection

The initial step involved obtaining the active registered patient list from the HCS secretariat as of the study date. From this list of 318 patients, records of 164 individuals who had received home health care continuously for at least one year were systematically reviewed. Demographic characteristics including age, gender, marital status and educational status were documented, alongside descriptive features such as bed dependency, excretory and nutritional status, presence of pressure ulcers, and concurrent diseases.

Nutritional status was assessed using the Mini Nutritional Assessment, pressure ulcer risk with the Braden Scale, and independence in daily living activities using the Katz Index. These assessments were conducted by certified physicians based on direct patient examination, with information supplemented by caregivers where necessary. All measurements were taken using calibrated devices.

Additionally, data on the number of visits conducted by the HCS team for each patient throughout the year (January to December 2022), the reasons for these visits, and the specific procedures performed were collected and incorporated into the study dataset.

Data Analysis

Data were analyzed using SPSS version 23.0 (IBM, Chicago, USA). Descriptive statistics were computed, and normal distribution of numerical variables was assessed using the Kolmogorov-Smirnov Z test. Numerical data were further analyzed using Spearman correlation analysis and the Mann-Whitney U test where appropriate.

Logistic regression analysis was employed to identify independent risk factors influencing the implementation of each medical procedure. Variables demonstrating a significance level of $p<0.05$ in individual comparisons were included in the regression model. Numerical data were presented as median [interquartile range], while categorical data were expressed as frequencies and percentages. Statistical significance was set at $p<0.05$.

Results

A total of 164 patients were included in the study, with a median age of 80 [14] years, and 99 (60.4%) were female. Detailed demographic characteristics and comorbidities are summarized in Table 1 and 2.

Visit data were unavailable for 2 patients receiving home health services, leaving 162 patients for analysis. Over the study period (January to December 2022), a total of 2774 visits were conducted, with a median of 16 [14] visits per patient (Table 3). The distribution of medical procedures performed during these visits is also detailed in Table 3.

Significantly more visits were observed among patients residing in urban areas, those fully dependent on bed use, using air beds, urinary catheters, enteral nutrition solutions, and with tracheostomy or pressure ulcers ($p=0.047$, $p=0.037$, $p=0.013$, $p<0.001$, $p=0.042$, $p=0.005$, $p=0.045$, $p=0.003$, respectively).

Multiple regression analysis (Table 4) revealed

the impact of patient characteristics on the implementation of key medical procedures such as wound dressing, blood tests, and urinalysis, which are commonly performed during home visits.

Table 1. Descriptive characteristics of patients

	n (%)
Age	
<18	5 (3.0)
18-64	22 (13.4)
65-84	87 (53.1)
>85	50 (30.5)
Living place	
Urban	68 (41.5)
Rural	96 (58.5)
State of being bedridden	
Fully dependent	119 (72.6)
Semi-dependent	40 (24.4)
Not dependent	5 (3.0)
Caregiver	
Child	89 (54.3)
Bride or groom	20 (12.2)
Mother or father	17 (10.4)
Wife or husband	16 (9.8)
Other relative	11 (6.7)
Hired caregiver	11 (6.7)
Functional bed	46 (28.0)
Air bed	44 (26.8)
Excretion status	
Diaper	140 (85.4)
Urinary catheter	50 (30.5)
Colostomy	4 (2.4)
Nutritional status	
Oral intake	117 (71.3)
Nutrition with PEG/NG	51 (31.1)
Use of enteral nutrition solution	62 (37.8)
Malnutrition status (n=106)	
Normal nutritional status	9 (8.5)
At risk of malnutrition	44 (41.5)
With malnutrition	53 (50.0)
Respiratory status	
Tracheostomy	22 (13.4)
Use of assisted breathing apparatus	35 (21.3)
Pressure ulcer	54 (32.9)

PEG: percutaneous endoscopic gastrostomy
NG: nasogastric tube

Table 2. Comorbidities of patients

	n (%)
Neurological disease	142 (86.6)
Dementia	79 (48.2)
Cerebrovascular event	70 (42.7)
Epilepsy	28 (17.1)
Parkinson's disease	19 (11.6)
Cerebral palsy	8 (4.9)
Cardiac disease	75 (45.7)
Atrial fibrillation	35 (21.3)
Coronary artery disease	30 (18.3)
Heart failure	24 (14.6)
Valvular heart disease	16 (9.8)
Hypertension	119 (72.6)
Hyperlipidemia	25 (15.2)
Diabetes	54 (32.9)
Hypothyroidism	18 (11.0)
Orthopedic disease	39 (23.8)
Lung disease	
Chronic obstructive pulmonary disease	18 (11.0)
Asthma	11 (6.7)
Pulmonary embolism	11 (6.7)
Psychiatric illness	45 (27.4)
Anxiety	19 (11.6)
Depression	17 (10.4)
Malignancy	13 (7.9)
Chronic kidney disease	11 (6.7)

Table 3. Medical procedures performed during home visits and how many patients these procedures were performed on.

	Number of patients n (%)	Total number of procedures
Wound dressing	69 (42.6)	423
Blood test	122 (75.3)	464
Coagulation monitoring (INR)	33 (20.4)	138
Urinalysis	46 (28.4)	123
Culture	10 (6.2)	13
Vaccination	39 (24.1)	56
Electrocardiogram	3 (1.9)	3
Urinary catheter	59 (36.4)	264
Nasogastric tube	9 (5.6)	22

Table 4. Multiple regression analysis data showing the effect of patient characteristics on wound dressing, blood test and urinalysis.

	Odds ratio [confidence interval]	p value
Wound dressing		
Using a functional bed	2.9 [1.1-7.6]	0.029
Having pressure ulcer	3.3 [1.4-7.7]	0.006
Blood test		
Living in rural	2.8 [1.3-6.1]	0.012
Having diabetes	2.9 [1.1-7.7]	0.038
Urinalysis		
Living in rural	3.4 [1.4-7.9]	0.005
Using a urinary catheter	3.1 [1.3-7.3]	0.010
History of pulmonary embolism	8.3 [1.9-35.6]	0.004

Variables observed to have p<0.05 in single comparisons were included in the multiple regression model.

Discussion

Our study revealed that patients received a median of 16 visits per year from HCS. The most common procedures during these visits were blood testing, wound dressing and urinary catheterization, aligning with findings from previous studies (Aslan et al., 10). However, our study observed a higher visit frequency compared to some literature reports (7,9).

Certain patient characteristics emerged as independent risk factors influencing the need for specific procedures. Patients using functional beds and those with pressure sores required more frequent wound dressings. Similarly, rural residence and diabetes were associated with increased need for blood testing while urinary catheter use and a history of pulmonary embolism were linked to higher rates of urinalysis.

The majority of HCS recipients in our study were women, consistent with broader trends observed in Turkiye (4,8,11,12), where elderly women constitute a significant portion of the population benefiting from HCS. This trend may reflect both longer life expectancy among women and their higher utilization rates of healthcare services.

A notable finding was the high prevalence of bedridden patients in our study, exceeding 70%. This contrasts with previous estimates, potentially due to our inclusion criteria focusing on patients receiving continuous HCS for at least one year, thereby capturing more chronic and severe cases. However, it's concerning

that less than one-third of these patients had access to functional or pneumatic beds, which are crucial for preventing complications like pressure ulcers.

Malnutrition emerged as a significant concern, with a substantial portion of patients at risk, often requiring specialized nutritional support such as percutaneous endoscopic gastrostomy (PEG) or nasogastric tube (NG) feeding. Malnutrition can significantly impact various aspects of patient health, including wound healing, immune function and overall quality of life.

Chronic conditions such as neurological and cardiovascular diseases were prevalent among our cohort, necessitating ongoing medical management through HCS. This highlights the importance of comprehensive care plans that address both acute medical needs and long-term management strategies, including regular monitoring and immunization schedules.

It is important to note the limitations of our study, including its retrospective nature and cross-sectional design, which preclude establishing causal relationships. Additionally, not all data may have been fully captured due to the study's retrospective nature, impacting the comprehensiveness of our findings.

Conclusion

This study has illuminated the demographic profiles and medical needs of patients receiving HCS at a tertiary hospital in a semi-rural setting. Patients requiring intensive monitoring include those with functional bed dependency, urinary catheter use, pressure ulcers, diabetes, a history of pulmonary embolism, and those residing in rural areas. These findings underscore the necessity for personalized care plans and the expertise of healthcare professionals in administering specialized procedures such as wound dressing and catheterization.

The dissemination of our findings can inform the development of comprehensive health policies tailored to address the specific needs identified within HCS. Implementing digital platforms to document patient characteristics and risk profiles holds considerable promise for enhancing service delivery and overall quality. Future research endeavors should explore these digital solutions further to optimize the effectiveness of HCS.

In conclusion, understanding the dynamic relationship between patient profiles and service requirements is pivotal for efficient resource allocation and improved outcomes in home care settings. This study contributes valuable insights to ongoing efforts aimed at refining and expanding HCS, ultimately enhancing care delivery for diverse patient populations.

Ethical Approval

Permission for the study was obtained from the hospital management and approved by the Trabzon Kanuni Training and Research Hospital, Clinical Research Ethics Committee with 27.06.2022 date and 2022/38 number.

Authorship Contribution Statement

Conception: C.Y., V.A., B.A.Y., Design: C.Y., V.A., B.A.Y., Supervision: C.Y., V.A., B.A.Y., Data Collection and/or Processing: C.Y., V.A., B.A.Y., Analysis and/or Interpretation: C.Y., Literature Review: C.Y., Writer: C.Y., V.A., B.A.Y., Critical Review: C.Y., V.A., B.A.Y.

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ORIGINAL ARTICLE

Determination of the Effects of Hand Hygiene Education Given to Nursing Students in Intensive Care Unit on Hand Microbiota

Yoğun Bakım Ünitesinde Hemşirelik Öğrencilerine Verilen El Hijyeni Eğitiminin El Mikrobiyotasına Etkisinin Belirlenmesi

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ABSTRACT

Purpose: This study is conducted with the purpose of comparing fourth-year nursing students' hand hygiene practices and beliefs with their hand flora. Additionally, we aim to assess the effectiveness of hand hygiene education in this context.
Material and Methods: This research has been conducted using a pre-test, post-test, and control group quasi-experimental design. The research was conducted with fourth-grade students studying at the Nursing Department of a Faculty of Health Sciences in the fall semester of the 2022-2023 academic year. Twenty students who volunteered to participate were included using a simple random sampling method and were then randomly assigned to experimental and control groups. The Hand Hygiene Application Inventory and the Hand Hygiene Belief Scale administered as pre-tests. Students underwent tape stripping and swab methods to collect samples for their hand flora before any interventions. Ten students in the experimental group were given education about hand hygiene rules by the researchers. A post-test was conducted for the experimental group.
Results: The hand hygiene beliefs and practices of both groups were similar before training. When the Hand Hygiene Application Inventory and Hand Hygiene Belief Scale scores before and after the training were examined, an increase was observed in the scale scores after training. In this study, the microorganisms present in the general hand flora were identified simplistically, and the changes were observed after hand hygiene education. Furthermore, the study shed light on the structure of hand flora after education in terms of microbial load.
Conclusion: It has been experimentally determined that there is a significant decrease in hand microbiota load and pathogenic groups with hand hygiene education.

Keywords: Hand hygiene, Hand microbiota, Intensive care, Nursing student.

ÖZ

Amaç: Bu çalışma hemşirelik dördüncü sınıf öğrencilerinin el hijyeni uygulama ve inançlarının el florası ile karşılaştırılması amacıyla yapılmıştır. Ayrıca bu bağlamda el hijyeni eğitiminin etkinliğini değerlendirmeyi amaçlıyoruz.
Gereç ve Yöntemler: Bu araştırma ön test, son test ve kontrol gruplu yarı deneysel desen kullanılarak gerçekleştirilmiştir. Araştırma, 2022-2023 akademik yılı güz döneminde bir Sağlık Bilimleri Fakültesi'nin Hemşirelik Bölümü'nde öğrenim gören dördüncü sınıf öğrencileri ile gerçekleştirilmiştir. Araştırmaya katılmaya gönüllü olan yirmi öğrenci basit rastgele örnekleme yöntemi kullanılarak seçilmiş ve daha sonra deney ve kontrol gruplarına rastgele atanmıştır. El Hijyeni Uygulama Envanteri ve El Hijyeni İnanç Ölçeği ön test olarak uygulanmıştır. Öğrencilere herhangi bir müdahale öncesinde el florası için örnek toplamak amacıyla bant çıkarma ve sürüntü alma yöntemleri uygulanmıştır. Deney grubundaki 10 öğrenciye araştırmacılar tarafından el hijyeni kuralları hakkında eğitim verilmiştir. Deney grubuna son test uygulanmıştır.
Bulgular: Her iki grubun el hijyeni inançları ve uygulamaları eğitim öncesinde benzerdi. El Hijyeni Uygulama Envanteri ve El Hijyeni İnanç Ölçeği puanları eğitim öncesi ve sonrası incelendiğinde eğitim sonrası ölçek puanlarında artış gözlendi. Bu çalışmada genel el florasında bulunan mikroorganizmalar basit bir şekilde tanımlanmış ve el hijyeni eğitimi sonrası değişimler gözlemlenmiştir. Ayrıca çalışma, mikrobiyal yük açısından eğitim sonrası el florasının yapısına ışık tutmaktadır.
Sonuç: El hijyeni eğitimi ile el mikrobiyota yükünde ve patojen gruplarda anlamlı bir azalma olduğu deneysel olarak belirlenmiştir.

Anahtar kelimeler: El hijyeni; el mikrobiyotası; yoğun bakım; hemşirelik öğrencisi.

Introduction

Healthcare-associated infections in intensive care units are important causes of preventable morbidity, mortality, and prolonged length of stay (1). The management of infectious diseases is progressively becoming more difficult, primarily due to the emergence of resistance mechanisms in bacteria. Non-adherence to proper hand hygiene stands as a paramount factor among the leading causes of healthcare-associated infections. Emphasizing proper hand hygiene practices in intensive care units is highlighted as a crucial measure for managing central catheter-associated infections (2) and controlling ventilator-associated pneumonia (3). In a recent study, it was observed that healthcare professionals exhibit a higher frequency of transitioning from tasks involving contamination to those involving cleanliness during patient care responsibilities. This dynamic has the potential to elevate the risks of transmission and infection (4). Due to the higher likelihood of healthcare workers transmitting pathogenic microorganisms to intensive care patients through their hands, addressing the knowledge and implementation gaps in hand

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hygiene practices among the staff is emphasized as an effective strategy in reducing infection rates (5).

In a study evaluating the hand hygiene practices of nurses in the hospital, it was found that only 65% of participants demonstrated proper hand hygiene compliance (6). To reduce the spread of healthcare-associated infections, continuous education is recommended for intensive care unit staff to induce behavioral changes in hand washing practices (3). A study focused on the adherence of neonatal intensive care unit nurses to standard infection control measures and the identification of facilitating factors revealed that clinical experience and educational qualifications are fundamental determinants in this regard (7). The study recommended periodic updates and evidence-based training related to the subject, highlighting the significance of staying current in the field (7). It has been observed that compliance with hand hygiene can be enhanced up to six months following the conducted training interventions (8). Therefore, it is recommended that the training programs are of high quality, tailored to the specific goals, and inclusive of all intensive care staff members (9).

Since nursing students are considered healthcare workers during their education, they could potentially serve as vectors for cross-contamination in the hospital setting (10). Additionally, due to the elevated risk of exposure to occupational biological hazards, it is recommended to provide training for students to enhance their knowledge and compliance with infection prevention practices (11). Training interventions have been found to foster positive attitudes towards hand hygiene and enhance awareness (10-12). While studies have determined that nursing students hold positive beliefs and value hand hygiene (13), there is also recognition of the need to improve compliance with hand hygiene (14, 15). The use of hand hygiene training videos has been observed to increase nursing students' handwashing skills and compliance rates (12). However, it is important to note that the outcomes of these studies are based on students' self-reports. Therefore, there is a need for observation-based studies concerning compliance with hand hygiene (12,13-16,17). As a result, this approach can enable healthcare workers to provide care to patients in a more efficient, effective, and safe manner (4).

The skin, our largest organ, possesses two distinct microbiotas: one permanent and one temporary, both enveloping the body. Human skin provides a habitat for commensal microbiota while also serving as a physical barrier to deter the invasion of foreign pathogens. It is colonized by various microbiotas, playing a dual role of hosting and repelling potential intruders (18).

The microbial load on hands varies considerably in comparison to other skin areas, with healthcare workers' hand microbial load reported to be between 3.9x104 and 4.6x106 CFU/cm2 (19). Different isolation methods can be employed to determine the presence of microorganisms in an environment (20, 21). Sampling through the swab method from clinical specimens is a widely used approach (22). In a study, the tape stripping method was compared to the swab method for collecting live skin bacteria without compromising the composition of the skin microbiome. It was demonstrated that the tape stripping method is comparable to the swab method (23).

The literature does not currently include a study comparing nursing students' hand hygiene practices and beliefs with their hand flora. Therefore, our research is conducted with the purpose of comparing fourth-grade nursing students' hand hygiene practices and beliefs with their hand flora. Additionally, we aim to assess the effectiveness of hand hygiene education in this context.

The hypotheses of the study are as follows:

H0: Hand hygiene training has no effect on hand microbiota load and pathogenic group amount.

H1: Hand hygiene training reduces hand microbiota load and pathogenic groups.

Material and Methods

Type of research

This research has been conducted using a pre-test, post-test, and control group quasi-experimental design.

Research population and sample

The research was conducted with fourth-grade students studying in the Nursing Department of a Faculty of Health Sciences in the fall semester of the 2022-2023 academic year. For the specified academic year, 20 volunteer students practicing in intensive care unit within the scope of clinical practice course were randomly selected by the instructor in charge of the course. Students were assigned to the experimental and control groups by using the lottery method.

Implementation of the research

The data of the study was collected between September and December 2022. Before the intervention, students in both groups were administered the Hand Hygiene Application Inventory (HHAI) and the Hand Hygiene Belief Scale (HHBS) as pre-tests. All students underwent tape stripping and swab methods to collect samples for their hand flora before any interventions. Ten students in the experimental group were given education about hand hygiene rules by the researchers. Ten students in the control group did not participate in the education. After the education, the students continued to care for patients in the intensive care unit. A post-test was conducted for the experimental group after the education. Subsequent to application, all students underwent sample collection using the same methods.

Implementation of hand hygiene education

The content of the hand hygiene education was designed in alignment with the existing literature. It encompassed key aspects such as proper handwashing techniques, the products utilized during

handwashing, strategies for ensuring effective hand hygiene, recommended frequency of handwashing, scenarios necessitating handwashing, potential barriers to handwashing, and the appropriate usage of alcohol-based antiseptics.

The training session took place in the hospital's designated meeting room and was structured to last for approximately 45 minutes. The content was tailored to suit the educational needs of the participants and was aimed at providing comprehensive insights into the topics outlined above.

Data collection instruments

Hand Hygiene Application Inventory (HHAI) and Hand Hygiene Belief Scale (HHBS): The HHAI is a 14-item inventory used to assess hand hygiene practices; whereas the HHBS is a 22-item scale designed to evaluate beliefs regarding hand hygiene. The Turkish validity and reliability of these instruments were established by Karadağ et al. in 2016 (24).

Both scales utilize a 5-point Likert scale. Scores for HHAI range from a minimum of 14 to a maximum of 70 while scores for HHBS range from a minimum of 22 to a maximum of 110. These instruments were employed to assess the participants' hand hygiene practices and beliefs in the context of the study.

Determining hand flora

To ascertain changes in the hand flora of participating students who received hand hygiene education and those who did not, isolation studies were conducted using swab and tape stripping methods on skin flora. This allowed for the revelation of the microbial profile. General and selective culture media were employed in the isolation process. Nutrient agar served as the general culture medium while Blood agar and Brain Heart Infusion (BHI) agar functioned as selective media.

Nutrient agar is a general-purpose medium suitable for the growth of various organism groups. Blood agar is a selective medium employed for the isolation of Streptococcus pneumoniae, other streptococci, Bacteriodes, Clostridium and yeast. BHI agar, being an enriched medium, can be used for the culture of challenging-to-culture organisms like streptococci, pneumococci and meningococci. The utilization of these media aided in determining the microbial composition present in the hand flora of the participants.

Swab Method

Sterile swab sticks were gently rubbed onto the surface of the hand to collect samples. Subsequently, the swab stick was cut and placed into a vial containing Ringer's solution, where it was left to stand for 30 minutes. Serial dilution was performed using the dilution plate method, and 200 µl was taken from each dilution to be inoculated onto prepared culture media using the streak plate method (21).

Tape Stripping Method

Acrylic adhesive medical permeable tape was sterilized using ultraviolet radiation and then applied to the hands of nursing students for a duration of one minute. Subsequently, using sterile forceps, the tape was peeled off the skin and, similar to the swab method, inoculated onto culture media using the dilution plate method. Following this, the plates were left to incubate at 30 °C and 37 °C for 24 hours, and the resulting colony formations were examined for differentiation. All colonies that had formed as single entities were subjected to tests for catalase and coagulase enzyme activities. Based on the test outcomes, the colonies were grouped into fundamental categories.

Determination of Isolated Bacteria's Enzyme Activities

Catalase Test

Catalase activity of microorganisms that appeared as single colonies on isolation plates was determined using hydrogen peroxide. For this test, S. aureus was used as a control group. The catalase test is employed for identifying aerobic bacteria containing cytochrome with catalase enzyme activity, along with certain facultative bacteria. A pure single colony of the microorganism from the solid culture medium was aseptically transferred onto a glass slide. A few drops of 3% hydrogen peroxide (H_2O_2) were added onto the colony using a sterile loop. The formation of bubbles after the reaction was evaluated as a positive result.

Coagulase Test

Coagulase enzyme, which is involved in plasma clotting and also possesses deoxyribonuclease (DNase) characteristics, is widely used for identifying staphylococci. It is particularly employed to determine the pathogenicity of staphylococci. In the coagulase test, S. aureus was used as the control group.

A clean glass slide was prepared, and a pure colony from the agar plate was suspended in sterile water. A few drops of fresh sterile human plasma were added onto the suspension. The clotting status was assessed after 3-5 seconds, and the result was determined as either positive or negative. This test is significant for evaluating the pathogenicity of staphylococci.

Data Analysis

The research data were analyzed using SPSS 21.0 software package. Descriptive statistics were presented in terms of numbers, percentages, means, and standard deviation values. For comparative analyses, the Mann-Whitney U test was used for independent groups, while the dependent t-test was employed for dependent groups. A significance level of $p<0.05$ was considered to determine the statistical significance of the results.

Ethical Considerations

The research was conducted in accordance with the Helsinki Declaration. Prior to implementation, approval was obtained from the Bilecik Şeyh Edebali University Non-Interventional Clinical Research Ethics Committee

with approval number 7/6 and date 22.11.2022. Permission for conducting the study at the intensive care unit where the students practiced was obtained, and written and verbal consent was obtained from the participants. The researchers informed the participants about the research topic, purpose, and process. Ethical principles were strictly followed throughout the study.

Results

The pre-training and post-training results of the HHAI and HHBS applied to the experimental and control groups are presented in Table 1. Before training, the experimental group had a mean HHAI score of 61.40±4.42 and an HHBS score of 79.30±5.18. The control group had a mean HHAI score of 64.30±4.16 and an HHBS score of 79.30±16.14 before training. After training, the experimental group's mean HHAI score was determined as 69.30±0.94, and the HHBS score was 94.60±5.25. There was no statistically significant difference in the HHAI and HHBS scores before training between the experimental and control groups (p>0.05). This indicates that the hand hygiene beliefs and practices of both groups were similar before training. When comparing the pre- and post-training HHAI and HHBS scores within the experimental group, a statistically significant increase was observed in scale scores after training (p<0.05).

Isolation to collect samples from the skin flora of both the experimental and control group students was conducted using the swab and tape stripping methods. Samples obtained from all students using these two methods were inoculated onto three different culture media using the dilution plate method. After the incubation period, bacterial colonies that developed on the plates were examined, and colony counts were performed. The obtained results are presented in Table 2. In this study, the aim was to determine bacterial groups in the hand flora using two different methods and three different media. For the samples obtained through the swab method, based on the results from BHI agar and blood agar media, no significant differences were observed in the growth of bacterial colonies before and after contact for both the experimental and control groups (p>0.05). However, when considering the results from the nutrient agar media, a significant difference was detected in the colony counts before and after contact for both groups (p<0.05). Regarding the samples obtained through the tape stripping method, no significant differences were found in colony counts between the experimental and control groups before contact for blood agar and nutrient agar media (p>0.05). However, a significant difference was observed in colony counts before contact for the BHI agar media (p<0.05). After contact, significant differences in colony counts were observed between the experimental and control groups for blood agar, BHI agar, and nutrient agar media (p<0.05). In all media, the experimental group exhibited significantly lower colony counts compared to the control group (p<0.05).

Table 1. HHAI and HHBS Results for Experimental and Control Groups

		Experimental Group (n=10)		Control Group (n=10)		
		Mean	Standard Deviation	Mean	Standard Deviation	p Z
Pre-education	HHAI	61.40	4.42	64.30	4.16	0.211 -1.252
Post-education	HHAI	69.30	0.94			
p Z		0.005 -2.805				
Pre-education	HHBS	79.30	5.18	79.30	16.14	0.363 -0.911
Post-education	HHBS	94.60	5,25			
p Z		0.005 -2.805				

Table 2. Colony Count Ratios of Samples Obtained Through Swab And Tape Stripping Methods In Different Media

	Swab Method					
	Before contact			After contact		
	Experimental Group	Control Group		Experimental Group	Control Group	
	Mean±SD	Mean±SD	p Z*	Mean±SD	Mean±SD	p Z*
BHI agar	1.20±2.25	202.80±419.69	0.195 -1.195	0.80±1.31	219.30±415.35	0.669 -0.428
Blood agar	1.40±3.09	407.10±509.92	0.123 -1.544	2.80±6.51	109.50±313.26	0.609 -0.512
Nutrient agar	3.50±9.68	599.70±515.49	0.024 -2.253	0.20±0.63	304.30±479.58	0.045 -2.008
	Tape Stripping Method					
	Before contact			After contact		
	Experimental Group	Control Group		Experimental Group	Control Group	
	Mean±SD	Mean±SD	p Z*	Mean±SD	Mean±SD	p Z*
BHI agar	1.40±4.08	424.70±495.45	0.003 -2.962	0.90±1.85	307.70±477.26	0.035 -2.112
Blood agar	1.10±3.47	308.00±477.52	0.090 -1.693	0	399.60±515.88	0.029 -2.179
Nutrient agar	1.00±2.82	299.90±482.42	0.130 -1.514	0.50±1.08	401.10±514.60	0.029 -2.187

*Mann whitney u test

Table 3. Comparison of sample collection methods for before and after contact media

		BHI agar		Blood agar		Nutrient agar	
		Before contact	After contact	Before contact	After contact	Before contact	After contact
Swappping	p	0,244	0,476	0,234	0,859	0,152	0,271
Stripping	Z*	-1,165	-0,713	-1,190	-0,178	-1,433	-1,101

*Mann Whitney u test

Table 4. Enzyme test results of bacteria obtained by swab method

Swab method							
		Coagulase Test					
		Blood agar		BHI agar		Nutrient agar	
			n (%)		n (%)		n (%)
Before contact	Experimental Group	+	1(10)	+	0	+	1(10)
		-	1(10)	-	2(20)	-	0
		*	8(80)	*	8(80)	*	9(90)
		T	10(100)	T	10(100)	T	10(100)
	Control Group	+	1(100)	+	1(100)	+	2(20)
		-	5(50)	-	5(50)	-	6(60)
		*	4(40)	*	4(40)	*	2(20)
		T	10(100)	T	10(100)	T	10(100)
		Blood agar		***BHI agar***		Nutrient agar	
			n (%)		n (%)		n (%)
After contact	Experimental Group	+	1(10)	+	3(30)	+	0
		-	2(20)	-	0	-	0
		*	7(70)	*	7(70)	*	10(100)
		T	10(100)	T	10(100)	T	10(100)
	Control Group	+	1(10)	+	1(10)	+	1(10)
		-	3(30)	-	5(50)	-	5(50)
		*	6(60)	*	4(40)	*	4(40)
		T	10(100)	T	10(100)	T	10(100)
		Catalase Test					
		Blood agar		BHI agar		Nutrient agar	
			n (%)		n (%)		n (%)
Before contact	Experimental Group	+	2 (20)	+	5 (50)	+	3(30
		-	2 (20)	-	1 (10)	-	1(10)
		*	6 (60)	*	4 (40)	*	6(60)
		T	10 (100)	T	10 (100)	T	10(100)
	Control Group	+	6 (60)	+	5 (50)	+	5(50)
		-	1 (10)	-	1 (10)	-	0
		*	3 (30)	*	4 (40)	*	5(50)
		T	10 (100)	T	10 (100)	T	10(100)
		Blood agar		BHI agar		Nutrient agar	
			n (%)		n (%)		n (%)
After contact	Experimental Group	+	2(20)	+	3(30)	+	0
		-	0	-	1(10)	-	0
		*	8(80)	*	6(60)	*	10(100)
		T	10(100)	T	10(100)	T	10(100)
	Control Group	+	4(40)	+	4(40)	+	4(40)
		-	0	-	0	-	0
		*	6(60)	*	6(60)	*	6(60)
		T	10(100)	T	10(100)	T	10(100)

+: Positive; -: Negative; *: Not determined; T: Total

Table 5. Enzyme test results of bacteria obtained by stripping with tape

Stripping Method							
		Coagulase Test					
		Blood agar		BHI agar		Nutrient agar	
			n (%)		n (%)		n (%)
Before contact	Experimental Group	+	0	+	0	+	0
		-	0	-	1(10)	-	0
		*	10(100)	*	9(90)	*	10(100)
		T	10(100)	T	10(100)	T	10(100)
	Control Group	+	2(20)	+	0	+	2(20)
		-	4(40)	-	8(80)	-	5(50)
		*	4(40)	*	2(20)	*	3(30)
		T	10(100)	T	10(100)	T	10(100)
		Blood agar		BHI agar		Nutrient agar	
			n (%)		n (%)		n (%)
After contact	Experimental Group	+	0	+	1(10)	+	0
		-	0	-	0	-	0
		*	10(100)	*	9(90)	*	10(100)
		T	10(100)	T	10(100)	T	10(100)
	Control Group	+	1(10)	+	1(10)	+	1(10)
		-	2(20)	-	4(40)	-	6(60)
		*	7(70)	*	5(50)	*	3(30)
		T	10(100)	T	10(100)	T	10(100)
		Catalase Test					
		Blood agar		BHI agar		Nutrient agar	
			n (%)		n (%)		n (%)
Before contact	Experimental Group	+	1(10)	+	1(10)	+	2(20)
		-	0	-	0	-	0
		*	9(90)	*	9(90)	*	8(80)
		T	10(100)	T	10(100)	T	10(100)
	Control Group	+	3(30)	+	6(60)	+	3(30)
		-	0	-	0	-	1(10)
		*	7(70)	*	4(40)	*	6(60)
		T	10(100)	T	10(100)	T	10(100)
		Blood agar		BHI agar		Nutrient agar	
			n (%)		n (%)		n (%)
After contact	Experimental Group	+	1(10)	+	0	+	2(20)
		-	0	-	0	-	0
		*	9(90)	*	10(100)	*	8(80)
		T	10(100)	T	10(100)	T	10(100)
	Control Group	+	1(10)	+	3(30)	+	2(20)
		-	1(10)	-	1(10)	-	2(20)
		*	8(80)	*	6(60)	*	6(60)
		T	10(100)	T	10(100)	T	10(100)

+: Positive; -: Negative; *: Not determined; T: Total

The results of the comparison of colony counts based on sample collection methods and media are presented in Table 3. When the results obtained from the tape stripping and swab methods were compared for both before and after contact conditions, it was determined that there was no statistically significant difference in colony counts between the sample collection methods ($p>0.05$). This suggests that the choice of sample collection method did not lead to significantly different colony counts in terms of culture media, regardless of whether the samples were collected before or after contact.

Isolation plates were used to perform catalase and coagulase enzyme tests on microorganisms that fell as single colonies. S. aureus was utilized as the control group for these tests. Isolates with catalase enzyme activity were considered positive if bubble formation occurred after the reaction. In the coagulase enzyme test, results were evaluated as positive or negative based on whether clotting occurred. The enzyme test results for bacteria obtained through tape stripping and swabbing methods in our study are shown in Table 4 and Table 5. For samples collected using both methods, the proportion of positive organisms in the coagulase test ranged from 10% to 80%. Prior to and after contact, the positivity rate for the experimental group ranged from 0% to 30%, whereas for the control group, it was 10% to 80%. Similarly, in the catalase test, the total positivity rate for the experimental group ranged from 10% to 60%. For the same group, this rate

was 0% to 50% for the control group, both before and after contact. It was observed that the experimental group receiving the education had lower rates of microorganisms with enzyme activity.

Discussion

Handwashing is the simplest, most effective, cost-efficient, and universally applicable method in the prevention of healthcare-associated infections (25). In addition to healthcare workers, nursing students are also among the groups that need to adhere to infection control measures in intensive care units and other hospital units. The purpose of education applied to these care providers is to increase their knowledge, enhance their skills and attitudes during healthcare delivery (5). In our study, nursing students' hand hygiene practices and beliefs were compared with their hand flora, and the effectiveness of hand hygiene education was evaluated.

In our study, the average HHAI scores before education were determined as 61.40±4.42 for the experimental group and 64.30±4.16 for the control group. In other studies, the average HHAI scores were reported as 64.67±5.03 by Türeyen and Artan (26), 63.97±6.37 by Okuroğlu et al. (12), 65.90±5.54 by Alcan and Dolgun (27), 67.42±4.98 by Artuvan and Çetin (28), 65.26±5.29 by Gürlek Kısacık et al. (29), 64.26±5.33 by Bayram et al. (30), 67.2±3.9 by Çakırlı Kozik et al. (31), and 64.96±9.09 by Şahbaz and Adana (32). In our study, the average HHBS scores before education were found as 79.30±5.18 for the experimental group and 79.30±16.14 for the control group. In other studies, the average HHBS scores were reported as 87.50±9.35 by Türeyen and Artan (26), 84.03±8.28 by Okuroğlu et al. (12), 85.04±8.20 by Alcan and Dolgun (27), 87.34±9.73 by Artuvan and Çetin (28), 86.01±9.08 by Gürlek Kısacık et al. (29), 76.00±18.76 by Bayram et al. (30), 82.7±8.7 by Çakırlı Kozik et al. (31), and 87.29±13.34 by Şahbaz and Adana (32).

It can be observed that the mentioned studies were conducted with different healthcare professionals, in various work settings, and some involved students as participants. Our HHAI and HHBS results are in line with the outcomes of these other studies, and overall, it's notable that participants' hand hygiene practices and beliefs tend to be high or close to high in other studies as well. Considering the significant increase in these results after the education provided in our study, the effectiveness of the education cannot be ignored.

In our study, the HHAI and HHBS results of the experimental and control groups were similar before the education. This indicates that the groups were comparable before the intervention. The statistically significant increase in post-test averages compared to pre-test averages after the education indicates that the provided education positively influenced the hand hygiene practices and beliefs of nursing students. In a study by Cruz and Bashtawi (10), it was determined that nursing students had a moderate level of hand hygiene knowledge. In another study, it was determined that providing hand hygiene education through a booklet and historical hand hygiene application significantly improved attitudes in the experimental group compared to the control group (33). In an examination of the effect of practical hand hygiene education provided to auxiliary service personnel on hand hygiene compliance, it was reported that the compliance of auxiliary service personnel working in the operating room significantly increased (34). In another study, it has been noted that hand hygiene education for patient relatives and healthcare workers increased awareness, but it is emphasized that these educations should be repeated to keep the topic on the agenda (35). In studies evaluating educational interventions, positive outcomes from the education are expected. In our study, besides the increase in measurement results after the education, the evaluation of hand flora is considered as a factor that enhances the quality of our study. However, it is recommended that similar trainings should not only target nursing students but should be periodically repeated for all healthcare workers to maintain their effectiveness.

Isolating different microorganisms that can grow vegetatively in various environments is possible through isolation methods (20, 21). Molecular methods such as metagenomic analysis are used to determine the presence of non-culturable bacteria (36). Sampling from clinical specimens or surface environments using the swabbing method is widely used (22). In this study, the differences between the swabbing method and the tape-stripping method were investigated. Additionally, the effectiveness of different media in bacterial isolation was determined. In samples collected using the swabbing method, significant differences in colony counts before and after contact were observed for the nutrient agar medium compared to the BHI agar and blood agar media. Accordingly, it can be inferred that the bacterial growth in the swabbing method and the nutrient agar medium was lower in the experimental group before and after contact, compared to the control group.

In the tape-stripping method, differences were observed in the samples collected before and after contact. Before contact, the tape-stripping method showed significant differences between the experimental and control groups in terms of colony counts on the BHI agar medium. After contact, significant differences in colony counts were observed in all three media. In all media, there was a statistically significant lower level of bacterial growth in the experimental group compared to the control group. As a result of the provided training, we can observe a reduction in microbial load in the samples collected from the experimental group after contact.

Swap and tape string methods are simple but effective invasive methods used for skin isolation. In different studies on these techniques, the effectiveness of the techniques and their advantages have been compared. In a study on the importance of the structure of the swab material used in the swab technique, 15 different swabs consisting of cotton (5), flocked foam

(7) and nylon (3) were used (37). The swab sampling efficiency of these swabs was evaluated and it was stated that cotton swabs and small foam swabs were advantageous in sampling non-absorbent surfaces. It is thought that the cotton swabs used in our study provide the desired level of effectiveness because they are the most suitable material for sampling. In a study conducted with the tape stripping technique, it was determined that the structure of the skin was effective in taking samples (38). In a different study, the washing process was compared with the band stripping method in the detection of antimicrobial peptides, and similar results were obtained in both methods (39). In the study conducted by Ogai et al. (40), swabbing and stripping techniques were compared with molecular methods. When next-generation sequencing results were compared to both sampling methods, it was determined that the tape scraping method collected a higher number and wider variety of live skin bacteria than the swabbing method. When our results were evaluated, it was determined that the tape string method generally yielded more bacteria. However, it has been determined that the medium used also changes the effectiveness of the method. For this reason, carrying out isolation studies with the appropriate method and appropriate medium will ensure more effective results.

In a study conducted by Öz et al. (22), they examined the bacterial composition of hand flora among healthcare workers, medical students, and patients along with their accompanying relatives. Similar to our study, they used biochemical tests to analyze the bacterial structure of hand flora. The results of their investigation revealed the presence of coagulase-negative staphylococci, micrococci, viridans streptococci, and coryneform bacteria. Furthermore, they highlighted that the proportion of bacteria not typically found in normal skin flora was notably high. It is particularly striking that this rate is higher among students. In a study conducted by Yayla using swab samples taken from healthcare workers in the intensive care unit and from inanimate surfaces within the unit, blood agar and Eosin-Methylene Blue (EMB) agar were employed for isolation purposes (41). The results showed growth in 15 samples, which were determined to contain Coagulase-Negative Staphylococcus, S. aureus, E. coli, Proteus spp., and Acinetobacter spp. This study provides insights into the microbial presence in the intensive care unit environment, shedding light on the types of bacteria that can thrive on surfaces and among healthcare workers in that setting.

In a study conducted by Mbanga et al. (42), samples were collected from inanimate surfaces and medical equipment (58 swab samples) as well as from hand swabs of healthcare personnel (six swab samples) within the intensive care unit. The results revealed the presence of various bacteria, including E. coli, Klebsiella spp., S. aureus, Coagulase-Negative Staphylococcus, and P. aeruginosa, in the samples obtained from healthcare personnel. This study provides valuable insights into the microbial composition of both surfaces and healthcare workers' hands within the intensive care unit setting. A study conducted with medical and nursing students in Jordan by Bataineh et al. (43) collected swab samples from hands, stethoscopes, and mobile phones. The results revealed that the highest level of contamination was observed on hands. Since it was determined that hands were the most contaminated surface among the sampled items, this study highlights the importance of hand hygiene practices among healthcare students and professionals.

In this study, it was observed that the proportion of bacteria with coagulase activity in the microorganisms obtained through the swabbing and tape-stripping methods in the experimental group was significantly lower compared to the control group. The coagulase test is commonly used for the identification of staphylococci. It is a test particularly utilized to determine the pathogenicity status of staphylococci. The significantly lower proportion of pathogenic staphylococci in the experimental group compared to the control group suggests a reduction in potential transmission rates. This, in turn, is anticipated to contribute to lower rates of healthcare-associated infections and consequently improve patient safety.

Catalase enzyme activity is used as a test for the identification of aerobic bacteria and certain facultative bacteria. In our study, the aerobic or facultative nature of bacteria present in the hand flora was determined. Samples were collected using both tape-stripping and swabbing methods from the experimental and control groups before and after contact. A significant presence of catalase-positive microorganisms was detected in these samples. However, after contact, there was a decrease in the proportion of catalase-positive microorganisms. In addition to biochemical tests that provide a general identification of microorganisms, the use of molecular techniques such as metagenomic analysis would offer a more precise characterization.

In this study, the microorganisms present in the general hand flora were identified simplistically, and the changes brought about by hand hygiene education were observed. Furthermore, the study shed light on the structure of hand flora after education in terms of microbial load. The results demonstrated experimental evidence that hand hygiene education leads to a reduction in hand microbiota load and a significant decrease in pathogenic groups. According to these results, hypothesis H1 is accepted.

Conclusion

In conclusion, reducing hand microbiota hand hygiene education is critical to preventing healthcare-associated infections, improving patient safety, and maintaining a sterile environment, which ultimately improves patient outcomes and overall healthcare quality.

Limitations

The most important limitation of the study is that the

study was carried out as a TUBITAK student project within the scope of 2209-A and the identification studies with molecular methods could not be carried out due to the budget limitations arising accordingly. The limited number of the study sample makes the generalizability of the results difficult. In addition, long-term results could not be evaluated due to time constraints. Another limitation is that since the main hypothesis of the study was to compare the hand flora of the participants, a post-test was not performed on the control group.

Conflict of Interest: The authors declare that there are no conflicts of interest.

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Ethics Committee Approval: This study was approved by the Bilecik Şeyh Edebali University Non-Interventional Clinical Research Ethics Committee with approval number 7/6 and date 22.11.2022.

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ORIGINAL ARTICLE

Prevalence of Digital Technology Use in Psychiatry Patients

Psikiyatri Hastalarında Dijital Teknoloji Kullanımının Yaygınlığı

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ABSTRACT

Objective: Digital technologies help to monitor patients remotely, collect medical data, recognize the disease and increase awareness through psychoeducation and self-help applications. However, literature on the utilization of digital technologies among psychiatric patients is scarce. The aim of this study was to investigate the prevalence of the use of digital technology in patients applying to psychiatry outpatient clinic and its distribution according to diagnoses.
Material and Methods: Between September-November 2023, 500 patients who applied to the Selcuk University Faculty of Medicine Psychiatry Outpatient Clinic and volunteered to participate were included in the study. After the psychiatric interviews were completed, a questionnaire was filled out asking about the characteristics of the use of mobile technologies, internet, social media and health applications.
Results: Of the study group, 69.4% were female (n=347) and the mean age was 33.9 (±13.01) years. The educational status of 50.4% of the participants was university or master's degree. While 96% of the participants used smartphones, 16% used wearable technology (n=80). Internet usage rate was 94.8% and social media usage rate was 91%. When 251 people who did not use any health application but would like to use one were asked which features they would like to have in the application they would like to use, 78.8% stated that they would like to create an appointment, 67.7% would like an appointment time reminder, 59.7% would like drug side effect query, 55.7% would like their physician to have access to their health information, and 54.9% would like online psychotherapy.
Conclusion: The prevalence of smartphone and internet use among patients admitted to psychiatry is similar to the national population. There is an unmet need in terms of health applications for the psychiatric patient group. Considering the desired characteristics of health applications, it should be taken into account that there are different demands in psychiatric diagnosis groups.

Keywords: Smartphone, Digital technology, Psychiatry, Bipolar disorder, Schizophrenia

ÖZ

Amaç: Dijital teknolojiler; hastaların uzaktan takip edilmesini, tıbbi verilerin toplanmasını, psikoeğitim ve kendine yardım uygulamaları ile hastalığın tanınması ve farkındalığın artmasına yardım etmektedir. Literatürde psikiyatrik hasta popülasyonunda dijital teknolojilerin kullanımına yönelik bilgi kısıtlıdır. Bu çalışmanın amacı, psikiyatri polikliniğine başvuran hastalarda dijital teknoloji kullanımının yaygınlığını ve tanılara göre dağılımını araştırmaktır.
Yöntem: Eylül-Kasım 2023 tarihleri arasında Selçuk Üniversitesi Tıp Fakültesi Psikiyatri Polikliniğine başvuran ve katılmaya gönüllü 500 hasta dahil edildi. Hastalara psikiyatrik görüşmelerinin tamamlanmasının ardından mobil teknolojiler, internet, sosyal medya, sağlık uygulamaları kullanım özelliklerinin sorulduğu bir anket doldurulduldu.
Bulgular: Çalışma grubunun %69,4'ü kadın (n=347) ve yaş ortalaması 33,9 (±13,01) idi. Katılımcıların %50,4'ünün eğitim durumu üniversite veya yüksek lisans idi. Katılımcıların %96'sı akıllı telefon kullanmaktayken %16'sı giyilebilir teknoloji (n=80) kullanmaktaydı. İnternet kullanım oranı %94,8 sosyal medya kullanım oranı %91 idi. Herhangi bir sağlık uygulaması kullanmayan ancak kullanmak isteyen 251 kişiye kullanmak istedikleri uygulamada hangi özelliklerin olmasını istedikleri sorulduğunda %78,8'i randevu oluşturmak, %67,7'si randevu saati hatırlatıcısı, %59,7'si ilaç yan etki sorgulaması, %55,7'si hekiminin kendi sağlık bilgilerine erişebilmesi, %54,9'u çevrimiçi psikoterapi özelliklerinin olmasını istediğini belirtti.
Sonuç: Psikiyatriye başvuran hastalar arasında akıllı telefon ve internet kullanım yaygınlığı ülke popülasyonuyla benzerlik göstermektedir. Psikiyatrik hasta grubu için sağlık uygulamaları açısından karşılanmamış bir ihtiyaç söz konusudur. Sağlık uygulamalarında bulunması istenen özelliklere bakıldığında psikiyatrik tanı gruplarında farklı taleplerin olduğu dikkate alınmalıdır.

Anahtar kelimeler: akıllı telefon, dijital teknoloji, psikiyatri, bipolar bozukluk, şizofreni

Introduction

Today, with the rapid development of digital technologies and their accessibility by the society, the use of digital products such as smartphones, computers and tablets that can access the internet has become widespread worldwide. With the widespread use of wearable technologies that can provide measurements such as heart rate, blood pressure, sleep cycle, digital technologies and digital health applications are manifested everywhere in the field of health, including psychiatry (1). The remote continuation of healthcare services during the Coronavirus Disease 2019 (COVID-19) pandemic has increased interest in this field. As a matter of fact, the budget allocated to digital health technologies in the United States of America (USA) was almost doubled in 2020 compared to 2019, and exceeded 14.7 billion dollars in the first half of 2021 (2). There are more than 350,000 health apps available for mobile use on digital platforms. More than 10,000 of these are specific applications related to mental health (2) and their number is increasing rapidly in response to the ever-increasing demand (3). E-Nabız is a public, digital

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health application supported by the Ministry of Health of the Republic of Türkiye. It is an application where health information produced on behalf of the person can be managed and medical information can be accessed from a single place, regardless of where the examination, tests and treatments are performed. All this emphasizes the growing demand in this field and the importance of the subject.

The lack of objective measurement in psychiatry causes many difficulties. Clinical follow-ups for diagnosis and routine follow-ups usually consist of cross-sectional symptom assessments based on self-reports, which have various limitations due to recall difficulties, bias and misinterpretation (4). There is an inability to monitor changes in mood, cognition and behavior. Therefore, more effective strategies for the clinical management of diseases are required. Advances in digital technologies may offer potential solutions to the above challenges (5).

Today, digital technologies are used in psychiatry for various purposes such as follow-up, treatment and monitoring (5). The widespread use of smartphones, many sensors on them, and the fact that people carry them every day and for most of the day make these devices ideal for digital healthcare and digital phenotyping (6). Many mobile applications specific to the diagnoses of depressive disorder (DD), anxiety disorder (AD), bipolar disorder (BD), psychotic disorder (PD), insomnia disorder, eating disorders and substance use disorders have been launched (7). Through these applications, it is aimed that patients can receive information about their diseases, remind appointments and medication, and receive the necessary therapeutic support from mental health professionals by providing remote access if necessary (8). Studies have also shown that personal data obtained from smartphones and wearable technologies can be used effectively in the early diagnosis of mental illnesses before exacerbations and in the follow-up process (9,10). In recent years, the increasing knowledge in this field suggests that digital phenotyping can be done by analyzing the behavioral patterns of the person and other data obtained, and that the perspective in the field of psychiatry can be further expanded thanks to digital phenotyping (11).

Determining the prevalence of individuals' technology use plays an important role in the process of transition to utilizing digital applications. Determining the frequency of digital use and willingness to use applications is the first step to identify unmet needs. Looking at the statistics on digitalization, it has been reported that 86.11% of the world population owns a smartphone and 65.7% use the internet (12,13). In our country, according to August 2023 Turkish Statistical Institute (TURKSTAT) data, 95.5% of the country's population owns a smartphone while 87.1% reported using the internet (14).

Studies conducted in different countries on smartphone and internet use by psychiatric patients indicate that the rates are close to the world population rates (15). In a study conducted in patients with chronic psychiatric illness, it was reported that the rate of smartphone use was 60% (16). In a study of inpatients in the USA, the rate of health-related app use was reported as 25% and 60% of participants reported a desire to use a health app (15). To the best of our knowledge, there is only one study in Türkiye investigating the prevalence of the use of digital technologies among psychiatric patients (17). In this study, which included 300 participants admitted to outpatient psychiatry outpatient clinics in 2021, 91.4% of the participants used smartphones and 93.3% had internet access (17). At the same time, the rate of using any health application was 35%, and the rate of those who conducted research on disease and health-related issues over the phone was 79% (17). However, no data was provided by diagnostic groups.

Our aims in this study are as follows; to determine the level of using smartphone, wearable technology, internet, social media and health application, to evaluate the desire to use a health application and the level of expectation from the application, to compare the data according to diagnostic groups in outpatients admitted to psychiatry outpatient clinic.

Material and Methods

Patients between the ages of 18-65 years with any psychiatric diagnosis, who were currently receiving treatment and only clinically in remission were included in this study. Patients under the influence of alcohol and drugs, mental retardation, autism spectrum disorder and chronic neurological comorbid disease (such as dementia, previous cerebrovascular accident, epilepsy) were excluded.

Between September and November 2023, 760 patients who applied to the Psychiatry outpatient clinic of Selcuk University Medical Faculty Hospital (XUTF) were invited to the study. Two hundred people who did not meet the inclusion criteria or refused to participate in the study were excluded from the study. Also, 60 people were not included in the analysis due to missing data. The final 500 participants who agreed to participate in the study were administered a data collection form including sociodemographic and clinical characteristics, use of social media and related technologies and their opinions on their use by their physicians before their routine outpatient examinations.

Statistical Analysis

In the evaluation of the data, mean and standard deviation were used for continuous variables and frequency tables were used for qualitative data. Chi-square test was used to investigate the relationship between qualitative data. Differences between continuous variables, t-test and their nonparametric equivalents were used. Statistical analyses were performed with SPSS 23 package program. Statistical significance was set at $p \leq 0.05$.

Results

In our study, 69.4% of the participants were female (n=347) and the mean age was 33.9 (±13.01) years. Half of the participants had university or master's

Table 1. Sociodemographic Data of Patients

Age (years)	Mean, SD	33.9. ±13.01
Gender/Female	N%	347. 69.4%
Education Status		
Illiterate/primary education	N%	131. 26.2%
High school	N%	117. 23.4%
University / Master's Degree	N%	252. 50.4%
Employment status		
Not working/Unemployed	N%	204. 40.8%
Working	N%	157. 31.4%
Retired	N%	28. 5.6%
Housewife	N%	111. 22.2%
Diagnosis Distribution		
Anxiety Disorders	N%	197. 39.4%
Depressive Disorders	N%	147. 29.4%
Bipolar Disorders	N%	46. 2.9%
Trauma Related Disorders	N%	23. 4.6%
Neurodevelopmental Disorders	N%	19. 3.8%
Psychotic Disorders	N%	16. 3.2%
Obsessive-Compulsive Disorders	N%	15. 3%
Others	N%	37. 7.4%
Smartphone Usage / Yes	N%	480. 96%
Use of Wearable Technology / Yes	N%	80, 16%
Internet Usage / Yes	N%	474, 94.8%
Social Media Use / Yes	N%	455. 91%
E- Nabız Use / Yes	N%	396. 79.2%
Use of health applications other than E-Nabız/ Yes	N%	93. 18.6%
If not using:Would he/she like to use a health app? / Yes	N%	251. 61.7%

Table 2. Distribution of Sociodemographic Data According to Diagnoses

	Age (years)	Gender (Female)	Employment Status (Employed / Retired / Housewife)	Education Duration (years)	Comorbidity	Smoking	Alcohol Use	Substance Use
AD	35.72 (±14.0)	71.6% (n=141)	27.4% (n=56) / 5.1% (n=10) / 27.4 %(n=54)	11.3 (±5.0)	35% (n=69)	29.4 % (n=58)	8.6% (n=17)	4.1% (n=8)
DD	32.37 (±12.2)	75.5% (n=111)	34% (n=50) / 4.8% (n=7) / 20.4 %(n=30)	11.6 (±4.0)	29.9% (n=44)	29.9% (n=44)	8.8% (n=13)	3.4% (n=5)
BD	37.67 (±12.7)	60.9% (n=28)	39.1% (n=18) / 10.9 % (n=5) /17.4 %(n=8)	12.3 (±5.3)	39.1% (n=18)	34.8 % (n=16)	15.2% (n=7)	0% (n=0)
TRD	30.00 (±15.8)	65.2% (n=15)	30.4% (n=7) / 13% (n=3) / %17.4 (n=4)	10.7 (±4.4)	30.4% (n=7)	30.4% (n=7)	13% (n=3)	4.3% (n=1)
ND	22.00 (±4.7)	68.4% (n=13)	52.6%(n=10) / 0% (n=0) / 0% (n=0)	15.3 (±1.8)	5.3% (n=1)	15.8% (n=3)	15.8% (n=3)	5.3% (n=1)
PD	35.50 (±11.0)	31.3% (n=5)	25% (n=4) / 6.3 % (n=1) / 6.3 % (n=1)	10.9 (±4.9)	12.5% (n=2)	31.3 % (n=5)	0% (n=0)	0% (n=0)
OCD	23.00 (±6.6)	73.3% (n=11)	13.3% (n=2) / 0%(n=0) / 13.3% (n=2)	13.6 (±3.8)	13.3% (n=2)	6.7% (n=1)	6.7% (n=1)	0% (n=0)
Others	33.81 (±10.3)	62.2% (n=23)	27%(n=10) / 5.4% (n=2) / 32.4% (n=12)	10.7 (±5.3)	37.8% (n=14)	37.8 % (n=14)	21.6% (n=8)	10.9% (n=4)

AD: Anxiety Disorders; DD: Depression Disorders; BD: Bipolar Disorders; TRD: Trauma Related Disorders; NDD: Neurodevelopmental Disorders; PD: Psychotic Disorders; OCD: Obsessive-Compulsive Disorders

Table 3. Distribution of Data on Technology Use According to Diagnoses

	Smartphone Usage	Wearable Technology Usage	Internet Usage	Social Media Usage	E-Nabız Usage	Health Application Usage Other than E-Nabız	If not using: Would like to use a health application / Yes
AD	97.5% (n=192)	15.2 % (n=30)	94.4 % (n=186)	91.9% (n=181)	80.2% (n=158)	21.3% (n=42)	58.7 % (n=91)
DD	94.6% (n=139)	17 % (n=25)	95.9% (n=141)	93.9% (n=138)	77.6% (n=114)	16.3% (n=24)	64.2% (n=79)
BD	93.5% (n=43)	10.9 % (n=5)	89.1% (n=41)	78.3% (n=36)	80.4% (n=37)	19.6% (n=9)	75.7% (n=28)
TRD	100% (n=23)	8.7% (n=2)	100% (n=23)	100% (n=23)	78.3% (n=18)	21.7% (n=5)	38.9% (n=7)
NRD	100% (n=19)	26.3% (n=5)	100% (n=19)	89.5% (n=17)	94.7% (n=18)	31.6% (n=6)	69.2% (n=9)
PD	93.8 % (n=15)	6.3% (n=1)	93.8% (n=15)	87.5% (n=14)	68.8% (n=11)	0% (n=0)	56.3% (n=9)
OCD	100% (n=15)	13.3% (n=2)	100% (n=15)	93.3% (n=14)	80% (n=12)	20% (n=3)	66.7% (n=8)
Others	91.9% (n=34)	27% (n=10)	89.2% (n=33)	86.5% (n=32)	75.7% (n=28)	10.8% (n=4)	60.6% (n=20)

AD: Anxiety Disorders; DD: Depression Disorders; BD: Bipolar Disorders; TRD: Trauma Related Disorders; NDD: Neurodevelopmental Disorders; PD: Psychotic Disorders; OCD: Obsessive-Compulsive Disorders

degree (50.4%, n=252) and 40.8% (n=204) were not working/unemployed. The majority of the participants were AD and DD patients (39.4%, n=197; 29.4%, n=147). Sociodemographic data and diagnosis distributions are summarised in Table 1.

Almost all of the participants used smartphones (96%, n=480) and 16% (n=80) of them also used wearable technology (smartwatch, etc.). Internet and any social media programme usage rates were also quite high (94.8%, n=474; 91%, n=455). While 79.2% (n=396) of the participants were using e-Nabız, only 18.6% (n=93) were using a health application other than e-Nabız. When 81.4% (n=407) who did not use a health application were asked whether they would like to use a health application, 61.7% (n=251) stated that they would like to use one (Table 1). When the e-Nabız users were asked for which purposes they used e-Nabız; 73% (n=289) stated that they used it to control tests and examinations, 48.2% (n=191) stated that they used it to make an appointment at the haspital.

Sociodemographic data according to diagnoses are presented in Table 2. Data on smartphone use, wearable technology use, internet use, social media use, use of e-Nabız application, use of a health application other than e-Nabız, and whether those who do not use a health application would like to use a health application according to diagnoses are presented in Table 3.

When 251 people who did not use any health application but would like to use one were asked which features they would like to have in the application, 78.8% (n=198) responded that they would like to use it to make an appointment, 67.7% (n=170) to be reminded of appointment times, 59.7% (n=150) to question drug side effect, 55.7% (n=140) to access to his/her own health information by his/her doctor and 54.9% (n=138) stated that they would like to have online psychotherapy features.

When 37 BD and PD patients who did not use any health application but would like to use it were asked about the features they would like to have in the health application; 75.6% (n=28) responded that they would like to use it to make an appointment, 64.8% (n=24) to question drug side effect (n=24), 62.1% (n=23) for mood tracking, and 62.1% (n=23) stated that they would like to have online meeting features with their doctor.

When those who would like to have online psychotherapy feature in the health application were categorised according to diagnostic groups, 71.4% (n=11) were trauma-related disorders, 62.0% (n=49) depressive disorders and 56.0% (n=51) were anxiety disorders.

Discussion

With the increase in digital technologies and the use of artificial intelligence in most areas of life, there are opinions that digital psychiatry applications will be used more frequently in psychiatric practices, especially in clinical practice such as diagnosis, treatment and follow-up. However, in order for these and similar technological developments to be used widely, the existing conditions should be open and ready for this development. The most important of these is to determine the interest of patients receiving psychiatry services towards digital technology, the reasons for using technology and their prevalence.

In this study, in which we sought answers to these questions, 96% of the participants used smartphones and 16% used wearable technology. The smartphone usage rates of our study group were above the world average (86.11%) (12, 13) and close to the Turkish average (95.5%) announced by TURKSTAT in August 2023 (14). In our study, internet usage rate was 94.8% and social media usage rate was 91%. Internet usage rate was significantly above the world average (65.7%) and above the average in Türkiye (87.1%). In the literature, data on the prevalence of technology use according to psychiatric diagnosis distribution are limited. In a study conducted in 2021 on 300 outpatients admitted to the psychiatry clinic at Akdeniz University, the rate of smartphone use was 91.4% and internet access was 93.3%, similar to our findings in our study (17). One of the reasons for the higher rates of smartphone and internet use in the psychiatric patient population compared to the general population may be that smartphone addiction, which is considered one of the behavioural addictions, frequently accompanies psychiatric diagnoses (18-20). It may also be due to the fact that patients with chronic psychiatric illness have lower social functionality and meet their needs in this area through online platforms (21). Finally, this may be related to the fact that the sample of our study consisted of a relatively young population (mean age 33.9 years (±13.01)) and was conducted with a limited sample. The rate of smartphone use is above 90% and the rate of internet use is above 89% in all diagnostic groups shows that the psychiatric patient population uses digital technologies at a similar level to the general population and that digital options can be used in the follow-up and treatment processes of these patients.

E-Nabız, which is widely used as a health application in our country, was also used at a high rate (79.2%) in our sample. The rate of participants using a health application other than E-Nabız is 18.6%. In a study conducted in 2019, e-Nabız usage rate in the general population was reported as 47.9% (22), while in 2022, according to Siemens Healthineers Turkiye's Health Literacy Research Report (23), this rate was reported as 86%. These rates show that the prevalence of the use of digital applications has increased over the years and that the psychiatric patient population has kept pace with digital developments. When the patients who did not use any health application (other than e-Nabız) but wanted to use it were analysed, it was observed that the rates were the highest in BD and PD patients (75.7%, 56.3%). The high rate of individuals with chronic psychiatric illnesses stating that they would like to use a health application indicates the existence of unmet needs in this area.

When the desired features of the application are analyzed, it is seen that appointment creation and

drug side effect query are the most demanded features while the demand for some features varies according to the diagnostic groups. While the online psychotherapy feature was more prominent in the diagnostic groups of TRD, DD, AD, the features of mood tracking and online consultation with the physician were more prominent in BD and PD patients. Individuals with chronic psychiatric illness have fewer hospital admissions, including primary health care services, primarily due to stigmatisation, and fewer physician admissions due to the frequently encountered complaint of reluctance reveals the importance of telepsychiatry practices in this patient group that requires regular follow-up and treatment (8). These findings indicate that psychiatric diagnostic groups and their needs should be taken into consideration in health practices developed for psychiatric patients.

Limitations

Our study has various limitations, the first limitation is that the study is a cross-sectional study. In today's world where the use of technology is increasing rapidly, the rates we have determined in our study will change day by day. Therefore, as time passes, the data presented in the study will lose its validity. The second limitation is that the majority of our sample consists of individuals with a university or master's degree, which may be a bias. The third limitation is that an objective measurement tool was not used. The fourth limitation is that a high proportion of the participants (69.4%) were women. Lastly, the number of participants diagnosed with TRD, NDD, PD and OCD was low. There is a need for further studies by scaling in larger sample groups.

Conclusion

The prevalence of smartphone and internet use among patients admitted to psychiatry is similar to the national population. There is an unmet need in terms of health practices for the psychiatric patient group. It should be taken into consideration that there are different demands according to psychiatric diagnosis groups for the features that health practices will contain.

Ethical Approval: This study was approved by the Selcuk University Faculty of Medicine Local Ethics Committee on 01.08.2023 with decision number 2023/385.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Authorship Contribution Statement

Conception: R.T., Design: R.T., Supervision: R.T., Materials: Ö.B., F.Ç., H.R.D., Data Collection and/or Processing: Ö.B., F.Ç., H.R.D., Analysis and/or Interpretation: R.T., Ö.B., Literature Review: R.T., Ö.B., Writer: R.T., Ö.B., Critical Review: R.T.

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ORIGINAL ARTICLE

Protective Factors, Stress and Anxiety Effects on the Resilience Levels of Healthcare Workers During COVID-19 Pandemic

Koruyucu Faktörler, Stres ve Anksiyetenin COVID-19 Pandemisi Sırasında Sağlık Çalışanlarının Psikolojik Dayanıklılık Düzeyleri Üzerindeki Etkileri

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ABSTRACT

Objective: This study investigated how protective factors, stress, and anxiety levels affected the resilience of healthcare workers (HCWs) during the COVID-19 pandemic. Specific aims included examining whether HCW resilience levels varied significantly according to demographic variables.
Methods: A total of 303 HCWs from two training and research hospitals completed the survey. The Protective Factors for Resilience Scale (PFRS), The Stress and Anxiety to Viral Epidemics–9 Items Scale, and Brief Resilience Scale were used as data collection tools. Confirmatory factor analysis, reliability analyses, construct validity analysis, discriminant validity analysis, structural equation modeling, t-test and ANOVA were conducted respectively.
Results: Only the impact of the individual sub-factor of PFRS on the resilience level of HCWs was positive and significant (b=.847, t= 8.670, p<.001); stress and anxiety levels of HCWs to viral epidemics on their resilience level were both insignificant (b= .039, t=-.468, p=.640; b= .095, t=1.073, p=.283). The resilience level of HCWs who were male (M=4.53, SD=.55), married (M=4.50, SD=.55), had high school graduates (M=4.87, SD=.27), had 31 years and above experience (M=5.00, SD=.00), had children (M=4.54, SD=. 53), and exercised 2-3 days a week (M=4.54, SD=.46) had significantly higher levels of resilience.
Conclusion: This study pointed out that individual protective factors (such as healthy skills and abilities) positively affect the resilience of HCWs and play a crucial for the mental health of HCWs. HCWs who were male, married, low educated, more experienced, had children and doing sports 2-3 days a week had significantly higher resilience.

Keywords: Resilience, Stress, Anxiety, Protective Factors, Healthcare Workers, Pandemics

ÖZ

Amaç: Bu çalışma, koruyucu faktörlerin, stres ve kaygı düzeylerinin COVID-19 salgını boyunca sağlık çalışanlarının psikolojik dayanıklılık düzeylerini nasıl etkilediğini araştırmıştır. Özel amaçlar arasında, sağlık çalışanlarının psikolojik dayanıklılıklarının demografik değişkenlere göre anlamlı farklılık gösterip göstermediğinin incelenmesi de yer almaktadır.
Gereç ve Yöntem: İki eğitim ve araştırma hastanesinden toplam 303 sağlık çalışanı anketi tamamlamıştır. Veri toplama araçları olarak Psikolojik Dayanıklılık için Koruyucu Faktörler Ölçeği, Viral Salgınlara Karşı Stres ve Kaygı Ölçeği ve Kısa Dayanıklılık Ölçeği kullanılmıştır. Sırasıyla doğrulayıcı faktör analizi, güvenilirlik analizleri, yapı geçerliliği analizi, ayırıcı geçerlilik analizi, yapısal eşitlik modellemesi, t-testi ve ANOVA yapılmıştır.
Bulgular: Psikolojik Dayanıklılık için Koruyucu Faktörler Ölçeği'nin sadece Bireysel alt faktörünün sağlık çalışanlarının psikolojik dayanıklılık düzeyi üzerindeki etkisi pozitif ve anlamlıdır (b=.847, t= 8.670, p<.001); sağlık çalışanlarının viral salgınlara karşı stres ve kaygı düzeylerinin psikolojik dayanıklılık düzeyleri üzerindeki etkisi ise anlamsız bulunmuştur (b= .039, t=-.468, p=.640; b= .095, t=1.073, p=.283). Erkek (M=4.53, SD=.55), evli (M=4.50, SD=.55), lise mezunu (M=4.87, SD=.27), 31 yıl ve üzeri deneyime sahip (M=5.00, SD=.00), çocuk sahibi (M=4.54, SD=. 53) ve haftada 2-3 gün egzersiz yapan (M=4.54, SD=.46) sağlık çalışanlarının dayanıklılık düzeyleri anlamlı derecede daha yüksek çıkmıştır.
Sonuç: Bu çalışma, bireysel koruyucu faktörlerin (sağlıklı beceriler ve yetenekler gibi) sağlık çalışanlarının psikolojik dayanıklılığını olumlu yönde etkilediğini ve sağlık çalışanlarının psikolojik sağlığı için önemli bir rol oynadığını göstermiştir. Erkek, evli, düşük eğitimli, daha deneyimli, çocuk sahibi ve haftada 2-3 gün spor yapan sağlık çalışanlarının psikolojik dayanıklılıkları ise anlamlı düzeyde daha yüksektir.

Anahtar Kelimeler: Psikolojik dayanıklılık, Stres, Anksiyete, Koruyucu Faktörler, Sağlık Çalışanları, Pandemi

Introduction

Viral epidemics adversely affect people from different countries and socioeconomic groups. In addition to economic and physical challenges, people may experience fear of infection, social isolation, uncertainty and grief (1). According to a systematic review, most populations experienced relatively high rates of anxiety, stress, post-traumatic stress disorder, depression and psychological distress symptoms during the COVID-19 pandemic (2). Health care workers (HCWs) were also affected psychologically in ways similar to the rest of the population (3), and with their increased care workloads, they were among the most exposed to the impacts of the pandemic.

During the COVID-19 pandemic, HCWs had to maintain their psychological well-being while working actively. Working on the health front-line triggered anxiety and depression in HCWs, and the uncertain course of the virus, the increasing number of deaths, long working hours and fatigue became significant stressors for

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HCWs (4). HCWs also had to manage the risk of virus exposure, increased workloads, changing practice environments, fear of bringing the virus to the home, and insufficient resting time (5). Thus, the challenges caused by the COVID-19 pandemic highlight the vital need to better understand the dynamics of resilience among HCWs.

Psychological resilience has various definitions from different perspectives, including 'the process of and capacity for successful adaptation despite challenging or threatening circumstances' (6), 'the personal qualities that enable one to thrive in the face of adversity'(7), 'a dynamic process encompassing positive adaptation within the context of significant adversity' (8) and 'protective factors which modify, improve or alter a person's response to some environmental hazard that predisposes to a maladaptive outcome' (9) — which share a core idea of being able to cope with a crisis both cognitively and emotionally.

Resilience served as a protective factor against the negative impacts of COVID-19 on the mental health of HCWs, such as incapacitating levels of depression, anxiety and stress (10). Social support and spirituality are crucial coping factors that increase resilience. Previous research has suggested HCWs' resilience is influenced by factors such as age, gender and profession, and better resilience is associated with better health status, self-care, and peer support (11). Understanding how HCWs cope with challenges such as pandemics and the factors that improve their resilience is crucial for developing effective support systems. The present study, thus, focuses on the relationship between HCWs resilience and the protective factors, stress and anxiety during the COVID-19 pandemic.

The aim of this study was to analyze the effect of protective factors (personal, family, peer dimensions) on the resilience of HCWs and their stress and anxiety levels to the viral epidemic on their resilience during the COVID-19 pandemic. The secondary objective of the study was to investigate whether there was a significant difference in the resilience level of HCWs according to the following variables: a) gender, b) age, c) working years, d) marital status, e) education level, f) occupation, g) having children, h) doing physical activity, and i) doing meditation and/or religious practices. Based on the study objectives and related literature, the following research questions were tested:

Q1 - Do protective factors for resilience a) individual, b) peer, and c) family have a positive and significant impact on the resilience levels of HCWs?

Q2 - Do the stress and anxiety levels of HCWs related to the viral epidemic a) subfactor 1-(F1) b) subfactor 2-(F2) have a negative and significant impact on the resilience levels of HCWs?

Q3 - Is there a significant difference in the resilience levels of HCWs according to their a) gender, b) age, c) working years, d) marital status, e) education level, f) occupation, g) children, h) physical activity and i) meditation and/or religious practice?

Materials and Methods

Study Model

This quantitative, one-sample, descriptive, and cross-sectional study was conducted in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Giresun University on 09.3.2022 (Decision No. E-50288587-050.01.04-80432) and informed consent was obtained from all participants included in the study.

Participants

The research population consisted of healthcare professionals serving in two hospitals, "The Training and Research Hospital" and "The Maternity and Children Training and Research Hospital". The research sample was formed using a simple random sampling method, and data were collected using face-to-face administered survey questionnaires between March 15 and May 20, 2022. The inclusion criteria for the participants to be included in the study were; being a healthcare professional, being over 18 years of age, and participate in the study voluntarily. After removing incomplete forms, 303 HCWs remained in the research sample. Although opinions on the ideal sample size vary, it is generally agreed upon that the rule of thumb should include ten participants for each research item (12-13). Based on the 30 research items, it was concluded that the sample size in this study was sufficient.

Data Collection Tools

The questionnaire constructed for the study first asked for demographic information: age, gender, marital status, education level, occupation, experience, children, physical activity (sports), and meditation/ prayer. Participants then completed the following scales:

• Protective Factors for Resilience Scale (PFRS): The original scale was developed by Harms, Pooley, & Cohen (14) and its Turkish validity and reliability study was reported by Tanko et al. (15). The scale consists of three 5-item dimensions (individual, peer and family dimensions) with a 7-point Likert response format. It has good fit values ($\chi 2/sd$= 1.99; $p < .001$; CFI= .98; NNFI = .97; SRMR = .053; RMSEA = .062) and a high alpha reliability coefficient (0.93).

• The Stress and Anxiety to Viral Epidemics–9 Items Scale (SAVE-9): This scale was originally developed by Chung et al. (16), and a Turkish validity and reliability study was also reported by Uzun et al. (17). The scale consists of 9 items and two dimensions in total, with six items (1, 2, 3, 4, 5, and 8) in the first dimension and 3 items (6,7,9) in the second dimension. A 5-point Likert response format was used. In the validity analysis, it was reported to have good fit values (TLI = 0.98, CF = 0.99, RMSEA = 0.04) and acceptable alpha internal consistency reliability (0.77).

• Brief Resilience Scale (BRS): The original scale was developed by Smith et al. (18) and its Turkish reliability validation study reported by Doğan T.(19) uses a 5-point Likert response format and consists of 6 items. Items 2, 4, and 6 were reverse coded. High scores indicate high psychological resilience. The internal consistency coefficient was high (0.83).

Data Analysis

IBM SPSS 26.0 and IBM SPSS Amos 22 were used for the analyses. First, descriptive statistics (frequency and percentage values) were used to determine the descriptive characteristics of the sample. For the normality test, the skewness and kurtosis values of the variables were examined, and it was observed that these values ranged from -1.848 to .611 for skewness, which were within the acceptable range of -+2 (20), and for kurtosis ranged from -.851 to 3.127, which were appropriate in range (21). It was concluded that parametric statistics could be used for the analyses. Confirmatory Factor Analysis (CFA) was used to assess the compatibility of the scales with the research data. The Cronbach Alpha and Composite Reliability were used for construct reliability. Construct validity was measured using both convergent validity (AVE values) and discriminant validity (Fornell-Larcker Criterion). Finally, path analysis, t-test, and ANOVA (Tukey and Dunnett's T3 for the Post-Hoc analyses) were conducted. A significance level of $p < 0.05$ was considered statistically significant.

Results

The demographic characteristics of the participants are presented in Table 1. According to the results, most of them were female (67%), aged between 18 and 30 (58%), single (60%), had a bachelor's or higher degree (64%), and the majority of them were nurses (42%) and had experience between 1 and 10 years (77%).

CFA was used to evaluate the study model, and assessing goodness-of-fit indices is the first step in CFA (22). In the CFA analysis, because of low loadings (< 0.50, Hair et al. (23)), item 6 from the PFRS, item 6 from the SAVE-9, and items 3 and 4 from the BRS were omitted. The obtained model fit indices were as follows: $\chi2(279) = 762.702$ ($p<0.001$), $\chi2/df = 2.605$, RMSEA=0.073 ($p<0.05$), CFI=0.904, TLI=0.889, SRMR=0.060 and these values are within the recommended values (20, 22, 24). On the basis of these results, it is possible to conclude that CFA met the goodness-of-fit criterion.

Construct reliability assessment determines how well a variable or combination of variables measures what is supposed to be measured (25). To assess the construct reliability of the model, Cronbach's Alpha and Composite Reliability (CR) were calculated. Both Cronbach's Alpha values, which ranged from 0.745 to 0.907, and CR values between 0.767 and 0.904 were over the 0.70 limit (26). As a result, the construct reliability for each research construct was obtained (Table 2).

Construct validity assesses how effectively the items selected for the construct measure the construct. Construct validity is determined by two types of validities: convergent and discriminant. Convergent validity is the extent to which many measures of a concept that need to be connected in theory are related in practice (27). By doing so, the multiple-item structures are guaranteed to be unidimensional, and any unreliable indications are removed (28). Average Variance Extracted (AVE) was used to evaluate convergent validity. Because the relevant latent variable accounts for over half of the variance in belonging indicators, an AVE greater than 0.50 offers empirical support for convergent validity (29). Each construct of the model has AVE values higher than 0.50, indicating appropriate convergent validity (Table 2).

Table 1. Characteristics of the participants

Variables (n=303)	Frequency (n)	Percentage (%)
Gender		
Female	204	67.3%
Male	99	32.7%
Age		
18-30	175	57.8 %
31-40	88	29 %
41-50	34	11.2 %
51 and above	6	2 %
Marital Status		
Single	181	59.7 %
Married	122	40.3 %
Education level		
High school	30	10 %
Undergraduate	78	25.7 %
Bachelor's degree	157	51.8 %
Post-graduate	38	12.5 %
Profession		
Doctor	24	8 %
Nurse	127	41.9 %
Other medical staff	84	27.7 %
Administrative staff	68	22.4 %
Work experience		
1-10 years	233	76.9 %
11-20 years	49	16.2 %
21-30 years	16	5.3 %
31 years and above	5	1.6 %
Having child/children?		
Yes	114	37.6 %
No	189	62.4 %
Physical activity (sports)?		
Every day	22	7.3 %
2-3 days a week	88	29 %
1 day a week	79	26.1 %
Never	114	37.6 %
Meditate/pray?		
Yes	215	71 %
No	88	29 %

Discriminant validity, also known as divergent validity, describes how different measurements differ from one another even if they do not exhibit strong correlation. The degree to which a particular construct varies from other constructs is indicated by discriminant validity (30). It was suggested that the square root of each latent variable's (LV) of the AVE should be larger than its correlations with all other LVs in the analysis (31). Thus, the factors of the study demonstrated acceptable discriminant validity (Table 2).

Table 2. Reliability, Convergent and Discriminant Validity

Constructs	Cronbach's Alpha	CR	AVE	PFRS-F1	PFRS-F2	PFRS-F3	SAVE-F1	SAVE-F2	BRS
PFRS-F1	0.846	0.862	0.557	0.746					
PFRS-F2	0.874	0.880	0.647	0.541	0.804				
PFRS-F3	0.877	0.877	0.589	0.492	0.551	0.767			
SAVE-F1	0.907	0.904	0.655	0.132	0.111	-0.088	0.809		
SAVE-F2	0.745	0.767	0.527	0.053	-0.006	-0.202	0.704	0.726	
BRS	0.843	0.848	0.583	0.746	0.297	0.256	0.135	0.131	0.764

Note: Square roots of the AVE are indicated on the diagonal in bold. correlations below the diagonal.
PFRS: Protective Factors for Resilience Scale (F1: Individual, F2: Peer, F3: Family), SAVE: Stress and Anxiety to Viral Epidemics Scale (F1: Subfactor-1, F2: Subfactor-2), BRS: Brief Resilience Scale, CR: Composite Reliability, AVE: Average Variance Extracted.

In the path analysis, the impacts of each sub-factor of Protective Factors for Resilience and Stress and Anxiety levels of HCWs in response to viral epidemics on their resilience level were analyzed (Table 3). According to the results, only the impact of the Individual sub-factor of Protective Factors for Resilience on the resilience level of HCWs was positive and significant (b=.847, t= 8.670, p<.001), supporting Q1a. Other sub-factors of Protective Factors for Resilience on the resilience level of HCWs were both negative and insignificant (b=-.110, t=-1.560, p=.119; b=-.084, t=-1.193, p=.233); hence, Q1b and Q1c were not supported. All sub-factors of stress and anxiety levels of HCWs to viral epidemics on their resilience level were negative and positive but both insignificant (b= .039, t=-.468, p=.640; b= .095, t=1.073, p=.283); thus, Q2a and Q2b were not supported.

Table 3. Path Analysis Results

Hypothesized Relationship	Standardized Estimates	t-values	p-values	Decision
PFRS-F1-> BRS	.847	8.670	.000*	Q1a: Accepted
PFRS-F2-> BRS	-.110	-1.560	.119	Q1b: Rejected
PFRS-F3-> BRS	-.084	-1.193	.233	Q1c: Rejected
SAVE-F1-> BRS	-.039	-.468	.640	Q2a: Rejected
SAVE-F2-> BRS	.095	1.073	.283	Q2b: Rejected

R2= 0.58, **p<0.001*
PFRS: Protective Factors for Resilience Scale (F1: Individual, F2: Peer, F3: Family), SAVE: Stress and Anxiety to Viral Epidemics Scale (F1: Subfactor-1, F2: Subfactor-2), BRS: Brief Resilience Scale

An independent sample t-test was performed to compare the resilience levels of HCWs according to gender (Table 4). There were significant differences (t(223.586)=-3.285, p=.001) in the scores, with the mean score for males (M=4.53, SD=.55) being higher than for females (M=4.29, SD=0.65); thus, Q3a was supported. In the second analysis, the resilience levels of HCWs differed significantly according to age (F3, 299 =5.396, p<.01). For the Post-Hoc test, Tukey's test was conducted as the variances were assumed to have been equally distributed, and the results showed that the mean score of 18-30 years (M=4.25, SD=.65) was significantly different from 31-40 years (M=4.49, SD=.59) and 41-50 years (M=4.56, SD=.48) at the p<.05 level. Therefore, Q3b was accepted. However, no significant differences were observed between 51 and 65 years and other groups. The resilience levels of HCWs differed significantly according to working years (F3, 299 =1.682, p< .05). For the Post-Hoc test, Dunnett's T3 test was conducted as the variances were not assumed to be equally distributed, and the results showed that the mean score of the age group of 31 and above (M=5.00, SD=.00) was significantly higher from 1 to 10 years (M=4.32, SD=.65), 11-20 years (M=4.56, SD=.45) and 21-30 years (M=4.25, SD=.58) at the p<.05 level. Therefore, H3c was accepted. The resilience level of HCWs differed significantly according to their marital status (t(286.524)=-3.116, p=.002). Married HCWs' resilience level (M=4.50, SD=.55) was higher than single HCWs (M=4.28, SD=.66); thus, Q3d was supported. According to the educational level of HCWs, their resilience level differed significantly (F3, 299 =10.441, p<.001). Dunnett's T3 test was used for the post-hoc test because equal variance was not assumed. The test indicated that the mean score of resilience for high school graduates (M=4.87, SD=.27) was significantly higher than undergraduate (M=4.42, SD=.56), bachelor's degree (M=4.22, SD=.65), and post-graduate (M=4.48, SD=.63) at the p<.05 level, therefore, Q3e was supported. The resilience level of HCWs did not significantly differ according to profession (F3, 299 =1.682, p=.171), thus, Q3f was not supported.

The resilience levels of HCWs according to having children and not having children had a significant difference (t(276.403)=3.944, p=.000), and HCWs who had children (M=4.54, SD=.53) had significantly higher resilience levels than those who had no children (M=4.26, SD=0.66); consequently, Q3g was supported. According to doing physical activity (sports) and not doing it, the HCWs' resilience level differed significantly (F3, 299 =5.388, p<.01). Dunnett's T3 test was used for the post-hoc test because equal variance was not assumed. The test indicated that those who did sports 2-3 days a week (M=4.54, SD=.46) had significantly higher resilience levels than those who did not do (M=4.21, SD=.72); thus, Q3h was supported. The resilience level of HCWs did not significantly differ according to doing meditation/praying (t(301)=.387, p=.699); so Q3i was not supported.

Table 4. Comparison of groups of participants on mean scores of the resilience level of HCWs

		Mean	SD	t/F	df	Sig.
Gender	Female	4.29	.65	-3.285	223.586	.001
	Male	4.53	.55			
Age	18-30*	4.25	.65	5.396		
	31-40*	4.49	.59			
41-50* 4.56 .48					3 299	.001
	51-65	4.83	.41			
Marital Status	Single	4.28	.66	-3.116	286.524	.002
	Married	4.50	.55			
Educational Level	High school*	4.87	.27	10.441	3 299	.000
	Undergraduate*	4.42	.56			
	Bachelor's deg.*	4.22	.65			
	Post-graduate*	4.48	.63			
Profession	Doctor	4.34	.71	1.682	3 299	.171
	Nurse	4.28	.64			
	Other medical staff	4.47	.51			
	Administrative staff	4.42	.68			
Work experience	1-10 years*	4.32	.65	3.867	3 299	.010
	11-20 years*	4.56	.45			
	21-30 years*	4.25	.58			
	31 and above*	5.00	.00			
Having children?	Yes	4.54	.53	3.944	276.403	.000
	No	4.26	.66			
Physical activity (sports)?	Each day	4.52	.49	5.388	3 299	.001
	2-3 days a week*	4.54	.46			
	1 day a week	4.37	.63			
	Never*	4.21	.72			
Meditate/pray?	Yes	4.38	.63	.387	301	.699
	No	4.34	.62			

T-test and ANOVA were performed. Tukey and Dunnett's T3 tests were used for post-hoc analyses.

Discussion

In this section, the research questions and their results are analyzed.

The relationship between protective factors and HCWs resilience

In this study, different dimensions of psychological resilience -individual, peers and family- were analyzed, and a positive and significant impact of HCWs' individual resilience was determined. Individual protective factors for resilience, such as healthy skills and abilities, can influence resilience level (32) and play crucial roles in promoting the well-being and mental health of HCWs. Therefore, HCWs with higher levels of individual resilience may handle stressors and challenges in their work environment (33). Higher resilience levels among HCWs are partially mediated by individual resilience. Individual resilience prevents the negative impact of stress on mental symptoms. Moreover, it decreased anxiety symptoms, especially among individuals experiencing higher levels of stress related to COVID-19 (34).

Relationship between HCWs stress and anxiety levels and resilience levels

The current study investigated the impact of stress and anxiety levels on HCW resilience during COVID-19. Despite the initial research question positing a negative, significant impact, the findings indicated that the relationships between stress, anxiety and resilience were both negative and positive but were statistically insignificant. In addition, there was no significant difference in the resilience levels of HCWs who were infected with COVID-19 and those who worked in a COVID-19 department. Several studies have consistently highlighted the negative correlation between psychological resilience and various stressors such as depression, anxiety, and COVID-19-related stress (5, 10). Higher resilience levels appeared to be associated with more positive stress responses, enhanced well-being, and reduced risk of burnout and distress, particularly during the COVID-19 pandemic (35). The literature highlighted the importance of resilience in mediating the effects of stress and anxiety on the mental health and quality of life of HCWs. Therefore, higher psychological resilience was associated with fewer mental disorders and better coping mechanisms among HCWs (36). Resilience not only plays a vital role in mediating the effects of stress and anxiety but also plays a crucial role in coping with the harmful effects of epidemic outbreaks (37). Previous studies have found that frontline HCWs experienced higher stress levels during the COVID-19 pandemic (38), and anxiety and fear of infection were negatively correlated with HCWs' resilience (39). While some studies have emphasized resilience as a protective factor against psychological stress and emotional exhaustion (10), others have underlined the role of specific resilience factors, such as perception of the future and self-perception, in influencing stress and anxiety levels (40). However, the present findings did not replicate this trend. There are also studies reporting insignificant relationships between resilience and anxiety, or COVID-19-related stress, and resilience (41). A possible explanation for this might be that the extreme, widespread, and complex nature of the pandemic and its effects on healthcare settings and staff may have weakened the observed relationships between stress, anxiety and resilience.

The difference in the resilience levels of HCWs according to their a) gender, b) age, c) working years, d) marital status, e) education level, f) occupation, g) children, h) physical activity, i) meditation and/or religious practice.

The difference between demographic variables in terms of resilience scores was analyzed, and for gender, it was found that male HCWs were more resilient. In contrast, some studies (42, 43) found that female HCWs were more resilient. It has also been

stated that women with higher educational levels or more work experience were more resilient (42). Other studies have found that females are more likely to report mental health problems and discomfort (40, 44). On the other hand, some studies (45, 46) did not find statistically significant differences in resilience scores according to gender. A previous study has pointed out that this relationship may not be applicable in all situations (45). Thus, further research is required to investigate the relationships among additional variables to better understand the differences in resilience between genders among HCWs.

In the current study, high school graduates HCWs were more resilient than those with undergraduate, bachelor's and post-graduate degrees. This finding is contrary to previous studies that have suggested that HCWs with higher educational levels are more resilient (45-47). Higher resilience levels among high school graduates may be attributed to the fact that the majority of high school graduates are administrative staff. Administrative staff or HCWs with managerial duties have previously been found to report lower resilience levels (48).

The findings also revealed a significant difference in resilience levels among the age groups. HCWs with 31 years or more of work experience had higher resilience scores than those with 1–10, 11–20, and 21–30 years of work experience. A comparison of the findings with those of other studies confirmed a positive correlation between older age and higher resilience levels (11, 34, 39, 45-49). A positive correlation was reported between longer working years in the profession and institution and better resilience scores (45). It seems that length of working experience emerges as a potential influencing factor, and older HCWs exposed to a wide range of difficult circumstances may become more resilient (46). However, some research found that there was no significant relationship between resilience levels and years of employment (35, 48). The relationship between resilience and experience can be moderated by personality characteristics, coping techniques and organizational support.

This study also found that married HCWs were more resilient on average. Contrary to previous findings in the literature, no statistically significant correlation was found between resilience scores and marital status (45, 46). Cultural and social factors may influence the relationship between resilience and marital status. Furthermore, resilience among HCWs was significantly related to parenthood. The results revealed that HCWs with children reported higher resilience levels. This result corresponds to a study finding that having children is positively correlated with higher resilience levels (34). Being a parent can provide a sense of drive and purpose that may contribute to resilience. HCWs with children may experience an additional level of stress because of their children's concerns about their parents' health and safety during difficult circumstances such as the pandemic. However, the responsibility of raising and protecting their children may serve as a powerful source of motivation for HCWs, helping them overcome subsequent challenges. HCWs may be motivated to increase their resilience against fear-induced stress.

Contrary to expectations, this study did not find a significant difference between the resilience scores of HCWs based on professional affiliation. It was pointed out that healthcare professionals differ in many ways and that clinical professionals, on average, report lower resilience levels than administrative staff and those with managerial duties (48). Nurses may report elevated levels of anxiety, sadness and PTSD symptoms, especially in difficult circumstances (11, 49, 50). Another study found that nurses report lower average resilience levels than physicians and ambulance technicians (51). It was found that doctors and nurses reported higher resilience levels than other medical professionals, such as paramedics and laboratory personnel (43). The significance of expertise and the possibility that through their extensive and varied training experiences physicians were more resilient than healthcare assistants and rehabilitation specialists (39). There was also a substantial difference in average levels of resilience among nurses compared with respiratory therapists, healthcare technologists and anesthetists. Thus, resilience in the healthcare workforce can be a complex and multidimensional concept. Distinct resilience traits may be advantageous for different professional affiliations (52). Such differences can be attributed to the diverse demands, stressors, obligations and technical skills associated with different healthcare professions. It is important to acknowledge that the present study may have some limitations because it examined several healthcare professions and may have overlooked differences within particular roles.

Another factor that may contribute to higher average resilience levels among HCWs is participating in sporting activities. HCWs who engaged consistently in sports were found to have higher average resilience levels, which is consistent with previous research reporting a beneficial relationship between resilience and sports involvement (53, 54). Studies in various contexts have highlighted the potential protective function of exercise against anxiety (54, 55). Our results support this finding, namely, that HCWs who practiced sports for two or more days a week demonstrated much higher average resilience levels than those who never played sports.

The results of the current study did not reveal any significant difference between the resilience levels of HCWs according to their meditation or praying habits. This outcome is not consistent with earlier studies' findings that so-called distraction coping activities, such as meditation, have a beneficial effect on the coping strategies used by HCWs (6, 35, 56, 57). Self-care strategies, such as such as mindfulness, gratitude, and kindness, have been identified as crucial elements in mitigating the negative effects of stress and promoting resilience (38). The literature supports the notion that mindfulness contributes to resilience (57). Although our study did not find a significant difference in resilience

levels based on whether or not participants reported meditation/praying practices, this question may well have failed to capture the multifaceted nature of spirituality.

Results

The main purpose of the current study was to examine how resilience protective factors, stress, and anxiety levels are related to HCW resilience during the COVID-19 pandemic. The findings revealed that individual resilience protective factors were associated with higher resilience levels among HCWs. The secondary aim of the study was to determine whether resilience levels among HCWs differed according to demographic variables, parental status, doing sports, meditation, and/or religious practices. The results suggest that having more experience and engaging in sports positively impact resilience levels. These results add to the rapidly expanding field of exploring resilience among HCWs.

This study offered valuable insights into relevant issues, such as the impact of protective factors on HCW resilience during the COVID-19 pandemic. In addition, comprehensive demographic variables such as gender, marital status, parental status, education level, experience and physical activity enriched the study by providing a better understanding of HCW resilience levels.

Limitations & Recommendations

There are some limitations in this study that need to be recognized. The small sample that contains 303 HCWs, which might make it a non-representative sample, relies on self-report questionnaires, which can introduce response biases, and the cross-sectional design of the study limits the ability to draw causal inferences about the relationships between protective factors, stress, anxiety, and resilience, cultural context and unexamined variables such as organizational support, which may affect generalizability. Finally, the study did not account for all possible variables that may influence resilience.

Despite attempts to ensure sample diversity, the findings may not be widely applicable. In this study, nurses were the dominant group in the sample. It would be beneficial to conduct future research with a larger, more diversed sample to validate and expand on these results. Additionally, the study was conducted within a specific geographical region and cultural context; thus, the findings may not be applicable to other settings or populations with different cultural norms or socio-economic backgrounds. Future research should aim to reproduce these findings in diverse contexts to enhance the external validity of the results. Finally, the cross-sectional design of the study limits our ability to establish causal relationships between variables. Longitudinal or experimental designs are necessary to explore the temporal relationships and causal mechanisms underlying the observed associations.

Based on the findings of this study, several recommendations can be made to enhance HCWs' resilience in future crises. Institutions should invest in stress management, problem-solving, and adaptive coping strategies. Encouraging physical activity through fitness facilities and group exercises is crucial for HCWs. Tailored support programs should address demographic factors such as gender, marital status, education level, and years of experience, and tailored support programs should be developed to offer additional support to individuals at greater risk. Family support programs and workplace physical well-being promotion can further increase resilience among HCWs.

Ethical Approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Giresun University on 09.3.2022 with decision number E-50288587-050.01.04-80432.

Conflict of Interest: The authors report there are no competing interests to declare.

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ORIGINAL ARTICLE

The Investigation of the Effect of Electrolyte Disorder on Sweat Test in Newborns with Positive Cystic Fibrosis Screening

Kistik Fibrozis Taraması Pozitif Yenidoğanlarda Elektrolit Bozukluğunun Ter Testine Etkisinin Araştırılması

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ABSTRACT

Background and objectives: The aim of this study is to investigate the effect of the electrolyte and acid-base status present at the time of admission to the hospital on the sweat test (ST) of the patients who were found to have a positive newborn screening test (NST) for Cystic Fibrosis (CF).
Methods: The patients who referred to pediatric pulmonology clinic for ST with positive NST for CF and diagnosed as CF were analyzed retrospectively. From the medical records, acid-base status measured simultaneously with the ST and with serum sodium, potassium, and chloride levels were included in the study.
Results: The study was completed with 37 patients who met the inclusion criteria. At the time of ST, the mean sodium, potassium and chlorine values were 134.83±4.25 (122.0-141.0), 4.94±0.95 (2.9-7.6) and 97.72±12.40 (64.0-116.0) mEq/L, respectively. Patients whose electrolytes were measured at the time of diagnosis, 27.0% (n=10) had hyponatremia, 8.1% (n=3) had hypokalemia, and 4.8% (n=1) had hypochloremia. There was a significant difference between serum chloride and bicarbonate levels according to the negative, borderline and positive ST groups (p=0,036). In addition, no significance was detected between the sweat test values of patients with and without Pseudo-Bartter Syndrome (PBS) (38.7%).
Conclusion: This study shows that the electrolyte disorders, low Na, Cl values and higher pH and HCO3' values than normal at the time of ST affects the ST results. So, it is important to check the serum electrolyte levels before ST of the NST positive newborn.

Keywords: Cystic fibrosis, Sweat test, Newborn screening, Serum electrolytes, Pseudo-Bartter syndrome.

ÖZ

Giriş ve Amaç: Kistik Fibrozis (KF) yenidoğan tarama testi pozitif olup ter testi yapılması için yönlendirilen hastaların başvuru anındaki elektrolit ve kan gazı değerlerinin ter testi üzerindeki etkisini araştırmak.
Yöntemler: Çocuk göğüs hastalıkları polikliniğine kistik fibrozis için yenidoğan tarama testi pozitif olan ter testi nedeniyle başvuran ve kistik fibrozis tanısı almış olan hastalar retrospektif olarak incelendi. Tıbbi kayıtlarda ter testi ile eş zamanlı ölçülen asit-baz değerleri, serum sodyum, potasyum ve klorür düzeyleri olan hastalar çalışmaya dahil edildi.
Bulgular: Çalışma, dahil edilme kriterlerini karşılayan 37 hasta ile tamamlandı. Ter testi sırasında ortalama sodyum, potasyum ve klor değerleri sırasıyla 134,83±4,25 (122,0-141,0), 4,94±0,95 (2,9-7,6) ve 97,72±12,40 (64,0-116,0) mEq/L idi. Tanı anında elektrolitleri ölçülen hastaların %27,0'ında (n=10) hiponatremi, %8,1'inde (n=3) hipokalemi, %4,8'inde (n=1) hipokloremi vardı. Negatif, borderline ve pozitif ter testi gruplarına göre serum klorür ve bikarbonat düzeyleri arasında anlamlı fark vardı (p=0,036). Ayrıca Psödo-Bartter Sendromu (PBS) (%38,7) olan ve olmayan hastaların ter testi değerleri arasında anlamlılık saptanmadı.
Sonuç: Bu çalışma, ST anında elektrolit bozukluklarının, düşük Na, Cl değerlerinin, pH ve HCO3' değerlerinin normalden yüksek olmasının ST sonuçlarını etkilediğini göstermektedir. Bu nedenle NST pozitif yeni doğanın ST öncesi serum elektrolit düzeylerinin kontrol edilmesi önemlidir.

Anahtar Kelimeler: Kistik fibroz, ter testi, yenidoğan taraması, serum elektrolitleri, psödo-Bartter Sendromu.

Introduction

Cystic Fibrosis (CF, OMIM#219700) is caused by a defect in the chloride channel called the CF transmembrane conductance regulator (CFTR) which is essential for the normal function of the epithelium in the airways, intestinal lumen, pancreas, testicles and sweat glands (1). The CF patients had the clinic of metabolic alkalosis defined by the increase of both plasma HCO3 level (>26 mmol/L) and blood arterial pH (>7.43) which is quite frequent and usually accompanied by hypokalemia. Its pathogenesis requires both the generation of alkalosis and its maintenance (2).

The presentation of CF is often due to chronic respiratory and gastrointestinal symptoms. However, in infants Pseudo Bartter syndrome (PBS), which is a symptom of dehydration accompanied by severe electrolyte and acid-base disturbances, may be the primary presentation especially in regions with hot climates (3-6).

PBS is known as complication of CF which is consisted of hyponatremic, hypochloremic dehydration with metabolic alkalosis without renal pathology. On the other side, Bartter Syndrome (BS) is a rare autosomal recessive disease accompanied by salt absorption disorder in the thick ascending limb of loop of Henle.

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It is generally characterized by normal blood pressure despite metabolic alkalosis, hypokalemia, hypercalciuria, and increased renin-aldosterone ratio (7).

CF was included in the newborn screening program by the Ministry of Health in 2015 in Turkey (7,8). Taking into account PBS accompanying CF in the literature especially in countries with a Mediterranean climate like Turkiye, it may be necessary to check electrolyte along with sweat test at the first diagnosis (6). Although it is not in the routine algorithm, serum sodium, potassium, chloride and acid-base status should be checked simultaneously. Because the low level in these electrolytes, especially in chloride, directly affects ST; and other low electrolyte levels affect the ST when sweat conductivity test is performed and this situation may cause the results to be normal (false negative) or in intermediate value. Although there are publications drawing attention to this issue, there are no studies that can constitute a basis for the need to examine sodium, potassium, and chloride and acid-base status simultaneously. The aim of this study is to investigate the effect of electrolyte and acid-base status on the ST of patients with positive NST and referred for ST.

Material and Methods

In this retrospective study, the files of the patients, who were referred to Necmettin Erbakan University Medical Faculty (NEUMF), Pediatric Pulmonology and whose sweat tests were performed after a high Immunoreactive Trypsinogen (IRT) value was detected in the NST and diagnosed as CF, were reviewed between January 2015 and December 2017. Children whose first blood IRT value was higher than 90 and the second IRT was higher than 70 were evaluated for CF and ST (8,9). The study was approved by the Ethics Committee of NEUMMF (Number: 2019/1826 Date: 10.05.2019).

Demographic data (age, gender), weight at diagnosis, month of admission to the polyclinic, family history (kinship between parents, siblings with CF), the IRT value evaluated in the heel prick screening test, the history of meconium ileus and jaundice, electrolyte levels (Na, K, Cl) measured simultaneously with the ST, arterial acid-base status (pH, HCO3) and the results of the ST was collected and evaluated.

Conductivity measurement was used in the ST with the method available in the hospital. In the evaluation, less than 50 mmol/L was considered negative, 50-90 mmol/L was borderline and above 90 mmol/L was positive (8). In heel prick screening test results of newborns, IRT-1 ≥90 ng/ml and IRT-2 ≥70 ng/ml were considered as positive (8,9). Normal ranges of serum values were accepted as 135-145 mEq/L for sodium, 98-107 mEq/L for chloride, 3.5-5.1 mEq/L for potassium. The normal pH values measured in acid-base status was 7.35-7.45 and the bicarbonate value between 21-27 mEq/L was accepted as normal (10,11).

Inclusion Criteria: Patients diagnosed with CF (patients with one or more clinical features of CF and with ST ≥90 mEq/l and patients diagnosed by showing two mutations for patients with normal or borderline ST with at least one clinical feature of CF, patients detected as positive in newborn screening, patients who underwent ST (ST is performed by Macroduct method) were included in the study.

1- Patients diagnosed with CF (Patients diagnosed by showing two mutations for patients with one or more Cystic Fibrosis clinical features and sweat test >90 mEq/l and for patients with at least one Cystic Fibrosis clinical feature with normal or borderline sweat test) were included in the study. (Sweat test is done by Macroduct method).)

2- Patients with positivity in newborn screening

3- Patients who underwent sweat test

4- Patients who come to the controls regularly. Cut off levels were defined according to the study of Sismanlar et.al. (6). They reported that according to the receiver operating characteristic (ROC) curve graph, the best conductivity cut-off value to make the CF diagnosis was 90 mmol/L and to exclude the CF diagnosis was 70 mmol/L. They suggested the conductivity measurement as a reliable and quantitative sweat chloride analysis to diagnose or exclude CF which can be used as a diagnostic test in addition to screening (6).

Exclusion Criteria: The patients whose heel prick screening test results could not be obtained or were not performed, the patients whose ST were postponed due to severe electrolyte disorder (especially hyponatremia) at the time of admission were excluded.

Data entry, statistical analysis and report writing processes were done in computer environment. SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL, USA) package program was used in the analysis. In summarizing numerical data; arithmetic mean, standard deviation, median, minimum and maximum values, frequency distributions and percentages were used to summarize categorical data. Relationships between data; Chi-square test, Mann-Whitney U test, Kruskal Wallis analysis of variance and Spearman correlation coefficient were used. Statistical significance was accepted as $p < 0.05$.

Results

There were 52 children diagnosed with CF but after the exclusion, the study continued with 37 patients. The 48.6% were girls (n=18) and there was a consanguinity between the parents of 29.7% (n=11). History of CF in siblings was 18.9% (n=7). The median age of diagnosis was 43 (11-366) days. The mean body weight at the time of diagnosis was 4345 ± 1480 (2030-10600) grams, and 72.3% (n=27) of them had weight-for-age below the 50% percentile.

CF NST of all patients included in the study was positive. At the time of admission to the hospital, 14 (43.75%) of the screened patients had a positive ST. The ST results of 14 (43.75%) patients were at borderline. There were five patients who did not sweat. The second ST

of 36.4% (n=4) of 14 patients with borderline ST was positive, and second ST of 36.4% (n=4) of the patients was at borderline. There were three patients who did not sweat.

When the ST and electrolyte levels were compared according to the seasons they were diagnosed, no significant difference was found between them (p>0.05). Patients whose electrolytes were measured at the time of diagnosis, 27.0% (n=10) had hyponatremia, 8.1% (n=3) had hypokalemia, and 4.8% (n=1) had hypochloremia. It was determined that 10.0% (n=3) of the patients had low pH and 36.7% (n=11) of the patients had high pH, that is, alkalosis. The bicarbonate level was found low in 13.3% (n=4) patients and high in 40.0% (n=12) patients. The mean of IRT, ST, and the electrolyte and acid-base status performed in the newborn screening is given in Table I, Table II shows the levels of ST, IRT and electrolytes of the study group.

IRT-1, IRT-2 values and chloride and bicarbonate levels according to patients' ST groups (negative, borderline, positive) were significantly different (p=0.010, p=0.001, p=0.036, p=0.048 respectively). Patients with positive ST had significantly higher IRT-1 and IRT-2 values. Chloride values were lower in the group with negative ST. In the first ST, one of the six patients with low chlorine value had a negative ST while four had intermediate and one had normal (Table-III).

At the time of admission, 38.7% (n=14) of the patients were in the PBS picture and 50% (n=7) of them were female. There was no significant difference between genders (p>0.05). Age-weight percentiles of 64.2% (n=9) of the patients were below 50% percentile. While 35.7% (n=5) had a sibling history with CF, consanguinity between the parents was 14.2% (n=2).

According to newborn heel prick screening test and ST there were no significant difference between the patients with and without PBS (p>0.05). Potassium and chloride values were significantly different (p=0.002, p=0.022) and potassium and chloride values were lower in the group with PBS. Bicarbonate level was significantly higher in the group with PBS (p=0,028). Some comparisons between the two groups are given in Table IV.

Table I. The median of IRT, ST and electrolyte values

	Avg±SD**	Median (Min-Max)
IRT-1* value	197.0±111.33	172.0 (69.0-565.80)
IRT-2* value	156.44±86.35	130.0 (39.0-368.0)
First sweat test result	77.73 ±24.14	87.30 (9.30-111.0)
Second sweat test result	70.30±30.85	82.50 (12.50-108.94)
Sodium (mEq/L)	134.83±4.25	136.0 (122.0-141.0)
Potassium(mEq/L)	4.94±0.95	5.0 (2.90-7.60)
Chloride(mEq/L)	97.72±12.40	102.0 (64.0-116.0)
Magnesium(mEq/L)	2.16±0.30	2.09 (1.56-2.77)
pH	7.44±0.08	7.44 (7.27-7.65)
HCO3	27.94±8.61	25.90 (14.80-52.60)

* IRT: (Immunoreactive Trypsinogen) Value in newborn heel prick screening

**SD: Standard deviation

Table II: Comparison of IRT electrolyte and acid- base status according to the results of the first sweat test

Parameters		1.Sweat Test 0-50: Negative n(%)	50-90: Borderline n(%)	90 and above: Positive n(%)	Total n(%)
1.IRT* value	Negative	0 (0.0)	1(100)	0 (0.0)	1(100)
	Positive	4(12.9)	13(41.9)	14(45.2)	31(100)
2.IRT* value	Negative	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Positive	4(12.9)	13(41.9)	14(45.2)	31(100)
Sodium	Low	1(11.1)	7(77.8)	1 (11.1)	9(100)
	Normal	3(13.0)	7 (30.4)	13(56.5)	23(100)
	High	0 (0.0)	0 (0.0)	0 (0.0)	0(0.0)
Potassium	Low	1(50.0)	0(0.0)	1(50.0)	2(100.0)
	Normal	1 (6.2)	10(62.5)	5(31.2)	16(100.0)
	High	2(14.3)	4(28.6)	8(57.1)	14(100.0)
Chloride	Low	1(16.7)	4(66.7)	1(16.7)	6(100.0)
	Normal	3(12.0)	10(40.0)	12(48.0)	25(100.0)
	High	0(0.0)	0(0.0)	1(100.0)	1(100.0)
Magnesium	Low	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	Normal	3(18.8)	5(31.2)	8(50.0)	16(100.0)
	High	0(0.0)	0(0.0)	1(100)	1(100)
pH	Low	1(50.0)	0(0.0)	1(50.0)	2(100.0)
	Normal	1(7.1)	5(35.7)	8(57.1)	14(100.0)
	High	1(11.1)	5(55.6)	3(33.3)	9(100.0)
HCO3	Low	0(0.0)	0(0.0)	4(100.0)	4(100.0)
	Normal	1(9.1)	5(45.5)	5(45.5)	11(100.0)
	High	2(20.0)	5(50.0)	3(30.0)	10(100.0)

Table III. Averages and comparisons of the first sweat test result with the condition of the IRT, electrolyte levels and acid-base status.

	First Sweat Test Average±SD* 0-50 (negative)[a]	50-90 (borderline)[b]	90 and more (positive)[c]	p
IRT-1** value	124.83±28.01	161.99±86.68	254.05±123.32	0.046[ac] 0.034[bc] (0.010)
IRT-2** value	85.01±16.75	118.59±38.79	221.12±87.52	0.003[ac] 0.017[bc] (0.001)
Sodium (mEq/L)	135.75±1.89	133.71±5.33	135.79±3.33	0.541
Potassium (mEq/L)	4.79±1.04	4.76±0.62	5.34±1.12	0.238
Chloride (mEq/L)	94.50±9.85	95.07±12.25	101.07±10.99	0.036
pH	7.45±0.15	7.45±0.6	7.42±0.08	0.626
HCO3	28.63±6.07	31.60±9.7	23.88±6.59	0.050[bc] (0.048)

*SD: Standard deviation

** IRT: Value (Immunoreactive Trypsinogen) in newborn heel prick screening

Table IV: Numbers and percentages of newborn sweat test screening results of the groups with and without PBS

PBS presence	Negative	Positive	P
	Average±SD**	Average±SD**	
Age at diagnosis	69±74	53±44	0.301
Diagnostic weight	4220±1778	4221±829	0.616
Week of birth	37±3	39±1	0.330
Birth weight	3059±539	3243±339	0.296
IRT-1 * value	185±87.08	215.39±144.60	0.719
IRT-2* value	155.99±90.79	157.15±82.23	0.615
First sweat test	77.54±26.76	78.03±20.11	0.741
Second sweat test	71.34±32.05	68.22±30.3	0.554
Sodium(mEq/L)	136.35±1.30	132.36±6.06	0.114
Potassi-um(mEq/L)	5.29±0.68	4.38±1.07	0.002*
Chloride(mEq/L)	103.13±4.27	88.86±14.08	0.022*
pH	7.42±0.06	7.47±0.11	0.078
HCO3	24.86±3.59	31.97±11.45	0.028*

*IRT: Value (Immunoreactive Tripsinojen) in newborn heel prick screening

**SD: Standard deviation

Discussion

CF is a metabolic disease with high mortality and morbidity. With early diagnosis, regular follow-up and compliance with treatment, the quality of life and lifespan of the cases increase. This study was conducted on electrolyte disorder which is one of the conditions that can affect the result of the ST, which is a very important test in diagnosis. It is also the first study because it does not investigate the effect of electrolytes on the ST by examining the serum electrolytes of the child before performing the ST after screening, and it tries to explain this effect. The results of the study will contribute significantly to further studies to be carried out on this subject, since there are limited studies on the search for the reasons that may affect the result of the ST.

The median age at diagnosis was 43 days, and all cases were diagnosed before the age of one year. European Cystic Fibrosis Society 2008-2009 data reported that 60% of the cases were diagnosed in the first year (13). A study in Iran in 2010, reported the median age at diagnosis as 5 months (14). The reason for the high rate of diagnosis under the of age one year in this study was considered as the inclusion of patients with positive CF screening.

ST and electrolyte levels were not different according to the seasons. It should be kept in mind that ST results may be false negative, especially in hot climates and in winter dressing warmly when room temperature is extremely high.

Chloride measurement in sweat is the gold standard for diagnosis. In a study conducted on ST results, 12% false negative and 15% false positive results were found (15) Hypochloremia was detected in 27.0% (10 patients) of 37 patients who came for screening without any complaints, and chlorine values were determined as 97.72±12.40 (64.0-116.0) mEq/L. Likewise, the results of the first ST were negative in one of the 6 patients with a low chlorine value, and an intermediate value was detected in 4 of them although these children were diagnosed with definite CF in the follow-up. This suggests that regardless of the method of the ST, the electrolyte levels of the children with positive CF screening test should at least be evaluated even if blood gas cannot be measured at first visit. Other researchers state that low blood chlorine levels also cause low sweat levels (6). Accordingly, it was determined that blood electrolytes were also low in pseudo-Bartter syndrome in children with CF, in which there is excessive salt loss from the skin. In the ST measurements made at this time, the chlorine level in the sweat may be lower at the limit. In these patients, they recommended that blood chlorine measurement should be performed after blood electrolyte levels returned to normal (5,16). Similarly, at the time of admission 27.0% had hyponatremia, 8.1% had hypokalemia, 36.7% alkalosis and 40.0% had high HCO3 levels and these results shows definite CF although these children do not have obvious findings. It indicates that these changes in electrolyte values may affect the ST. Since this situation will delay the diagnosis of patients with a negative ST, it will not be possible for children to receive early treatment. This situation will also lead to a newborn with a high IRT being referred to a screening program and being misdiagnosed as not having CF. Detecting low chloride level with a negative result in sweat cannot exclude the diagnosis of CF (14). In this study, the ST of 43.8% of the cases was in the range of 50-90 mmol/L. Edmondson et al. (17) reported that 17% of the patients with negative ST results and positive newborn screening test were diagnosed with CF during the follow-up period. Because the clinical spectrum of CF is highly variable, the follow-up of the patients with positive screening tests, leading to negative and intermediate values on clinical suspicion, should continue. Intermittent sweat testing can help diagnose these patients. Although there were patients with CF in this study, not all ST results were positive. It should be kept in mind that PBS, which is a common complication in CF patients, or other electrolyte disturbances or other pathologies may be the reason that causes false negative. If the patients with positive heel prick screening test and negative ST need to be followed up for CF for a while, the diagnosis should be confirmed with further examinations. In the study, the difference between the ST, low serum chloride and the bicarbonate value at the time of admission was associated with the fact that these patients were in PBS picture at the time of admission or their low ST result due to electrolyte disorder. So, it is important to check the electrolyte levels while ST was being performed.

Chloride and bicarbonate levels according to their ST groups (negative, borderline, positive) were significantly different. Bicarbonate value was higher in the group with negative ST and in the borderline group compared to the group with positive ST while chloride levels were lower in the group with borderline and negative STs. It was thought that if patients

had hypochloremic metabolic alkalosis, this would cause the ST results to be false negative, and this is an important result. In the literature, there is no study comparing electrolytes and ST results. Knowing that normal serum electrolytes performed in the laboratory and clinic when these patients came for ST had an effect on ST, and ST is not considered only as a test suggests that the patient should be evaluated by the doctor first and the ST should be performed after the serum, chloride control, if possible. Otherwise, normal ST results of the patients in warmer countries like Turkiye than in northern European countries with high IRT values as a result of scanning may lead to delayed or misdiagnosis.

Some researchers did not find significant difference in ST of patients with and without PBS although the ST results of patients with PBS were higher (15,18). Similarly, Tutar et al. (19) did not find significant difference in ST in sweat chloride test values. However, in this study, the ST was not performed in children when they had PBS. Sismanlar et al. (6) reported that the first sweat chloride test value was not significantly lower in PBS patients, but the second sweat chloride test value was significantly lower in PBS patients. Similarly, although the mean of the second ST was lower in the group with PBS, the first and the second ST result of patients with PBS and without PBS were not different significantly.

PBS, a disease with hyponatremia, hypochloremia and metabolic acidosis, is a common complication in CF and often missed as simple dehydration or BS (20,21). The mean potassium and chloride values were significantly lower, the mean bicarbonate value was significantly higher in the patients with PBS. In favor of our findings a study with 2,664 patients, 16 children had sweat conductivity values higher than 80. Age, pH, HCO3, Na, Cl, K and the sweat conductivity test were found statistically related (22). The difference of our report is that ST was applied to the children who just came for CF screening test positivity. It is important in these children that the blood electrolyte values are in the normal range because the low level of electrolytes especially Na, K, Cl, is assumed to affect the ST. So, we think that before ST controlling serum electrolytes levels are important. Another important issue in this study is that the patients had a PBS picture when they applied for a ST after they had a positive screening test result even though there was no clinical symptom. This situation can be thought to cause the ST results to be normal or at borderline.

Since sweat testing is of great importance in the diagnosis of CF, blood electrolyte levels and acid-base status should be checked in patients before performing a ST and if an electrolyte disorder is detected, ST should be performed after correcting electrolytes. A study claims that the management of PBS is focused on rehydration and correction of electrolyte abnormalities in children with CF (4). However, when ST is performed regardless of electrolytes in hot countries like Turkiye, in an undetected electrolyte disorder, the ST may turn out to be false negative. In this case, the success of the newborn CF screening program will be affected and the patient's diagnosis will be delayed. False negativity causes a delay in diagnosis and affects the prognosis of patients by delaying treatment, which affects not only the patients and their families but the whole society. It causes deviations in the targeted results of the CF screening program in health services. In addition to adverse social and psychological impacts, increased health costs and improper use of the health workforce have both national and international impacts.

In very hot weather, PPH and electrolyte abnormalities may be seen even in elderly cystic fibrosis patients (23). Main limitation of the study may be seen as making the diagnose via conductivity ST for sweat chloride test, but Mattar et al. (22) says that this way of testing is as accurate as sweat chloride test for the diagnose of CF. Similarly, in another study in Turkiye with a high number of participation, authors used this way of testing (24). The second limitation is the number the patients with full records showing the importance of patient follow up and recording.

Conclusion

In conclusion, infants with positive CF screening test and no symptoms referred for ST may have low Na, Cl values, and higher pH and HCO3' values than normal at the time of ST. This study shows that the electrolyte disorder which is present during the ST affects the ST result. It is important to see that the electrolyte and blood gas values are normal before the ST is performed after CF scanning, and to perform a ST after that, regardless of the method. Thus, after the CF screening test, false normal ST results and negative CF diagnosis will be avoided. As we suggested here, all can be prevented via simple, cost-free attention.

Ethics statement: The study was approved by the Ethics Committee of Necmettin Erbakan University Meram Medical Faculty (Number: 2019/1826 Date: 10.05.2019).

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ORIGINAL ARTICLE

Evaluation of Toenail Findings and Ingrown Nails in Athletes

Sporcularda Ayak Tırnak Bulgularının ve Tırnak Batmasının Değerlendirilmesi

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ABSTRACT

Background/Aims: Professional athletes often encounter foot nail issues due to the demands of their intensive training and the conditions within their sports footwear. The aim of this study is to assess the prevalence of nail disorders affecting professional athletes, characterize their types, and identify predisposing factors, shedding light on a critical but often neglected area in sports-related health.
Methods: We surveyed 120 professional athletes from football and basketball teams across three major sports clubs. Data on sociodemographic factors and nail issues were collected via a detailed questionnaire and corroborated with dermatological exams.
Results: The research included 108 football players and 12 basketball players, with 13 female athletes among them. The average age of the participants is 22.87, and their average sports career duration is 6.72 years. Ingrown toenails were reported by 81 athletes (67.5%), with 35 cases involving multiple regions and 9 cases a single region. The condition was most frequently found in the first toe, presenting in 41 instances. A significant association was found between ingrown toenails and both age and sports activity duration ($p=0.006$ and $p<0.001$, respectively). Drying between toes was more prevalent among those with ingrown toenails ($p=0.005$). No significant relationship was observed with other factors such as shoe type, nail cutting habits, pedicure history, fungal infections or symptoms like sweating and swelling. Dermatological assessments also identified subungual hematoma in 25 athletes, hyperkeratosis in 5, and nail dystrophy in 23.
Conclusion: In professional athletes, a high incidence of ingrown toenails has been associated with increased duration of sports activity; however, no correlation was found with known predisposing factors such as improper nail cutting or incorrect footwear selection, suggesting that the meticulous foot care practices of athletes may mitigate these risks. Proactive dermatological surveillance and tailored educational interventions are imperative for athletes to preemptively address podiatric ailments and uphold optimal performance.

Keywords: Nails; Athletes; Nails, Ingrown; Football

ÖZ

Amaç: Profesyonel sporcular, yoğun antrenman koşulları nedeniyle sıklıkla ayak tırnak sorunlarıyla karşılaşırlar. Bu çalışma, profesyonel sporcuları etkileyen tırnak hastalıklarının yaygınlığını değerlendirmeyi, tiplerini karakterize etmeyi ve predispozan faktörleri tanımlamayı, sporla ilgili sağlığın kritik ancak sıklıkla ihmal edilen bir alanına ışık tutmayı amaçlamaktadır.
Yöntem: Üç büyük spor kulübünün futbol ve basketbol takımlarından 120 profesyonel sporcunun ayak tırnak sorunları değerlendirildi. Sosyodemografik faktörler ve tırnak sorunlarına ilişkin veriler ayrıntılı bir anket aracılığıyla toplandı ve dermatolojik muayeneleri yapıldı.
Bulgular: Araştırmaya 13'ü kadın sporcu olmak üzere 108 futbolcu ve 12 basketbolcu dahil edildi. Katılımcıların ortalama yaşı 22,87, ortalama spor kariyeri uzunluğu ise 6,72 yıldı. Ayaklarda tırnak batması 81 sporcu (%67,5) tarafından bildirildi; 35 vaka birden fazla bölgede ve 9 vaka tek bir bölgede batma tanımladı. Bu durum en sık 41 vakada birinci ayak parmağında görüldü. Tırnak batması ile yaş ve spor aktivite süresi arasında anlamlı ilişki bulundu (sırasıyla $p=0,006$ ve $p<0,001$). Tırnak batması olanlarda ayak parmak aralarını kurulama alışkanlığı daha sık görüldü ($p=0,005$). Ayakkabı tipi, tırnak kesme alışkanlığı, pedikür geçmişi, mantar enfeksiyonu, terleme, şişlik şikayeti gibi diğer faktörlerle anlamlı bir ilişki gözlenmedi. Dermatolojik değerlendirmelerde 25 sporcuda subungual hematom, 5'inde hiperkeratoz ve 23'ünde tırnak distrofisi tespit edildi.
Sonuçlar: Profesyonel sporcularda, yüksek oranda görülen ayaklarda tırnak batması, artan spor aktivitesi süresi ile ilişkilendirilmiştir; ancak uygunsuz tırnak kesimi veya yanlış ayakkabı seçimi gibi bilinen predispozan faktörlerle hiçbir korelasyon bulunamamıştır; bu da sporcuların dikkatli ayak bakımı uygulamalarının bu riskleri azaltabileceğini düşündürmektedir. Proaktif dermatolojik gözetim ve kişiye özel eğitim müdahaleleri, sporcuların podiatrik rahatsızlıkları önleyici bir şekilde ele alması ve optimum performansı sürdürmesi için zorunludur.

Anahtar kelimeler: Tırnak, sporcular, tırnak batması, futbol

Introduction

Physical activity is universally acknowledged for its health benefits, enhancing both physical and mental well-being. However, professional athletes, due to the nature of their rigorous training and competitive environments, often face a unique set of health challenges. Among these, foot-related ailments are particularly common owing to the combination of mechanical stress, repeated trauma and the microenvironments created by sports footwear.

The foot is a complex anatomical structure that bears the brunt of repetitive impacts and pressures during athletic activities. This constant stress, coupled with the confined conditions of sports footwear—often under moist and frictional circumstances—increases the risk of developing a range of podiatric conditions, including various nail disorders. Such afflictions can range from common fungal infections to more serious structural nail changes resulting from repeated trauma. Moreover,

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the close quarters of locker rooms and communal showers facilitate the spread of infectious agents, compounding the likelihood of dermatological issues.

The implications of neglected foot health extend beyond discomfort; they can adversely affect an athlete's performance, potentially leading to more severe injuries and even impacting team dynamics. Prompt identification, effective management, and preventive strategies are therefore crucial components in the holistic healthcare of athletes.

In the light of these considerations, the aim of this study is to investigate the prevalence and types of foot nail issues among professional athletes. By doing so, we hope to contribute valuable insights to the domain of sports medicine, particularly in the field of preventative dermatological care for athletes.

Material and Methods

Study Population and Data Collection

Between February 2021 and November 2023, we conducted a survey involving 120 professional athletes from the football and basketball teams of three major sports clubs. A questionnaire, designed by our research team, gathered data on the athletes' sociodemographic characteristics and nail-related issues. Alongside the questionnaire, we performed dermatological physical examinations on the participants.

Questionnaire Design

The questionnaire commenced with a preamble explaining the study's goals and the responsible academic department's information. A consent form was presented at the outset, offering options to 'agree to participate' or 'decline participation'. Those who chose 'decline participation' were excluded from further contact. The questionnaire was enhanced with visual aids to help participants, pinpoint the location of their nail problems, specify their shoe type, and describe their nail-cutting practices.

Inclusion and Exclusion Criteria

Eligible participants for this study must provide informed consent and have played basketball or football professionally for at least one year with a valid license. Conversely, individuals will be excluded from the study if they do not provide informed consent or have played basketball or football professionally for less than one year. This approach ensures that all participants have a comparable level of professional experience, crucial for the reliability and validity of the study findings.

Ethical issues and permissions

Ethical permission was obtained from the Karadeniz Technical University, Medical Faculty Clinical / Human Research Ethics Committee for this study with date 2017 and number 44, and Helsinki Declaration rules were followed to conduct this study.

Statistical Analysis

Data analysis was conducted using SPSS version 23.0. Descriptive data were summarized with counts and percentages. For categorical variables, the comparison was made using the Chi-square test. The Kolmogorov-Smirnov test assessed the normality of the distribution. For normally distributed continuous variables, we applied the Student's t-test, while the Mann–Whitney U test was used for variables not normally distributed. Spearman's correlation test facilitated the correlation analysis. We considered a p-value of less than 0.05 as indicative of statistical significance.

Results

Participant Demographics

A total of 120 athletes were assessed, comprising 13 females (10.8%) and 107 males (89.2%). The mean age of participants was 22.87 years (SD ±4.68, range 17-35). The majority were football players (108, 90%), while the rest were basketball players(12, 10%). The athletes trained for an average of 1 hour and 15 minutes per day, 5-6 days a week with a mean sports involvement of 6.72 years (SD ±4.89, range 1-20 years).

Education and Health

Educational levels among 104 athletes were as follows: primary education (36, 34.6%), secondary education (54, 51.9%), and university graduates (14, 13.5%). One athlete was on adalimumab and azathioprine treatment for a rheumatological condition. Dermatological issues were limited to vitiligo (2 athletes) and contact dermatitis (2 athletes). Reported medication use included vitamin supplements (3 athletes), systemic isotretinoin (1 athlete), escitalopram (1 athlete), and the aforementioned adalimumab and azathioprine (1 athlete). Pedicures were common (50 athletes, 43.5%), with one reporting complications. Non-sports-related foot trauma was reported by 13 athletes.

Ingrown Toenails

A history of ingrown toenails was reported by 81 athletes (67.5%). Demographic and behavioral characteristics stratified by the presence of ingrown toenails are presented in Table 1. Age and duration of sports activity were significantly associated with ingrown toenail occurrence ($p=0.006$ and $p<0.001$, respectively), as detailed in Table 2, which illustrates the correlation between these variables and ingrown toenail incidence. The practice of drying between toes was significantly more common in those with a history of ingrown toenails ($p=0.005$). No significant correlations were found with other researched factors.

The number of past ingrown toenail episodes was recorded for 46 athletes, with a distribution as follows: one episode (11 athletes), two episodes (12 athletes), three episodes (2 athletes), four episodes (20 athletes) and five episodes (1 athlete).

Figure 1. Photographic representations of participant cases. Figures 1-11 depict dystrophic nail changes attributed to sports-related trauma. Figures 12-15 demonstrate subungual hematomas alongside traumatic nail alterations.

Preventative Measures and Treatments

For prevention purposes, 27.6% cut the nail corner, 2.6% rested their feet elevated, 9.2% applied antibiotic cream, and 60.5% received professional help.

For treatment, athletes consulted manicurists/pedicurists (41.8%), podiatrists (18.2%), family physicians (16.4%), orthopedic specialists (14.5%), general surgeons (3.6%), and dermatologists (5.5%). Despite being included as an option in our survey, none of the participating athletes selected the choice indicating that they had consulted with a plastic surgery specialist.

Ingrown Toenail Characteristics

In terms of location, 35 cases involved multiple regions, and 9 cases involved a single region. The distribution was as follows: bilateral involvement on all four sides of the first toe in 19 cases, bilateral medial edges of the first toe in 5 cases, bilateral lateral edges of the first toe in 5 cases, bilateral involvement with one medial and the other mediolateral side of the first toe in 3 cases, bilateral involvement of the fourth and fifth toes in 1 case, involvement of all four sides on the first toe plus one side of the second toe in 2 cases, and unilateral involvement of the first toe (medial side in 4 cases, lateral side in 3 cases) and the lateral sides of the second toe in 2 cases.

Treatment Modalities

Treatments included nail avulsion (24 cases, 61.5%), nail brace and tube treatments (3 cases, 7.7%), oral

Table 1. Demographic and Behavioral Characteristics by Presence of Ingrown Toenails

Variables	Overall Population (n=120)	No Ingrown Nails (n=39)	Ingrown Nails (n=81)	p-value
Age (years)	22.87±4.68	21.39±4.32	23.60±4.70	0.006
Gender Female Male	 13 107	 6 33	 7 74	0.348
Duration of sports activity (years)	6.72±4.89	4.24±4.08	7.65±4.88	0.000
Type of Sports Basketball Soccer	 12 108	 5 34	 7 74	0.523
Pedicure History Absent Present	 65 50	 23 11	 42 39	0.150
Non-Occupational Trauma Absent Present	 104 13	 35 1	 69 12	0.063
Preferred Non-Sport Shoes tip type Narrow Wide	 8 30	 1 11	 11 19	0.393
Preferred shoe size Large Fitting	 25 41	 5 15	 20 26	0.179
Person who cuts nails Self Others	 103 13	 33 2	 70 11	0.339
Nail Cutting Style Short and Deep Rounded Deep Corners Straight Across	 6 71 12 25	 1 19 3 10	 5 52 9 15	0.542
Sweating Absent Present	 97 20	 30 6	 67 14	0.935
Bad Odor Absent Present	 112 5	 33 3	 79 2	0.169
Swelling Absent Present	 111 6	 36 0	 75 6	0.175
History of fungal Mycosis Absent Present	 99 21	 34 5	 65 16	0.603
Onychomycosis Absent Present	 109 11	 36 3	 73 8	0.698
Frequency of Washing Feet Once a day Less often	 102 11	 33 3	 69 8	0.672
Drying Between Toes Absent Present	 48 68	 22 14	 28 54	0.005

Table 2. Correlation Between Age, Duration of Sports Activity, and Incidence of Ingrown Toenails

variable	Correlation Coefficient	P-value
Age	**0.264**	**0.006**
Duration of sports activity	**0.348**	**<0.001**

antibiotics (4 cases, 10.3%), antibiotic creams (7 cases, 17.9%), and pain medication (1 case, 2.6%).

Physical examination findings

We observed subungual hematoma in 25 cases, subungual hyperkeratosis in 5 cases and dystrophic changes such as nail splitting, ridging, and pigmented bands at the nail tips in 23 cases (Figure 1).

Discussion

Athletes especially soccer players are prone to specific nail dystrophies due to the considerable forces exerted on the feet during abrupt kicking motions. The nail plate and surrounding periungual area are subject to significant pressure and trauma during athletic activities. The specific forces exerted on the feet vary by sport, leading to distinct sport-related nail changes (1,2). Trauma to the nail unit is a common cause of onychodystrophy and may be acute, resulting from a single severe injury, or chronic, due to repetitive minor injuries. Acute trauma can promptly lead to splinter hemorrhages, subungual hematomas, and potential nail loss. In soccer players, traumatic injuries to the toenails frequently result in subungual hematoma. This condition is analogous to 'tennis toe', which typically affects the first and second digits as a result of abrupt stops and starts, as well as 'jogger's toe', commonly involving the third to fifth digits (1). In our study, subungual hematoma was observed in the first toe of 22 soccer players and 2 basketball players, while

separately, a hematoma was detected in the second toe of another soccer player.

Delayed nail deformities may encompass nail splitting and ridging, pterygium development, hook nails, pigmented bands and ectopic nail formation (3). Chronic sports-related trauma is also associated with subungual hyperkeratosis, as indicated in the study by Ergun et al. with a prevalence of 14.6% among the subjects examined (4,5). Our study identified subungual hyperkeratosis in 5 soccer players and dystrophic changes such as nail splitting, ridging, and pigmented bands in 23 athletes, 21 of whom were soccer players. In our study, the low incidence of subungual hyperkeratosis and dystrophic nail changes is attributed to the high rate of ingrown toenails and the subsequent increased attention to foot care.

Sporting activities may be regarded as a potential risk factor for onychocryptosis (ingrown nails), but the sparse data available do not establish a direct correlation between these factors (6-10). Onychocryptosis is an exceedingly uncomfortable and painful condition, occurring when the lateral edge of the nail embeds or is forced into the lateral nail fold (6,7). The prevalence of this condition is not well-defined; however, a screening study in the United States identified a rate of ingrown nails at 24 cases per 1,000 individuals (11). Trauma is recognized as one of the causative factors for ingrown nails (7-10). In our previous study, which assessed the clinical features of 206 adult patients with ingrown toenails, we found that 20.5% had a history of engagement in sports activities and 24.3% had a history of trauma (12). In our current study, we detected onychocryptosis in 67.5% of professional athletes. Only 14.8% of the cases with onychocryptosis had a history of non-sport related trauma. We found a statistically significant correlation between the age of our subjects and the duration of their sports activities with the frequency of onychocryptosis.

One of the most significant factors known to contribute to the development of ingrown nails is the use of inappropriate footwear, such as shoes with pointed toes, or socks that cause recurring trauma (12,6,7,10,13). Tight shoes or socks can compress the lateral part of the nail, leading to penetration of the soft tissue. Consequently, inflammation and foreign-body reactions may occur in this area. In our previous study, an alarmingly high rate of 46.2% of subjects were found to be wearing unsuitable shoes (12). Additionally, the practice of nail cutting has been correlated with ingrown nails in several studies, with improper techniques being identified as common etiological factors (12,6,7,10,13). Cutting the nail at an angle can result in the formation of spicules. As the nail grows out, these spicules can embed into the distal lateral nail fold, thereby provoking a foreign-body response. Therefore, trimming the nail too short or at an angle can cause the corners of the nail to be situated more proximally, leading to the corners growing inward towards the depth of the fold. In our previous study, 73.5% of patients trimmed their nails in a rounded fashion (12).

Prevention strategies are crucial and should include the use of well-fitting footwear that provides midfoot stability and ample space in the toebox to avert compression-related issues. It is also recommended to trim nails straight across to distribute force evenly and reduce the likelihood of nail dystrophies (2,14). When our subjects developed symptoms of onychocryptosis, they frequently sought initial treatment from manicurists and podiatrists. We believe that early diagnosis and proper management are crucial for professional athletes with onychocryptosis to prevent impairment of performance and quality of life. Therefore, providing education on this topic to both athletes and those who support them is essential.

However, in this current study involving professional athletes, when we assessed the predisposition to ingrown nails in relation to incorrect cutting habits and footwear choices, we did not find any significant difference in cases with ingrown nails. This suggests that professional athletes may be more attentive to their foot care.

Hyperhidrosis can compromise foot hygiene by causing maceration of the skin, and this moist environment may lead to foot infections. The edema associated with such infections can create conditions that promote the development of ingrown nails (6,7,15,16). In our previous study, the incidence of hyperhidrosis in patients with ingrown toenails was reported as 16.8% (12). Similarly, in this study focused solely on athletes, we found a comparable hyperhidrosis frequency of 15.7%. However, we did not observe a significant difference in the prevalence of hyperhidrosis between patients with ingrown nails and those without.

Ingrown nails are commonly observed in the hallux, which is the medical term for the big toe (12,17). The hallux bears a significant portion of the body's weight during walking, which can push the soft tissue upward around the edge of the nail, leading to ingrown nails. The hallux is also the toe most affected by the interaction between the foot and the shoe, as well as by any abnormalities in pedal biomechanics. The literature often reports a higher incidence of ingrown nails on the lateral (outer) margins of the nail (6,12,15,18). When a person stands, the hallux tends to rotate medially (inward), and when the foot is lifted, it returns to its original position. Concurrently, the body of the nail may move laterally, which is why ingrown nails are more commonly observed on the lateral side (15). Additionally, within the confines of a shoe, the second toe may be pressed against the lateral margin of the hallux, increasing pressure on that side and thus promoting ingrowth (13). Consistent with these findings, our study also found that ingrown nails were present in the first toe (hallux) of 41 cases.

Pico et al.'s study found a notable occurrence of onychocryptosis in athletes, linking it to nail plate hardness, which may be caused by the mechanical stress of sports activities. (8,9,19) Their research, involving 140 young athletes and non-athletes, also suggests that active males and non-active females

are more prone to ingrown toenails, indicating that physical activity and gender may influence the development of this condition. However, our study did not find a significant gender-related difference in the incidence of onychocryptosis, which could be due to variations in sample size, sporting activities included, or diagnostic methods. These contrasting findings highlight the complexity of factors contributing to onychocryptosis.

Zaraa et al.'s study examined sports-related skin issues among 30 athletes, consisting of 18 soccer players and 12 basketball players, and reported that 87% prevalence of skin infections were mostly fungal (20). The average age of the cohort was 25.3 years, ranging from 18 to 35 years. In addition to infections, traumatic skin lesions were also common, with 20 of the 30 athletes affected, primarily by calluses and nail disorders, which comprised 80% of the traumatic dermatoses noted. These findings highlight the importance of routine dermatological screenings for athletes to ensure early detection and treatment of sports-related dermatoses that could impair performance. The higher occurrence of dermatoses compared to our younger cohort may reflect the older age and longer sports involvement of Zaraa et al.'s participants.

Athletes, including soccer players, are prone to cutaneous mycotic infections. The chronic sweating experienced by athletes leads to skin maceration, which compromises the protective barrier of the stratum corneum and increases susceptibility to infections. The interdigital spaces of the feet are particularly vulnerable. The combination of warmth, friction, and physical contact, along with communal use of showers and changing areas, contributes to the high incidence of viral, bacterial, and fungal infections in athletic populations. Onychomycosis in athletes commonly affects nails that have been damaged or are under trauma, and this may be exacerbated by bacterial infections, potentially leading to paronychia. Prompt diagnosis and treatment are essential to reduce the spread of these conditions.

In a study by Purim KS et al., which involved 105 soccer players and 24 control subjects, tinea pedis was observed more frequently in the control group whereas onychomycosis was more prevalent among the athletes. The reduced incidence of tinea pedis in soccer players was attributed to professional foot care and health education initiatives (21).

Ergun et al. examined 137 football players for superficial fungal infections (4). Onychomycosis was diagnosed in 9.5% of the players (13 cases), with one case also displaying concurrent tinea pedis. Isolated tinea pedis was found in 3 cases (2.2%). Additionally, 20 players (14.6%) presented with subungual hyperkeratosis, 14 (10.2%) with yellow nail discoloration, 11 (8%) with onycholysis, and 5 (3.6%) with black discoloration of the nail. In 9 of the 20 players with subungual hyperkeratosis, no fungal growth was detected through direct microscopy or culture. Similarly, 6 of the 14 players with yellow nail discoloration showed no fungal growth. Another study found that 18 out of 23 soccer players (78.26%) displayed no signs of mycotic infection. However, two players (8.70%) were diagnosed with tinea pedis, and three participants (13.04%) had onychomycosis concurrent with tinea pedis (22). Our study did not include a laboratory evaluation for fungal infections as per our research design. Nevertheless, medical histories revealed that 21 cases (17.5%) had a history of foot fungus, and 11 cases (9.2%) had a history of nail fungus.

Poor foot hygiene and a higher rate of fungal and bacterial infections can lead to inflammation and edema, which may predispose individuals to developing ingrown toenails (6,15). The discomfort caused by ingrown toenails typically results in increased attention to foot care. This level of care is likely to be even more pronounced among professional athletes.

Conclusion

It is imperative that athletes undergo routine dermatological screenings to identify and manage skin conditions early, preventing any adverse impact on their athletic performance. Within the population of professional athletes, we have observed a significant prevalence of ingrown toenail occurrences that directly correlate with the extended periods of sporting engagement. Interestingly, our study did not establish any significant relationship between this condition and the commonly acknowledged contributory factors, such as the practice of incorrect nail trimming techniques or the selection of inappropriate footwear. This unexpected finding might be attributed to the heightened diligence that athletes typically apply to their foot care routines, which could potentially counterbalance the effects of these otherwise contributory factors. Implementing an educational program specifically designed for athletes is vital. This program would teach athletes to recognize the early signs of nail and skin disorders, underscore the significance of maintaining proper foot hygiene, guide them in choosing suitable footwear, and instruct them on appropriate responses to injuries or infections.

Conflict of Interest:

The authors declare that there is no conflict of interest.

Financial Disclosure:

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Ethical Declaration

For research articles:

Ethical permission was obtained from the Karadeniz Technical University, Medical Faculty Clinical / Human Research Ethics Committee for this study with date 2017 and number 44, and Helsinki Declaration rules were followed to conduct this study.

Authorship Contributions

Concept: D.A.A., L.B.S., Design: D.A.A., L.B.S., E.A., C.Y., İ.E.A., Supervising: D.A.A., L.B.S., EA, C.Y., İ.E.A., Financing and equipment: D.A.A., L.B.S., C.Y., İ.E.A.,

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ORIGINAL ARTICLE

Prevalence and Determinants of Depression Among Medical Students: A Comprehensive Investigation

Tıp Öğrencileri Arasında Depresyonun Yaygınlığı ve Belirleyicileri: Kapsamlı Bir Araştırma

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ABSTRACT

Aim: Depression is a prevalent mental health disorder globally, impacting individuals' quality of life significantly. Medical students, due to the demanding nature of their education, are particularly susceptible to depression. This study aimed to investigate the prevalence and severity of depression among medical students and explore associated factors.
Materials and Method: This cross-sectional study was conducted over three months at a tertiary healthcare institution affiliated with a university. A face-to-face questionnaire was used to assess depression levels and associated factors among medical students. The Beck Depression Inventory was utilized for depression assessment. Statistical analyses were performed using IBM SPSS Statistics.
Results: The study included the demographic characteristics, lifestyle factors, and depression scores of medical students. Female students exhibited significantly higher depression scores than male students (p=0,019). Factors such as family income, smoking habits, social media usage, and regular studying showed significant associations with depression levels (p<0.05). Additionally, students who were satisfied with their medical education and those who did not experience semester/internship loss demonstrated lower depression levels (p<0.05).
Conclusion: Several factors, such as gender, family background, lifestyle choices, and academic performance were found to influence depression levels among medical students. Notably, social media use, regular studying habits, and satisfaction with medical education emerged as significant predictors of depression. Depression among medical students is a multifaceted issue influenced by various factors. Addressing these factors through targeted interventions and support services is crucial for promoting the psychological well-being of medical students and ensuring their long-term success in the medical profession.

Keywords: Depression, Medical students, education process, Diversities

ÖZ

Amaç: Depresyon, bireylerin yaşam kalitesini önemli ölçüde etkileyen, dünya çapında yaygın bir ruh sağlığı bozukluğudur. Tıp öğrencileri, eğitimlerinin zorlu doğası nedeniyle depresyona karşı özellikle hassastır. Bu çalışmanın amacı tıp öğrencileri arasında depresyonun yaygınlığını ve şiddetini araştırmak ve ilişkili faktörleri incelemektir.
Gereç ve Yöntem: Bu kesitsel çalışma, bir üniversiteye bağlı üçüncü basamak bir sağlık kurumunda üç ay boyunca yürütülmüştür. Tıp öğrencileri arasında depresyon düzeylerini ve ilişkili faktörleri değerlendirmek için yüz yüze bir anket kullanılmıştır. Depresyon değerlendirmesi için Beck Depresyon Envanteri kullanılmıştır. İstatistiksel analizler IBM SPSS Statistics kullanılarak gerçekleştirilmiştir.
Bulgular: Çalışma tıp öğrencilerinin demografik özelliklerini, yaşam tarzı faktörlerini ve depresyon puanlarını içermektedir. Kız öğrencilerin depresyon puanları erkek öğrencilere göre anlamlı derecede yüksekti (p=0,019). Aile geliri, sigara içme alışkanlığı, sosyal medya kullanımı ve düzenli ders çalışma gibi faktörler depresyon düzeyleri ile anlamlı ilişkiler göstermiştir (p<0.05). Ayrıca, tıp eğitiminden memnun olan ve dönem/staj kaybı yaşamayan öğrencilerin depresyon düzeyleri daha düşük bulunmuştur (p<0.05).
Sonuç: Cinsiyet, aile geçmişi, yaşam tarzı seçimleri ve akademik performans gibi çeşitli faktörlerin tıp öğrencileri arasında depresyon düzeylerini etkilediği bulunmuştur. Özellikle, sosyal medya kullanımı, düzenli ders çalışma alışkanlıkları ve tıp eğitiminden memnuniyet depresyonun önemli belirleyicileri olarak ortaya çıkmıştır. Tıp öğrencileri arasında depresyon, çeşitli faktörlerden etkilenen çok yönlü bir sorundur. Bu faktörlerin hedefe yönelik müdahaleler ve destek hizmetleri aracılığıyla ele alınması, tıp öğrencilerinin psikolojik esenliğini teşvik etmek ve tıp mesleğinde uzun vadeli başarılarını sağlamak için çok önemlidir.

Anahtar Kelimeler: Depresyon, Tıp öğrencileri, Eğitim süreci, Farklılıklar

Introduction

Depression is a common mental health disorder that can have a significant impact on an individual's quality of life. According to the World Health Organization, more than 264 million people suffer from depression. This has made depression one of the leading health problems worldwide (1). Depression can manifest itself in a variety of ways, including feelings of sadness, hopelessness, and helplessness, as well as physical symptoms such as fatigue, sleep disturbances, and changes in appetite (2). Poor sleep, stress, and significant life events are key risk factors for depressed mood, while physical activity and quality of social interactions are protective factors (3,4). Despite being a common condition, many people continue to suffer in silence, either due to fear of stigmatization or a lack of access to mental health services. However, depression is a treatable condition, and there are many practical strategies and interventions available to manage its symptoms.

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The demanding nature of medical education and training is a significant source of stress, leading to depression among students. Studies have shown that medical students have a higher risk of developing depression compared to their peers in other academic programs. In a meta-analysis conducted by Rotenstein et al. in 2016, they found that the overall prevalence of depression or depressive symptoms among medical students was 27.2%, which is significantly higher than that of the general population (5). Dyrbye et al. reported that approximately 11% of medical students had suicidal thoughts at some point (6).

Studies in the literature show that depression among medical students is not only a common problem but also a serious threat. Therefore, this research aims to delve deeper into depression among medical students and to elucidate the complex factors that influence this condition. By taking into account a wide range of variables such as social media usage habits, family economic status, family relationships, etc., it aims to reveal the complex dynamics underlying depression. This comprehensive analysis aims to make a significant contribution to the development of not only medical students' but also the general mental health approach, and to provide more effective and original solutions by getting to the roots of the problem.

Materials and Method

This study was conducted within three months in a tertiary healthcare institution affiliated with a university. Ethical approval for the study was obtained from the non-interventional Ethics Committee of İzmir Katip Çelebi University, dated 26.01.2023 and numbered 0004. The study was conducted using a face-to-face questionnaire method with students studying at the university's medical faculty affiliated with the hospital. The questionnaire aimed to assess the depression levels of the students and to investigate the factors associated with depression. All students except the final year of the faculty were included in the study, and students with incomplete questionnaire data and those who refused to participate were excluded from the study. Final-year students were excluded due to the lack of in-semester examinations in the last year of medical school and the possibility that additional major stress factors, such as specialty examinations and employment at the end of the faculty, might affect an objective result. By the parameters specified in the study protocol, each participant was administered a meticulously prepared questionnaire covering various sociodemographic variables. These variables included factors such as age, gender, education, marital status, employment status, income level, place of residence, dependency and health status. The classification of students' family income level was based on the poverty and hunger thresholds set by the government at the time of the study. In addition to the sociodemographic questionnaire, participants were assessed using the Beck Depression Inventory (BDI). The data obtained were recorded on forms specially designed for the study. Scores were calculated according to the answers given to the scaled questions, and the relationships between the depression levels of the participants and the factors that may cause depression were evaluated by statistical analysis.

Beck Depression Inventory

Developed in 1961 by Aaron T. Beck, the BDI has undergone several revisions and updates over the years, the most recent version being the BDI-II. The BDI-II is a 21-item questionnaire that assesses various symptoms of depression, including sadness, hopelessness, guilt, irritability, and fatigue. It has been validated in many studies and is considered a reliable and valid measure of depression severity (7). The BDI is a self-report questionnaire that individuals can complete in approximately 5–10 minutes. Each item is scored on a scale of 0 to 3, with higher scores indicating more severe symptoms of depression. The total score ranges from 0 to 63, with 0–13 indicating minimal depression, 14–19 indicating mild depression, 20–28 indicating moderate depression, and 29–63 indicating severe depression.

Statistical Analysis

Data were evaluated using the statistical package program IBM SPSS Statistics Standard Concurrent User V 26 (IBM Corp., Armonk, New York, USA). Descriptive statistics were given as number of units (n), percentage (%), mean ± standard deviation ($\bar{x}$ ±ss), median (M), minimum (min) and maximum (max) values. The Shapiro-Wilk normality test evaluated the normal distribution of the data of numerical variables, and it was determined that the data did not meet the normal distribution conditions. Beck Depression Scale total score was compared with the Mann-Whitney U test in variables with two groups and the Kruskal Wallis test in variables with three or more groups. Bonferroni post hoc test was applied for multiple comparisons. The relationships between continuous data were evaluated with the Spearman correlation coefficient. $p<0.05$ was considered statistically significant.

Results

Regarding gender distribution, 56% of the participants were female, and 44% were male. When we look at the grade distribution of the participants, it can be seen that the highest number of participants is in the first grade, with 27.9%.

Notably, 99.6% of the participants are single, and only 0.4% are married. While 20.3% of the participants live alone, 33.3% live with roommates, 29.7% live with their families, and 16.7% live in dormitories. It is observed that 89.2% of the participants' parents live together, 6.7% live separately, 1.6% of the participants' mothers, and 2.5% of the participants' fathers are decedent. While 38.6% of mothers have a bachelor's degree, this rate is 48.3% for fathers. Of the mothers, 46.8% are not working, 26.6% work for the government, 12.6% work in the private sector, and 14.0% are retired. On the other hand, 28.7% of the fathers were employed in the government, 34.6% were employed in the private sector, and 30.3% were retired. Family monthly

income level shows that 14.7% of the participants have a monthly income of <₺9,752, 59.6% have a monthly income of ₺9,752 - ₺33,754, and 25.7% have a monthly income of >₺33,754. 77.4% of the participants do not smoke, 18.3% smoke less than one pack a day, and 4.3% smoke more than one pack a day. In terms of alcohol consumption, 55.3% prefer a life without alcohol, 42.0% consume alcohol less than three days a week, and 2.7% consume alcohol more than three days a week.

Table 1: Descriptive Properties and Evaluation of the Relationship of Beck Depression Total Score with Each Variable

Variables	Statistics	**Beck Depression Scale Total Score** *M (IQR)*	Test Statistics		
	n		Test Value	*p* Value	%
Gender					
Female	249	13 (12)	z=2.343	0.019	56.0
Male	196	12 (12)			44.0
Grade					
1	124	13 (11)			27.9
2	65	14 (12,5)			14.6
3	71	11 (11)			16.0
4	62	16 (13)	*H*=4.775	0.444	13.9
5	65	13 (13)			14.6
6	58	12.5 (11)			13.0
Marital Status					
Single	443	13 (12)	z=1.726	0.084	99.6
Married	2	4 (-)			0.4
Place of Residence					
I live alone	90	13 (13)			20.3
I live with my roommate/ friends	148	13 (12.75)	*H*=1.895	0.594	33.3
I live with my family	132	12 (12.5)			29.7
I live in a dormitory	74	14 (9.25)			16.7
Which is true about your parents?					
They live together	396	12.5 (12)			89.2
They live separately	30	16 (8.5)	*H*=1.467	0.690	6.7
My mother passed away	7	17 (12)			1.6
My father passed away	11	14 (13)			2.5
Mother's Education Status					
Did not go to school	32	15.5 (15.75)			7.2
Primary school graduate	80	13.5 (12.75)			18.1
Secondary school graduate	40	12 (12.5)	*H*=8.814	0.184	9.0
High school graduate	76	12 (12.25)			17.2
License	171	12 (11)			38.6
Master's Degree	38	16.5 (13.75)			8.6
PhD	6	19.5 (13.5)			1.4
Fathers's Education Status					
I did not go to school	8	18.5 (25.25)			1.8
Primary school graduate	58	15 (15.5)			13.1
Secondary school graduate	25	12 (12)			5.6
High school graduate	79	12 (10)	*H*=5.015	0.542	17.8
License	214	13 (11.25)			48.3
Master's Degree	48	13 (11.75)			10.8
PhD	11	16 (16)			2.5
Mother's Employment Status					
Not working	208	13 (12)			46.8
Working for the government	118	13 (12.25)	*H*=0.211	0.976	26.6
Work in the private sector	56	12.5 (12)			12.6
Retired	62	12.5 (11)			14.0
Father's Employment Status					
Not working	28	16 (16)			6.3
Working for the government	127	14 (14)	*H*=4.360	0.225	28.7
Works in the private sector	153	12 (10)			34.6
Retired	134	12 (11)			30.3
Family Monthly Income					
<₺9.752	65	16 (10.5)[a]			14.7
₺9.752 - □33.754	264	12 (10.75)[b]	*H*=9.695	0.008	59.6
>₺33.754	114	12 (12.5)[b]			25.7
Smoking					
No.	343	12 (11)[a]			77.4
Yes, less than 1 pack per day	81	15 (10)[a]	*H*=11.274	0.004	18.3
Yes, more than one pack per day	19	21 (22)[b]			4.3
Alcohol					
No.	245	13 (13)			55.3
Yes, less than three days a week	186	12 (9)	*H*=1.317	0.518	42.0
Yes, more than three days a week	12	15.5 (17.5)			2.7
Sport					
No.	224	13.5 (12)			50.5
Yes, less than three days a week	123	13 (10)	*H*=5.283	0.071	27.7
Yes, more than three days a week	97	12 (12.5)			21.8
Social Media					
No.	12	13 (12.25)[a]			2.7
Yes, less than 4 hours a week	243	12 (11)[ab]	*H*=13.864	<0.001	54.9
Yes, more than 4 hours a week	188	14 (12)[ac]			42.4
Listening to Music					
No.	12	7 (13.5)[a]			2.7
Yes, Less than 3 hours a day	309	12 (11)[a]	*H*=8.827	0.012	69.4
Yes, more than 3 hours a day	122	14.5 (11)[b]			27.5
TV series/movie					
No.	50	17 (16.5)			11.3
Yes, less than three days a week	225	13 (11)	*H*=3.247	0.197	50.7
Yes, more than three days a week	169	12 (11)			38.1
Video Game					
No.	213	13 (13)			48.0
Yes, less than three days a week	129	13 (10)	*H*=0.960	0.619	29.1
Yes, more than three days a week	102	13 (11)			23.0
Studying					
I do not study regularly	184	14 (11)[a]			41.3
Yes, less than 4 hours a day	184	11 (11.75)[b]	*H*=13.852	<0.001	41.3
Yes, more than 4 hours a day	75	12 (13)[b]			16.9
Disease History					
No	200	12 (11)	z=2.723	0.006	73.3
Yes	73	15 (12.5)			26.7
Regular Medication					
No	197	12 (10.5)	z=2.432	0.015	71.1
Yes	80	14 (13)			28.9
History of disease in first-degree relatives					
No	149	12 (11)	z=1.493	0.135	47.0
Yes	168	14 (11.75)			53.0
History of drug use due to chronic physical diseases in first-degree relatives					
No	149	12 (12)	z=0.847	0.397	49.7
Yes	151	13 (12)			50.3
Suicidal ideation					
No	317	11 (11)[a]			71.2
Yes, Once	46	18 (9.5)[b]	*H*=45.358	**<0.001**	10.3
Yes, more than once	82	17.5 (16)[b]			18.4
Suicide Attempt					
No	423	13 (12)			95.5
Yes, Once	17	17 (16.5)	*H*=4.009	0.135	3.8
Yes, more than once	3	2 (-)			0.7
Being Willing When Choosing a Medical Faculty					
No	83	16 (10)	z=4.549	<0.001	18.7
Yes	362	12 (12)			81.3
Being Satisfied with Choosing a Medical School					
No	133	17 (11.5)	z=6.205	**<0.001**	29.9
Yes	312	11 (11)			70.1
Choose Medicine Again					
No	138	16 (12.25)	z=4.513	**<0.001**	31.2
Yes	305	12 (11)			68.8
Loss of Period					
No	363	12 (11)	z=3.269	0.001	81.8
Yes	81	17 (15)			18.2

%: Row percentage *M: Median, IQR: Interquartile Range, z: Mann Whitney U test, H: Kruskal Wallis test*

Table 2: Comparison of Average Scores of Medical Faculty Grade 1 and Grade 5 Students According to Beck Depression Levels

	BECK DEPRESSION INVENTORY LEVELS								Test Statistics†	
	1		2		3		4			
									F	p
Average Scores of Faculty of Medicine Students										
Grade 1	81.89	4.89	78.80	13.32	80.0	8.03	83.0	0	0.297	0.827
Grade 5	73.28	8.32	73.33	9.49	82.0	11.31	66,0	0	0,841	0,478
Test Statistics ‡	7.525		1.412		0.072		1.820			
p	0.008		0.240		0.790		0.183			

$\bar{x}$: mean, ss: Standard deviation. *Two-way analysis of variance in repeated measures, †: Comparisons between groups at each measurement time, A and B superscripts indicate groups with statistically significant differences in each measurement. Groups with the same superscript are statistically similar. ‡: Within-group comparisons between measurements in each group.

50.5% of the participants do not do sports, 27.7% do sports less than three days a week, and 21.8% do sports more than three days a week. It is seen that 54.9% of the participants use social media less than 4 hours a day, and 42.4% use it more than 4 hours a day. While 69.4% of the participants listen to music less than 3 hours a day, 27.5% listen to music more than 3 hours a day. 50.7% of the participants watch T.V. series/movies less than three days a week, while 38.1% watch more than three days a week. It is seen that 48.0% of the participants do not play games, 29.1% play games less than three days a week, and 23.0% play games more than three days a week. 41.3% of the participants do not study regularly, 41.3% study less than 4 hours a day, and 16.9% study more than 4 hours a day.

According to health-related data, 73.3% did not have a history of illness, while 26.7% had a history of illness. While 71.1% of the participants do not take medication, 28.9% take medication regularly. Regarding the history of illness and medication in first-degree relatives, 53.0% and 50.3% had a history of illness, while 47.0% and 49.7% had no history. 71.2% of the participants stated that they had never had suicidal thoughts, 10.3% had had suicidal thoughts once, and 18.4% had had suicidal thoughts more than once. Among the participants, 18.7% said they did not want medical education, and 81.3% said they wanted it. It was observed that 29.9% of the participants were happy, and 70.1% were unhappy with their medical education. The rate of those who intend to participate in medical education again is 68.8%. Finally, the rate of those who experienced a semester loss is 18.2%, while the rate of those who did not is 81.8%.

The Beck Depression Scale scores of female students were statistically significantly higher than those of male students (p=0.019). There is no significant difference in Beck Depression Scale scores regarding students' education period, marital status, place of residence, information about mother and father, mother and father's education level, and mother and father's working status (p>0.05). However, the Beck Depression Scale scores of students whose family monthly income is below 9.752 ₺ are statistically significantly higher than those with other income levels (p=0,008). In addition, Beck Depression Scale scores of students who smoked more than one pack of cigarettes per day were higher than the others, and this difference was statistically significant (p=0.004). Students' alcohol use and sports participation did not have a significant effect on their Beck Depression Scores (p>0.05). On the contrary, Beck Depression Scores of students (BDSS) who used social media more than 4 hours a day were statistically significantly higher than those who used social media less (p<0.001). Similarly, the BDSS of students who listened to music more than 3 hours a day were higher than those who listened to less music, and this difference was statistically significant (p=0.012). There was no significant difference between the duration of watching T.V. series/movies and playing games regarding BDSS (p>0.05). BDSS of those who did not study regularly were higher than those who studied regularly, and this difference was statistically significant (p<0.001). BDSS with a history of physical illness and regular medication use were higher (p=0.006; p=0.015). However, history of chronic physical illness in first-degree relatives and regular medication use did not have a significant effect on Beck Depression Score (p>0.05). BDSS of the students who did not have suicidal ideation were significantly lower than those who had suicidal ideation (p<0.001). There was no significant effect of having attempted suicide on the Beck Depression Score (p=0.135). Finally, the BDSS of those who did not choose medical school willingly were statistically significantly higher than those who did (p<0.001). The BDSS of the students who were not happy to be medical school students were also higher than those of students who willingly chose medical school, and this difference was statistically significant (p<0.001). Finally, the BDSS of those who experienced semester/internship loss in medical school were statistically significantly higher than those who did not experience semester/internship loss (p<0.001).

According to the table, the mean scores of Grade one students in Beck depression levels are similar (p=0.827). The mean scores of Grade five students at the Beck depression level were similar (p=0.478). The mean scores of students with Beck depression 1 level were higher in Grade one than in Grade 5 (p=0.008). The average scores of students with Beck Depression 2 were similar in Grade one and Grade 5 (p=0,240). The Grade one and Grade 5 mean scores of students with Beck Depression 3 were similar (p=0.790). The mean points of students with Beck depression level 4 in Grade one and Grade 5 were similar (p=0.183).

Discussion

In our study, depression in medical students and the factors affecting these conditions were investigated. When demographic factors were analyzed, no significant relationship was found between age and depression. The relatively narrow age range can explain this result since the study population consisted of university students. The data obtained show that the rate of depression is significantly higher in female students compared to male students. S. Nolen-Hoeksema et al. reported that women were twice as likely to experience depression than men and that stress experiences and reactions to stress played a role in making women more vulnerable to depression (8). This may support the effect of gender on depression.

It was found that increasing the number of siblings increased the depression status of the individual in our study. Having more siblings may mean that familial resources such as money, time, and parental attention are divided more among individuals. It can be predicted that this situation may increase the person's susceptibility to depression due to the difficulty in meeting individual needs. In a study conducted in 1989 on 144 university students, it was reported that the number of siblings and depression status were not related, which is inconsistent with the results of this study (9). An inadequate sample size of the study may explain this inconsistency.

In this study, it was observed that depression was higher in individuals who grew up in families with lower education levels and income. While economic difficulties create stress and pressure on individuals, limited social support networks and lack of access to mental health services may be among the parameters that trigger depression (10,11). In addition, a low educational level may reduce self-esteem and hope by limiting job opportunities and social status. Under these conditions, a person may be more prone to depression.

High amount of smoking has been found to be associated with depression. Studies in the literature also support these findings (12,13). In addition to chemical effects, the addictive feature of smoking, decreased ability to cope with stress, the effect of social and psychological factors and other independent variables may play a role in this situation.

The findings show that as the duration of social media use increases, the incidence of depression increases in parallel. In a study conducted by M. Block et al. 2014 on 19776 individuals; social media use was directly associated with significant depression, which is consistent with the results of this study (14). Social media use may lead people to compare themselves with others, which may lower self-esteem and lead to a depressive state. Long-term social media use may disrupt sleep patterns, lead to social isolation, and weaken the social support system by reducing real-world relationships. However, more in-depth research and examination of other factors may be needed to determine whether this relationship is causal.

Depression was less common in the group that listened to more music. Music may be a tool to provide emotional balance and express emotions, which may increase emotional well-being. Many studies have reported that music improves depression (15,16). S. Castillo-Perez et al. reported that music was more effective than psychotherapy in patients with low and moderate depression (17). It can be said that artistic activities such as music may help prevent depression by increasing the mental condition of the person.

In this study, the frequency of depression was found higher in students who studied regularly compared to those who did not study regularly. Medical students are relatively more achievement-oriented and competitive than the average student population. Failure to study regularly may lead to social and academic underachievement. In a study conducted among university students, Amir M. et al. reported that low academic achievement was directly related to depression, which supports this study (18). In line with these results, it can be said that academic failure or failure anxiety triggers depression by creating pressure on the student.

Students who willingly chose medical education and were satisfied with their medical education had lower rates of depression compared to the other group. In addition, depression was higher in students who lost a semester or internship during their education. In a study conducted in 2013 on 194 medical students, it was reported that medical students who passed the final exam experienced lower psychological distress and showed fewer symptoms of anxiety and depression than those who failed (19). In individuals directed to medical education due to familial and social pressures, there may be a severe lack of motivation during medical education due to failure to meet personal expectations and uncertainties in the future planning of the individual. This situation may cause pressure and stress on the individual, leading to failure and may lead to depression.

In our study, no significant difference was found between the depression levels of first-grade and fifth-grade medical students. The lack of a significant difference between first-grade and fifth-grade medical students may suggest that students are exposed to similar levels of stress and pressure at different stages of the medical education process or that these processes have similar psychological effects in both groups. In a study conducted in Pakistan, it was reported that students in the first year of medical education were more likely to be depressed than students in the final year (20). Factors such as curriculum structure, timing of clinical experiences, and cultural differences may affect the stress levels experienced by students. These differences may cause individuals to have different depression thresholds.

Our study focuses on an enriched dataset based on a large sample encompassing various sociodemographic variables and potential confounding factors. This approach enhances the methodological robustness

of the study, leading to more reliable results. However, there are certain limitations to this study. Firstly, the sample used in the data collection process is drawn only from a specific geographic region, thereby limiting the generalizability of the findings. There is a risk of subjectivity in the data based on participants' self-reports. In the future, including a broader sample from different geographic regions and using objective data collection methods could enhance the overall validity of the results.

Conclusion

It should be taken into consideration that depression in medical students is affected by many factors and that preventive and supportive interventions should be made by considering these factors. The long-term benefits and drawbacks of the psychological health of young physicians who have just started their professional lives should be considered.

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ORIGINAL ARTICLE

The Use of Minimally Invasive Surgical Techniques in Pediatric Patients with Partial Anomalous Pulmonary Venous Return

Parsiyel Anormal Pulmoner Venöz Dönüş Anomalili Pediatrik Hastalarda Minimal İnvaziv Cerrahi Tekniklerin Kullanımı

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ABSTRACT

Aim: The use of minimally invasive procedures in low-risk congenital heart surgeries has increased recently. Compared to traditional median sternotomy, minimally invasive techniques offer better cosmetic results and provide more satisfaction to both the patient and their parents. Partial anomalous pulmonary venous return (PAPVR) can be safely repaired using these techniques.
Material and Methods: The perioperative data of right-sided PAPVR patients who were operated on with minimally invasive approaches in our clinic between March 2019 and January 2023 were reviewed retrospectively. The perioperative data of the patients' including type of surgery, cardiopulmonary bypass duration, cross-clamp duration, postoperative cardiac rhythm, total operation duration, total drainage, total intensive care unit duration and total hospital stay duration were obtained. The results were compared with the data in the current literature.
Results: During the study period, 14 patients underwent surgical repair. Five (36%) of them were female and nine (64%) were male. Patients underwent right infra-axillary vertical thoracotomy (RIAVT) and right anterolateral thoracotomy (RALT) had mean ages of 48±26.6 and 42±18.2 months, respectively. High venosum type atrial septal defect (ASD) was detected in 12 (85.7%) of the patients. The most frequently used surgical treatment was the double patch technique which was used in 12 patients (85.7%). This was followed by single patch repair in one patient (7.1 %). The Warden procedure was used in one patient (7.1%) who was operated on with the RIAVT technique. Patients' cross-clamp, cardiopulmonary bypass (CPB), and total operation durations were comparable to those reported in the medical literature.
Conclusion: RIAVT and RALT are two of the frequently used minimally invasive surgical techniques in congenital heart surgery. After gaining sufficient experience, both of these methods can be safely applied to PAPVR repair.

Keywords: Anomalous pulmonary venous return, pediatrics, minimally invasive surgical procedure, thoracotomy

ÖZ

Amaç: Son zamanlarda, düşük riskli doğumsal kalp cerrahisinde minimal invaziv prosedürlerin kullanımı artmaktadır. Geleneksel median sternotomiye kıyasla minimal invaziv teknikler daha iyi kozmetik sonuçlar sunmakta ve hem hastaya hem de ebeveynlerine daha fazla memnuniyet sağlamaktadır. Pediatrik hastalarda , parsiyel anormal pulmoner venöz dönüş anomalisi (PAPVD) , bu teknikler kullanılarak güvenle onarılabilmektedir.
Gereç ve Yöntem: Mart 2019 ile Ocak 2023 tarihleri arasında kliniğimizde minimal invaziv yaklaşımlar kullanılarak ameliyat edilen sağ taraflı PAPVD hastalarının perioperatif verileri retrospektif olarak incelendi. Hastaların perioperatif verileri çerçevesinde , uygulanan cerrahi tipleri, kardiopulmoner bypass süreleri, kross klemp süreleri, postoperatif kardiyak ritimleri , toplam operasyon süreleri, toplam drenajları, toplam yoğun bakım süreleri , toplam hastanede kalış süreleri ve mortalite verileri toplandı. Sonuçlar mevcut literatürdeki verilerle karşılaştırıldı.
Bulgular: Çalışma döneminde 14 hasta opere edildi . Bunların beşi (%36) kadın ve dokuzu (%64) erkekti. Sağ infraaksiller vertikal torakotomi(SIAVT) ve sağ anterolateral torakotomi(SALT) yapılan hastaların yaş ortalamaları sırasıyla 48±26,6 ve 42±18,2 aydı. Hastaların 12'sinde (%85,7) yüksek venöz tip atriyal septal defekt tespit edildi. En sık kullanılan cerrahi tedavi çift yama tekniği olup, bu yöntem 12 hastada (%85,7) kullanıldı. Bunu, bir hastada (%7,1) tek yama onarımı izledi. SIAVT tekniği ile ameliyat edilen bir hastada (%7,1) Warden prosedürü uygulandı. Hastaların kross klemp, kardiopulmoner bypass ve toplam operasyon süreleri, tıbbi literatürde bildirilenlerle benzer olarak izlendi.
Sonuç: SIAVT ve SALT , konjenital kalp cerrahisinde sıkça kullanılan minimal invaziv cerrahi tekniklerdir. Yeterli deneyim kazandıktan sonra, bu yöntemlerin her ikisi de PAPVD onarımında güvenle uygulanabilir.

Anahtar Kelimeler: Anormal pulmoner venöz dönüş, pediatri, minimal invaziv cerrahi prosedür, torakotomi

Introduction

It is estimated that 1% of all congenital heart defects (CHD) involve a partial anomalous pulmonary venous connection (1). It is a congenital anomaly characterized by one or more pulmonary veins, but not all, draining directly or indirectly into the right atrium instead of the left atrium. Indirect ways of pulmonary venous drainage might be tributaries of the superior vena cava (SVC), inferior vena cava (IVC) , coronary sinus or left innominate vein (2). There are more than 20 anatomical variations of PAPVR. However , abnormal drainage of the pulmonary veins originating from the right lung is the most prevalent form (3). An additional

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secundum atrial septal defect (ASD) is observed in approximately 80% of patients (4). In approximately 50% of these, ASD is of the sinus venosus type (5).

The application of minimally invasive techniques in congenital cardiac surgery are gradually increasing in the pediatric population. Due to their safe application and cosmetic benefits, these techniques are widely accepted as the "new standard" by many centers, particularly in patients with low-risk CHD. The most significant drawbacks of these techniques are that achieving a clear surgical exposure is more difficult than the conventional sternotomy and that a considerably long learning period is required for safe surgery (6). Currently, the combination of the right-sided PAPVR and ASD can be repaired safely by using a variety of minimally invasive techniques (6-8).

In this study, we hypothesized that minimally invasive surgical techniques can be safely used by experienced surgeons in pediatric patients with PAPVR. In order to investigate the safety and reproducibility of minimally invasive techniques in the surgical repair of the right-sided PAPVR and ASD in pediatric patients, we analyzed the data on perioperative morbidity and mortality, comparing them with the data in the current literature.

Material and Methods

This retrospective study was conducted between March 2019 to January 2023, by reviewing the medical records of all pediatric patients diagnosed with right-sided PAPVR concomitant with ASD and operated using minimally invasive surgical techniques. Excluded from the study were the patients with Scimitar syndrome or other concomitant complex cardiac anomalies as well as patients with conduction abnormalities before surgery. Indications for surgery include presence of an ASD with at least two pulmonary veins draining to right atrium, SVC or its tributaries resulting in dilatation of right sided cardiac structures or significant left-to-right shunt leading to Qp/Qs ratio of greater than 1.5:1 on an invasive cardiac catheterization study. In selected cases where the pulmonary vein connections could not be clearly observed by echocardiography, computed tomography imaging was utilized (9).

The patients were operated on after the localization of all pulmonary veins to the right atrium or SVC was determined. Since 2020, in accordance with our clinical policy we have started to use minimally invasive surgical techniques in low risk cardiac pathologies. RIAVT has become the most preferred technique in our clinic. In addition, we also frequently employ RALT. The surgical method that would be used was left to the discretion of the senior cardiac surgeons performing the operation. The perioperative data of the patients' including cardiopulmonary bypass time, cross-clamp time, postoperative cardiac rhythm, total operation time, total drainage, total intensive care unit time and total hospital stay time were obtained.

Statistical Analysis

Categorical measurements were summarized as numbers and percentages, and numerical measurements were summarized as mean and standard deviation. All statistical analyses were performed using IBM SPSS (Statistical Package for the Social Sciences) version 25.

Surgical Technique

Central cannulation was performed in all patients. In patients who underwent RALT and RIAVT, 4-5 cm incisions were made in the fourth intercostal space to gain access to the thorax (Fig.1a). After retracting the lung from the surgical field with a moist sponge, the pericardium was opened 2 centimeters anterior to the phrenic nerve in the superior inferior direction. Holding sutures were placed at frequent intervals. Removing the slack of the previous holding suture after each one is a crucial manipulation for improving surgical exposure and bringing cardiac structures closer together. The atrial appendage was then retracted in an inferior direction with another suspending suture. This procedure provides exceptional exposure of the aortic root (Fig.1b). After exposing the entire aortic root and ascending aorta, the pericardium over the SVC was released without damaging the phrenic nerve by sharp dissection up to the junction with the left innominate vein. All anomalous pulmonary veins draining into SVC or cavoatrial junction and azygos vein were exposed (Fig.1b). After aortic cannulation, selective cannulations of the SVC and IVC were performed. SVC cannulation was performed at the junction point of right and left innominate veins with either a right-angle metal-tipped cannula or a small diameter plastic straight cannula (Fig.1c). Subsequently, cardiopulmonary bypass was initiated and continued under mild hypothermia (34˚C). The heart was then arrested with del-Nido cardioplegia solution after achieving targeted temperature.

Three different repair techniques were used in patients following cardiac arrest; double-patch repair, single patch repair and Warden procedure. The preferred surgical method was chosen after careful consideration of several aspects. These include; (1) distance between the entrance point of pulmonary venous connection to SVC and cavoatrial junction, (2) the presence of persistent left SVC (PLSVC) and the diameter of right SVC and (3) the localization of the ASD in the interatrial septum. In cases with wide SVC and short distance (<1 cm) between the pulmonary venous connection and the cavoatrial junction, the single patch technique was used. If the patient had a well-developed superior limbus combined with a small SVC or if the pulmonary venous connection to the SVC was more than 1 cm from the cavoatrial junction, the double patch or Warden procedure was preferred. All restrictive ASDs was expanded towards the direction of the fossa ovalis. If the patient's PLSVC or ASD was not of the high venosum type, we preferred the double patch technique or Warden procedure rather than the single patch technique.

Care was taken to ensure that the patch was sewn generously to avoid stenosis in the baffle, and the double patch or Warden procedure was favoured in every case where SVC stenosis was suspected to develop after the interior patch was sutured (Fig.2).

Results

During the study period, 14 patients underwent surgical repair. Five (36%) of them were female and 9 (64%) were male. The mean ages of the patients who underwent RIAVT and RALT 48±26.6 and 42±18.2 month, respectively. The mean weight of the RIAVT and RALT patients were 14.6 kg and 24 kg, respectively.

In the majority of cases, 12 patients (85.7%) had both the right upper and right middle lobe pulmonary veins draining into right-sided heart structures. ASD of the high venosum type was identified in 12 patients (85.7%). On 12 patients (85.7%), the double patch technique was employed most frequently in surgical treatment. This was then followed by a single patch repair in one (7.1%) patient. The Warden procedure was performed on only one patient (7.1%) underwent RIAVT surgery. In both minimally invasive techniques, the cross-clamp time, CPB time and total operation time were comparable. Nevertheless, due to the complexity of the surgical procedures involved in the double patch and Warden procedures, the duration of these operations was slightly longer than those of the single patch technique. Table 1 lists the demographic, anatomical and surgical details of the patients.

The postoperative intensive care morbidity variables of the patients, such as the need for mechanical ventilation, the total length of stay in the intensive care unit, and the total amount of drainage were similar to each other, and no significant difference was observed between the RIAVT and RALT techniques. However, CPB, cross-clamp and total operation time was slightly longer in the RALT group. This was attributed to the fact that fewer patients were operated on and less experience was gained in the group with less RALT.

During the surgical procedure, none of the patients required inotropic support. All patients were extubated within the first six hours postoperatively. No mortality was observed in any patient. In addition, no complications that would prolong their hospital stay were observed in any of the patients.

In the early postoperative period, a heart rhythm other than normal sinus rhythm was observed in two patients. Since the heart rates of these patients were within the acceptable range, no additional intervention was performed, and they were discharged with close monitoring. In the first month of follow-up, it was observed that one patient with low atrial rhythm treated with the double patch technique returned to normal sinus rhythm. The rhythm of the remaining patient did not change in the first month of follow-up and close monitoring continued. The variables in postoperative intensive care unit and early-term following discharge are shown in Table 2.

Table 1. Demographic and Surgical Data of the Patients

	Minimal Invasive Surgery(N=14)	
Route of Surgery	RIAVT(N=10)	RALT (N=4)
Age (month)	48±26.6	42±18.2
Weight (kg)	14.6±3.51	24±2.64
Male Sex, n (%)	6(60%)	3 (75%)
Right pulmonary veins		
RUL	1(10%)	1(25%)
RUL+RML	9(90%)	3(75%)
RUL+RML+RLL	0(0%)	0(0%)
High venosum ASD, n	9(90%)	3(75%)
Surgical Technique		
Double Patch ,n	9 (90%)	3(75%)
Single Patch ,n	0(0%)	1(25%)
Warden, n(%)	1(10%)	0(0%)
Cross clamp time(min)	35.6±4.9	49±17.7
CPB time(min)	61.6±7.8	75.6±24.5
Operation Duration (h)	4.55±0.62	4.82±0.76

RIAVT; right infra axillary vertical thoracotomy, RALT; right anterolateral thoracotomy, RUL; right upper lobe, RML; right middle lobe, RLL; right lower lobe, ASD; atrial septal defect, CPB; cardiopulmonary bypass

Table 2. The variables in postoperative intensive care unit and early-term following discharge

	Minimal Invasive Surgery(N=14)	
Surgical Approach	RIAVT(N=10)	RALT (N=4)
Mechanic Ventilator Time (h)	6.4±2.2	5.8±3.3
ICU stay time (d)	2.2±0.2	2.4±0.6
Total Drainage (ml)	171±37.5	185±34.1
Total Hospital Stay (d)	4.1±0.6	4.2±0.4
Early Postoperative rhythm		
Normal sinus rhythm	8	4
Lower atrial rhythm	2*	0
Junctional rhythm	0	0
Rhythm at the postoperative 1st month		
Normal sinus rhythm	9	4
Lower atrial rhythm	1*	0
Junctional rhythm	0	0

RIAVT; right infra axillary vertical thoracotomy, RALT; right anterolateral thoracotomy, RUL; right upper lobe ,RML; right middle lobe, RLL; right lower lobe ICU ; intensive care unit ,* Double Patch repair was used

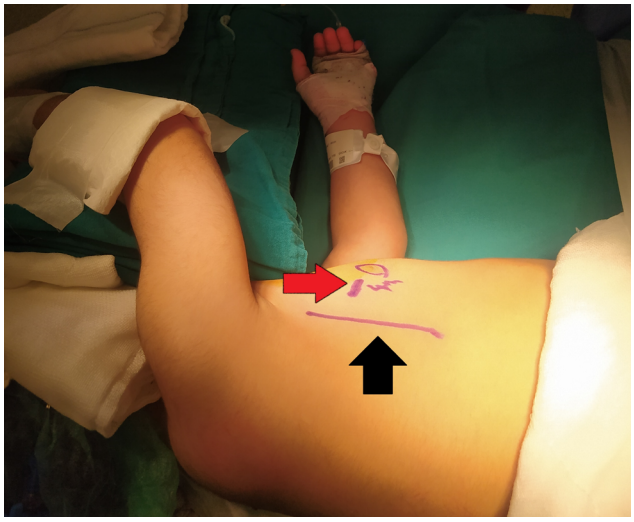

Fig 1a: Preoperative marking of the patient : the red arrow indicates the 4th intercostal space , the black arrow shows the vertical skin incision to be performed.

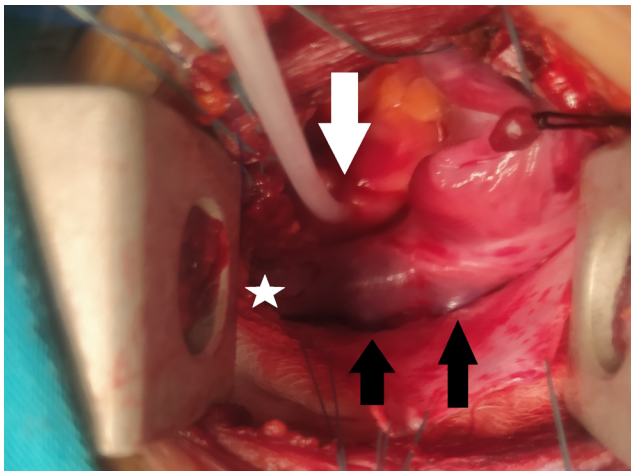

Fig 1b: The view of he surgical field from the primary surgeon's side: White asteriks indicates the SVC , black arrows indicate anomalous pulmonary veins draining to SVC and atriocaval jounction and white arrow shows aortic purse string sutures.

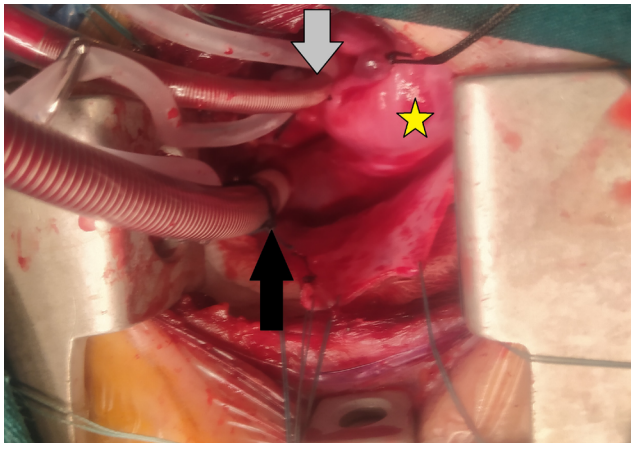

Fig 1c: Central cannulation of the patient: Black and grey arrow indicate SVC and aortic cannulations, respectively.Yellow asteriks marks the right atrium..

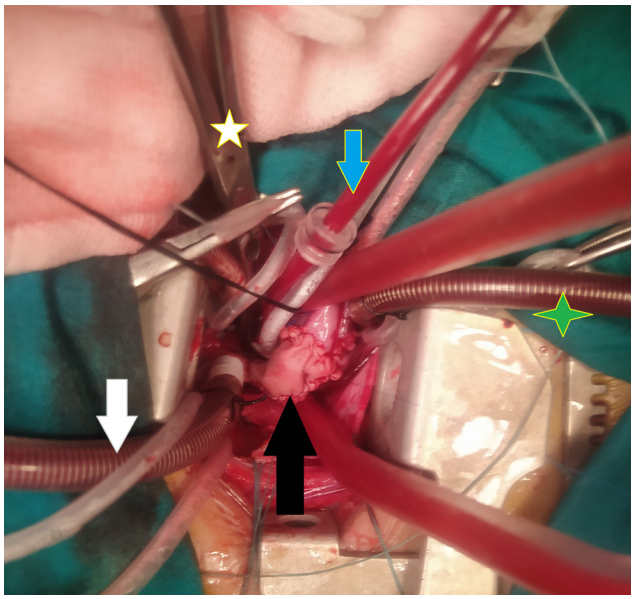

Fig 2: Surgical field of the patient during cardioplegic arrest : White , blue and black arrows indicate SVC cannula, cardioplegia cannula and pericardial patch , respectively. White arrow marks aortic cross clamp and green arrow indicates IVC cannula.

Discussion

The use of minimally invasive surgical methods in congenital heart anomalies continues to increase. Contrary to the disadvantages of traditional median sternotomy, minimally invasive techniques provide superior cosmetic outcomes and greater patient and parent satisfaction. In many cases of CHD, minimally invasive surgical procedures have become the standard of care in recent years as a result of advancing surgical techniques and growing experience. Among these techniques, right vertical or horizontal infra-axillary thoracotomy, ministernotomy and RALT are the techniques used most commonly. In many high-volume centers around the world, low-risk CHD have substantially been repaired using these techniques, and the conventional median sternotomy has gradually been used less frequently. The most common congenital heart anomaly in which these techniques are used is secundum ASD. In addition, many other anomalies such as, PAPVR, ventricular septal defect, partial or complete atrioventricular septal defect, double chamber right ventricle and tetralogy of fallot can also be repaired using these methods. However, in more complex congenital heart anomalies, conventional sternotomy is still recommended because minimally invasive techniques cannot provide sufficient exposure to allow comfortable access to the cardiac structures to perform successful surgical repair.

RALT and RIAVT have been used safely in the surgical repair of right-sided PAPVR and ASD. Unlike the standard secundum ASD repair, selective cannulation of the superior vena cava is one of the most challenging parts of the surgical procedure. It is troublesome to insert metal-tipped right-angle cannulas into the SVC, especially in cases where the anomalous

pulmonary vein has connected to the SVC at superior segments. In these cases, the use of smaller, straight cannulas may provide simplicity in surgical technique. Alternatively, the thorax may be reentered through the 3rd intercostal space for more comfortable SVC and aortic cannulation. Thus, the surgical procedure can be completed using both intercostal spaces. However, in certain cases where the thorax has been entered through the fourth intercostal space, IVC cannulation and snaring may still be challenging. Especially for inferior type sinus venosus secundum ASDs with weak inferior rims, it is crucial to cannulate the IVC as distally as possible. For this reason, we cannulate the IVC with CPB support in cases where exposure is insufficient and do not hesitate to cleave the lower rib to gain enough exposure instead of performing peripheral cannulation if necessary. As a result of our experience with post-discharge patient follow-ups, we did not observe any cosmetic or functional abnormalities in patients whose lower ribs were severed and repaired at the conclusion of the surgical procedure.

There are many studies that report PAPVR repair could be conducted with minimally invasive approaches. Zubritskiy et al.(8) reported that they successfully performed the Warden procedure using the right infra axillary thoracotomy approach in 21 pediatric patients with an average weight of 25 kg, and diagnosed with PAPVR and ASD. In that study population, central cannulation was performed in all patients and surgical repair was performed with ventricular fibrillation under CPB support. No morbidity or mortality was observed in the patients in the postoperative period and all patients were discharged with a normal sinus rhythm. Similarly, Rao et al.(7) reported that they performed the surgical treatment of 14 pediatric patients with PAPVR and sinus venosus type ASD via a modified RIAVT. The average weight of the patients was 21 kg. Peripheral cannulation was performed using the internal jugular vein and femoral vein in patients instead of central venous cannulation. They stated that with this method, the venous cannulas that disturb clear exposure of the surgical field can be avoided and the skin incision can be kept shorter (7). In the study of Amirghofran et al. (10), in which minimally invasive methods and conventional sternotomies were compared in PAPVR and ASD repair in pediatric and adult patients, it was reported that surgical repair of patients could be successfully performed with an anterior mini thoracotomy method. The mean age of 25 pediatric patients who underwent minimally invasive approaches was 4.99 years. It was stated that peripheral cannulation was avoided and central venous cannulation was applied to these patients whenever possible. In addition, high SVC cannulation was not used selectively in pediatric patients, instead, a malleable cannula was sent through the right atrial appendage to the upper segments of the SVC to provide drainage. In all patients, double patch repair was performed and SVC stenosis was only detected in a 3.5-year-old patient. This patient was reoperated to relieve the SVC stenosis. The authors concluded that the anterolateral mini thoracotomy method can be safely applied to pediatric patients (10).

In PAPVR repair, the superiority of single patch, double patch and Warden procedures to each other in terms of the development of sinus node dysfunction, SVC stenosis or pulmonary venous baffle stenosis in the long term has not been fully clarified. Each technique has its own advantages and disadvantages. Single patch repair is a practical and reproducible method in patients with large SVCs and where the pulmonary venous connection is close to the SVC-right atrial junction. However, it is not recommended in cases where the SVC is small and the pulmonary venous connection is away from the SVC-right atrial junction due to the development of potential stenosis in SVC or baffle. In these patients, double patch repair or the Warden procedure is preferred. Although SVC stenosis can usually be avoided with double patch repair, it may still develop in cases where the pulmonary venous connection is very high in SVC or the left SVC is accompanied and the right SVC is smaller than the normal size (8,11). In such cases, the Warden procedure may be a more viable option. Although the long-term survival results of both surgical techniques are excellent, there are publications showing that the Warden procedure gives better results than the double patch technique in terms of sinus node dysfunction (12, 13). Despite the fact that the Warden procedure appears to be a safe and effective surgical technique, it is not without its drawbacks. Particularly in cases where the right atrial appendage is underdeveloped and the SVC caudal segment is short, end to end anastomosis of the SVC to the right atrial appendix cannot be performed and pericardial augmentation or PTFE tube graft interposition may be required to reduce anastomotic tension. In addition, the pectinate muscles in the appendix must be radically resected to prevent stenosis at SVC- right appendix anastomosis (3). Patients undergoing this surgery should be monitored for stenosis in this region during the follow-up period (2, 3, 14).

Double patch repair has been our first choice in the vast majority of PAPVR cases in our clinic (2). This was because all of our patients had a well-developed SVC and we were confident that the patch on the SVC lateral wall would greatly relieve SVC flow. Although it is thought to cause sinus node dysfunction in the long term (11), we did not encounter such a complication in the patients we operated on with this method in our clinic. None of our patients needed a permanent pacemaker. There are many scientific publications showing that the Warden procedure is a superior surgical method that offers very good results in terms of postoperative mortality and morbidity in PAPVC patients (12, 15-18). In one of our patients, we preferred to use the Warden procedure because the pulmonary vein-SVC connection was located very superiorly. There were three reasons why we did not prefer the double patch in this patient. The first reason was that the diameter of the SVC was not wide enough and we suspected that the baffle to be created might critically narrow the total diameter of the SVC. The second

reason was that a very long and wide buff had to be created to divert the pulmonary vein to the left atrium. The third reason was that internal baffle creation was a technically difficult procedure due to the high insertion of the pulmonary vein to the SVC and the presence of the venous cannula close to the surgical area.

The most important limitation of this study is that the small number of cases in the RIAVT and RALT groups made it impossible to compare these two minimally invasive techniques with each other in terms of early and long-term results. In addition, the long-term echocardiographic follow-up of the patients has not been completed yet. After obtaining these data, the reliability of these two techniques used in terms of the development of stenosis in the venous structures where patches are used and the development of cardiac rhythm problems can be clarified.

Conclusion

In conclusion, minimally invasive surgical techniques have better cosmetic results than conventional sternotomy incisions. All surgical techniques that are used in right-sided PAPVR repair with conventional sternotomy methods can also be applied easily and safely with minimally invasive methods. In the following years, minimally invasive approaches may become standard practices in right-sided PAPVR repair.

Ethics Committee Approval: The study was evaluated by the Ankara City Hospital Ethics committee and received ethical approval on 01.02.2023 with the number E2-23-3285. Every procedure was carried out in compliance with the moral guidelines outlined in the 1964 Helsinki Declaration and its subsequent revisions.

Informed Consent: Informed consent was obtained from each subject.

Peer-review: Internally peer-reviewed.

Authorship Contributions: MY wrote the primary draft of the article. BST took part in collecting the data of the article. ANE took a primary role in the preparation of the ethics committee file of the article. YŞÖ and HAG worked on the editing of the article. AA reviewed the final version of the article. The authors have read and approved the final manuscript.

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

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ORIGINAL ARTICLE

Understanding the Social Variations of Nursing Students' Service-Learning and its Effect on Development of Vocational and Social Responsibility

Hizmet Ederek Öğrenme Yaklaşımının Hemşirelik Öğrencilerinin Mesleki ve Sosyal Sorumluluk Gelişimine Etkisinin İncelenmesi

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ABSTRACT

Aim: The study which was carried on to define the effectiveness of the service-learning approach was realised with 2nd Grade nursing students of the faculty of health sciences of a state university operating in Turkiye during the fall semester of the 2022-2023 academic year (14 weeks).
Material and Methods: In this study using mixed methods, the sample group of the quantitative research consisted of 132 students. For this purpose, "Personal and Social Responsibility Questionnaire and Service-Learning Scale", validity and reliability of which was proved, was used. The qualitative part of the research was conducted with 10 participants who participated in the whole process of the study and a semi-structured questionnaire was used. In the qualitative part of the study, it was aimed to gain profound knowledge through the experiences that participants gained during the service-learning process.
Results: It was determined that the average score of the students participating in the research was 58.51±17.59 in the pre-test application of the personal and social responsibility survey and 62.59±10.13 in the post-test application. In addition, the average of the scores the students received in the pre-test from the total service-learning scale was 82.78±13.88; It was determined that the average score they received in the post-test was 86.00±10.69. Qualitative data show that the service-learning approach positively contributed to the development of the participants' insight into the importance of community work, helped them understand social diversity, helped them develop social skills and increased their sense of responsibility.
Conclusion: Service-learning positively affected students' knowledge of vocational and social responsibility and their self-assessment of knowledge-skill-attitudes. It is recommended that the service-learning approach be used to teach nursing vocational and social responsibility.

Keywords: Nursing education, Nursing students, Service-learning, Social responsibility, Vocational development.

ÖZ

Amaç: Hizmet ederek öğrenme yaklaşımının etkililiğini belirlemek amacıyla yürütülen çalışma, Türkiye'de faaliyet gösteren bir devlet üniversitesinin sağlık bilimleri fakültesi 2. sınıf hemşirelik öğrencileri ile 2022-2023 eğitim-öğretim yılı güz döneminde (14 hafta) yapılmıştır.
Gereç ve Yöntem: Karma yöntem kullanılarak yapılan bu çalışmada nicel araştırmanın örneklem grubu 132 öğrenciden oluşmuştur. Bu amaçla geçerliliği ve güvenirliği kanıtlanmış "Bireysel ve Sosyal Sorumluluk Ölçeği ve Hizmet Ederek Öğrenme Ölçeği" kullanılmıştır. Araştırmanın nitel kısmı çalışmanın tamamına katılan 10 katılımcı ile gerçekleştirilmiş olup yarı yapılandırılmış anket kullanılmıştır. Araştırmanın nitel kısmında ise katılımcıların hizmet ederek öğrenme sürecinde edindikleri deneyimler aracılığıyla derinlemesine bilgi edinmesi amaçlanmıştır.
Bulgular: Araştırmaya katılan öğrencilerin Bireysel ve Sosyal Sorumluluk Ölçeği'nin ön test uygulamasında ortalama puanının 58,51±17,59, son test uygulamasında ise 62,59±10,13 olduğu belirlenmiştir. Ayrıca öğrencilerin hizmet ederek öğrenme toplam ölçeğinden ön testte aldıkları puanların ortalaması 82,78±13,88; Son testte aldıkları puan ortalamasının 86,00±10,69 olduğu saptanmıştır. Araştırmanın nitel verileri, hizmet ederek öğrenme yaklaşımının katılımcıların toplum için çalışmasının önemine dair içgörülerinin gelişmesine olumlu katkıda bulunduğunu, sosyal çeşitliliği anlamalarına yardımcı olduğunu, sosyal becerilerinin gelişmesine yardımcı olduğunu ve sorumluluk duygularının arttığını göstermektedir.
Sonuç: Hizmet ederek öğrenme, öğrencilerin mesleki ve sosyal sorumluluk bilgilerini ve bilgi-beceri-tutumlarına ilişkin öz değerlendirmelerini olumlu yönde etkilemiştir. Hemşireliğin mesleki ve sosyal sorumluluğunu öğretmek için hizmet ederek öğrenme yaklaşımının kullanılması önerilmektedir.

Anahtar kelimeler: Hemşirelik eğitimi, Hemşirelik öğrencileri, Hizmet ederek öğrenme, Sosyal sorumluluk, Mesleki gelişim.

Introduction

Social responsibility, associated with the activities that a person or an institution works for for the benefits of community without taking into account her own interests or putting herself in the forefront, is an ideological concept aiming institutions or communities not to behave unethically, instead to contribute voluntarily to the welfare of the community where they interact and operate. As a matter of fact, educational institutions fulfil their responsibilities by educating their students as individuals responsive to the environment and society (1). At this point, the question "what is the concept of the service-learning (CSL) in terms of its relation with social responsibility" is thought to be appropriate. Tens of descriptions have been developed for the CSL and it is generally stated that the service-learning is shaped around a "programme type and educational philosophy" theme (2). When the relevant literature taken into consideration, this concept is

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understood to be defined as "educational experience based on modular (credit) lessons where students participate in organized service activities that meet the defined social needs; and also the experience where they reflect through service activities that enable students to gain a better understanding about the content of the lessons, to grasp the importance given to this discipline and to increase their commitment to personal values and civic responsibilities. According to the definition in question, it is expected that the service-learning should have an academic activity, contribute to the objectives of the lessons and create meaningful learning, and should carry a meaning for both the student and stakeholder of the society. However, one of the most important objectives of the service-learning is to gain civic responsibility (3). Facts such as offering meaningful and relevant services to the society, encouraging academic learning and preparation of the individual for active citizenship process are among the criteria required to enable learning by service and to make it a part of an academic programme (4).

The CSL is a reflective and relational pedagogy connecting community and public services with structural learning opportunities. This method prepares students to solve community-based problems on a practical level rather than focusing on preparing them for a specific job. Students are offered to discover the connections between the theoretical area of the classroom and the practical needs of the society. Perhaps the most important benefit of the service-learning is students' connection to a community and the motivation and the opportunity that the CSL would provide for them to define their own roles within that community (5). It increases academic achievement, enables school attendance in terms of learning responsibility and provides additional support for commitment to classroom work and high exam grades (6).

At the same time, while developing self-concept, self-esteem, self-efficacy in terms of identity development (7), it enables establishing positive relations by connecting the student with the society (8), and therefore supports fair society (9). In order for learning from service experience to have the desired level of impact, the CSL policy needs to be designed to facilitate the development of these skills as part of or in addition to other learning objectives. It is stated that the way to realise this is including students in the environments, processes, and interactions where the concept in question exists and can be critically examined and by comparing different worldviews (10).

No study has been found in the literature examining the service-learning approach of nursing students. In this regard, the study will be conducted to examine the effect of the service-learning approach on the professional and social responsibility development of nursing students.

Material and Methods

Subject of the Research

In the research conducted with the combination of qualitative and quantitative method and details of which are given in methodology chapter, it is aimed to find out whether the CSL activities contribute to the social responsibility and vocational skills of the students; and the study is designed in a way to answer the questions below:

If there are any significant difference between pre-test and post-test performances of the students participating in the CSL activities

To compare the results gained with the students who did not participate in the CSL activities

To find out whether the CSL activities contribute to the development of the social responsibility skills of the students.

Universe and sample

The population of the research consists of the 2nd Grade nursing students of the faculty of health sciences of a state university in Turkiye. Sample of the research consists of the students taking an "Emergency Care and First Aid" lesson, in which the social responsibility levels of the students came to the fore the most. In this study, the sample size calculation developed by Krejcie and Morgan in 1970 was used. In the mentioned method, it is stated that according to a=0.05 significance and ± 5% error margin in a population consisting of 168 people, the required sample number is supposed to be 126. (11). Starting from these data, the research has been realised with 132 students (78.5% of the universe has been reached). The qualitative research part of the study has been carried out with 10 students who have participated in the pre- and post- tests.

Data collection tools

The research is based on a combined qualitative and quantitative approach. In the quantitative part of the research "The CSL Scale and Social Responsibility Scale" validity and reliability of which was proven was used. In the qualitative part 10 participants were asked a semi-structured questionnaire. Before the interview, participants were briefly informed about the content of the research. It was stated that voice recorders would be used in order not to lose any data, and these would be used under the scope of the research and never be shared with the third parties. It was informed that participating in the research was voluntary and interviews lasted around 30 minutes on average. As the data from the participants were protected, they were coded as P1, P2, P3, … and so on; no changes were made in the views of the participants and they were directly transferred.

The service-learning scale

The original form of the scale is "Short Version of Scale of Service-Learning Involvement (SSLI)" and developed by Olney and Grande in 1995. Original language of the scale is English. Küçükoğlu and Ozan adapted The

Service-Learning Scale into Turkish in 2015. The internal consistency reliability parameter of the scale was found as .85 and the test-retest reliability coefficient was .81. The adapted scale consists of 30 items and is in 4-point Likert type (12).

Personal and social responsibility questionnaire

The original form of the scale is "Personal and Social Responsibility Questionnaire (PSRQ)" and developed by Li Weidong, Paul M. Wright, Paul B. Rukavina and Molly Pickering in 2008. Original language of the scale is English. Filiz and Demirhan adapted the Personal and Social Responsibility Questionnaire (PSRQ) into Turkish in 2015. PSRQ can be used for different disciplines covering studies on responsibility behaviours. Within the scope of the reliability study, the internal consistency parameter was calculated as .925. It was determined that the Pearson Product Moment Correlation Coefficient calculated for the test-retest reliability study was significant. Findings from Confirmatory Factor Analysis showed that the structure composed of Exploratory Factor Analysis was at an acceptable level. The adapted scale consists of 13 items and is in 6-point Likert type (13).

Semi-structured questionnaire

Research questions were prepared by taking the national and international literature into consideration. The reason why semi-structured questions were preferred was that they were neither as rigid as structured questions nor as flexible as unstructured questions. Therefore, since it is located between the two extremes, it was aimed to enable the participants to express their views on the subject more clearly. For this purpose, 11 questions were directed to the participants.

Implementation background of the research

The research was completed in 14 weeks in the Fall Semester of the 2022-2023 Academic Year. First of all, the pre-test of the research was presented on 12 October 2022 and the CSL was introduced to this group. In the following weeks, workshops in and outside the classroom and activities based on social responsibility were carried out with the students participating in the study within the scope of the CSL. For instance, as part of extracurricular activities, a "Healthy Life Activity" was organized in the foyer area of the university campus on 29 December 2022. The last test of the study was conducted on 10 January 2023, which was in the last week of the Fall Semester. Qualitative interviews were held again this week. Qualitative data were checked using "Standards for Reporting Qualitative Research (SRQR)".

Analysis of data

Data of the study were analyzed with IBM SPSS 23v package programme. After that, reliability of both the pre-test and post-test implementations of the scales used in the research was presented through the Cronbach Alpha internal consistency coefficient. An alpha coefficient of less than 0.5 is unacceptably reliable, between 0.5 and 0.6 is poorly reliable, between 0.6 and 0.7 is acceptably reliable; between 0.7 and 0.9 means good reliability and if it is higher than 0.9, it shows that it is perfectly reliable (14).

After determining those scales yielded reliable results, the normal distribution situation of both the scales and the differences between the pre-test and post-test scores were examined in order to decide on the tests to be used in the analysis. Due to the normal distribution of the pre-test scores of the Personal and Social Responsibility Questionnaire and The CSL Scale, the relationship between the scales was examined with Pearson Product Moment Correlation; since the post-test scores did not show normal distribution, the relationship between the scales was examined through Spearman Rank Differences Correlation; and significant differences between the scores were examined using the Dependent Samples t-Test as the differences between the measurements showed a normal distribution.

Correlation coefficients between 0 and 0.30 were interpreted as low, between 0.30 and 0.70 as medium, between 0.70 and 1 as an indicator of a high level of correlation (15). For the pre-test and post-test measurements, the size of the differences between the units was calculated by Eta squared. An eta square (η2) of 0.01 was interpreted as low, 0.06 medium, and 0.138 as an indicator of a difference with a high effect size (16).

Reliability analysis

Alpha coefficient was found as 0.977 in the pre-test application of the one-dimensional Personal and Social Responsibility Questionnaire and 0.901 in the post-test application and it was seen that it was perfectly reliable for both applications. Alpha coefficient was found as 0.826 for the pre-test application and 0.817 for the post-test application of the CSL Scale in general, and it was highly reliable for both applications.

Results

According to Table 1, 0.8 % of the students participating in the research were 18 years old (n=1) , 22.7 % of them 19 (n=30), 34.8 % of them 20 (n=46), 21.2 % of them 21 (n=28), 6.8% of them 22 (n=9), 6.8 % of them 23 (n=9), 0.8 % of them 24 (n=1), 3.8 % of them 25 (n=5), 1.5 % of them 26 (n=2) and 0.8 % of them were 30 years old (n=1). 3 % of the students participating in the research were married (n=4), 97 % of them were single (n=128) 72.7 % of the students were female (n=96) and 27.3 % of them were male (n=36). The place where 14.4% of students lived the longest was a village (n=19), 31.8 % of them lived in a district (n=42), 22.7 % of them lived in a province (n=30) and 31.1 % of them lived in a big city (n=41). 21.2 % of the students still lived with their parents (n=28), 19.7 % of them lived with their friends at home (n=26) and 50.8 % of them lived in a state hotel (n=67) and 8.3 % of them lived in a private hostel (n=11). According to Table 2, 34.8 % of the students participating in the research were 20 years old (n=46), 97 % of them were single (n=128), 72.7 % of them were

female (n=96). The place where 31.8 % of students lived the longest was a district (n=42) and during the research was conducted 50.8 % of the students were staying in the state dormitory (n=67).

Table 1. Information on students participating in the research.

Variable	Category	N	%
Age	18	1	.8
	19	30	22.7
	20	46	34.8
	21	28	21.2
	22	9	6.8
	23	9	6.8
	24	1	.8
	25	5	3.8
	26	2	1.5
	30	1	.8
Marital Status	Married	4	3.0
	Single	128	97.0
Gender	Female	96	72.7
	Male	36	27.3
The place where they have lived the longest	Village	19	14.4
	District	42	31.8
	Province	30	22.7
	Big city	41	31.1
The place they live in now	With the family	28	21.2
	At home with friends	26	19.7
	State hostel	67	50.8
	Private hostel	11	8.3
Total		132	100

According to Table 2, 69.7 % of the students stated that the income and expenses of their families were equal (n=92). Mothers of 50.8% of the students are primary school graduates (n=67) and fathers of 38.6 % of the students are high school graduate (n=51). 57.6 % of the students participating in the study stated that they took part in social responsibility activities (n=76), when the social activities they took part examined, it was found out that 28 % of them were giving health training (n=37). Families of 44.7 % of the students (n=59) and social environment of 43.9 % of the students (n=74) involved in social responsibility activities.

According to Table 3, 22 % of the students stated that their income was less than their expenses (n=29), 69.7 % of them stated that their income and expenses were equal (n=92), 8.3 % of them stated that their income was more than expenses (n=11). Mothers of 4.5 % of the students were illiterate (n=6), 50.8 % were primary school graduates (n=67), 28 % of them were high school graduates (n=37) and 16.7 % of them had a university degree or above (n=22). Fathers of 0.8 % of the students were illiterate (n=1), 34.8 % of them primary school graduates (n= 46), 38.6 % of them were high school graduates (n=51) and 25.8 % of them had a university degree or above (n=34). Of the students participating in the study, 57.6 % stated that they took part in social responsibility activities (n=76), and 42.4 % stated that they did not (n=56). When the social activities they took part examined, it was seen that 28 % of them planted trees (n=37), 28 % of them gave health training (n=37), 23.5 % of them helped those who needed (n=31), 15.2 % of them donated blood to the Red Crescent (n=20), 3.8 % of them paid support visits to the elderly and sick people (n=5) and 1.5 % of them fed the stray animals (n=2). Families of 44.7 % of the students participated in social responsibility activities (n=59) while 55.3 % of them did not (n=73). When the social circle of the students was examined, 43.9 % of them took part in social activities (n=58) while 56.1 % did not (n=74).

Table 2. Information on the family and participation status in social activities.

Variable	Category	N	%
Income Level of the Family	Income is less than expenses	29	22.0
	Income is equal to expenses	92	69.7
	Income is more than expenses	11	8.3
Mother's Education	Illiterate	6	4.5
	Primary School	67	50.8
	High School	37	28.0
	University Degree or above	22	16.7
Father's Education	Illiterate	1	.8
	Primary School	46	34.8
	High School	51	38.6
	University Degree or above	34	25.8
Status of Participating in the Social Responsibility Activities	I participated	76	57.6
	I did not participate	56	42.4
Social Activities Participated	Planting trees	37	28.0
	Giving health training	37	28.0
	Helping those who need help	31	23.5
	Donating blood to the Red Crescent	20	15.2
	Organizing support visits to the sick/ elderly people	5	3.8
	Feeding stray animals	2	1.5
Family Participating in the Social Responsibility Activities	They participated	59	44.7
	They did not participate	73	55.3
Social Environment Participating in the Social Responsibility Activities	They participated	58	43.9
	They did not participate	74	56.1
Total		132	100

Results related to the quantitative methods

Descriptive statistics about Personal and Social Responsibility Questionnaire are given in Table 3.

Table 3. Descriptive statistics about personal and social responsibility questionnaire.

Measu-rement	N	X̄	SS	The Lowest	The Highest	Item Averages
Pre-test	132	58.51	17.59	15.00	78.00	4.50
Post-test	132	62.59	10.13	16.00	78.00	4.81

According to the findings in Table 3, it is seen that the average score (X̄) of the students who participated in the study was 58.51 in the pre-test application of the personal and social responsibility questionnaire, the standard deviation was (SD) 17.59, the lowest score gained from the scale was 15, and the highest was 78, and item averages were 4.50. In accordance with the item averages, personal and social responsibility levels of the students seemed "high" in the pre-test implementation. As regards the findings in Table 4, it was determined that the average score (X̄) of the students who participated in the study was 62.59 in the post-test application of the personal and social responsibility questionnaire, standard deviation was (SD) 10.13, the lowest score gained from the scale was 16, and the highest was 78, and item averages were 4.81. In accordance with the item averages, personal and social responsibility levels of the students seemed "high" in the post-test implementation.

With regard to the findings in Table 3, it is found that the average score of the students who participated in the study was 58.51±17.59 in the pre-test application and 62.59±10.13 in the post-test application of the personal and social responsibility questionnaire. In accordance with the item averages, personal and social responsibility levels of the students were determined as "high" in the pre and post-test implementation. Descriptive statistics about The Service-Learning are given in Table 4.

Table 4. Descriptive statistics about the service-learning.

Scale/Sub-Dimension	Measure-ment	N	X□	SS	The Lowest	The Highest	Item Avera-ges
Exploring	Pre- Test	132	27.62	4.91	16.00	38.00	2.76
	Post- Test	132	29.06	4.30	17.00	38.00	2.91
Realising	Pre- Test	132	28.69	6.53	13.00	37.00	2.87
	Post- Test	132	30.08	4.86	13.00	39.00	3.01
Internalization	Pre- Test	132	26.46	4.17	17.00	35.00	2.65
	Post- Test	132	26.86	3.24	18.00	38.00	2.69
Total	Pre- Test	132	82.78	13.88	48.00	102.00	2.76
	Post- Test	132	86.00	10.69	50.00	110.00	2.87

In Table 4, it was determined that in the pre-test application of the exploration sub-dimension of the CSL scale, the average score obtained by the students participating in the research was 27.62±4.91. Considering the item averages, exploring levels of the students was seen as "medium" in the pre -test implementation. It was detected that in the post-test application of the exploration sub-dimension of the CSL scale, the average score obtained by the students participating in the research was 29.06±4.30. In compliance with the item averages, exploring levels of the students were seen as "high" in the post -test implementation.

According to the findings in Table 4, it is seen that the average score (X̄) of the students who participated in the study was 27.62 in the exploration sub-dimension pre-test application of the CSL Scale, standard deviation was (SD) 4.91, the lowest score gained from the sub-dimension was 16, and the highest was 38, and item averages were 2.76. In comparison with the item averages, exploring levels of the students were "medium" in the pre -test implementation. It was determined that the average score (X̄) of the students who participated in the study was 29.06 in the exploration sub-dimension post-test application of the CSL Scale, standard deviation was (SD) 4.30, the lowest score gained from the sub-dimension was 17, and the highest was 38, and item averages were 2.91. In accordance with the item averages, exploring levels of the students were "high" in the post -test implementation.

According to the findings in Table 4, it was established that the average score (X̄) of the students who participated in the study was 28.69±6.53 in the realization sub-dimension pre-test application of the CSL Scale. In reference to the item averages, realization levels of the students were "high" in the pre -test implementation. The average score of the students who participated in the study was 30.08±4.86 in the realization sub-dimension post-test application of the CSL Scale. With respect to the item averages, realization levels of the students were "high" in the post -test implementation.

According to the findings in Table 4, the average score (X̄) of the students who participated in the study was 28.69 in the realization sub-dimension pre-test application of the CSL Scale, standard deviation was (SD) 6.53, the lowest score gained from this sub-dimension was 13 and the highest was 37 and item averages were 2.87. In regard to the item averages, realization levels of the students were "high" in the pre -test implementation. It is seen that the average score (X̄) of the students who participated in the study was 30.08 in the realization sub-dimension post-test application of the CSL Scale, standard deviation was (SD) 4.86, the lowest score gained from this sub-dimension was 13 and the highest was 39 and item averages were 3.01. In accordance with the item averages, realization levels of the students were "high" in the post -test implementation.

In proportion to the findings in Table 4, the average scores (X̄) of the students participating in the research in the internalization sub-dimension were 26.46±4.17 in the pre-test application and 26.86±3.24 in the post test application of the CSL scale. In accordance with the item averages, internalization levels of the students were "medium" in the pre and post -test implementation.

According to the findings in Table 4, the average

score ($\bar{X}$) of the students who participated in the study was 26.46 in the internalization sub-dimension pre-test application of the CSL Scale, standard deviation was (SD) 4.17, the lowest score gained from this sub-dimension was 17 and the highest was 35 and item averages were 2.65. In reference to the item averages, internalization levels of the students were "medium" in the pre -test implementation. It was detected that the average score ($\bar{X}$) of the students who participated in the study was 26.86 in the internalization sub-dimension post-test application of the CSL Scale, standard deviation was (SD) 3.24, the lowest score gained from this sub-dimension was 18 and the highest was 38 and item averages were 2.69. In accordance with the item averages, internalization levels of the students were seen as "medium" in the post -test implementation.

With respect to the findings in Table 4, it is seen that for the total of the CSL scale, the average of the scores that the students who participated in the research got in the pre-test was 82.78±13.88. As regard the item averages, the CSL level of the students were at the "medium" level in the pre-test application. It was determined that for the total of the CSL scale, the average scores that the students participating in the research got in the post-test application was 86.00±10.69. Considering the item averages, the CSL level of the students were at the "high" level in the post-test application.

Considering the findings in Table 4 in the post-test application for the total of the CSL scale of the students participating in the research, the average ($\bar{X}$) of the scores obtained in the pre-test application for the total of the CSL scale was 82.78, the standard deviation (SD) was 13.88, and the lowest score obtained from the scale. 48, the highest score is 102, and the item average is 2.76. With respect to the item averages, the CSL level of the students were at the "medium" level in the pre-test application. Pursuant to the findings in Table 5, the average ($\bar{X}$) of the scores obtained in the post-test application for the total of the CSL scale was 86, the standard deviation (SD) was 10.69, and the lowest score obtained from the scale was 50 and the highest score was 110 and the item averages were 2.87. In terms of the item averages, the CSL level of the students were at the "high" level in the post-test application. Findings regarding the determination of the relations between Personal and Social Responsibility Questionnaire and The Service-Learning Scale are given in Table 6.

When Table 5 is examined, it is seen that the scores of the students in the pre-test application from the individual and social responsibility scale in general have a moderately significant positive correlation with the exploration sub-dimension scores of the CSL scale (p<.01; r=.596). a moderately significant positive correlation with the scores of the realization sub-dimension (p<.01; r=.599), a moderately significant positive correlation with internalization sub-dimension scores (p<.01; r=.408), and a moderately significant positive correlation (p<.01; r=.616) with the total scores of the CSL.

Table 5. The relations between personal and social responsibility questionnaire and the service-learning scale.

Implementation	Scale/Sub-dimension	The Service-Learning			
		Exploring	Realizing	Internalization	Total
Pre-test	Personal and Social Responsibility	.596**	.599**	.408**	.616**
Post- Test		.379**	.443**	.222*	.421**

**p<.01; *p<.05

When Table 5 is examined, it was determined that the scores of the students in the post-test application from the individual and social responsibility scale in general had a moderately significant positive correlation with the exploration sub-dimension scores of the CSL scale (p<.01; r_s=.379), and a moderately significant positive correlation with the realization sub-dimension scores (p<.01; r_s=.443), a low-level significant positive correlation with the internalization sub-dimension scores (p<.01; r_s=.222) and a moderately significant positive correlation with the total scores of the CSL scale (p<.01; r_s=.421).

The t-Test results, which were carried out to determine whether there was a significant difference between the pre-test and post-test average scores of the Personal and Social Responsibility Questionnaire, are given in Table 6.

According to Table 6, there is a significant difference in small effect size between personal and social responsibility questionnaire pre-test scores and post-test scores (t_132=-2.207, p<0.05, η2=0.036). The average of the personal and social responsibility questionnaire scores of the students after the community service implementation ($\bar{X}$=62.59) is higher than the average of the personal and social responsibility questionnaire scores before the community service implementation ($\bar{X}$=58.50).

Table 6. The *t*-test results of the pre-test and post-test average scores of the personal and social responsibility questionnaire.

Measurement	N	$\bar{X}$	SS	sd	t	p	η^2
Pre- Test	132	58.50	17.58	131	-2.207	0.029*	0.036
Post-Test	132	62.59	10.12				

*<p,05

The t-Test results, carried out to determine whether there was a significant difference between the students' personal and social responsibility questionnaire pre-test scores, and the pre-test and post-test average scores of the CSL Scale according to Table 6, are given in Table 7.

Table 7. The *t*-test results of the pre-test and post-test average scores of the service-learning scale. X̄

Scale /Sub-dimension	Measurement	N	X̄	SS	sd	t	p	η^2
Exploring	Pre- Test	132	27.62	4.92	131	-2.368	0.019*	0.041
	Post-Test	132	29.06	4.30				
Realizing	Pre- Test	132	28.69	6.53	131	-1.894	0.060	-
	Post-Test	132	30.08	4.86				
Internalization	Pre- Test	132	26.46	4.17	131	-0.898	0.371	-
	Post-Test	132	26.86	3.25				
Total	Pre- Test	132	82.78	13.88	131	-2.065	0.041*	0.032
	Post-Test	132	86.00	10.70				

*p<, 05

According to Table 7, there is a significant difference in the small effect size between the students' pre-test scores of the exploration sub-dimension of the CSLscale and the post-test scores of the exploration sub-dimension of the CSL scale (t_132=-2.368, p<.05, η2=0.041). The average of the scores of the students for the scale exploration sub-dimension (X̄=29.06) of the CSL Scale after the community service application is higher than the average of the scores before the community service application (X̄=27.62). There is no significant difference between the students' pre-test scores and the post-test scores the of the realization sub-dimension of the CSL scale (t_132=1.894, p>.05). There is no significant difference between the students' pre-test scores and the post-test scores the of the internalization sub-dimension of the CSL scale (t_132=-0.898, p>.05). There is a significant difference in small effect size between the students' total pre-test scores and the total post-test scores of the CSL scale (t_132=-2.065, p<.05, η2=0.032). The average scores of the students after the community service practice (X̄=86.00) of the L CSL scale is higher than the ones before the community service practice (X̄=82.78).

Results on the qualitative method

Social responsibility and social awareness perception

Social responsibility is a phenomenon that has material and spiritual elements. The concept in question has been tried to be defined by associating it with different points of views by the participants. In an approach, in which conscience is prominent, social responsibility is described as follows:

"Social responsibility, to me, is to help people – financially and morally - by taking care of their needs. Social responsibility, of course, is a situation that is up to the conscience of the person; you should be willing to help others. I think we can meet a lot of needs of the people within the scope of social responsibility" (P1).

Empathy approach that can be described as sympathy is to internalize a subject or an event by the individual by understanding the emotional state of another person. Another participant points out the relationship between social responsibility and empathy.

"Man, first of all, is a social being. As we live in a state order after all, we have to show empathy. We are all a community, that is we are like combined chains. If we become selfish, we become the weak link in the chain" (P2).

Social responsibility concept is not limited only with its material dimension. At the same time, it should be taken into consideration with its spiritual aspects in accordance with the phenomenon that is put in the centre. Therefore, social responsibility is defined as follows:

"I think the concept of social responsibility is to show people what they do not know or to express their important problems and help them develop methods to cope with their problems. This could be material or spiritual" (P10).

In this respect, it seen that various approaches emerge when considering whether financial or moral assistance is provided to any person with or without close or distant relationship, and if so, what kinds of assistance is provided for them.

"Of course, I did. I mean, I have helped people- either old, or a child or at my age … I love to help people. I mean, seeing their works are done or their problems are settled at that moment makes me very happy. Because, even this much is enough. The simplest one for example helping an elderly patient cross the street is something I do daily basis. I become happy when I help people solve their issues; that's why I help" (P1).

In another example it is understood that there happens discrimination among the people to be helped and priority is given to the immediate environment. The background reason of this is the real situation of the person to be helped is not known exactly.

"I mostly help my close ones. My priority is my immediate environment, because I am not in a close relationship and I cannot sense the needs of those who are far away, I help my immediate environment" (P6).

When the expectations from the individuals that are helped are focused on, it is understood that the subject is taken in a simple way and only a positive attitude from them will be sufficient.

"When I am helping, I do not expect anything as the other side already has a problem or needs something at that time. But of lesson, if the person I help is to resent me or bite my head off, this situation frankly makes me feel uneasy. The only thing I expect from the other side is to thank me. That's all. I do not expect anything else. Apart from this, I think if they are not able to do this, they can at least smile and that would be enough" (P1).

It is seen that another participant also shares the same thoughts and due to her/his religious belief s/he says positive wishes would be enough.

"I have no expectations. It is enough if they pray for me or thank me" (P7). "This is both the feeling of sympathy

and happiness and also it is because of our religion. This would help on the other side when we die" (P6).

When the motivations directing an individual to help are taken into consideration, it is understood that different meanings are attributed to the aids, but a psychological border emerges in terms of the size of the aids.

"I have limits in both financial and moral aids. After all I am a human being. Although I say I have no mental limits, I would say stop somewhere. But I do my best until the time my mind tells me to stop, of course, within the limits of my budget" (P2).

One participant who states that s/he can act in a more unlimited way in terms of moral assistance along with financial aid says s/he will not give up on this behaviour despite the possible negative consequences. S/he says that:

"I have a limit when sacrificing, I mean, I think I can help until the point that I hurt myself. It would be wrong to say I do not have any limits. I cannot continue after a point that I might give harm. I cannot continue helping financially but morally I might. Because there are people we love and we do not want them to be upset, we want to help them. In return we give harm to ourselves, but personally I would continue moral help" (P4).

The issue of the abuse of aid is another aspect of the border drawn.

"This happened a lot when I helped a person. They start using me for their benefits. I say stop to this situation now because I feel used – my good will is being abused. In this case, I would stop myself but other than that, I do my best to help" (P5).

However, there are examples that are exceptions to these approaches; it is stated that when necessary, aids are directed to those who are in need by taking from the others.

"I can sacrifice financially till the end. I can even give the last money in my pocket, really, if I feel that person really needs and if my money is not enough, I can ask from the people around me. I mean, I do not have limits when it comes to helping" (P3).

The contribution of the csl activities to the education process and the development of social responsibility

In the CSL approach, a form of learning in which academic objectives and services for the benefit of the society are combined, academic learning is supported with real-life experiences. Thus, the experience of being an effective citizen is also provided. Moreover, it should be noted that, the phenomenon in question is widely used by all disciplines when the CSL contribution to the system and the personal development is taken into consideration. In this respect, when the contribution of the practices and theoretical information provided during the research to the education process and social responsibility understanding of the participants is examined, positive feedback that can be classified under different headings draw attention. For instance, the importance of knowing an individual closely in the nursing profession is expressed as such:

"I think this approach has great contribution to the nursing field. Because, the nursing profession requires acting in line with the people's care needs. That is why; we assess each person we see outside differently. Thanks to these practices, I have been able to more closely experience that people's needs are various. We are given such an opportunity. Moreover, it also gave me the opportunity to practice taking blood, measuring blood sugar or checking blood pressure, it made me feel more useful for the society" (P1).

Learning is an action realized with different methods by seeing, hearing and doing by considering the characteristics differences between individuals. Activities carried out during the research process presented learning by doing experience to the participants. This approach, depending on the features of the practices, creates the feeling of being useful to the society, while combining theory and practice.

"We learn a lot of theoretical things in the lessons and in fact we do know a lot. But the knowledge can be fleeting, that is why practice is more important as it is visual, we were able to get good opportunities; we had the chance to practice what we learned. But more importantly, what we did was rewarded. Sometimes people can face bigger problems due to small precautions. We took blood and measured blood pressure; maybe with a small precaution we will be able to solve a bigger problem. This is a good feeling" (P10).

The CSL process arouses an interest in social problems while assisting development of social responsibility consciousness. At the same time, it supports the development of competences such as working based on collaboration, solidarity and communication.

"We study nursing in health sector. As a requirement of our profession, we will be in communication with patients all the time. I think the most important contribution of this experience was the opportunity to improve communication. Learning their needs by observing is very important for our job. There is something like this; we do not work only in the intensive care unit, emergency unit, or in other services. For instance, some of our friends are choosing public health; I believe the activities we carry on here will contribute to them a lot. I think social responsibility projects can contribute a lot more to public health nursing as there are old and infant patients here. A different experience is needed to deal with such groups, I believe, such approaches may help understand our profession" (P9).

While daily problems occur in the CSL concept, methods to solve these problems are tried to be developed. In this process, while enabling the individual to take responsibility through academic and social activities, it also contributes to their self-confidence development.

"Last year we could not do an internship at the hospital,

so this year when we went for internship, we faltered a bit. I am not talking about everyone but many friends of mine faltered when they approached people and helped them. Thanks to this lesson we learned how to approach people and we gained confidence" (P4).

There are many alternative methods to integrate CSL activities into the curricula. Therefore, different models can be developed in accordance with the learning objectives, the number of the students, education level of the students, and also the projects and the opportunities of the institution to be collaborated with in the community. Determining the suitable model is the most important stage of the preparation phase. In this respect, one of the questions wondered in this study was "outside clinical practices in nursing education, whether the education process with CSL could be reinforced or not". Although participants gave different and alternative answers to this question, they expressed as their common thought that a significantly positive benefit gained.

"As I stated in the previous questions, I think this approach can be very useful for instance in public health. After all, it will certainly help at the stage when we put the theoretical knowledge we learned into practice. Moreover, it contributes to the development of communication and empathy skills but the most importantly it helps us become a part of the community as an individual. I think this is what we need most, and this approach gives us a good opportunity" (P9).

Another participant offered a little bit more different approach in terms of the impact of this approach on the education process, and highlighted the contribution that emerged in reinforcing cognitive and affective competences.

".....for example, I am an excited and sensitive person. When I do something related with my job or in social life, my hands shake. I started learning how to get over these problems by taking part in the activities in this lesson. It was a good experience for me to communicate with people, otherwise my hands used to shake while measuring blood pressure; "I think I feel a little more confident now." (P7).

Another feature of the CSL approach is its offering participants the opportunity to express themselves in a more relaxed atmosphere. In this way, alternative approaches can emerge in terms of the benefit of the society and personal development outside the formal atmosphere. Thus, while the individual is acting at the centre of the social expectations, at the same time starts becoming a part of the society.

"We used to hesitate by thinking if people would misunderstand. Bu in this lesson, we found a more relaxed atmosphere beyond a formal approach and spoke to people more comfortably. Sometimes when we speak to the patients at the hospital, they become aggressive and we cannot get along. How to put it, it was as if we were provided with an experience outside the hospital and I think we felt more comfortable." (P8).

Discussion

The CSL offers various benefits to the stakeholders, moreover, research in this field shows that the approach in question is frequently used in several academic disciplines such as medicine, nursing, business, economy, social sciences, education (17). This study carried out with nursing students for a long period of time shows that the CSL concept is an approach which is appropriate for the health sector. In this regard, the students who participated in the study stated that they had the opportunity to "learn by experiencing" through service-learning practices and that they integrated theoretical and practical knowledge with these approaches. In addition, students stated that this approach was effective in strengthening cognitive and affective competencies and that their self-confidence increased.

There are programmes making the CSL management a part of the education system. For instance, this approach is evaluated as an important component of graduate training program at the Fisher Institute of Health and Gerontology at Ball State University. Each student who is accepted to this programme as an assistant is trained in their responsibilities including social assistance to the elderly people living in that community and they present their experiences regularly through the Monthly Report Form. The results obtained from the analysis of a report selected as an example within the scope of the study show that students gained new competences in the professional and social fields, they understood disabled and elderly individuals better, that is, their feeling of sympathy improved, and the fear of working with the elderly that they used to have diminished (18). Students interviewed within the scope of the study gave similar feedback to the research in question and stated that their empathy skills improved and that coming together with different communities at early stages had advantages.

In the service-learning, learning objectives of the students are as important as the benefits of the services offered to society; more importantly both are interconnected and strengthen each other. Studies show that the service-learning contributes positively to the development of personal qualifications in different ways. However, when the CSL is implemented based on a compulsory curriculum, debates on its potential benefits are still ongoing (19). In the study students examined the effects emerged at the implementation stage of a compulsory the service-learning lesson, the results showed that learning experiences students gained from the service-learning had a strong impact on their personal developments. The benefit of the the service-learning approach is inevitable in the approaches in which field practices are not enough due to the large number of the students and the students are hesitant to contact the patient. Findings obtained from this research present similar results. The participants stated that there was a significant difference in their personal developments when they compared their situation before and after the research.

Scientific articles and studies on the CSL display various approaches, and present a wide perspective about the experiences obtained from the perspectives of the students, lecturers and the administrative staff. Most of these studies build a bridge between theory and practice; besides enabling students and the future professionals to gain competences and skills, they provide social awareness which is especially necessary for their professional performances (20). Based on these contributions the service-learning to professional performance, it is stated that when the CSL based academic learning process is integrated with community experience, students gain both personal/social and academic skills. At the same time, on one hand critical awareness with leadership and communication skills, on the other hand the ability to adapt and respond to real-world challenges as well as time and resource management are developing and all of which contribute significantly to the transition to the labor market.

A study carried out at a university in Portugal points out that how important it is to adopt "education market" understanding in order for students to be prepared to live in a community and therefore be raised with the perspective of existence. The results of the study in question show that when academic learning is combined with community experience, students gain both academic and social competences and at the same time they develop critical awareness about the real world and all of which are beneficial in the transition phase to the labour market (21,22). Participants taking part in the study gave similar feedback at the first stage of their personal developments when the experiences they gained were taken into consideration.

The world is experiencing a period in which great transformations have occurred in both education and labour market. It is thought that there is knowledge-based competence lies at the background of this transformation, especially in terms of employment. The most important concept stepping in at this point is a special or technical competence – that is cross competence – which consists of certain skills, values and attitudes and is at the same time valid in the environments they are developed. This concept has begun to be attributed more and more importance by organizations in order to adapt to today's competitive conditions. Within this framework, in a study carried out at a university in Spain, the impact of cross-competences on the employability degree of university students was examined within the framework of the CSL concept. One of the questions the answer to which was sought in the research was "Is there a significant difference between the students participating and not participating in the experimental activities in terms of the development of cross-competences?" The results showed that there was a positive relation between cross-competences and experimental activities connecting students to professional or social practices (23). The students taking part in the study expressed those similar contributions emerged at the point of development of cross-qualifications. It was stated that this concept offered both the opportunity to practice in terms of professional experience and the chance to be an active member of the society.

Conclusion

The CSL is a philosophical approach combining services for community or public field with structured learning opportunities. By means of this approach the individual is prepared to solve community-based problems. Moreover, students are offered the opportunity to discover the connections between theoretical atmosphere of the classroom and practical needs of the community. In this respect, the CSL transforms the individual into a phenomenon that helps the individual develop critical thinking ability by nature, enables them to take part in collective activities, develops civic consciousness, and strengthens his ability to become an active member of society.

The results of the study show that the CSL approach develops students' insight into the importance of community works and helps them to understand social diversity and contributes positively to the development of the sense of responsibility social skills of the individual. Moreover, participants stated that the service-learning helped them clarify the concepts they learned in their classes. On the other hand, they expressed that thanks to this programme, learning became a more enjoyable activity. This study, which lasted for 14 weeks, was realised by presenting an alternative method for learning experiences of the students by collecting data from different individuals in the same time of period. Therefore, when viewed from a general and limited framework, it is possible to state that a special effort to determine the latitudinal effect stands out a little more. In terms of future studies, it is thought that this method can be redesigned to include different time periods and through studies in which the longitudinal effect is prominent. For example, the attitude and behaviour changes of the students trained with the concept of the CSL after completing the program can be chosen as a research topic.

Ethical considerations

Institutional permission (05.10.2022-E-43687250) and ethics committee approval (26.09.2022-2022/07) were obtained from the university where the research would be conducted. Written permission from the students was obtained and they were informed that their personal information would be used for research purposes only.

Author contributions

Bora Balun: Conception, Resource, Materials, Analysis, Literatüre Review, Supervision, Writer, Critical Review. Yılmaz Olcay: Conception, Resource, Analysis, Literatüre Review, Writer. Durdane Yılmaz Güven: Conception, Design, Data collection, Analysis, Writer, Critical Review.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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ORIGINAL ARTICLE

Carpal Tunnel Syndrome and Migraine Lateralization

Karpal Tünel Sendromu ve Migren Lateralizasyonu

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ABSTRACT

Background/Aims: Within the scope of this research, we aimed to elucidate the relationship between carpal tunnel syndrome and migraine to explore both the pain intensity and the localization of carpal tunnel syndrome (CTS) in concomitant migraine. The primary outcome variable was elaborated as the pain lateralization, and the secondary outcome variable was the pain intensity.
Method: This is a cross-sectional, observational prospective study of 500 patients with preliminary carpal tunnel syndrome diagnosis at our institution. After patients with missing data were excluded from the study, 413 remained, 365 (88.4%) women and 48 (11.6%) men. After recording the demographic characteristics, the patient's migraine pain year of onset, pain characteristics, localization, frequency, duration, severity, triggering factors, symptoms, and findings accompanying the pain were recorded.
Results: The lateralization of migraine was on the right side (only on the right or mostly on the right) in 25.9% and on the left side (only on the left or mostly on the left) in 26.4% of the patients. Almost half of the patients (47.7%) experienced bilateral migraine headaches. Carpal tunnel syndrome was in the right hand in 13.3%, in the left hand in 11.6%, and bilateral in 75.1%. Of 197 patients with bilateral pain, 68 (34.5%) had mild, 116 (58.9%) had moderate, and 13 (6.6%) had severe CTS. The VAS level of migraine pain was higher only in patients with CTS in the left hand and in those with moderate CTS.
Conclusion: It has been determined that those with carpal tunnel syndrome on the right side have migraines mostly on the right, those with carpal tunnel syndrome on the left have migraines on the left, and those with carpal tunnel syndrome in both directions have migraines predominantly in both directions.

Keywords: Migraine; Carpal tunnel syndrome; Lateralization; Visual Analog Scale (VAS); Pain

ÖZ

Amaç: Bu araştırma kapsamında, eşlik eden migrende karpal tünel sendromunun (KTS) hem ağrı yoğunluğunu hem de lokalizasyonunu araştırmak için karpal tünel sendromu ile migren arasındaki ilişkiyi aydınlatmayı amaçladık. Birincil sonuç değişkeni, ağrının lateralizasyonu olarak detaylandırıldı ve ikincil sonuç değişkeni, ağrının yoğunluğuydu.
Yöntemler: Bu araştırma, kurumumuzda karpal tünel sendromu ön tanısı alan 500 hastanın katıldığı kesitsel, gözlemsel, prospektif bir çalışma olarak planlanmıştır. Verileri eksik olan hastalar çalışma dışı bırakıldıktan sonra 365'i (%88,4) kadın, 48'i (%11,6) erkek olmak üzere 413 kişi kaldı. Hastanın demografik özellikleri kaydedildikten sonra migren ağrısının başlangıç yılı, ağrının özellikleri, lokalizasyonu, sıklığı, süresi, şiddeti, tetikleyici faktörler, ağrıya eşlik eden semptomlar ve bulgular kaydedildi.
Bulgular: Migrenin lateralizasyonu hastaların %25,9'unda sağ tarafta (sadece sağda veya çoğunlukla sağda), %26,4'ünde ise sol tarafta (sadece solda veya çoğunlukla solda) idi. Hastaların neredeyse yarısında (%47,7) iki taraflı migren baş ağrısı görüldü. Karpal tünel sendromunun %13,3'ü sağ elde, %11,6'sı sol elde, %75,1'i ise iki taraflıydı. Bilateral ağrısı olan 197 hastanın 68'inde (%34,5) hafif, 116'sında (%58,9) orta ve 13'ünde (%6,6) şiddetli KTS vardı. Migren ağrısının VAS düzeyi sadece sol elde KTS'si olanlarda ve orta derecede KTS'si olanlarda daha yüksekti.
Sonuç: Sağ tarafta karpal tünel sendromu olanların migren hastalarının çoğunlukla sağda, solda karpal tünel sendromu olan hastaların migren ağrılarının solda, her iki yönde de karpal tünel sendromu olanların her iki yönde migren ağırlıklı olduğu belirlendi.

Anahtar Kelimeler: Migren, Karpal tünel Sendromu, Lateralizasyon, Vizüel Analog Skala (VAS), Ağrı

Introduction

Carpal tunnel syndrome (CTS) is the most common upper extremity peripheral neuropathy, which develops due to pressure on the median nerve at the wrist level within the wrist canal for different reasons. It accounts for approximately 90% of all entrapment neuropathies. It is seen in all age groups, especially between the ages of 40 and 60, and is nearly two times more common in women than men [1]. Although definite risk factors (most importantly environmental factors) are associated with CTS, they are mostly idiopathic. Long-term wrist flexion and extension repetitive movement of the flexor muscles and exposure to vibration are among the factors that facilitate the development of CTS [2]. While the prevalence of CTS has been reported as 10% and its incidence as 1–5% in previous studies, the incidence of CTS in the general

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population is 3 – 4 % [3]. The prevalence of carpal tunnel syndrome is 6% in men and 9% in women. It has been shown that CTS develops at a higher rate (14.5%) in specific occupational groups (especially in the dominant hand, due to straining and repetitive movements) in Western societies [3, 4].

Migraine is a common primary headache disorder that causes disability. Many epidemiological studies have documented the high prevalence of migraine and its socioeconomic and personal effects. In the Global Burden of Disease Study, migraine was ranked as the third most prevalent disorder in the world. Additionally, it ranked third in terms of causes of disability among men and women under the age of 50 worldwide [5]. According to the World Health Organization (WHO), migraine headaches are among the top 10 most common diseases in men and among the top five most common diseases in women. The estimated prevalence of migraine is between 12% and 16% of the population, and it is higher in women than men [6].

It has come to our attention that these two conditions, in addition to being common in society, have common characteristics such as being unilateral or bilateral, being more common in women, being affected by genetic and environmental factors, and having unclear physiopathogenesis. It brings to mind whether it is a coincidence that these two conditions have so much in common or whether there is a common mechanism for their co-occurrence. In recent years, a few studies have investigated whether these two conditions are related and reported positive results on their coexistence, but this relationship has not been clarified. For this reason, it was planned to evaluate the relationship between these two tables from a different perspective. Migraine occurring on the same side may be a trigger for carpal tunnel syndrome on the same side. Within the scope of this research, we aimed to elucidate the relationship between carpal tunnel syndrome and migraine to explore both the pain intensity and the localization of CTS in concomitant migraine. The primary outcome variable was elaborated as the pain lateralization, and the secondary outcome variable was the pain intensity.

Method

This is a cross-sectional, observational prospective study of 500 patients with preliminary carpal tunnel syndrome diagnosis at our institution. After patients with missing data were excluded from the study, 413 remained, 365 (88.4%) women and 48 (11.6%) men.

All procedures followed are in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution with protocol number 12129, and informed consent has been obtained from all participants.

Patient Selection

The patient selection was conducted in two stages. In the first stage, it was planned to include patients who came to our institution's electrophysiology laboratory with a preliminary diagnosis of carpal tunnel syndrome and were diagnosed with carpal tunnel syndrome due to nerve conduction measurements. Individuals who agreed to participate in the study were required to complete a questionnaire prepared according to the criteria determined by the International Headache Committee (IHC). Patients with migraine headaches were enrolled after completing the survey. After recording the demographic characteristics of all patients included in the study (age, gender, weight, comorbidities), the characteristics of the patient's migraine pain (year of onset of pain, pain characteristics, localisation, frequency, duration, severity, triggering factors, symptoms and findings accompanying the pain) were recorded. It was planned to examine separately the characteristics of CTS symptoms (initiation time, severity, localisation, time day/night, triggering factors, symptoms accompanying pain).

Statistical Analysis

The Kolmogorov-Smirnov test was used for normality distribution checking of continuous variable. Independent Sample t–test was used for the comparison between two independent normally distributed groups, and t statistics values were given. For non-normal independent two groups comparison, Mann-Whitney U test was used and Z values were presented. Kruskal-Wallis test was used more than non-normal two independent groups comparison, and Chi-square value was given. Mean and standard deviation for continuous variables were given as descriptive values. In addition, minimum and maximum values were given because of presence of non-normal continuous variables in tables.

Pearson Chi-Square test was used to compare categorical variables in crosstable and chi-square statistics value was given. Frequency and percentage for categorical variables were also presented.

The results were considered statistically significant when the p-value was less than 0.05. Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program.

Results

A total of 500 patients were included in the study. After the patients with missing data were excluded, 413 patients remained: 365 (88.4%) women and 48 (11.6%) men. Among the patients' data examined in the study, Table 1 denotes the lowest, highest, and average values according to patient age, duration of headache, duration, frequency, and severity. Although it was observed that the severity of CTS increased with age, no statistical significance was achieved (p=0.111).

The lateralization of migraine was on the right side (only on the right or mostly on the right) in 25.9%

Tablo 1. Baseline demographics of the study population

	Gender	N	Mean	Standard Deviation	Minimum	Maximum	Test	P-value
AGE	Female	365	47.8	10.80	18.0	82.0	t=-1.309	0.191
	Male	48	50.0	12.25	25.0	78.0		
BMI	Female	364	30.5	5.62	16.0	66.0	Z=-1.268	0.205
	Male	48	29.5	5.22	17.5	44.0		
VAS MIGRAINE	Female	364	6.9	1.54	3.0	10.0	Z=-0.333	0.740
	Male	48	6.8	1.67	3.0	9.0		
Duration of Migraine	Female	365	14.2	8.38	1.0	40.0	Z=-0.511	0.610
	Male	48	15.1	9.39	2.0	35.0		
Migraine Attacks (hours)	Female	365	13.3	15.22	2.0	72.0	Z=-1.303	0.192
	Male	48	13.2	16.6	3.0	72.0		
Migraine Attach Frequency	Female	365	8.4	6.22	1.0	35.0	Z=-0.243	0.808
	Male	48	8.1	4.94	1.0	20.0		

Tablo 2. The lateralization/localization of migraine and carpal tunnel syndrome

Migraine Lateralization	Carpal Tunnel Syndrome			Total
	Right N (%)	Left N (%)	Both N (%)	
Right	22(20.6)	11(10.3)	74(69.2)	107(25.9)
Left	13(11.9)	17(15.6)	79(72.5)	109(26.4)
Both	20(10.2)	20(10.2)	157(79.7)	197(47.7)
Total	55(13.3)	48(11.6)	310(75.1)	413(100)

*Chi-square=9.026, p=0.060

Tablo 3. The association between carpal tunnel syndrome (CTS) and VAS in migraine patients

	Severity of CTS	N	Mean	Standard Deviation	Minimum	Maximum	Kruskal Wallis Test	P-value
General	Low	136	6.8	1.84	3.0	10.0	Chi-square=1.411	0.494
	Medium	247	7.0	1.35	3.0	9.0		
	Severe	29	6.6	1.68	3.0	9.0		
Right hand	Low	34	7.1	1.72	4.0	9.0	Chi-square=1.206	0.272
	Medium	16	6.6	1.66	4.0	9.0		
Left hand	Low	22	5.9	1.92	3.0	9.0	Chi-square=5.119	0.024*
	Medium	19	7.2	1.31	4.0	9.0		
Both hands	Low	80	6.9	1.81	3.0	10.0	Chi-square=1.140	0.565
	Medium	212	7.1	1.33	3.0	9.0		
	Severe	29	6.7	1.68	3.0	9.0		

Table 4. CTS severity and number of years of headache experience

	Severity of CTS	N	Mean	Standard Deviation	Minimum	Maximum	Kruskal Wallis Test	P-value
General	Low	136	12.4	8.32	2.0	35.0	Chi-square=12.903	0.002*
	Medium	248	15.2	8.49	1.0	40.0		
	Severe	29	15.5	8.04	1.0	30.0		
Right hand	Low	34	11.9	8.48	2.0	35.0	Chi-square=2.486	0.115
	Medium	16	15.5	8.79	5.0	30.0		
Left hand	Low	22	13.1	8.32	3.0	28.0	Chi-square=2.400	0.121
	Medium	19	17.0	8.18	1.0	30.0		
Both hands	Low	80	12.4	8.3	2.0	35.0	Chi-square=7.802	0.020*
	Medium	213	15.0	8.5	1.0	40.0		
	Severe	29	15.5	8.0	1.0	30.0		

and on the left (only on the left or mostly on the left) in 26.4% of the patients. Almost half of the patients (47.7%) experienced bilateral migraine headaches. Carpal tunnel syndrome was in the right hand in 13.3%, in the left hand in 11.6%, and bilateral in 75.1%. It was observed that 20.6% of the patients with migraine pain on the right side had CTS on the right while 15.6% of those with migraine on the left had CTS on the left, and 79.7% of those with bilateral headaches had bilateral CTS (Table 2).

Of the 107 patients with migraine pain on the right side, 27 (25.2%) had mild, 71 (66.4%) had moderate, and 9 (8.4%) had severe CTS. Of the 109 patients with migraine pain on the left, 41 (37.6%) had mild CTS, 61 (56.0%) had moderate CTS, and 7 (6.9%) had severe CTS. Of 197 patients with bilateral pain, 68 (34.5%) had mild, 116 (58.9%) had moderate, and 13 (6.6%) had severe CTS.

When the VAS values showing the severity of CTS and the severity of migraine headaches were compared, the VAS level of migraine pain was higher only in patients with CTS in the left hand and in those with moderate CTS. Migraine pain levels were partially lower in those with low and severe CTS. As a result, no statistical significance was found between CTS severity and migraine pain level VAS (p=0.494) (Table 3).

When all groups were included, it was determined that those with mild CTS had headaches for an average of 12.4 years while those with moderate CTS had headaches for 15.2 years, and those with severe CTS had headaches for 15.5 years. This showed that as the number of years of headache experience increased, the severity of CTS also increased statistically significantly (p□0.002) (Table 4). However, the severity of CTS and the duration of headache exposure in hours was not statistically significant.

When the relationship between CTS severity and headache frequency (month/day) was examined, it was observed that those with mild CTS experienced pain for an average of 8.4 days per month while those with severe CTS experienced pain for an average of 9.8 days per

month. Similar results were found in those with bilateral headaches and those with bilateral CTS.

Discussion

Migraine and carpal tunnel syndrome are two separate diseases that affect the peripheral nervous system, and migraine affects the central nervous system. They are completely different from each other but are common in society. Some recent studies have investigated whether these two tables coexist and published positive results. Although these studies have published results indicating that this relationship may exist, it is unclear whether it exists. In our recently published article, Koyuncu reported that 80.3% of the patients with carpal tunnel syndrome had migraines, and 12.6% of individuals with migraines had carpal tunnel syndrome [7]. In a large cohort of 401.656 individuals from the United Kingdom Biobank, migraine and carpal tunnel syndrome denoted a significant epidemiological association. A genetic correlation with shared genetic susceptibility at the TRIM32 locus underpinned this association [8]. Nerve compression also triggered an inflammatory response in the affected area. Inflammation is also known to play a role in migraine pathophysiology that might contribute to an overall increase in inflammation, potentially exacerbating migraines [2, 4].

In previous literature, it was reported that head and neck compressive neuropathies triggered headaches. However, the entrapment neuropathies of the extremities have traditionally been perceived as separate clinical entities. Gferer et al. claimed a significant clinical presentation, treatment, and anatomical abnormality overlap. The relationship between nerve compression headaches, carpal tunnel syndrome, and other upper extremity compression neuropathies have common pathologies and comorbidities [9]. Upper extremity nerve compression syndromes and migraines caused by nerve entrapment have many similarities, including patient presentation, anatomical findings, and treatment by surgical decompression of affected nerves, thus indicating a possibility of shared predisposition. Gferer et al. have stated that patients who undergo median and multiple nerve decompression are more likely to experience migraine headaches [10].

Recent evidence has suggested that some types of migraine headaches may be associated with nerve compression [11–14]. Members of the American Headache Society (AHS) commonly use nerve blocks and trigger point injections to treat migraine headaches, and several other studies support targeted injections of botulinum toxin or local anesthetic for the treatment of migraine headaches [15, 16]. The first community-based study that demonstrated an association between carpal tunnel syndrome and migraine headaches was published by Law et al. (2010) [17]. It utilized the data from 25.880 respondents of the cross-sectional 2010 National Health Interview Survey. They stated that 34% of people with carpal tunnel syndrome had migraine, compared to 16% of people without the syndrome. Additionally, 71% of the participants underwent median nerve decompression surgery performed on the wrist to relieve nerve pressure, and thus reduce carpal tunnel syndrome symptoms, 14% of participants underwent ulnar nerve decompression, and 6.5% had decompression surgery at multiple sites in the body. Those who had median nerve decompression and multiple nerve decompression were 30% and 70% more likely to have migraine than those who had ulnar nerve decompression [17].

Migraine is a typically unilateral disorder, and its lateralization is thought to be related to manual dominance. La Pegna et al. [18] conducted retrospective research and reported that the right-handers had 3412 unilateral episodes; 62.8% of the pain attacks were on the right side and 37.2% by pain on the left. On the other hand, the left-handed subjects had 803 unilateral pains, with 63.5% of unilateral pain episodes on the left side and 36.5% of attacks with

lateralized pain on the right (p<0.001). Their data suggested that manual dominance might influence the side of pain lateralization in migraine [18]. Similar to these outcomes, an association between carpal tunnel syndrome and hand dominance has been identified [19].

Blum et al. [20] published an interesting review stating that left- and right-sided migraine differed across a wide range of domains, raising the possibility that the left- and right-side pathophysiology may not be identical. They indicated that left- and right-sided migraine was found to differ across multiple domains as left- and right-sided migraine was associated with ipsilateral handedness, tinnitus, onset of first Parkinson's symptoms, white matter hyperintensities on MRI, activation of the dorsal pons, hippocampal sclerosis, and thalamic NAA/Cho and NAA/Cr concentrations [20]. In our study, the intensity of migraine headaches and carpal tunnel syndrome was found as follows: in right-sided migraine, 25.2% had mild, 66.4% had moderate, and 8.4% had severe carpal tunnel syndrome. In left-sided migraine, 37.6% had mild, 56.0% had moderate, and 6.9% had severe carpal tunnel syndrome. In patients with bilateral pain, 34.5% had mild, 58.9% had moderate, and 6.6% had severe carpal tunnel syndrome.

Last but not least, left-sided migraine was associated with worse quality of life, anxiety, bipolar disorder, PTSD, lower sympathetic activity and higher parasympathetic activity. In contrast, right-sided migraine was associated with poorer performance on multiple cognitive tests, a greater degree of anisocoria, changes in skin temperature, higher diastolic blood pressure, changes in blood flow through the middle cerebral and basilar arteries, and changes in EEG [20]. In our study, the lateralization of migraine was on the right side in 25.9% of the patients and on the left side in 26.4%. Almost half of the patients (47.7%) experienced bilateral migraine headaches. Carpal tunnel syndrome was in the right hand in 13.3%, in the left hand in 11.6%, and bilateral in 75.1%. It was observed that 20.6% of the patients with migraine pain on the right side had carpal tunnel syndrome on the right. In comparison,15.6% of those with migraine on the left had carpal tunnel syndrome on the left, and 79.7% of those with bilateral headaches had bilateral carpal tunnel syndrome.

One expected result was the increase in the intensity of headaches and duration of migraine, as denoted by VAS scores. As the severity of carpal tunnel syndrome deteriorated, migraine attack periods increased.

Conclusion

Regarding the outcomes of this research, it has been determined that those with carpal tunnel syndrome on the right side have migraines mostly on the right, those with carpal tunnel syndrome on the left have migraines on the left, and those with carpal tunnel syndrome in both directions have migraines predominantly in both directions.

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Competing interests

The authors declare that they have no competing interests.

AI Statement

The authors used AI and AI-assisted Technologies (Grammarly and MS Word Editor) in the writing process. These technologies improved the readability and language of the work. Still, they did not replace key authoring tasks such as producing scientific or medical insights, drawing scientific conclusions, or providing clinical recommendations. The authors are ultimately responsible and accountable for the contents of the whole work.

Consent for Publication

The original article is not under consideration by another publication, and its substance, tables, or figures have not been published previously and will only be published elsewhere.

Data Availability

The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethical Declaration

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. Informed consent has been obtained from participants.

Author Contributions:

Research idea, design of the study, acquisition of data for the study, analysis of data for the study, ınterpretation of data for the study, drafting the manuscript, revising it critically for important intellectual content: GK

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ORIGINAL ARTICLE

Evaluation of Adhesin Antigen Test Results in Samples Sent with Suspicion of Amebiasis

Amibiyazis Şüphesiyle Gönderilen Örneklerde Adezin Antijen Test Sonuçlarının Değerlendirilmesi

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ABSTRACT

Objective: In this study; it is aimed to evaluate E. histolytica-specific ELISA adhesin antigen test results in stool samples sent to the medical microbiology laboratory with suspicion of amebiasis.
Material and Methods: ELISA (Cellabs, Entamoeba Celisa Path, Brookvale, NSW Australia) adhesin antigen test results, examined on stool samples sent to the medical microbiology laboratory with suspicion of amebiasis in a two-year period between January 2022 and December 2023 were evaluated retrospectively. The data including the test results, gender, age, date and clinical information of the cases of the examined sample were obtained from our hospital's laboratory data software system. Fisher's exact chi-square test was used in statistical analyses.
Results: Of the 1120 samples in the study, 578 (51.6%) belong to male patients and 542 (48.4%) belong to female patients. The ages of the patients ranged from 0 to 94 years, and the average age was 33.92 (standard deviation: ±24.33). There were 335 (30%) samples from pediatric patients, and the mean age was determined as 4.48 ±4.78. One hundred and sixty-one (14.3%) samples were found positive with the ELISA adhesin antigen test specific to E. histolytica. Of patients with positive test results, 77 (47.8%) were male and 84 (52.2%) were female. Among the positive samples, there were 55 (34.1%) samples from pediatric patients. While there was no statistically significant difference between the positivity status and age and gender of the patients (p>0.05), the seasonal difference was considered significant (p<0.05).
Conclusion: In our study, E. histolytica specific ELISA adhesin antigen test positivity was determined as 14.3%, and this rate was found close to the country's literature data. It has been determined that amoebiasis is more common in tropical and subtropical climates. With the use of ELISA adhesin antigen test specific to E. histolytica, which is cheap, fast and does not require experienced personnel, the rate of misdiagnosis can be reduced and unnecessary treatment applications can be reduced.

Keywords: Amebiasis, Entamoeba histolytica, ELISA adhesin antigen test

ÖZ

Amaç: Bu çalışmada amibiyazis şüphesiyle tıbbi mikrobiyoloji laboratuvarına gönderilen dışkı örneklerinde E. histolytica'ya spesifik ELISA adezin antijen test sonuçlarının değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntem: Ocak 2022 ile Aralık 2023 tarihleri arasındaki iki yıllık dönemde amibiyazis şüphesiyle tıbbi mikrobiyoloji laboratuvarına gönderilen dışkı örneklerinde incelenen ELISA (Cellabs, Entamoeba Celisa Path, Brookvale, NSW Avustralya) adezin antijen testi sonuçları retrospektif olarak değerlendirilmiştir. Olgulara ait test sonuçları, cinsiyet, yaş, tarih ve örneğin geldiği klinik bilgileri hastanemiz laboratuvar bilgi sisteminden elde edilmiştir. İstatistiksel analizlerde Fisher kesin ki-kare testi kullanılmıştır.
Bulgular: Çalışmadaki 1120 örneğin 578 (%51.6)'i erkek, 542 (%48.4)'si kadın hastalara aittir. Hastaların yaşları 0 - 94 yaş aralığında olup, yaş ortalaması 33.92 (standart sapma: ±24.33) olarak bulunmuştur. Çalışmada çocuk hastalara ait 335 (%30) örnek bulunmaktadır ve bu hastaların yaş ortalamaları 4.48 (standart sapma: ±4.78) olarak tespit edilmiştir. E. histolytica' ya spesifik ELISA adezin antijen testi ile 161 (%14.3) örnek pozitif bulunmuştur. Pozitif örneklerin 77 (% 47.8)'si erkek, 84 (%52.2)'ü kadın hastalara aittir. Pozitif örnekler içinde çocuk hastalara ait 55 (%34.1) örnek bulunmaktadır. Hastaların pozitiflik durumu ile yaşı arasında ve pozitiflik durumu ile cinsiyeti arasında istatistiksel olarak anlamlı bir farklılık görülmemişken (p>0.05), mevsimler arasındaki farklılık anlamlı kabul edilmiştir (p<0.05).
Sonuç: Çalışmamızda E. histolytica' ya spesifik ELISA adezin antijen testi pozitifliği %14.3 oranında belirlenmiş ve bu oran ülke literatür verilerine yakın bulunmuştur. Amibiyazisin tropikal ve subtropikal iklim özelliklerinde daha sık görüldüğü belirlenmiştir. Ucuz, hızlı ve deneyimli personel gerektirmeyen E. histolytica'ya spesifik ELISA adezin antijen testi kullanımı ile yanlış tanı oranı düşürülerek gereksiz tedavi uygulamaları azaltılabilmektedir.

Anahtar Kelimeler: amibiyazis, Entamoeba histolytica, ELISA adezin antijen testi

Introduction

Amoebic dysentery (amobiasis) is a parasitic infection caused by Entamoeba histolytica (1). Entamoeba has six known species which are Entamoeba histolytica, Entamoeba dispar, Entamoeba moshkovskii, Entamoeba hartmanni, Entamoeba coli and Entamoeba polecki. The only species that causes amebiasis in humans is reported as E. histolytica. Amebiasis is widely detected all over the world and is considered a public health problem (2). Every year, 50 million cases of amebiasis are reported in the world, and approximately 100,000 of these cases result in death (3). The studies in our country have reported that the incidence of infection varied between 0% and 29.5% (1).

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E. histolytica infection was determined endemic in regions where temperate climate prevails, and it is associated with low socioeconomic status and inadequate hygiene conditions in developing countries (4). In developed countries, the cause of this infection is thought as travel to endemic regions (5).

Most of the infected individuals are asymptomatic (3). In 10% of patients, the infection progresses symptomatically and clinical courses such as dysentery, ameboma, acute necrotizing colitis, toxic megacolon, perianal fistula and ulcer and liver abscess may be observed (6,7,8).

In the diagnostic examination of stool samples, differentiating E. histolytica from E. dispar, which is a morphologically identical but genetically different species, is important in terms of planning the correct treatment protocol and preventing transmission. The World Health Organization states that cases with E. dispar should not be treated, and all symptomatic or asymptomatic E. histolytica cases should be treated. (9).

The most commonly used method in the diagnosis of amebiasis is direct microscopy. However, since this method cannot discriminate E. histolytica and non-pathogenic E. dispar, more reliable diagnostic methods are needed (10).

Recently, the use of molecular tests that detect the genetic material of E. histolytica and have higher sensitivity and specificity compared to microscopic examination and culture methods has been increasing. These diagnostic tests work is integrated with automated systems and provides the opportunity to give the results in a short time. Therefore, it gives a great advantage especially in laboratories with high workload. Also, with the use of commercial panels, it has become possible to detect more than one pathogen at the same time. However, its high cost causes limitations in its use (11).

Serological diagnostic techniques for detection of antibodies are especially useful in the diagnosis of extra intestinal amebiasis. However, the fact that the antibody response can be detected for a long time after treatment causes limitations in distinguishing between active and previous infection (12,13).

Antigen-detecting ELISA (Enzyme-Linked Immunosorbent Assay) tests can also differentiate E. histolytica and E. dispar. These tests have advantages such as high specificity and sensitivity, objective and rapid results, no need for experienced personnel, low cost especially compared to the molecular techniques, and the ability to process a large number of samples at the same time (14).

This study aimed to detect the frequency of intestinal amebiasis in stool samples sent with suspicion of amebiasis using ELISA adhesin antigen test specific to Entamoeba histolytica.

Material and Methods

This study was performed with the approval of the Ethics Committee of Necmettin Erbakan University Faculty of Medicine (Date: 01.03.2024 and Decision No: 2024\4832).

ELISA (Cellabs, Entamoeba Celisa Path, Brookvale, NSW Australia) adhesin antigen test results examined on stool samples and sent to the medical microbiology laboratory with suspicion of amebiasis in a two-year period between January 2022 and December 2023 were evaluated retrospectively.

In the ELISA method, the stool sample is emulsified with the sample dilution liquid. The diluted stool sample and the conjugate with a monoclonal antibody specific to the parasite antigen are placed in the wells of the microplates. These wells contain polyclonal antibodies that will bind to the E.histolytica antigen. If antigen is present in the stool sample, it combines with the polyclonal antibodies in the microplates and the specific monoclonal antibodies in the conjugate. Non-specific compounds are removed by washing. When the substrate is added, color formation occurs due to the enzyme-antibody-antigen complex.

The data including the test results, gender, age, date and clinical information of the cases of the examined samples were obtained from our hospital's laboratory data software system. The statistical analysis was performed by using SPSS, 22.0 for windows. Descriptive statistics were used to define demographic data, and the outcomes were expressed by number, mean and percentages. Fisher's exact Chi-square test was used in statistical analyses. A value of $p<0.05$ was considered statistically significant.

Results

Of the 1120 stool samples included in the study, 578 (51.6%) were from male patients and 542 (48.4%) from female patients. The ages of the patients ranged from 0 to 94 years, and the mean age was 33.92 years (standard deviation: ±24.33). Of the samples, 335 (30%) of them were obtained from pediatric patients, among them 184 (55%) were boys and 151 (45%) were girls. The mean age of these patients was 4.48 years (standard deviation: ±4.78).

The Entamoeba histolytica ELISA antigen test positivity rate was 14.3% (n=161). Of the 161 patients with a positive antigen test, 77 (47.8%) were male and 84 (52.2%) were female. The mean age of the antigen test positive patients was found as 31.5 years (standard deviation: ±24.48). In the study, 55 (34.1%) samples were positive in pediatric patients, and the mean age of these patients was 4.72 years (standard deviation: ±5.34). Pediatric patients with a positive test result constituted 16.4% of the general pediatric population. Additionally, 22 (40%) of positive pediatric patients were male and 33 (60%) were female. There was no statistically significant difference between the positivity status and age and gender of the patients ($p>0.05$).

The clinical departments where the 161 positive patients included the study were followed are presented in Table 1.

Table 1. Distribution and rates of ELISA antigen test positive patients according to clinical departments

	N	%
Hepatology \Inflammatory bowel diseases	39	24.2
Pediatric emergency	33	20.5
Gastroenterology	26	16.1
Pediatrics	14	8.7
Infectious diseases	11	6.8
Pediatric Hematology-Oncology	8	5
Medical Oncology	7	4.3
Organ and Tissue Transplantation Center	6	3.8
Hematology	5	3.1
Nephrology	5	3.1
Internal Medicine	4	2.5
Other Departments	3	1.9
Total	161	100

When the seasonal distribution of Entamoeba histolytica infection was examined, antigen test positivity was observed at a rate of 9.3% (n=15) in winter, 14.9% (n=24) in spring, 18.6% (n=30) in summer and 57.1% (n=92) in autumn. Additionally, it was determined that this positivity peaked in September with a rate of 33% (n = 54). It was determined that the positivity rate observed in the autumn season was significantly higher than other seasons. (p=0.001)

Discussion

Amebiasis is reported as a cause of serious morbidity and mortality all over the world (15). The prevalence of this infection in the world is reported as 10%, however, this rate increases up to 50%, especially in underdeveloped countries (4,16,8). When the previously performed studies were evaluated, the prevalence of E. histolytica was detected as 4.2% in Bangladesh, 8.4% in Mexico, 15% in Brazil, 20% in Saudi Arabia, 17.1% in Yemen, 25.9% in Tajikistan, and 18% in Tanzania (15,4,16,17). There are many studies in the literature to determine the prevalence of amebiasis in different regions of our country. According to the studies, the prevalence of E. histolytica was 0.5% in Kırıkkale 0.8% in Bursa, 7% in Istanbul, and 7.7% in Mersin (18,19,20,21).

The methods such as direct and trichrome staining techniques and microscopic examination, serological techniques based on antigen or antibody detection, culture and molecular tests are used for the diagnosis of E. histolytica infections (22). The fact that the previous prevalence studies were based on microscopic examination causes a limitation in the reliability of the prevalence of intestinal amebiasis. The low sensitivity of microscopic examination and the inability to differentiate E. histolytica trophozoites and cysts from leukocytes and other Entamoeba species in the feces caused false reporting of the prevalence of the infection (2).

In a study, only 25 (61%) of the 41 stool samples in which E. histolytica positivity was determined by other diagnostic methods could be identified by direct microscopic examination. (14). In a study conducted in Iraq, 47.66% E. histolytica positivity was detected by microscopic diagnostic method (23). In another study, 87 stool samples were suspected for E. histolytica by direct microscopy. E histolytica positivity was reported in 21.7% of these samples by ELISA and in 26.4% by trichrome staining technique (24). In India, 167 stool samples were examined and 9% (n=15) of E. histolytica/E. dispar were detected in microscopic examination, and the rate of E. histolytica was determined as 6% (n=9) by antigen-specific ELISA (25).

It is possible to reveal the accurate prevalence of E. histolytica infection by identifying other Entamoeba species by using diagnostic techniques with high specificity and sensitivity (26,27). E. histolytica-specific monoclonal ELISA antigen tests are frequently preferred today, especially because they do not show cross-reactivity with other enteric pathogens (28). In the previous studies, it was reported that the results of the ELISA method and molecular techniques used in the detection of E. histolytica were similar. Another study reported that the sensitivity of microscopic examination was 60% and the specificity was 79% while the sensitivity of antigen screening techniques was 80% and the specificity was 99% (3). In the discrimination of E. histolytica/E. dispar sensitivity of ELISA was 95% and the specificity was 93%, when compared to the zymodem technique (29). In our study, the Entamoeba histolytica ELISA antigen test positivity rate was detected as 14.3% (n = 161).

There are studies in the literature reporting that there is no significant relationship between E. histolytica positivity and gender. (30,6). In our study, it was also determined that gender had no effect on the detection of E. histolytica.

In a study in which microscopic examination, culture and isoenzyme analysis diagnostic methods were used to examine the stool samples of children with diarrhea living in the city, E. histolytica infection was detected in 4.2% and E. dispar infection was detected in 6.5%. While in children living in rural areas E. histolytica infection was detected in 1% and E. dispar infection was in 7% (15). In a study conducted in Iran, E. histolytica was reported at a rate of 1% in 10982 children (31). In a study conducted in Ethiopia, E. histolytica positivity was reported at a rate of 13.17% in 501 school children (32). In another study, E.histolytica/E.dispar positivity was established by microscopic examination in 6% of 500 randomly selected cases from the pediatric age group, while it was 3.2% by antigen-detecting ELISA (33). In our study, E. histolytica positivity was determined in 16.4% (n=55) of 335 pediatric patients by ELISA adhesin antigen test.

In a study conducted by using adhesin antigen, regarding the seasons and clinical departments in Kırşehir, positivity was in 4% (n = 6) of the patients, and it was reported that these patients mostly came from the gastroenterology clinic in the autumn season (34). In a study conducted in Sivas, positivity was in 25% (n=65) of the patients with the ELISA adhesin antigen test and it was reported that positivity was highest in 40% (n=22) in winter season. In this study, it was stated

that 28.6% of the patients with a positive antigen test came from the internal medicine clinic, 26.4% from the gastroenterology clinic, 25% from the pediatrics clinic, and 20% from the infectious diseases department (30). In our study, the positivity rate was 14.3% (n=161) and this positivity was the highest in the autumn season at a rate of 57.1% (n=92). In our study, 24.2% of the positive patients came from the hepatology/inflammatory bowel diseases (IBD) department, 20.5% from the pediatric emergency department, 16.1% from the gastroenterology department, 8.7% from the pediatrics department and 6.8% from the infectious diseases department.; We believe that the clinical distribution of E. histolytica positive patients in the studies and the seasonal characteristics when positivity is most common varies based on factors such as the patient's clinical condition, the clinician's differential diagnosis approach, personal hygiene, socioeconomic level and sanitation infrastructure.

Conclusion

In our study, E. histolytica specific ELISA adhesin antigen test positivity was determined as 14.3%, and this rate is close to the country's literature data. It has been determined that amoebiasis is more common in tropical and subtropical climates. The diagnostic algorithm of E. histolytica infections should be based on confirmation of microscopic examination with a different diagnostic technique and discriminating E. histolytica from E. dispar in stool samples. We believe that the use of ELISA adhesin antigen test specific to E. histolytica, which is cheap, fast and does not require experienced personnel, will reduce unnecessary treatment procedures by decreasing the rate of misdiagnosis.

Ethical Approval: This study was performed with the approval of the Ethics Committee of Necmettin Erbakan University Faculty of Medicine (Date: 01.03.2024 and Decision No: 2024\4832).

Authorship Contribution Statement

The authors have contributed to the article as the following:

Spec. Dr. Duygu Beder: Data Collection, Processing, and Reporting, Logical interpretation and presentation of findings, conducting the literature review, and writing the article.

Assoc. Prof. Fatma Esenkaya Taşbent: Generating ideas for the article, supervising, taking responsibility for executing the project, and intellectually examining the study content before submission.

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ORIGINAL ARTICLE

Periventricular Leukomalacia: Comparison of Parenchymal Signal and Volume Changes on Brain MRI in Paediatric Cases with Healthy Peers

Periventriküler Lökomalazi: Pediatrik Vakalarda Beyin MR'ında Parankimal Sinyal ve Hacim Değişikliklerinin Sağlıklı Akranlarla Karşılaştırılması

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ABSTRACT

Background/aims: Previous MRI studies have revealed white matter (WM) and gray matter (GM) of cerebrum and cerebellum, corpus callosum (CC) abnormalities in periventricular leukomalacia (PVL). However, the WM FLAIR signal ratio in MRI may provide quantitative data in the diagnosis and follow-up as a new radiologic method. Thalamic involvement may be a biomarker for neuronal damage and disease severity. We aimed to re-investigate both WM and GM volume changes of cerebrum and cerebellum, CC surface area in PVL, and to evaluate the diagnostic accuracy of the thalamus L sign and FLAIR signal ratio.
Methods: MRI scans of 30 pediatric patients with PVL and 42 healthy controls were analyzed to examine WM and GM volume changes, FLAIR signal ratio, CC surface area, and thalamus L sign. Volumetric analyses were done with the Volbrain program.
Results: Decreased subcortical GM volumes were found in PVL ($p<0.001$). There was a significant positive correlation between FLAIR signal ratio, various GM and cerebellum volumes. In patients with thalamus L sign, decreased GM volume and increased abnormal signaled WM volume were observed. The most important variable in the diagnosis of PVL was abnormally signaled WM volume ($p>0.001$).
Conclusions: Our results emphasize the role of MRI in the detection of PVL, the evaluation of GM changes and brain damage, and the importance of thalamus L sign and FLAIR signal ratio in the evaluation of the severity of the disease. Comprehensive studies in this direction may contribute to the development of targeted treatment strategies aimed at reducing cognitive and motor impairments in PVL.

Keywords: Brain volume, Corpus callosum, FLAIR signal ratio, Gray matter, Periventricular leukomalacia, Thalamus L sign

ÖZ

Amaç: Önceki MRG çalışmaları periventriküler lökomalazide (PVL) serebrum ve serebellumun beyaz cevher (BC) ve gri cevher (GC), korpus kallozum (KK) anormalliklerini göstermiştir. Ancak MRG'de BC FLAIR sinyal oranı yeni bir radyolojik yöntem olarak tanı ve takipte kantitatif veri sağlayabilir. Talamik tutulum nöronal hasar ve hastalık şiddeti için bir biyobelirteç olabilir. Bu çalışmada PVL'de serebrum ve serebellumun BC ve GC hacim değişikliklerini, KK yüzey alanını detaylı araştırmayı, talamus L işareti ve FLAIR sinyal oranının tanısal doğruluğunu değerlendirmeyi amaçladık.
Gereç ve Yöntemler: PVL'li 30 pediatrik hastanın ve 42 sağlıklı kontrolün MRG taramaları, BC ve GC hacim değişikliklerini, FLAIR sinyal oranını, KK yüzey alanını ve talamus L işaretini incelemek için analiz edildi. Volümetrik analizler Volbrain programı ile yapıldı.
Bulgular: PVL'de subkortikal BC hacimlerinde azalma saptadık ($p<0.001$). FLAIR sinyal oranı ile çeşitli GC ve serebellum hacimleri arasında anlamlı pozitif korelasyon bulduk. Talamus L işareti bulgusu olan hastalarda azalmış GC hacmi ve artmış anormal sinyalli BC hacmi gözledik. PVL tanısında en önemli değişken olarak anormal sinyalli BC hacmini bulduk ($p>0.001$).
Sonuç: Sonuçlarımız PVL'nin saptanmasında, GC değişikliklerinin ve beyin hasarının değerlendirilmesinde MRG'nin rolünü ve hastalığın ciddiyetinin değerlendirilmesinde talamus L işaretinin ve FLAIR sinyal oranının önemini vurgulamaktadır. Bu yönde kapsamlı çalışmalar PVL'de bilişsel ve motor bozuklukları azaltmayı amaçlayan hedefe yönelik tedavi stratejilerinin geliştirilmesine katkıda bulunabilir.

Anahtar Kelimeler: Beyin hacmi, FLAIR sinyal oranı, Gri madde, Korpus kallozum, Periventriküler lökomalazi, Talamus L işareti

Introduction

Periventricular leukomalacia (PVL) is an important neuropathological condition observed in childhood, predominantly affecting premature infants and leading to a range of motor and cognitive deficits. It is associated with the loss of cerebral white matter (WM), characterized by damage to the WM adjacent to the lateral ventricles. This condition occurs when there is insufficient oxygen or blood flow to the periventricular region of the brain (1, 2). The etiology involves a combination of several factors such as premature birth, hypoxic-ischemic events, intraventricular hemorrhage, infection and inflammation. In radiological diagnosis, sonography is useful as the first choice when the fontanelle opening allows imaging; MRI is frequently used in the suspicion of PVL because it detects WM signal change and its extent from the early stages. It has an important role in the diagnosis with its high image sensitivity, detailed visualization of the WM, the ability to evaluate the brain as a whole, its use in long-term follow-up, and its contribution to differential diagnosis.

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On MRI, the first signs of PVL are usually T2W and FLAIR hyperintensity areas. In time, cavity formation and periventricular cysts may be observed in these areas. In the last stage, ventriculomegaly and thinning of the corpus callosum (CC) may be observed with progressive necrosis of the periventricular tissue (3, 4). In the literature, PVL has been associated with widespread abnormalities in WM signal intensity (5). It has also been shown that the effect of PVL extends beyond WM and affects cortex and subcortical grey matter (GM) structures. It is known that as a result of these injuries, there is a decrease in WM and CC volumes, especially in the long term. There are a sufficient number of satisfactory studies on this subject in the literature. However, GM changes in PVL encephalopathy and its developmental effects are not completely understood (1, 2).

In MRI, WM signal changes are detected in T2W-FLAIR series. As a hypothesis, FLAIR signal intensity ratio can be useful in determining the severity of PVL. There is no study in the literature regarding this radiological method. Moreover, considering the role of the thalamus in cognitive and motor dysfunctions, the presence of the thalamus L sign in PVL may be a potential biomarker for the degree of neural damage and disease severity (6).

The goal of this study was to compare the WM and GM volume changes, CC surface area of children with PVL with those of healthy children, as well as to evaluate the diagnostic efficiency of the presence of the thalamus L sign and the FLAIR signal ratio value. In this way, we hope to provide a more comprehensive understanding of PVL's neurodevelopmental sequelae and inform early intervention and potential therapeutic targets for affected individuals.

Material and Methods

Study Design and Population

This study was performed as a retrospective observational study at a single center.

Between 2021 and 2023, the images of patients aged 0–17 years referred to the radiology clinic for brain MRI with a prediagnosis of PVL by the pediatric neurology clinic were accessed using hospital automation (Octomed) and the archive system (Infinitt). The images were retrospectively evaluated by the consensus of two radiologists with at least 5 years of experience in neuroradiology. As a control group, images of age and sex-matched healthy children who presented to our clinic for different reasons and underwent cranial MRI were evaluated. Patients with MRI findings in favor of PVL (T2W high signal areas, cavitations, periventricular cysts, ventriculomegaly with ventricle wall irregularities, WM volume loss, CC thinning) and optimal imaging quality were included in the study (Fig. 1). The control group included children with no pathology detected on brain MRI and no clinical and laboratory abnormalities that could affect neurological status in the hospital system. Patients with pathology detected on MRI, a current or past history of hemorrhagic stroke, parenchymal hematoma, a history of malignancy/cranial surgery/trauma, known metabolic diseases, artifacts in MRI images, or acute diseases that may affect neurological status were excluded from the study.

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the hospital ethics committee (27.09.2023).

MRI technique and analysis method

Imaging was performed with a 1.5 Tesla (T) MRI device (Philips Ingenia, The Netherlands). The sequences used in imaging are: axial spin echo T1W (TR/TE: 470-570/12-30ms), axial and sagittal T2W (TR/TE: 4500-6000/90-110ms), axial and coronal FLAIR (TR/TE: 6000-9000/100-120ms), and diffusion weighted imaging (DWI) (b = 0,500,1000). WM and GM T1W, T2W, FLAIR signal changes, FLAIR signal ratio, CC morphology and surface area, and the and the presence of the thalamus L sign were evaluated in MRI. To calculate the FLAIR signal ratio in PVL cases, we measured the signal intensity in the periventricular region where white matter signal abnormalities peak and in the adjacent normal-appearing cerebral parenchyma by verifying these signal intensities on T2W sequences. Similarly, we measured the FLAIR signal intensity of periventricular white matter and adjacent subcortical white matter in the control group. We determined the FLAIR signal ratio by proportioning these signal intensities for each hemisphere (Fig. 2). To minimize the margin of error, the measurements were taken three consecutive times, averaged, and recorded. We identified the FLAIR signal ratios measured in the right and left cerebral hemispheres and compared their averages with each other in the groups. We used a circular 5mm-diameter region of interest (ROI) in signal measurements.

We evaluated the presence of the thalamus L sign on axial T2W and FLAIR images as defined by Misser et al. (7) (Fig. 3).

Brain MRI volumetric analysis was conducted using Volbrain, a free, automated online platform designed for research. MR images were anonymized, optimized for quality, and converted to NIFTI format. The platform employs machine learning for automatic segmentation of brain regions, applying normalization and standardization for comparison. Volumetric data, calculated in cubic millimeters, is generated using multi-atlas label fusion techniques and compared against a normative database (8, 9). In our study, we measured various brain volumes using Volbrain analysis, including total WM, normal and abnormally signaled WM, total GM, subcortical and cortical GM, cerebrospinal fluid (CSF), and total brain volume (encompassing both WM and GM). In addition, intracranial cavity, total cerebrum, cerebrum WM, cerebrum GM, total cerebellum (excluding vermis), cerebellum WM and cerebellum GM volumes were measured (Fig.4).

We evaluated the MRI findings comparatively between PVL cases and an age- and sex-matched healthy group.

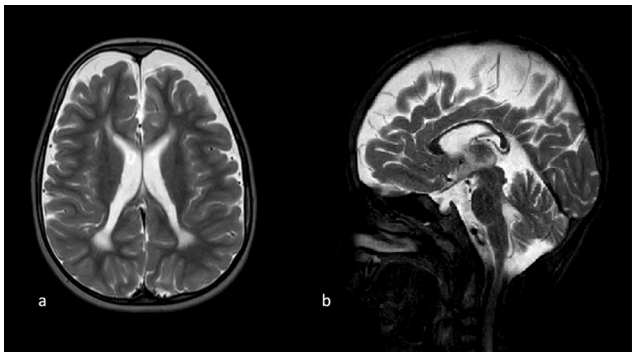

Fig. 1 T2W MRI images in the axial and sagittal planes in a PVL case show periventricular abnormal high signal areas, increased peripheral CSF distance anteriorly, ventricular wall irregularities, mild ventriculomegaly, white matter volume loss, and corpus callosum thinning

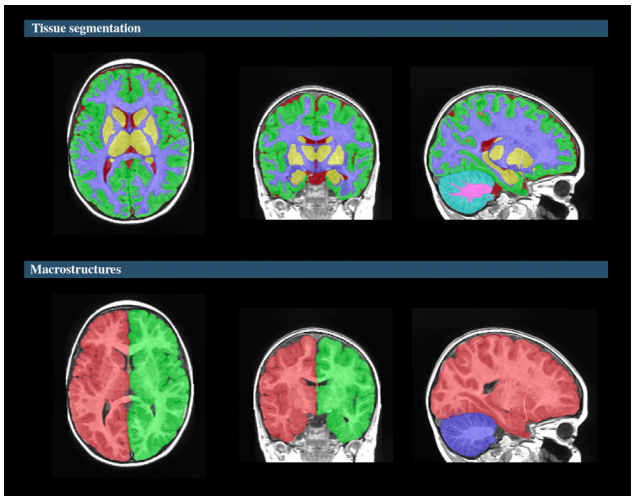

Fig. 4 Brain MRI volumetric analysis of cases with the Volbrain program

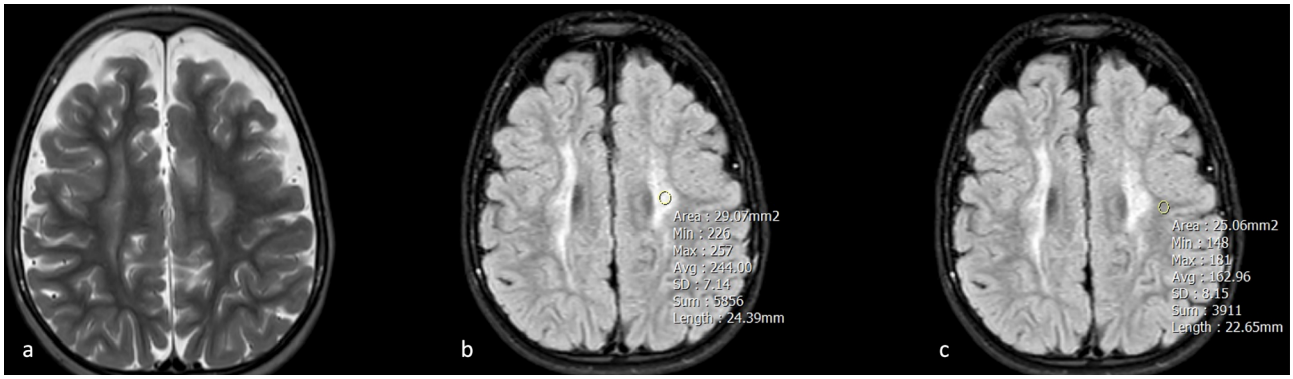

Fig. 2 The FLAIR signal ratio measurement in a PVL case: Signal intensity measurement method with ROI from periventicular abnormally high signaled white matter (b) and adjacent normal signaled white matter (c) in axial FLAIR images

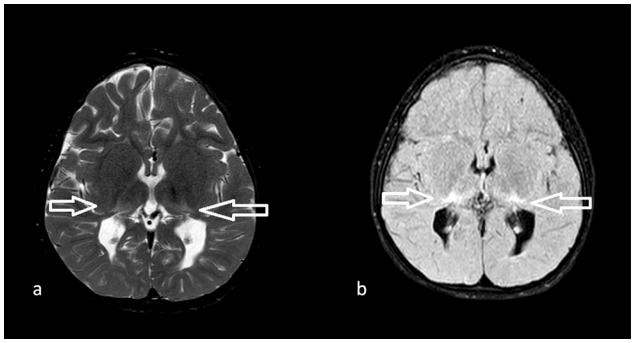

Fig. 3 Thalamus L sign in a case of PVL: Abnormal signal increases in posterolateral extension in both thalamus on T2W (a) and FLAIR (b) MR images in the axial plane (arrows)

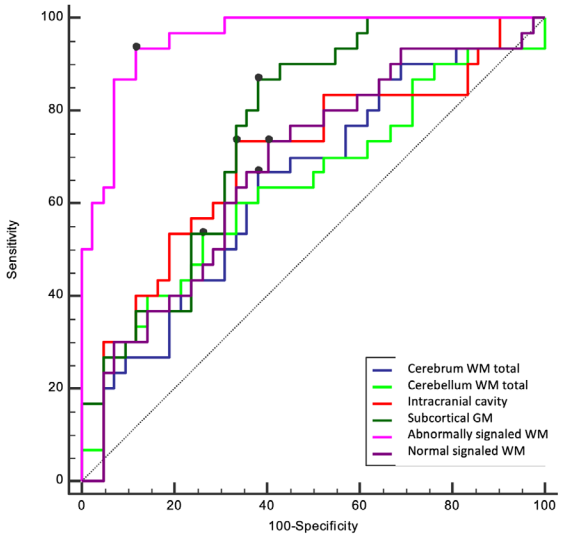

Fig. 5 ROC curves of variables that can be used to diagnose PVL

Table 1. Descriptive statistics and comparison results for PVL and control groups

	Control (n=42)	PVL (n=30)	Z / t	p
Total WM	390.67±103.87	348.03±105.09	1.709	0.092
Normally signaled WM	386.03±105.03	324.49±100.01	2.500	0.015
Abnormally signaled WM	3.15 (1.46-5.87)	22.72 (14.04-27.17)	-6.545	<0.001
Total GM	702.87 (494.36-779.73)	629.11 (492.15-708.98)	-1.416	0.157
Subcortical GM	40.94 (32.23-45.34)	32.57 (21.23-37.38)	-3.735	<0.001
Cortical GM	568.79 (396.45-629.25)	508.24 (398.71-574.24)	-1.371	0.170
Brain total (WM+GM)	1127.91 (826.32-1243.57)	928.69 (822.38-1047.32)	-1.885	0.059
Cerebrum total	1013.95 (736.69-1101.61)	827.80 (725.27-919.81)	-1.953	0.051
Cerebrum WM	369±97.26	328.32±94.77	1.768	0.081
Cerebrum GM	609.05 (425.36-673.26)	542 (419.68-609.99)	-1.588	0.112
Cerebellum total	114.42 (82.35-122.24)	98.38 (91.28-118.14)	-0.845	0.398
Cerebellum WM	21.39 (16.05-26.26)	17.21 (12.58-24.11)	-2.010	0.044
Cerebellum GM	97.71 (69.95-107.25)	87.81 (69.31-102.44)	-0.880	0.379
CSF	103.15 (69.82-301.73)	125.83 (95-150.40)	-0.628	0.530
Intracranial cavity	1232.36±212.91	1108.01±97.26	2.511	0.014

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

Table 2. The correlation analysis findings between the mean FLAIR signal ratio and volumetric measurements in the PVL group

	Mean FLAIR signal ratio	
Total WM	r=	-0.083
	p=	0.662
Normally signaled WM	r=	-0.070
	p=	0.715
Abnormally signaled WM	r=	-0.034
	p=	0.857
Total GM	r=	0.406
	p=	0.026
Cortical GM	r=	0.369
	p=	0.045
Subcortical GM	r=	0.520
	p=	0.003
Brain total (WM+GM)	r=	0.331
	p=	0.074
Cerebrum total	r=	0.316
	p=	0.089
Cerebrum WM	r=	-0.064
	p=	0.738
Cerebrum GM	r=	0.382
	p =	0.037
Cerebellum total	r=	0.399
	p=	0.029
Cerebellar GM	r=	0.536
	p=	0.002
Cerebellum WM	r=	0.034
	p=	0.856
CSF	r=	0.399
	p=	0.029
Intracranial cavity	r=	0.427
	p=	0.019

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

Statistical Analysis

Statistical analyses of the study were performed using SPSS software (IBM SPSS Statistics for Windows, Version 27.0). Armonk, NY: IBM Corp. Whether the quantitative variables are suitable for a normal distribution was analyzed by the Kolmogorov-Smirnov test. Independent groups were compared with an independent sample t test for normally distributed variables and a Mann-Whitney U test for non-normally distributed variables. The relationship between qualitative variables was analyzed by chi-square analysis. Pearson or Spearman correlation analysis was applied to examine the relationship between quantitative variables. Variables that can be used as markers for the diagnosis of PVL were analyzed by ROC analysis. Descriptive statistics of quantitative variables that conform to normal distribution are shown as mean±standard deviation, and descriptive statistics of quantitative variables that are not normally distributed are shown as median (25th–75th percentile). Descriptive statistics for qualitative variables were expressed as frequency (%). Statistical significance was defined as $p<0.05$ values.

Results

Considering the inclusion and exclusion criteria, 30 patients (16 girls, 14 boys) aged 0–18 years (3 (1.50–6.25)) diagnosed with PVL were included as the patient group, and 42 healthy children (23 girls, 19 boys) aged 0–18 years (3 (1.58–7)) were included as the control group, resulting in a total of 72 individuals.

Descriptive statistics and comparison results for PVL and control groups are given in Table 1. Normal signaled WM, subcortical GM, intracranial cavity, and cerebellum WM volumes were significantly greater in the control group ($p=0.015$, $p<0.001$, $p=0.014$, and $p=0.044$, respectively), while abnormally signaled WM volume was significantly higher in the PVL group ($p<0.001$) compared to controls.

Table 2 shows the correlation analysis findings between the mean FLAIR signal ratio and volumetric measurements in the PVL group. The mean FLAIR signal ratio showed a weak positive correlation with total GM, cortical GM, intracranial cavity, CSF, and total cerebellum volume ($r=0.406$, $p=0.026$; $r=0.369$, $p=0.045$; $r=0.427$, $p=0.019$; $r=0.399$, $p=0.029$; and $r=0.399$, $p=0.029$, respectively). A moderate positive correlation was observed with subcortical GM and cerebellar GM volumes ($r=0.520$, $p=0.003$ and $r=0.536$, $p=0.002$, respectively).

Table 3. Descriptive statistics and comparison results of the PVL group with and without the thalamus L sign

	TALAMUS L SIGN		Z / t	p
	(+) (n=16)	**(-)** (n=14)		
Age	15.25±9.40	12.64±9.35	0.760	0.454
Right FLAIR signal ratio	1.53±0.19	1.56±0.19	-0.515	0.611
Left FLAIR signal ratio	1.56±0.21	1.64±0.30	-0.892	0.382
Mean FLAIR signal ratio	1.54±0.19	1.60±0.24	-0.768	0.449
Corpus callosum surface area	237.81±53.96	147.29±51.75	4.672	**<0.001**
Total WM	313.45±71.28	387.55±124.97	-2.028	0.052
Normally signaled WM	297.27±74.86	355.61±117.86	-1.640	0.112
Abnormally signaled WM	16.18±7.66	31.91±15.23	-3.644	**0.001**
Gray matter	634.23±121.53	574.02±205.10	0.993	0.329
Subcortical GM	32.92±6.69	27.41±11.16	1.611	0.122
Cortical GM	512.78±105.79	457.87±169.82	1.078	0.290
Brain total (WM+GM)	947.68±170.94	961.57±189.67	-0.211	0.834
Cerebrum total	843±154.96	849.04±154.96	-0.102	0.919
Cerebrum WM	297.31±66.59	363.77±111.27	-2.015	0.054
Cerebrum GM	545.70±108.50	485.27±180.30	1.129	0.269
Cerebellum total	96.93 (86.36-117.20)	99.94 (93.39-120.72)	0.480	0.498
Cerebellum WM	15.78±5.47	23.78±14.89	-2.004	0.055
Cerebellum GM	85.52±19.40	88.75±25.96	-0.389	0.700
CSF	112.63 (74.96-185.62)	132.34 (96.14-143.10)	0.678	0.697
Intracranial cavity	1109.17±182.64	1106.69±222.85	0.033	0.974

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

Tablo 4. The ROC analysis findings regarding the volume variables that can be used to diagnose PVL

	AUC	SH_{AUC}	p	% 95 CI		Sensitivity (%)	Specificity (%)	Cut-off point
				Lower	Upper			
Abnormally signaled WM	0.955	0.021	<0.001	0.878	0.990	93.33	88.10	>7.23
Subcortical GM	0.760	0.056	<0.001	0.644	0.852	86.67	61.90	≤39.11
Intracranial cavity	0.690	0.065	0.004	0.571	0.794	73.33	66.67	≤1190.37
Normal WM	0.678	0.064	0.006	0.557	0.783	73.33	59.52	≤370.89
Cerebrum WM	0.640	0.066	0.036	0.518	0.750	66.67	61.90	≤351.07
Cerebellum WM	0.640	0.068	0.041	0.518	0.750	53.33	73.81	≤17.38
Total WM	0.638	0.067	0.039	0.516	0.748	66.67	61.90	≤372.91
Cerebrum total	0.636	0.069	0.048	0.514	0.746	83.33	61.90	≤956.82

** All the volumes are presented in absolute value (measured in cm3), WM: white matter, GM: gray matter*

There is also a negative, moderate correlation between FLAIR signal ratio and CC surface area (r=-0.585, p<0.001).

The mean CC surface area was significantly larger in patients without thalamus L sign compared to those with thalamus L sign (p<0.001), and abnormally signaled white matter volume was significantly higher in patients with thalamus L sign (p=0.001). No significant difference was found between the groups in other variables (p>0.05).

Table 4 shows the ROC analysis findings regarding the volume variables that can be used to diagnose PVL. In the analysis performed to determine which variables were more important in diagnosing PVL, the AUC value of the abnormally signaled WM volume variable was significantly greater than the AUC values of the cerebrum WM, cerebellum WM, intracranial cavity, subcortical GM, and normally signaled WM volume variables (p<0.001 for all comparisons) (Fig. 5). Accordingly, the most important variable that can be used to diagnose PVL is the abnormally signaled WM volume (AUC = 0.955, p<0.001).

Discussion

MRI is a neuroradiological marker for the detection of the presence of PVL. Any positive findings on the MRI are valuable for early diagnosis and the immediate initiation of rehabilitation measures. To the best of our knowledge, our study is unique and valuable as it is the first study to evaluate conventional MRI findings, FLAIR signal ratio, the presence of the thalamus L sign, and brain volumetric analysis together in PVL cases.

In children with PVL, MRI studies have revealed changes in both WM and GM volumes. In our study, there was an increase in the abnormally signaled WM volume and a decrease in the normal signaled WM volume in our PVL cases (p<0.001). In our study of PVL cases, volumes of normal signaled WM, intracranial cavity, and cerebellum WM were significantly reduced compared to the healthy control group (p = 0.015, p = 0.014, and p = 0.044, respectively), whereas CSF volume was notably higher (125.83 vs. 103.15). In PVL, which is characterized by a decrease in WM volume, an accompanying increase in CSF volume indicates loss of brain tissue in these regions (1, 10).

This reduction in WM correlates with the motor and cognitive deficits observed in affected children (10). Simultaneously, it has been reported that changes in GM volume are also observed in PVL, but these are more complex and region-specific. Some studies have reported decreased GM volume in areas associated with cognition and memory such as the hippocampus, amygdala and frontal lobes (2). This reduction in GM volume in specific regions may contribute to the cognitive impairments seen in children with PVL (2, 11, 12). In our study, subcortical GM volumes were significantly lower in PVL cases than in the healthy control group ($p<0.001$). A decrease in subcortical GM volume may reflect secondary degeneration resulting from disruption of the white matter pathways connecting these regions (12).

There are also studies in the literature that found that GM volume increased in certain regions of the putamen, thalamus, globus pallidus, and temporal, parietal, and occipital lobes (1, 2). In our study, we discovered a positive relationship between the average FLAIR signal ratio variable, total GM, cortical GM and subcortical GM volume. We believe that brain plasticity mechanisms like axonal sprouting, neuronal hypertrophy and neurogenesis, which may represent the brain's attempt to compensate for damage are associated with increases in GM volume (1). Our findings showing GM volume increases correlated with increased WM involvement are consistent with the idea that brain plasticity may lead to regional GM volume increases in response to WM damage (13). However, the clinical significance of these changes remains to be fully elucidated. Additionally, in our study, we observed a positive correlation between the increase in FLAIR signal ratio and cerebellar GM volume as well as cerebellar subcortical GM volume. This could potentially be explained by compensatory mechanisms or brain plasticity, as suggested by the increased GM volume observed in certain regions in preterm children with PVL (13). In addition to motor coordination, the role of the cerebellum in cognitive functions may also be reflected in these volumetric changes (14). Furthermore, the resistance of the cerebellum to WM damage may be attributed to distinct developmental and cellular states that may provide some degree of protection against the widespread WM damage observed in conditions such as PVL (14). Further research is needed to understand the effects of these volumetric changes on the long-term neurodevelopmental outcomes of pediatric patients with PVL. Our study underscores the importance of MRI techniques in elucidating the complex relationships between structural brain changes and clinical manifestations in pediatric neurology.

It is reported in the literature that the presence of GM damage in PVL is not limited to the cerebral cortex, and that subcortical structures such as the thalamus, basal ganglia, and cerebellar dentate nucleus are affected (15, 16). For this reason, it has been stated that white matter damage in PVL does not occur alone and that it may be appropriate to define the neuropathology as "perinatal panencephalopathy" (15). Thalamic involvement is particularly important as it plays a role in the cognitive and motor dysfunctions observed in children with PVL. As reported in the literature, the bilateral decrease in thalamic volume may be related to the presence of the thalamic L sign on MRI in our cases. In our study, the presence of lower CC surface area ($p<0.001$) and higher abnormally signaled WM ($p = 0.001$) in PVL cases with a positive thalamic L sign suggests that the thalamic L sign is a potential biomarker for the extent of neural damage in PVL, as stated in the literature (16).

In our study, the most important variable that can be used to diagnose PVL was the abnormally signaled WM volume (AUC=0.955, $p<0.001$). This highlights the critical role of abnormally signaled WM volume on MR imaging as an important diagnostic variable for PVL in children. Diffuse WM signal intensity abnormalities have been shown to be associated with PVL (5). The increased signal on MRI is thought to correspond neuropathologically to regions containing increased reactive astrocytes and microglia, decreased oligodendroglial cells, and a striking reduction in axon number (17). The intensity of the abnormal WM signal on MRI reflects underlying microstructural tissue damage. MRI of premature white matter disorders, including PVL, highlights the widespread excessively high signal intensity and its potential association with cognitive and behavioral disorders (18).

The negative relationship we found between FLAIR signal ratio and CC surface area is consistent with previous research showing that WM changes are associated with reductions in WM volume, as well as motor and cognitive deficits. There is also a study suggesting that there is a positive correlation between the thickness of the CC and the volume of cerebral WM in children with cerebral palsy and developmental delay and that damage to the corpus callosum may reflect the extent of white matter loss (19). The literature specifically reports a significant reduction in CC size associated with the severity of motor and cognitive impairments in PVL (1). Our results confirm the idea that the structural integrity of the CC is impaired in PVL, which may contribute to the functional deficits observed in PVL. We contribute to this understanding by highlighting the specific effect of PVL on the corpus callosum. Furthermore, the negative correlation between FLAIR signal ratio and CC surface area suggests that it may be useful in follow-up as a potential indicator of the disease severity.

The underlying neuropathology of PVL includes both WM damage and secondary GM changes (1, 2, 11, 15). As a basic diagnostic tool, MRI is extremely sensitive in detecting the characteristic findings of PVL, especially WM damage and changes in the periventricular area, by providing detailed images of brain tissue. In addition to the decrease in WM volume on MRI, both decreased and increased GM volumes in various regions indicate a complex interaction between the adaptive responses of the brain (2, 12, 15). The

relationship between structural and volumetric brain changes in PVL and functional outcomes highlights the importance of early diagnosis and intervention to reduce potentially its long-term neurodevelopmental impact.

Limitations

Our study had some limitations. Among these was the lack of follow-up data of the patients and the lack of correlation with the clinical severity score due to its retrospective nature. These parameters could be the focus of another study. Additionally, our relatively small sample size and the fact that the cases were not divided into etiological subgroups may also be a limitation. Since there were no 3D thin-section T1 sequences in the volumetric evaluation of the brain, we could not perform detailed microstructural analysis of the subanatomical regions of the brain. Therefore, we can consider our inability to detect specific regions of GM changes as a limitation. Another limitation is the inclusion of patients with chronic, long-term effects of PVL in this study. Another study can examine the effects in the early or subacute phase.

Conclusion

In conclusion, the use of MRI in the early diagnosis of PVL allows for more effective management of the disease and the early initiation of necessary treatment strategies. In addition to white matter involvement, regional GM volumetric changes, morphological changes in the corpus callosum, and their relationship with the increase in abnormal white matter signal intensity may be valuable for the development of targeted treatment strategies aimed at reducing cognitive and motor disorders in PVL.

Statements and Declerations

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

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Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors. This study was approved by the local medical ethical committee (2023/514/258/25), and all data was processed anonymously, according to the privacy legislation.

Authorship Contribution Statement

Conception: H.G.D., E.C., Design: H.G.D., E.C., T.B., Supervision: H.G.D., E.C., Materials: E.C., İ.S., S.G.S., Data Collection and/or Processing: H.G.D., E.C., S.G.S., İ.S., Analysis and/or Interpretation: F.C.T., Literature Review: H.G.D., E.C., T.B., Writer: H.G.D., E.C., Critical Review: H.G.D., E.C., S.G.S., İ.S., F.C.T., T.B.

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ORIGINAL ARTICLE

The Use of Propofol to Induce Anesthesia can Mitigate the Oxidative Stress Created by Laparoscopic Cholecystectomy, but not Thiopental

Anestezi Indüksiyonu için Propofol Kullanımı Laparoskopik Kolesistektominin Yarattığı Oksidatif Stresi Hafifletebilir Ancak Tiyopental Bunu Azaltamaz

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Çeliksu AG, Aksoy ŞM, Dumanlı Özcan AT, Gokcinar D. The Use of Propofol to Induce Anesthesia can Mitigate the Oxidative Stress Created by Laparoscopic Cholecystectomy, but not Thiopental. Genel Tıp Derg. 2024;34(4):554-8.

ABSTRACT

Aim: Laparoscopic cholecystectomy is one of the treatment methods employed in symptomatic cholelithiasis cases, and pneumoperitoneum has been shown to increase oxidative stress. Our aim is to compare propofol and thiopental in terms of their effects on oxidative stress parameters in laparoscopic cholecystectomy cases.
Materials and Methods: After obtaining Ethics Committee permission, patients who underwent laparoscopic cholecystectomy were divided into thiopental and propofol groups according to the agent used for anesthesia induction in the randomized and prospective study. Serum oxidative stress parameters levels were measured in all patients twice before induction of general anesthesia and at the 30th minute postoperatively.
Results: When comparing the preoperative period with the postoperative period, total antioxidant status (TAS) levels increased statistically significantly in the propofol group (preoperatively 1.21±0.21 mmolH2O2/L, postoperatively 1.31±0.18 mmolH2O2/L, p<0.001) compared to the thiopental group (preoperatively 1.23±0.14 mmolH2O2/L, postoperatively 1.27±0.14 mmolH2O2/L, p=0.055). arylesterase (ARES), serum native thiol, total thiol, and disulfide levels decreased statistically significantly in both groups. While Paraoxonase-1 (PON1) level did not change in the propofol group, it decreased in the thiopental group.
Conclusion: We concluded that propofol had a significantly greater oxidative stress reduction effect than thiopental. By increasing the TAS levels, propofol may have a more positive effect on oxidative stress than thiopental. However, neither propofol nor thiopental have oxidative stress-reducing effects on other oxidative stress parameters.

Keywords: Antioxidants, Disulfides, Laparoscopic cholecystectomy, Oxidative stress, Propofol, Thiol, Thiopental

ÖZ

Amaç: Semptomatik kolelitiazis vakalarında laparoskopik kolesistektomi tedavi metodlarından biridir ve pnömoperitoniumun oksidatif stresi arttırdığı gösterilmiştir. Bizim amacımız laparoskopik kolesistektomi olgularında oksidatif stres parametreleri üzerine etkileri açısından propofol ve tiyopentali karşılaştırmaktır.
Gereç ve Yöntem: Etik Kurul izni alındıktan sonra, randomize ve prospektif olarak planlanan çalışmada laparoskopik kolesistektomi geçiren hastalar anestezi indüksiyonu için kullanılan ajana göre tiyopental ve propofol gruplarına ayrıldı. Tüm hastalardan serum oksidatif stres parametreleri düzeylerinin ölçümü için genel anestezi indüksiyonu öncesi ve postoperatif 30. dakikada olmak üzere iki kez kan örnekleri elde edildi.
Bulgular: Total antioxidant statü (TAS) düzeyleri, preoperatif dönem ile postoperatif dönem karşılaştırıldığında propofol grubunda (preoperatif olarak 1.21±0.21 mmolH2O2/L, postoperatif olarak 1.31±0.18 mmolH2O2/L, p<0.001) tiopental grubuna (preoperatif olarak 1.23±0.14 mmolH2O2/L, postoperatif olarak 1.27±0.14 mmolH2O2/L, p=0.055) göre istatistiksel olarak önemli oranda arttı. Arilesteraz (ARES), serum native tiyol, toplam tiyol, disülfid düzeyi her iki grupta istatistiksel olarak önemli oranda azaldı. Paraoxonaz-1 (PON1) düzeyi ise propofol grubunda değişmemiş saptanırken, tiyopental grubunda azalmış olarak tespit edilmiştir.
Sonuç: Propofolün tiyopentalden anlamlı derecede daha fazla oksidatif stres azaltma etkisine sahip olduğu sonucuna vardık. TAS düzeylerinde artış sağlayarak, propofol tiyopentale göre oksidatif stres üzerine daha olumlu etkiye sahip olabilir. Ancak diğer oksidatif stres parametreleri üzerine ne propofolün ne de thiopentalin oksidatif stresi azaltıcı etkileri yoktur.

Anahtar kelimeler: Antioksidanlar, Disülfitler, Laparoskopik kolesistektomi, Oksidatif stres, Propofol, Tiyol, Tiyopental

Introduction

Laparoscopic cholecystectomy is the excision of the gallbladder using a laparoscope. Pneumoperitoneum is provided by insufflating carbon dioxide to obtain vision inside the abdomen (1). It may increase intra-abdominal pressure. Excessive increase in intra-abdominal pressure may lead to deterioration in splanchnic perfusion. This may increase reactive oxygen species through ischemia reperfusion injury (2). Free radicals, which are reactive oxygen species play a beneficial role in the immune system, intracellular signaling cascades and induction of mitogenic response at low or moderate concentrations. Oxidative stress occurs when the balance between production and detoxification of free radicals is disrupted. Lipids, proteins and DNA are negatively affected by oxidative stress (3). PON1 enzyme is largely produced in liver cells

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and high-density lipoprotein stimulates its release. PON1 protects against lipid peroxidation by binding to cell membranes in tissues and it is effective as an antioxidant (4). Thiols are organic compounds containing sulfhydryl groups and act as antioxidants in oxidative stress. TAS and TOS provide information about oxidant-antioxidant capacity status (5). The effects of intravenous anesthetic agents on oxidative stress are wondered. An animal study comparing the effects of propofol and thiopental on oxidative stress on dogs found an increase in TAS and a decrease in TOS levels with both agents (6). In a study comparing propofol and thiopental in an ischemia reperfusion model caused by testicular torsion in rats, it was found that propofol attenuated tissue malondialdehyde and nitric oxide levels (7). In another study, researchers determined oxidative stress based on glutathione levels in platelet cytoplasm. Citrated blood obtained from surgical patients was centrifuged and it was shown that propofol reduced oxidative stress in platelets more than thiopental (8). Propofol and sevoflurane were compared in terms of serum native thiol and nitric oxide levels in patients undergoing transsphenoidal pituitary surgery. It was suggested both agents had similar antioxidant effects (9). Since there is little information on comparing thiopental and propofol used in anesthesia induction, more clinical research on oxidative stress is needed. Our goal is to compare the effects of thiopental and propofol on oxidative stress in patients undergoing laparoscopic cholecystectomy.

Material and Methods

The randomized and prospectively planned study was carried out after obtaining Ethics Committee permission. Sixty adult patients with American Society of Anesthesiologists Physical Status classification I and II, Mallampati score I and II, and scheduled for laparoscopic cholecystectomy were included in the study. All patients signed informed consent. Patients with severe heart disease, obstructive and restrictive lung disease, kidney and liver failure, patients with a history of alcohol, sedatives, those using sedatives and long-term analgesics were excluded from the study.

Patients were fasted for at least 8 hours and no premedication was administered for preoperative sedation before entering the operating room. Randomization was performed to pick from an envelope labeled 30 propofol and 30 thiopental. Age, gender, smoking, past surgical history, American Society of Anesthesiologists (ASA) Physical Status classification, Mallampati score, duration of anesthesia and duration of operation of the patients were recorded. All patient monitored with the electrocardiography, noninvasive blood pressure device, pulse oximeter, and capnometer. Before induction, 100% oxygen was breathed for 3 minutes. In the propofol group, anesthesia was induced with IV lidocaine 1-1.5 mg/kg (Aritmal 2%, Osel) and IV propofol 2-3 mg/kg, IV remifentanil 1 mcg/kg (Ultiva 2mg GlaxoSmithKline) and IV rocuronium 0.6-1.2 mg/kg (Esmeron 50mg, 5ml vial, Organon). Anesthesia was applied to the Thiopental group with IV lidocaine 1-1.5 mg/kg, IV thiopental 4-7 mg/kg (Pental sodium 0.5 g, I.E. Ulugay) IV remifentanil 1 mcg/kg and IV rocuronium 0.6-1.2 mg /kg. Anesthesia maintenance was continued with remifentanil (0.05 – 0.25 mcg/kg/min) and 40% O2-Air mixture with 2-3% sevoflurane (Sevorane, Abbott Lab.).

It was planned to stop the study if the patient had uncontrolled bleeding and the surgery could not be completed with laparoscopic surgery.

Venous blood samples were taken from all patients twice before anesthesia induction and at the end of the surgery to measure serum TAS, TOS, PON1, ARES, native thiol, total thiol, and disulfide levels. Blood samples were centrifuged at 3600 rpm for 10 minutes in the biochemistry laboratory and then stored at -80 degrees. They analyzed on the Roche 501/701 modular system automatic analyzer.

Statistical analysis

Data were analyzed using IBM SPSS for Windows V22.0 program. Descriptive statistics were showed as mean±standard deviation, frequency distribution and percentage. To evaluate categorical variables, Pearson Chi-Square Test was used. The suitability of the variables to normal distribution was analyzed with visual (histogram and probability graphs) and analytical methods (Shapiro-Wilk Test). For variables conforming to normal distribution, statistical significance was determined between two independent groups using the Student T Test. Paired Sample T Test was applied between two dependent groups. If there was no normal distribution, Whitney U Test was used between two independent groups and Wilcoxon Signed Rank Test was employed between two dependent groups. Spearman Test was used to find the relationship between variables. $P<0.05$ was accepted as statistically significant.

Results

There was no significant difference between the two groups in terms of clinical characteristics of the patients ($p>0.05$; Table 1).

When comparing the preoperative period with the postoperative period, TAS levels increased statistically significantly in the propofol group (preoperatively 1.21±0.21 mmolH2O2/L, postoperatively 1.31±0.18 mmolH2O2/L, $p<0.001$; Table 2) compared to the thiopental group (preoperatively 1.23±0.14 mmolH2O2/L, postoperatively 1.27±0.14 mmolH2O2/L, $p=0.055$; Table 2). Postoperative PON1 values in the thiopental group decreased significantly. In the propofol group, PON1 levels did not change significantly ($p>0.05$; Table 2).

Postoperatively, ARES, native thiol, total thiol and disulfide levels decreased significantly in both the thiopental and propofol groups.

Table 1. Clinical characteristics of patients

	Thiopental group (n=30)	Propofol group (n=30)	p
Age, yr	47.67±13.05	42.83±13.91	0.170
Gender			
Male	7 (23.3)	6 (20.0)	0.754
Female	23 (76.7)	24 (80.0)	
Smoking	8 (26.7)	11 (36.7)	0.405
Past surgical history	19 (63.3)	14 (46.7)	0.194
ASA			
I	13 (43.3)	14 (46.7)	0.795
II	17 (56.7)	16 (53.3)	
Mallampati score			
I	9 (30.0)	11 (36.7)	0.584
II	21 (70.0)	19 (63.3)	
Duration of Anesthesia (min)	73.17±18.50	74.57±25.71	0.810
Duration of Operation (min)	55.53±20.39	57.33±25.55	0.764
Continuous variables were presented as "mean±standard deviation" and categorical variables were presented as "number (percentage)".			

Table 2. Oxidative stress parameters detected in patients anesthesia induced with thiopental or propofol

	Preoperative	Postoperative	p
Total antioxidant status (mmolH_2O_2/L)			
Thiopental group	1.23±0.14	1.27±0.14	0.055
Propofol group	1.21±0.21	1.31±0.18	<0.001
Total oxidant status (µmolH_2O_2/L)			
Thiopental group	5.26±2.28	5.47±2.35	0.742
Propofol group	4.75±1.47	4.94±1.47	0.943
Paraoxonase (U/L)			
Thiopental group	171.68±95.29	159.83±94.95	0.007
Propofol group	135.55±81.63	131.35±82.78	0.131
Arylesterase (U/L)			
Thiopental group	213.61±51.53	200.78±47.89	0.012
Propofol group	205.53±40.01	194.63±46.13	0.041
Native thiol (µmol/L)			
Thiopental group	359.16±57.07	323.42±51.18	<0.001
Propofol group	375.68±52.04	340.65±54.26	0.002
Total Thiol (µmol/L)			
Thiopental group	384.13±60.69	343.61±53.61	<0.001
Propofol group	402.27±53.71	363.06±58.93	0.001
Disulphide (µmol/L)			
Thiopental group	12.49±3.09	10.10±3.79	0.014
Propofol group	13.30±3.53	11.20±5.11	0.027
Disulphide/Native thiol%			
Thiopental group	3.49±0.74	3.15±1.18	0.216
Propofol group	3.58±0.99	3.30±1.41	0.325
Disulphide / Total Thiol%			
Thiopental group	3.25±0.65	2.94±1.04	0.196
Propofol group	3.33±0.85	3.06±1.24	0.297
Native thiol/ Total Thiol%			
Thiopental group	93.50±1.30	94.12±2.08	0.196
Propofol group	93.34±1.71	93.87±2.49	0.297

Discussion

In this study, we showed that TAS levels increased statistically significantly in the propofol group, but not in the thiopental group, when we compared the pre- and postoperative periods. While there was no change in PON1 level in the propofol group, a decrease was observed in the thiopental group. De La Cruz et al. administered IV 4 mg/kg thiopental or IV 2 mg/kg propofol for patients undergoing curettage, ligation fallopian tubes, inguinal hernia or cholecystectomy. They found that propofol decreased thiobarbituric acid reactive substances production by 25.7% and increased total glutathione content by 24.6%. On the other hand, thiopental did not change any of the variables of platelet oxidative stress (8). Zhang et al. showed protective effects of propofol on H2O2-induced cardiomyocyte injury and myocardial ischemic/reperfusion injury in rats (10).

The effects of antioxidants and anesthetic agents on oxidative stress due to ischemia-reperfusion injury have been investigated in some previous studies (11). Lee J Y et al. showed that oxidative stress in the propofol group was significantly lower than in the thiopental group in dogs underwent surgery (6). Kanbak et al. found that propofol attenuated the effects of ischemia-reperfusion injury on tissues (12). Tsuchiya et al. showed that propofol had a safe keeping effect against oxidative damage in red blood cell (13).

Thiopental may increase oxidative stress in the heart, bronchial tissues and brain of rats (14). In another study, Nishina et al. reported that thiopental significantly may decrease reactive oxygen products released from lymphocytes (15). Yağmurdur et al. stated in a study on testicular ischemia-reperfusion injury in rats that propofol reduced germ cell apoptosis more than thiopental did (7).

PON1 has an antioxidant effect against lipid peroxidation (16). Turkoglu et al. has reported that PON1 levels in patients with metabolic syndrome are lower than in healthy individuals without metabolic syndrome (17). In Parkinson's patients compared to healthy individuals, PON1, arylesterase and TAS levels were lower and TOS levels were higher (18). There are few studies investigating the effects of propofol and thiopental on oxidative stress in humans. Yagmurdur et al. compared the effects of etomidate, thiopental and propofol on malondialdehyde levels during laparoscopic cholecystectomy. They showed that malondialdehyde levels were lower both before and after desufflation in the propofol group. On the contrary, malondialdehyde levels were higher in the etomidate and thiopental groups than in the propofol group at both times (19). Propofol and sevoflurane were compared in patients underwent transsphenoidal pituitary surgery and it was suggested that both agents had similar antioxidant effects (20). Kutluhan et al. compared the effects of propofol and desflurane on surgical stress response in vertebra surgery. They found that post-operative thiol values were higher in the propofol group ($p<0.05$). However, the disulfide level was lower (21).

Simsek et al. compared the thiol-disulfide balance in general and spinal anesthesia in total knee replacement surgery. They used propofol for induction of general anesthesia. They found an increase in natural thiol and total thiol levels in the propofol group compared to the spinal anesthesia group and a decrease in disulfide (22).

Limitations

Limitations of this study include the possibility that multiple factors may influence the outcome. It was not possible to measure an agent given only for anesthesia induction without the effect of other applications during anesthesia maintenance.

Conclusion

In conclusion, TAS level increased statistically significantly in the propofol group than the thiopental group. ARES, native thiol, total thiol and disulphide levels decreased in both groups. PON1 level did not change in the propofol group, however it decreased in the thiopental group. Compared with thiopental, propofol can significantly increase TAS levels, therefore, it may preferable anesthetic agent for patients undergoing laparoscopic cholecystectomy.

Ethical Approval

Yıldırım Beyazıt University Faculty of Medicine Clinical Research Ethics Committee approved the study with decision number 235 on 17 December 2014.

Author Contributions: AGÇ generated the study conception. AGÇ and ŞMA designed the study. AGÇ acquired the data. AGÇ and ŞMA analyzed and interpreted the data. AGÇ, ATDÖ, DG and ŞMA were involved in writing of the manuscript. ŞMA and DG critically reviewed the manuscript. The manuscript has been approved by all authors for publication.

Conflicts of Interest: The authors have no conflicts of interest.

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ORIGINAL ARTICLE

Quality of Life and Employment Among Patients with Epilepsy

Epilepsili Hastalarda Yaşam Kalitesi ve İstihdam

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ABSTRACT

Objective: Seizures significantly affect quality of life among patients with epilepsy while employment significantly contributes to the quality of life in general. Thus, in our study, we aimed to determine how the demographic and disease-related characteristics of patients with epilepsy impact quality of life and employment.
Material and Methods: Our sample included 202 patients who had been diagnosed with epilepsy for at least a year and admitted to the Neurology Polyclinic between October 2023 and March 2024. Data about patients' characteristics were collected using a sociodemographic information form while quality of life was measured using the Turkish Quality of Life in Epilepsy Inventory-31 (QOLIE-31).
Results: On average, patients were 29.07 ± 10.84 years old and had had epilepsy for 10.5 ± 8.92 years. Patients' lowest mean score on the QOLIE-31's subscales was for "Total Quality of Life" whereas their highest mean score was for "Social Function". The total quality of life score of patients with low education level and low income was found significantly lower. Among other results, patients with a seizure frequency of 6 or more per month had significantly lower scores on all subscales except "Emotional Well-Being", and patients with refractory epilepsy and/or receiving polytherapy had significantly lower total scores and scores on all subscales.
Conclusion: Our results indicate that employment does not significantly affect quality of life among patients with epilepsy whereas their clinical features do. Even so, physicians should take all conditions into account to ensure the highest-possible quality of life for patients with epilepsy.

Keywords: Employment, Epilepsy, Seizure, Quality of Life, QOLIE-31

ÖZ

Amaç: Nöbetler epilepsi hastalarında yaşam kalitesini önemli ölçüde etkilerken, istihdam da genel olarak yaşam kalitesine önemli ölçüde katkıda bulunmaktadır. Bu nedenle çalışmamızda epilepsi hastalarının demografik ve hastalıkla ilişkili özelliklerinin yaşam kalitesini ve istihdamını nasıl etkilediğini belirlemeyi amaçladık.
Gereç ve Yöntemler: Örneklemimize Ekim 2023 ile Mart 2024 tarihleri arasında Nöroloji Polikliniği'ne başvuran, en az bir yıldır epilepsi tanısı olan 202 hasta dahil edildi. Hastaların özelliklerine ilişkin veriler sosyodemografik bilgi formu kullanılarak toplandı. Yaşam kalitesi, Epilepside Yaşam Kalitesi Envanteri-31 (QOLIE-31) kullanılarak ölçüldü.
Bulgular: Hastalar ortalama 29,07 ± 10,84 yaşındaydı ve 10,5 ± 8,92 yıldır epilepsi hastasıydı. Hastaların QOLIE-31 alt ölçeklerinden en düşük ortalama puanları Toplam Yaşam Kalitesi, en yüksek ortalama puanları ise Sosyal İşlev alanındaydı. Eğitim düzeyi ve geliri düşük olan hastaların toplam yaşam kalitesi puanının anlamlı derecede düşük olduğu görüldü. Diğer sonuçların yanı sıra, nöbet sıklığı ayda 6 veya daha fazla olan hastaların Duygusal İyilik dışındaki tüm alt ölçeklerde anlamlı derecede düşük puanları vardı ve dirençli epilepsisi olan ve/veya politerapi alan hastaların tüm alt ölçeklerde puanları ve toplam puanları anlamlı derecede düşüktü.
Sonuç: Sonuçlarımız, epilepsi hastalarında çalışmanın yaşam kalitesini anlamlı derecede etkilemediğini ancak klinik özelliklerinin etkilediğini göstermektedir. Yine de hekimlerin epilepsi hastalarında mümkün olan en yüksek yaşam kalitesini sağlamak için tüm koşullarını dikkate alması gerekir.

Anahtar Kelimeler: İstihdam, Epilepsi, Nöbet, Yaşam Kalitesi, QOLIE-31

Introduction

Epilepsy is a brain disorder characterized by recurrent seizures that significantly impact quality of life, meaning "an individual's perception of his/her position in life in relation to his/her goals, expectations, standards and concerns in the context of the culture and value systems in which s/he lives" (1).

Although the principal goal of treatment for epilepsy is to stop seizures from occurring, health is not only the absence of disease or infirmity but also a state of complete physical, mental, and social well-being, at least as defined by the World Health Organization (2). In this respect, patients with epilepsy not only experience seizures but may also experience emotional distress, low self-esteem, decreased social interaction, decreased job opportunities and problems with activities of daily living even if their seizures are well controlled (3).

Employment is a factor that determines social outcomes and contributes greatly to quality of life, especially for patients with epilepsy (4). Having a job not only facilitates financial independence but also

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reinforces self-esteem and supports social functioning (5). However, epilepsy is a major cause of uncertainty about not only employment but also social interactions and may also impose limits on aspects of independent living, including driving (6).

A recent large, multicenter, cross-sectional study on determinants of quality of life among patients with epilepsy has shown that, for such patients, seizure frequency, tolerability of anti-seizure drug, depression, stigma, and concern about the recurrence of seizures are associated with relatively low quality of life (7). Beyond that, numerous international studies have examined employment-related variables among patients with epilepsy, including a survey of 262 patients with epilepsy at four epilepsy centers in the United States. According to their results, being younger, having a higher socioeconomic status, and have fewer comorbidities were associated with higher levels of employment (8). Meanwhile, another cross-sectional study has revealed that a higher level of education, having well-controlled epilepsy, and having good mental health are associated with greater employability among patients with epilepsy (9). Taken together, those findings indicate that epilepsy is not an insurmountable barrier to achieving a productive work life but that other socioeconomic variables are important as well.

Against that background, in our study we aimed to determine how the demographic and disease-related characteristics of patients with epilepsy from our clinic, gathered using through the QOLIE-31 questionnaire, affect their quality of life and employment, with the overarching goal of highlighting the potential benefits of incorporating such a tool in clinical practice.

Material and Methods

Research Design and Sample

In our descriptive study, we aimed to determine the quality of life and employment status of patients with epilepsy as well as conditions related to those factors. Our sample consisted of 202 patients at least 18 years old who had been diagnosed with epilepsy for at least a year and admitted to Harran University Neurology Clinic between October 2023 and March 2024.

Data Collection Tools

To collect data, we used a sociodemographic information form and the Quality of Life in Epilepsy Inventory-31 (QOLIE-31), a scale that developed by the researchers in light of the literature. All data were collected via face-to-face interviews that lasted approximately 10 min each. The interviews were conducted by senior residents.

Sociodemographic Information Form

For data about participants' age, sex, income level, occupation, marital status, level of education, employment status, comorbidity status, years diagnosed with epilepsy, age at first seizure, seizure frequency, seizure type, seizure control, and type of treatment used, we used a sociodemographic information form consisting of 19 items.

Quality of Life in Epilepsy Inventory-31 (QOLIE-31)

The QOLIE-31 contains 31 of the 89 items on the Turkish version of the QOLIE-89, whose validity and reliability were determined by Mollaoğlu et al (10) The QOLIE-31 does not include any SF-36 items on the QOLIE-89 or items regarding symptoms not specific to epilepsy (e.g., pain). That is, the QOLIE-31's items concern epilepsy and epilepsy-related issues only. Its seven subscales contain 30 items in total: Seizure Worry (i.e., 5 items), Emotional Well-Being (i.e., 5 items), Energy/ Fatigue (i.e., 4 items), Social Function (i.e., 5 items), Cognitive Function (i.e., 6 items), Effects of Medications (i.e., 3 items), and overall quality of life (i.e., 2 items). The 31st item, which gives the QOLIE-31 its name, assesses overall health status. Altogether, scores on the QOLIE-31 range from 0 to 100, and a higher score reflects a higher quality of life. Cronbach's alpha of the original scale was 0.91 and in our study it was 0.91.

Statistical Analysis

The statistical analysis of the data was performed in the Statistical Package for Social Sciences version 22.0. Whether the data conformed to normal distribution was evaluated with the Shapiro–Wilk test on normal distribution graphs developed by examining skewness and kurtosis coefficient values together. Descriptive statistics (i.e., number, percentage, and mean) were used to evaluate the data, and an independent sample t test and ANOVA were used to analyze normally distributed variables, whereas the Kruskal–Wallis test was used for non-normally distributed variables. All p values less than .05 were considered to indicate statistical significance.

Ethical Considerations

Ethics approval for the study was obtained from Harran University's Non-Interventional Clinical Research Ethics Committee (HRÜ/23.19.24) while the necessary institutional permissions were obtained from the hospital where the study was conducted. Permission to use the scales was obtained from the researchers who validated the Turkish versions of the scale used in the study. Patients who agreed to participate in the study were informed about the study and told that their participation was voluntary, and their written consent was obtained.

Results

Of the 202 patients with epilepsy who participated in the study, 50.5% were female, and 49.5% were male. On average, they were 29.07 ± 10.84 years old (range: 18–77) and had had epilepsy for 10.5 ± 8.92 years, with seizures beginning at the age of 17.0 ± 13.34 years on average. Regarding the level of education, 59.4% of the patients had at least a high school degree.

Although 28.2% of patients reported not having any seizures in the past year, 10.4% reported having more than 6 seizures per month. When the patients were evaluated according to seizure control, 76.7% were in the well-controlled epilepsy group and 23% were in

Table 1. Demographic and clinical characteristics of epilepsy patients

	Patients n (%)
Gender	
Female	102 (50.5)
Male	100 (49.5)
Marital status	
Married	91(45.0)
Single	111 (55.0)
Level of education	
Uneducated	38(18.8)
Primary Education	44 (21.8)
High School and Above	120 (59.4)
Profession	
Housewife	46 (30.2)
Worker/Tradesman	44 (22.8)
Officer	12 (21.8)
Farmer	5 (5.9)
Student	22 (2.5)
Not Working	73 (69.8)
Have you considered working?	
Yes	83 (41.1)
No	116 (58.9)
Have you applied for a job?	
Yes	62 (30.7)
No	140 (69.3)
Employment status	
Full Time	50 (24.8)
Part Time	11 (5.4)
Unemployed	119 (58.9)
Other	22 (10.9)
Income level	
Income less than expenses	123 (60.9)
Income equals expenses	48 (23.8)
More income than expenses	31 (15.3)
Comorbidity	
Yes	64 (31.7)
No	138 (68.3)
Family history of epilepsy	
Yes	35 (17.3)
No	167 (82.7)
Seizure frequency	
No Seizures in the last year	57 (28.2)
1-5 /Month	124 (61.4)
6 or >6/Month	21 (10.4)
Epilepsy type (Onset)	
Fokal	56 (27.7)
Generalized	100 (49.5)
Unknown	46 (22.8)
Number of ASM taken	
Monotherapy	109 (54.0)
Polytherapy	93 (46.0)
Seizure control	
Uncontrolled	47 (23.3)
Controlled	155 (76.7)
Use of vehicles	
Yes	56 (27.7)
No	146 (72.3)

ASM: anti-seizure medication

Table 2. Quality of Life in Epilepsy-31 (QOLIE-31) scale average scores of epilepsy patients

	Number of Items	Min-Max	Mean	Sd
Seizure Worry	5	0-96	45.00	20.81
Overall Quality of Life	2	1-55	33.54	10.21
Mood	5	0-96	52.23	13.09
Energy/Fatigue	4	0-90	43.14	15.44
Cognition	6	16-100	63.99	16.01
Medication Effects	3	0-100	65.82	24.49
Social Function	5	0-100	67.82	21.47
Total	30	12.4-84.9	54.80	12.91

Min: minimum, max: maximum, Sd: standard deviation

the refractory epilepsy group. While 49.5% of patients had generalized seizures and 27.7% had focal seizures, 54.0% were receiving monotherapy and 46% were receiving polytherapy. Table 1 presents these and other demographic and clinical characteristics of the patients.

Table 2 shows the patients' mean scores on the QOLIE-31. Their lowest mean score on the QOLIE-31's subscales was for Total Quality of Life, whereas their highest mean score was for Social Function.

Next, Table 3 allows a comparison of the sociodemographic and clinical characteristics of the patients in the light of their mean subscale scores on the QOLIE-31. Considering sociodemographic characteristics, 18–25-year-old patients and female patients received significantly lower scores on the Seizure-Related Concerns subscale than all other groups ($p = .049$ and $p = .005$, respectively). Scores on the Total Quality of Life subscale among unmarried patients were significantly lower than among married ones ($p = .029$). Considering level of education, scores for Seizure-Related Concerns, overall quality of life, Energy/Fatigue, Cognitive Function, and Social Function, and Total Quality of Life were significantly lower among patients with lower levels of education ($p < .05$). As for socioeconomic status, 69.8% of patients were unemployed, and 60.9% reported having an income that was less than their expenses. Unemployed patients had significantly higher scores on the Emotional Well-Being subscale than other groups, while patients with lower income had significantly lower scores. Moreover, low-income patients had significantly lower Energy/Fatigue and total quality of life scores ($p < .05$). Last, regarding the use of vehicles, patients who did not drive got significantly lower scores on all subscales except Effects of Medication ($p < .05$).

When we evaluated the patients according to their clinical characteristics, we observed that patients with a seizure frequency of 6 or more per month had significantly lower scores on all subscales except Emotional Well-Being ($p < .05$). Patients with refractory epilepsy and patients receiving polytherapy had significantly lower scores on all subscales and Total Quality of Life ($p < .05$).

Table 3. Socio-demographic and clinical characteristics of participants and QOLIE-31

Variables	Seizure Worry	Overall Quality of Life	Mood	Energy/Fatigue	Cognition	Medication Effects	Social Function	Total
Age								
18-25	41.4± 19.8	32.3± 10.2	50.3± 13.5	42.1± 15.6	63.0± 16.0	65.1± 23.7	66.5± 23.1	53.4± 13.7
26-35	46.2± 22.4	34.1± 10.7	51.4± 13.2	42.9± 15.4	63.2± 17.3	64.1± 26.0	68.1± 21.6	54.6± 13.1
35-77	50.6± 18.9	35.1± 9.0	57.6± 10.2	45.5± 15.0	67.2± 13.5	70.1± 23.5	70.0± 17.5	58.0± 10.0
p-value	**0.049**	0.299	0.009	0.487	0.333	0.433	0.686	0.156
Gender								
Female	40.9±22.4	32.9± 10.3	50.7± 13.7	41.1± 14.6	63.5± 16.7	62.9± 25.7	65.5± 23.0	53.2 ± 13.6
Male	49.1±18.2	34.1± 10.1	53.8± 12.2	45.1± 15.9	64.4± 15.2	68.8± 22.8	70.1± 19.6	56.3 ± 12.0
p-value	**0.005**	0.421	0.093	0.067	0.680	0.087	0.137	0.085
Marital status								
Married	47.5± 20.3	35.0± 9.7	54.1± 12.6	44.2± 15.0	66.3± 15.2	67.8± 23.6	70.9± 19.4	56.9 ± 11.7
Single	42.95± 21.0	32.3± 10.4	50.6± 13.2	42.2± 15.7	62.3± 16.4	64.1± 25.1	65.2± 22.7	53.0 ± 13.5
p-value	0.122	0.060	0.059	0.342	0.054	0.295	0.063	**0.029**
Level of education								
Uneducated	36.8± 21.9	27.9± 11.4	47.7± 15.6	36.9± 25.9	56.4± 16.0	62.6± 24.2	54.7± 27.2	47.0±14.6
Primary education	51.0± 20.2	33.4± 10.6	52.7± 10.5	44.8± 15.4	63.5± 14.7	69.0± 24.4	70.3± 16.5	56.0± 9.9
High school and above	45.3± 19.9	33.3± 9.0	53.4± 12.8	44.4± 14.9	66.5± 15.8	65.6± 24.6	71.0± 19.5	56.7± 12.4
p-value	**0.008**	**0.001**	0.063	**0.023**	**0.003**	0.494	**0.001**	**0.001**
Employment status								
Yes	44.0± 21.5	32.9± 10.5	50.9± 13.2	41.7± 14.5	62.8± 16.4	65.0± 24.1	67.1± 22.5	53.8± 13.3
No	47.0± 19.1	34.9± 9.3	55.2± 12.3	46.3± 17.1	66.6± 14.8	67.6± 25.3	69.3± 18.	57.0± 11.6
p-value	0.349	0.202	**0.030**	0.055	0.125	0.494	0.501	0.098
Income level								
Income less than expenses	49.8± 13.0	40.4± 15.2	62.9± 15.7	64.8± 23.4	64.8± 23.4	66.5± 23.4	66.5± 21.4	53.2± 12.7
Income equals expenses	55.3± 13.9	47.3± 16.2	63.1± 17.5	63.1± 17.5	64.1± 26.4	64.1± 26.4	66.3± 22.5	55.4± 13.8
More income than expenses	56.7± 9.8	47.4± 12.7	69.5± 13.6	69.5± 13.6	72.2± 25.0	72.2± 25.0	75.0± 18.8	59.8± 10.7
p-value	0.485	0.067	**0.005**	**0.007**	0.109	0.284	0.129	**0.035**
Comorbidity								
Yes	41.1± 21.4	29.9± 11.1	50.8±15.5	40.3±15.5	59.1± 16.4	62.1± 26.3	60.7± 25.4	50.5± 14.4
No	46.7± 20.3	35.2± 9.3	52.8±11.8	44.4± 11.8	66.2± 15.35	67.5± 23.4	71.1± 18.5	56.7± 11.6
p-value	0.074	**0.001**	0.293	0.076	**0.003**	0.147	**0.001**	**0.001**
Seizure frequency								
No seizures in the last year	54.1± 22.5	36.8± 10.6	54.2± 13.5	47.5± 16.0	67.9± 17.9	70.6± 26.2	75.3± 21.8	59.6± 13.2
1-5 /month	43.4± 18.4	32.9± 9.3	52.1± 12.2	42.0± 14.2	64.2± 13.5	67.4± 20.7	67.0± 19.1	54.4± 11.1
6 or >6/month	29.2± 17.6	27.8± 11.3	47.4± 15.9	37.3± 18.3	51.7± 18.6	42.9± 28.4	52.0± 24.9	44.0± 15.1
p-value	0.001	0.001	0.123	0.016	0.001	0.001	0.001	0.001
Epilepsy type (onset)								
Fokal	46.7± 22.0	34.1± 9.5	53.3± 11.2	41.7± 13.2	67.4± 15.8	69.0± 24.0	68.9± 19.7	56.2± 12.3
Generalized	44.0± 19.8	34.4± 9.2	52.0± 12.5	43.1± 14.9	65.4± 14.7	66.7± 24.6	70.1± 20.2	55.7± 12.0
Unknown	44.8± 21.7	30.9± 12.6	51.3± 16.0	44.7± 18.8	56.6± 16.9	59.8± 24.1	61.4± 25.0	50.9± 14.8
p-value	0.739	0.134	0.730	0.624	**0.001**	0.143	0.068	0.071
Number of ASM taken								
Monotherapy	50.8± 18.6	37.0± 8.3	54.6± 11.6	45.1± 14.6	67.9± 15.2	70.8± 24.0	74.5± 16.9	59.0± 11.0
Polytherapy	38.1± 21.1	29.3± 10.6	49.3± 14.0	40.7± 16.1	59.4± 15.7	59.8± 23.4	59.9± 23.5	49.8± 13.2
p-value	**0.001**	**0.001**	**0.004**	**0.004**	**0.001**	**0.001**	**0.001**	**0.001**
Seizure control								
Uncontrolled	28.4± 17.0	24.4± 11.0	45.9± 14.8	36.4± 17.0	52.8± 13.2	51.7± 26.4	47.2± 22.3	42.7± 11.8
Controlled	50.0± 19.2	36.2± 8.2	54.1± 11.9	45.1± 14.3	67.3± 15.2	70.0± 22.2	74.05± 16.9	58.4.± 10.8
p-value	**0.001**	**0.001**	**0.001**	**0.001**	**0.001**	**0.001**	**0.001**	**0.001**
Use of vehicles								
Yes	51.4± 19.9	36.7± 8.7	57.0± 12.8	47.4± 16.5	68.8± 16.7	69.9± 26.2	76.5± 17.9	60.2± 12.0
No	42.5± 20.6	32.3± 10.5	50.4± 12.7	41.5± 14.7	62.1± 15.3	64.2± 23.7	64.4± 21.8	52.7± 12.6
p-value	**0.006**	**0.005**	**0.001**	**0.015**	**0.007**	0.135	**0.001**	**0.001**

Discussion

Using QOLIE-31, the Turkish version of an epilepsy-specific questionnaire, we examined the quality of life and employment status of patients with epilepsy and the factors affecting these conditions. Our results identified several factors that significantly impact the quality of life of patients with epilepsy, including marital status, level of education, income level, driving and frequency of seizures, seizure control and number of anti-seizure drugs. Patients received the lowest score for on the Total Quality of Life subscale and the highest on the Social Function subscale. Regarding these aspects, the managment of patients experiencing physical and psychosocial difficulties is possible with appropriate recommendations regarding psychological, social, and medical care (11).

Patients' sociodemographic characteristics can affect their quality of life. In our study, despite no significant difference in Total Quality of Life scores between younger participants and females, both groups received significantly lower scores for Seizure-Related Anxiety. Although multiple studies have shown that being female is a significant determinant of low quality of life (12, 13), multiple studies have also not observed that relationship (14, 15). These mixed results may indicate some intercultural differences between countries, for being female can be an important predictor of poor quality of life in countries where health and social care for females is inconsistent. Even so, poorer quality of life among females with epilepsy has also been reported in developed countries, which likely reflects some biological and psychosocial factors affecting their quality of life (13). Studies evaluating age's effect on quality of life have also produced conflicting results. In addition to studies showing that patient age is negatively related to quality of life (16), other studies have also shown that the health-related quality of life of people with epilepsy does not depend on age, as in our study (17, 18).

It has additionally been documented that patients with epilepsy have lower levels of education and income and experience relative difficulty in securing employment (19). A low level of education is indeed associated with unemployment (9). A study comparing the quality of life between patients with epilepsy and healthy controls in the same environment, with the same social relationships, and under the same living conditions showed a lower level of education, higher unemployment rate, higher unskilled employment rate and lower income among patients than controls (20). In our study, patients' scores for Seizure-Related Concerns, Total Quality of Life, Energy/Fatigue, Cognitive Function, Social Function, and total quality of life were significantly lower among patients with lower levels of education. However, the relationship between employment status and quality of life remains controversial in the literature. Although some studies have revealed that employment status is a primary factor affecting quality of life (21, 22), others have shown that socioeconomic status does not predict quality of life (23).

In a literature review of 95 articles reporting the employment status of people with epilepsy, an average employment rate of 58% was found (24). Employment makes a major contribution to the quality of life of people with epilepsy (4), because having a job not only facilitates financial independence but also reinforces self-esteem and supports social functioning (25). Even so, the 69.8% of patients who were unemployed in our study had significantly higher scores on the Emotional Well-Being subscale than all other groups. However, 60.9% of those patients also stated that their income was less than their expenses, and patients with low income had significantly lower Energy/Fatigue and Total Quality of Life scores. Although the mean Total Quality of Life and all subscale scores for unemployed patients with epilepsy were lower than for patients with epilepsy working in any job, the effect of employment status on quality of life did not make a significant difference as in the past research (23). Especially in the province where our study was conducted, unemployment and low income are common in the general population(26), which may explain why employment status did not significantly affect reported quality of life among the patients in our study.

The factors with the most significant impact on quality of life in our study were clinical features. It is suggested in the literature that polytherapy negatively affects the quality of life of patients with epilepsy and that the quality of life scores of patients receiving polytherapy are less than those of patients receiving monotherapy (23). In particular, Taskıran et al. (27) found a negative correlation between drug use and quality of life but also found that freedom from seizures was a positive factor affecting quality of life.

The literature demonstrates a lack of consensus about the effects of monotherapy and polytherapy on quality of life (28). Some studies have shown that the increased use of anti-seizure drugs or polytherapy is associated with decreased health-related quality of life (28) whereas others have not proven any association (15). In a recent study, the number of anti-seizure drugs was found to predict quality of life among patients with epilepsy, and the more anti-seizure medications taken by the patients, the lower their scores for Total Quality of Life (29). In our study, patients with refractory epilepsy and/or receiving polytherapy had significantly lower scores than other patients on all subscales. In terms of pharmacotherapy, our study revealed that patients taking two or more anti-seizure drugs had lower quality of life scores than ones receiving monotherapy. Accordingly, along with the adverse effects of anti-seizure drugs(30), the number of different anti-seizure drugs used by each patient should be carefully considered when making decisions about treatment. Our results also confirm that poor seizure control combined with a high frequency of seizures is significantly associated with poor quality of life. Patients who had not had a seizure in the past year had the highest score for Total Quality of Life and highest scores on all subscales. In a recent study,

people with epilepsy taking three or more anti-seizure drugs reported poorer health and were more likely to have difficulty performing daily activities than ones taking only two anti-seizure drugs (31). Previous studies have also suggested that a greater number of anti-seizure drugs is associated with worse quality of life, possibly due to an increased risk of multidrug-related side effects (32, 33). Since patients with well-controlled epilepsy have been shown to have a quality of life similar to control participants (34), and frequency of seizures is a key factor influencing quality of life (35), the higher number of seizures may contribute to patients' poorer quality of life.

Possible causes of poorer quality of life due to a higher frequency of seizures include seizure-related injuries, fear of new seizures, and limitations in daily life, including driving (7). This may also be due to taking more anti-seizure medications to reduce the frequency and severity of seizures, resulting in the potential for more side effects. (7).

In some countries, having a driver's license and transportation to work are important factors affecting employment (36). Driving restrictions have been shown to carry social stigma and limit the employment of patients with epilepsy, regardless of seizure status (37). In a study evaluating the chief variables affecting quality of life among patients with epilepsy, patients who did not drive in their daily lives had lower scores for quality of life and some subscales (i.e., Emotional Well-Being, Energy/Fatigue, Cognitive Function, and Social Function) (29) In our study, besides driving, patients who did not drive had significantly lower scores on all subscales except Effects of Medication. The purpose of driving restrictions for patients with epilepsy is public as well as personal safety; however, the same restrictions also prevent patients with seizures from socializing, being employed, and maintaining self-confidence. The freedom to drive has indeed been recognized as an important determinant of social independence and quality of life among patients with epilepsy (38).

Limitations

Although our sample was formed in a third-level epilepsy clinic, our results are not sufficient for generalization due to the study's sample size and cross-sectional nature. More comprehensive multicenter studies are therefore needed on the subject.

Conclusion

Our study has shown that clinical characteristics such as seizure frequency, seizure control, and the number of anti-seizure drugs used have a more significant impact on quality of life than sociodemographic characteristics. The goal of treatment for epilepsy is to control seizures. However, in chronic diseases such as epilepsy, it is also important to consider the conditions accompanying patients in order to ensure the highest-possible quality of life. The use of validated measurement tools, including the QOLIE-31, to assess quality of life among patients with epilepsy should become routine clinical practice even if challenging. Information collected in that way can tailor treatment for those patients and improve outcomes by illuminating the impact of the disease and other modifiable factors in daily life.

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Conflict of interest

The authors have stated explicitly that there are no with this any financial support or relationships that may pose potential conflict of interest in this article.

Ethical Considerations & Disclosure

The study was approved by the Ethics Committee of Harran University's Faculty of Medicine (HRU/23.19.24).

Authors' Contributions

TGD: Data curation, Methodology, Conceptualization, Formal Analysis, Writing – original draft.

SH: Investigation, Methodology, Supervision, Validation.

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ORIGINAL ARTICLE

Evaluation of Adolescent and Adult Cases Presenting with Suicide Attempt: A Five-Year Retrospective Study

İntihar Girişimi İle Başvuran Adölesan ve Erişkin Yaştaki Olguların Değerlendirilmesi: Beş Yıllık Retrospektif Bir Çalışma

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ABSTRACT

Objective: The objective of this study is to evaluate the applications to the Emergency Departments in Uşak province between 2019 and 2023 due to suicide attempts and to provide guidance for social preventive programmes.
Material and Method: This cross-sectional study was conducted with the approval of the Uşak University Non-Interventional Research Ethics Committee, dated 21 September 2023 and numbered 176-176-09. The study examined The archive of the Uşak Provincial Health Directorate was consulted to obtain records of cases of suicide attempts among individuals aged 13 years and over between the years 2019-2023. These records were examined between 1 November-31 December 2023.
Results: A total of 947 patients participated in the study, 635 of whom were women. The majority of suicide attempts (43.2%) occurred between the ages of 13 and 24 years. The highest number of suicide attempts occurred between 18:00 and 23:59 (40.5%) and in summer (29.8%). The highest number of suicide attempts occurred in August (10.5%). The majority of those who attempted suicide were primary school graduates (47.0%) and unemployed (39.4%). The suicide attempt rate of farmers (42.9%) was significantly higher than other occupational groups (p=0.009). Family problems (31.3%) were the most common reason for suicide attempt. The most common method of suicide attempt was drug-toxic substance use (92.6%). Among the study participants, 21.1% had attempted suicide previously. Among those who attempted suicide, 24.2% had a previous psychiatric diagnosis. Medication (activated charcoal) was administered to 60.4% of the suicide attempters, while psychiatric consultation was requested for 11.5%. A total of 69.5% of the suicide attempts resulted in a single interview.
Conclusion: Most of the suicide attempters were adolescent and young age group, female, illiterate, primary school graduate and unemployed. According to our study, the most common causes and methods of suicide attempts were familial problems and drug-toxic substance use. It is recommended that regulations should be implemented to ensure psychiatric consultation for all suicide attempters and that the follow-up and treatment of suicide attempters should be carried out by a team consisting of family physicians, psychiatrists, psychologists and social workers.

Keywords: Suicide attempt, Drug-toxic substance, Demographic factors, Psychiatric consultation.

ÖZ

Amaç: Bu çalışmada, 2019-2023 yılları arasında Uşak ilindeki Acil Servislere intihar girişimi nedeniyle yapılan başvuruların değerlendirilmesi ve toplumsal koruyucu programlar için yol gösterici olması amaçlanmaktadır.
Gereç ve Yöntem: Bu kesitsel çalışma, Uşak Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulu'nun 21.09.2023 tarihli ve 176-176-09 numaralı onayıyla, 1 Kasım-31 Aralık 2023 tarihleri arasında Uşak İl Sağlık Müdürlüğü arşivinde bulunan 2019-2023 yılları arasındaki 13 yaş ve üzeri intihar girişimlerinde bulunan vakaların kayıtlarının incelenmesiyle gerçekleştirilmiştir.
Bulgular: Çalışmaya toplam 947 hasta katıldı, bunların 635'i kadındı. İntihar girişimlerinin çoğunluğu (%43,2) 13-24 yaş arasındaydı. En fazla intihar girişimi, saatlerine göre 18.00-23.59 arasında (%40,5) ve yaz mevsiminde (%29,8) gerçekleşti. En fazla intihar girişimi Ağustos ayında (%10,5) oldu. İntihar girişiminde bulunanların çoğunluğunu ilköğretim mezunları (%47,0) ve işsizler (%39,4) oluşturdu. Çiftçilerin (%42,9) intihar girişim oranı diğer meslek gruplarına göre anlamlı derecede daha yüksekti (p=0,009). Ailesel sorunlar (%31,3), en sık gözlenen intihar girişim nedeniydi. En sık kullanılan intihar girişim yöntemi ilaç-toksik madde kullanımıydı (%92,6). Çalışmaya katılanların %21,1'i daha önce intihar girişiminde bulunmuştu. İntihar girişiminde bulunanların %24,2'sinin daha önce psikiyatrik tanısı konulmuştu. İntihar girişiminde bulunanların %60,4'üne ilaç tedavisi (aktif kömür) uygulanırken, %11,5'ine psikiyatrik konsültasyon istendiği gözlendi. İntihar girişiminde bulunan vakaların %69,5'i tek görüşme ile sonuçlandı.
Sonuç: İntihar girişiminde bulunanların çoğu adölesan ve genç yaş grubundan, kadın, okur yazar olmayan, ilköğretim mezunu ve işsizlerden oluşmaktaydı. Çalışmamıza göre intihar girişimlerinin en sık nedeninin ve yönteminin ailesel sorunlar ve ilaç-toksik madde kullanımı olduğu saptandı. İntihar girişiminde bulunanların tamamına psikiyatrik konsültasyon yapılmasını sağlayacak düzenlemelerin uygulanması, intihar girişiminde bulunanların takibi ve tedavilerinin aile hekimi, psikiyatrist, psikolog ve sosyal hizmet uzmanlarından oluşan bir ekip tarafından yapılması önerilir.

Anahtar Kelimeler: İntihar girişimi, İlaç-toksik madde, Demografik özellikler, Psikiyatrik konsültasyon.

Introduction

The term "suicide" is defined as the death resulting from self-destructive behaviour with the intention of dying. In contrast, a "suicide attempt" is defined as a potentially self-destructive behaviour with the intention of death, but not fatal (1).

The World Health Organization (WHO) reports that 703,000 people die by suicide each year. There are more than 20 suicide attempts for every suicide. Previous suicide attempts are one of the most significant risk

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factors for suicide. Other risk factors include psychiatric illnesses, alcohol and drug use, separation or divorce, violence, harassment, economic problems, illnesses, chronic pain, losses, conflicts, disasters and social isolation. Suicide is the fourth most common cause of death between the ages of 15 and 29, with 77% of suicides occurring in middle and low-income countries (2). In Turkey, the number of suicides has risen from over 3,000 annually since 2012 to 4,158 per year as of 2021. The most common age groups in which suicide was observed were 25-29 years old (n=523), 20-24 years old (n=508) and 30-34 years old (n=448), respectively (3).

Protective factors related to suicide include self-esteem, self-efficacy, social skills, family and friendship relationships. Individuals with positive levels of self-esteem and self-efficacy tend to exhibit higher problem-solving and coping skills, which in turn result in a lower incidence of suicide attempts. Individuals with high levels of social anxiety are unable to establish effective support networks or have difficulty accessing them, which results in elevated suicide rates (4). In suicide-related deaths, hanging is the most prevalent method, with a higher prevalence among men, whereas drugs are more commonly used by women who attempt suicide (5).

Materials and Methods

Study Design and Data Collection Form

This cross-sectional study was conducted between 1 November and 31 December 2023. The study analysed all files in the archive of the Uşak Provincial Health Directorate between 2019 and 2023, which were admitted due to suicide attempt/crisis. Cases in which the standard suicide attempt/crisis form of the Ministry of Health was completed were included in the study. The form included the reason for presentation, sociodemographic characteristics, time of suicide attempt, time of arrival at the emergency room, method of suicide, reason for suicide, previous suicide attempts, treatment and follow-up status in the last six months, type of medical treatment applied and presence of psychiatric consultation.

Participants

As the standard suicide attempt/crisis form is completed for cases with a minimum age of 13 years, applicants from this age group were included in the study. The data set comprised the records of cases aged 13 years and over admitted to the emergency departments of the hospitals in Uşak province for suicide attempt/crisis between 2019 and 2023. The data were sourced from the archive of the Uşak Provincial Health Directorate.

Ethical Considerations

The requisite permissions and approvals were duly obtained from the Uşak University Non-Interventional Research Ethics Committee (21 September 2023, Decision No. 176-176-09).

Statistical Analysis

The data obtained in this study were analysed using the SPSS 22 package programme. Frequency and percentage distributions of the data were presented. The relationship between variables was examined using the Chi-Square independence test, with a significance level of 0.05. The results were interpreted as follows: $p<0.05$ indicated a significant dependence, while $p>0.05$ indicated no significant dependence.

Results

The distribution of patients according to the reasons for presentation to the emergency department is as follows: 97.7% (n=904) suicide attempts, 1.4% other reasons, 0.5% suicide threats and 0.3% crisis. The study included 904 patients who were admitted due to a suicide attempt. Of the participants, 67.2% (n=607) were female. It was observed that females attempted suicide at a significantly higher rate than males (p=0.0001). The mean age of the women who participated in the study was 28.90 ± 10.9 (min-max 13.0-72.0), while the mean age of the men was 30.88 ± 10.9 (min-max 15.0-71.0).

Table 1. Sociodemographic Characteristics of Suicide Attempters

	Gender	Woman		Man		Total	
	Number / Percentage	n	%	n	%	n	%
Age groups	13-24	283	46.9	105	35.5	388	43.2
	25-34	148	24.5	85	28.7	233	25.9
	35-49	144	23.9	76	25.7	220	24.5
	50-64	22	3.6	24	8.1	46	5.1
	>65	6	1.0	6	2.0	12	1.3
	Total	603	67.1	296	32.9	899	100.0
Marital status	Married	251	41.7	116	39.6	367	41.0
	Single	300	49.8	158	53.9	458	51.2
	Divorced	29	4.8	10	3.4	39	4.35
	Widow	17	2.8	6	2.0	23	2.6
	Engaged	2	0.3	1	0.3	3	0.3
	Living separately	3	0.5	2	0.7	5	0.6
	Total	602	67.3	293	32.7	895	100.0
Education status	Illiterate	15	2.5	7	2.4	22	2.4
	Literate	66	10.9	29	9.8	95	10.6
	Primary education	267	44.2	156	52.9	423	47.0
	High School	161	26.7	70	23.7	231	25.7
	University	68	11.3	24	8.1	92	10.2
	Unknown	27	4.5	9	3.0	36	4.0
	Total	604	67.2	295	32.8	899	100.0
Profession Group	Unemployed	143	43.6	79	36.9	222	41.0
	Other	50	15.2	69	32.2	119	22.0
	Labour	35	10.7	31	14.5	66	12.2
	Housewife	43	13.1	0	0.0	43	7.9
	Not specified	20	6.1	15	7.0	35	6.5
	Student	25	7.6	3	1.4	28	5.2
	Pensioner	7	2.1	8	3.7	15	2.8
	Farmer	5	1.5	9	4.2	14	2.6
	Total	328	100.0	214	100.0	542	100.0

A statistically significant relationship between marital status and past suicide attempts was not observed (p=0.161). However, a non-statistically significant trend was identified, whereby those who were separated, widowed or divorced had a higher rate of suicide attempts in the past.

Table 2. Basic Characteristics of Suicide Attempt - 1

	Gender	Woman		Man		Total	
	Number / Percentage	n	%	n	%	n	%
Suicide attempt time interval	06.00-11.59	69	11.7	32	11.3	101	11.6
	12.00-17.59	134	22.8	58	20.4	192	22.0
	18.00-23.59	236	40.1	118	41.5	354	40.5
	24.00-05.59	150	52.5	76	26.8	226	25.9
	Total	589	100.0	192	22.0	873	100.0
The season of the suicide attempt	Winter	144	23.8	78	26.3	222	24.6
	Spring	156	25.8	78	26.3	234	25.9
	Summer	186	30.7	83	27.9	269	29.8
	Autumn	119	19.7	58	19.5	177	19.6
	Total	605	100.0	297	100.0	902	100.0
Month of Suicide Attempt	January	66	10.9	25	8.4	91	10.09
	February	39	6.5	21	7.1	60	6.7
	March	60	9.9	21	7.1	81	9.0
	April	43	7.1	20	6.7	63	7.0
	May	53	8.7	37	12.5	90	10.0
	June	53	8.7	31	10.4	84	9.3
	July	67	11.1	23	7.7	90	10.0
	August	66	10.9	29	9.8	95	10.5
	September	49	8.1	22	7.4	71	7.9
	October	44	7.3	25	8.4	69	7.7
	November	39	6.5	27	9.1	66	7.3
	December	26	4.3	16	5.4	42	4.7
	Total	605	100.0	297	100.0	902	100.0
Year of Suicide Attempt	2019	178	29.4	83	27.9	261	28.9
	2020	88	14.5	42	14.1	130	14.4
	2021	65	10.7	38	12.8	103	11.4
	2022	143	23.6	68	22.9	211	23.4
	2023	131	21.7	66	22.2	197	21.8
	Total	605	100.0	297	100.0	902	100.0
Suicide Attempt Location	City centre	486	80.5	239	80.5	725	80.5
	Rural	118	19.5	58	19.5	176	19.5
	Total	604	100.0	297	100.0	901	100.0

attempted suicide before (30.4%) was significantly higher than in other years.

Among those who attempted suicide, 24.2% (n=206) (F: 22.9%, M: 26.8%) had a previous psychiatric diagnosis. A significant correlation was observed between those with a previous psychiatric diagnosis and suicide attempts (p=0.0001). The prevalence of previous suicide attempts was found to be significantly higher among individuals with a psychiatric diagnosis (50.2%) than among those without a diagnosis (11.7%).

The rate of previous suicide attempts in the families of the participants was 4.9% (n=42). This rate was 5% (n=29) in women and 4.6% (n=13) in men. There was a statistically significant correlation between the rate of previous suicide attempts in the family and the rate of previous suicide attempts in the participants (p=0.0001). The rate of previous suicide attempts was found to be significantly higher in those with a family history of suicide attempts (47.5%) than in those without a family history of suicide attempts (18.8%).

In 6.0% (n=51) (F: 6.3%, M: 5.5%) of the families of suicide attempters, a psychiatric diagnosis had been made previously. The most common psychiatric diagnoses were as follows: 41.7% unspecified (F: 40.0%, M: 44.4%), 16.7% depression (F: 20.0%, M: 11.1%), 12.5% anxiety disorder (F: 13.3%, M: 11.1%) and 12.5% bipolar disorder (F: 13.3%, M: 11.1%). A significant correlation was observed between the participants who had a previous psychiatric diagnosis in their family and the participants' previous suicide attempts (p=0.0001). The rate of previous suicide attempts in those with a family history of psychiatric diagnosis (54.9%) was significantly higher than those without a family history of psychiatric diagnosis (18.0%). No significant relationship was observed between family psychiatric diagnoses and suicide attempts (p>0.05).

The rate of psychiatric follow-up or treatment in the last six months among those who attempted suicide was 23.4% (n=199) (F: 24.0%, M: 21.9%). The proportion of those who received drug treatment was 73.7% (F: 75.4%, M: 70.3%), psychotherapy was 7.0% and other treatments was 19.4%. There was a significant relationship between receiving psychiatric follow-up or treatment in the last six months and suicide attempts (p=0.0001). Among those who had received psychiatric follow-up or treatment in the last six months, the proportion of those who had attempted suicide before (44.4%) was significantly higher than those who had not received follow-up or treatment (13.5%). No significant correlation was observed between the treatment modality (e.g. medication, psychotherapy, psychotherapy and other) and previous suicide attempts among those who received psychiatric follow-up or treatment in the last six months (p>0.05).

Table 3. Years of Suicide Attempt and Previous Suicide Attempt

		2019		2020		2021		2022		2023		Total		Chi-Square Analysis	
Number / Percentage		n	%	n	%	n	%	n	%	n	%	n	%	Chi-Square	p
Has he/she attempted suicide before?	Yes	41	16.8	31	24.0	31	30.4	37	18.4	43	22.5	183	21.1	9.76	0.045

A statistically significant correlation was not found between educational status and past suicide attempts (p=0.053). The rates of suicide attempts in the past of those with primary and high school education were found to be 24.0% and 22.1%, respectively, higher than the other groups.

The highest rate of suicide attempts was observed among the unemployed. A significant difference was found between the rate of previous suicide attempts in farmers (42.9%) and in other occupational groups (p=0.009).

A statistically significant relationship was not observed between gender and the year of suicide attempt (p=0.912). Although not statistically significant, it was found that the rate of previous suicide attempts was higher in rural areas.

There was a significant correlation between previous suicide attempts and the year of suicide attempt (p=0.045). In 2021, the proportion of those who had

Table 4. Basic Characteristics of Suicide Attempt - 2

	Gender		Woman		Man		Total
	Number / Percentage	n	%	n	%	n	%
	Family problems	195	33.3	80	27.3	275	31.3
	No reason given	141	24.1	82	28.0	223	25.4
	Mental illness	44	7.5	26	8.9	70	7.9
	Communication problems	30	5.1	13	4.4	43	4.9
	Problems with the opposite sex	30	5.1	10	3.4	40	4.5
	Domestic violence	28	4.8	9	3.0	37	4.2
	Loneliness	15	2.6	11	3.8	26	2.9
	Economic	4	0.7	19	6.5	23	2.6
	Alcohol and substance addiction	6	1.0	12	4.1	18	2.0
	Parental conflicts	13	2.2	2	0.7	15	1.7
	Job	6	1.0	7	2.4	13	1.5
	Developmental problems	11	1.9	1	0.3	12	1.4
Reasons for Suicide Attempts	Marriage	8	1.4	4	1.4	12	1.4
	Children	11	1.9	1	0.3	12	1.4
	Disease	6	1.0	5	1.7	11	1.2
	Test anxiety	8	1.4	3	1.0	11	1.2
	School	8	1.4	2	0.7	10	1.1
	Homeless	5	0.5	2	0.7	7	0.8
	Chronic illness	4	0.7	1	0.3	5	0.6
	Harassment	5	0.9	0	0.0	5	0.6
	Death and Loss	1	0.2	3	1.0	4	0.4
	Rape	3	0.5	0	0.0	3	0.3
	Sexual problems	3	0.5	0	0.0	3	0.3
	Total	585	66.6	293	33.4	878	100.0
Suicide Attempt Method	*Drug-toxic substance*	572	94.9	261	87.9	833	92.6
	With a cutting instrument	19	3.2	15	5.1	34	3.8
	Hanging	4	0.7	12	4.0	16	1.8
	Jumping from a height	5	0.8	2	0.7	7	0.8
	Unknown	1	0.2	3	1.0	4	0.4
	Firearm	0	0.0	2	0.7	2	0.2
	Other	2	0.3	0	0.0	2	0.2
	Bottled gas, natural gas	0	0.0	1	0.3	1	0.1
	Jumping under the vehicle	0	0.0	1	0.3	1	0.1
	Total	603	100.0	297	100.0	900	100.0
	*Not stated**	25	23.4	22	37.9	47	28.5
	Depression	31	29.0	11	19.0	42	25.5
	Anxiety disorder	24	22.4	12	20.7	36	21.8
Previous psychiatric diagnosis	*Bipolar disorder*	11	10.3	5	8.6	16	9.7
	Other	8	7.5	3	5.2	11	6.7
	Panic Attack	5	4.7	2	3.4	7	4.2
	Alcohol and substance abuse	3	2.7	3	5.2	6	3.6
	Total	107	100.0	58	100	165	100.0
Has he/she attempted suicide before?	Yes	120	20.6	63	22.0	183	21.1
	No	463	79.4	223	78.0	686	78.9
	Total	583	100.0	286	100.0	869	100.0
Psychiatric consultation requested?	Yes	54	10.1	39	14.3	93	11.5
	No	480	89.9	233	85.7	713	88.5
	Total	534	100.0	272	100.0	806	100.0
Case Outcome	Single visit	431	70.7	199	67.0	630	69.5
	Psychiatry outpatient clinic referral	135	22.2	79	26.6	214	23.6
	Referral to another institution	20	3.3	12	4.0	32	3.5

*** Not stated:** It defines the cases who answered "yes" to the question of whether they had a previous psychiatric diagnosis in the questionnaire form, but did not know or did not want to tell their psychiatric diagnosis.

Medication (activated charcoal) was administered to 60.4% (n=498) (F: 61.0%, M: 59.3%) of those who attempted suicide. The number of people to whom other treatments were applied was 36 in total.

Discussion

The findings of this study indicate that individuals who have attempted suicide exhibit a number of characteristics. These include a history of suicide attempts, a female gender, familial issues, a low socio-economic status, a lack of education, psychiatric disorders and an easy access to drugs and poisons. The identification and analysis of the characteristics of suicide attempters may prove instrumental in the prevention of future suicides.

A systematic review and meta-analysis study conducted by Miranda-Mendizabal et al. revealed that female gender was 1.96 times more likely to attempt suicide than males (6). Another study conducted on adolescents indicated that girls were significantly more likely to attempt suicide due to conflicts with their parents and peers, guilt, helplessness and loneliness. Male adolescents are more likely to attempt suicide as a result of pressure (e.g. from peers or cyber environments) (7). A study on soldiers showed that workplace difficulties increased the suicide risk of female soldiers more than their male counterparts (8). Tsirigotis K. et al. found that although women attempted suicide more frequently, they were more likely to survive compared to men, while men were more likely to complete suicide and choose more violent suicide methods (9). In this study, it was observed a similar pattern to that observed in the literature, namely that females were more likely to attempt suicide. We hypothesise that this is due to the fact that women are more likely to use suicide attempts as a method of seeking help.

In two different studies conducted in our country, it was observed that approximately half of the suicide attempts (49.8%-48.1%) occurred in the evening (18.00-23.59) hours (10,11). In this study, similar to the literature, 40.5% of suicide attempts occurred between 18.00-23.59 pm. Considering that the most common reason for suicide attempts is familial problems, we think that suicide attempts increase in the evening hours when the family gathers together due to an increase in family conflicts.

A review of the literature reveals that suicide attempts are most prevalent in the summer and spring seasons (11-13). This study found that the majority of suicide attempts occurred in the summer (29.8%) and spring (25.9%) seasons, in accordance with the literature. It is postulated that the exacerbation of underlying psychiatric disorders, the announcement of university examinations and their results, and the return to family life following the closure of educational institutions may be among the potential reasons for the observed increase in suicide attempts during these seasons.

A gradual decline in the incidence of suicide and suicide attempts was observed in France between 2009 and 2018. The average annual decrease was 14.5% for suicide and 11.7% for suicide attempts (13). According to the Turkish Statistical Institute (TÜİK), the crude suicide rate of Uşak province was lower than the national average (4.21) in 2019 (2.44), but higher than the national average in In 2020, the suicide rate was 5.95 per 100,000 inhabitants, while in 2021 it was 6.46 per 100,000 inhabitants. In 2022, the rate increased to 10.15 per 100,000 inhabitants (3). In this study, the rate of suicide attempts in 2022-2023 was found to be significantly higher than in other years. It is hypothesised that this is due to a number of factors, including the impact of the COVID-19 pandemic on the emergence of new mental health issues and the exacerbation of existing ones, as well as the socioeconomic challenges experienced in the post-pandemic period. Furthermore, the postponement of routine health screenings due to the pandemic has made it more difficult for individuals to access health services during this period.

A study conducted in Sweden observed that the rates of completed suicide and suicide attempts were higher in rural and semi-rural areas than in cities (14). Another study conducted in Erzurum found that 75.6% of suicide attempts took place in the city centre, while the rest occurred in villages and districts (15). In the present study, 4/5 of the suicide attempts took place in the city centre, while the remaining attempts occurred in the districts. It is postulated that the fact that the majority of the Uşak population (69.3%) resides in the city centre may contribute to this elevated rate (16). While not statistically significant, the rate of previous suicide attempts was higher in those residing in rural areas. Potential factors contributing to this result include difficulties in accessing psychiatric care following a suicide attempt in rural areas, a lack of adequate follow-up and treatment, and the ease of access to drugs and toxic substances.

In Türkiye, 75% (n=3111) of those who committed suicide in 2022 were male. While the number of men and women who committed suicide was equal in Uşak province in 2017 (F:6, M:6), the majority of those who committed suicide in the following years were men (17). In a study by San Sebastián et al, suicide attempts were generally observed in young people and women (M/F: 106.2-252.3/100,000) (14). In another study conducted in France, 62% of suicide attempts were made by women in the 15-19 and 40-49 age groups (13). In this study, similar to the literature, 2/3 of the attempted suicides were female and 43.2% were in the 13-24 age group.

A study by Yağcı et al. found no significant association between marital status and suicide attempts (18). However, another study found that the risk of a repeat suicide attempt increased in unmarried individuals (19). In this study, although it was not statistically significant, it was found that the rate of suicide attempts was higher in separated, widowed and divorced individuals, similar to the literature. While marriage may reduce the risk of suicide due to factors such as the presence of social support systems and finding

meaning in life, marital status other than marriage has been associated with factors such as social isolation and lack of support.

Several studies have found that low levels of education are associated with increased rates of suicide attempts (20, 21). For example, a study conducted in Denmark found that more than a third of people in the 16-20 age group who attempted suicide had not completed upper secondary school (21). In this study, almost half of the people who attempted suicide were illiterate (2.4%) and had completed primary school (47.0%). Reasons for the association of low educational attainment with increased suicide attempts include socioeconomic vulnerability, limited access to help and inability to cope with stressors that lead to suicide attempts.

A meta-analysis and systematic review study found that unemployment was associated with repeated suicide attempts (19). Another study conducted in Greece during the economic crisis found a negative association between regional unemployment and suicide attempt rates in men and women (22). The recent global COVID-19 pandemic has led to an increase in the frequency of suicide and suicide attempts, which can be attributed to a number of factors, including unemployment, economic difficulties, social isolation, loneliness, and mental and physical burnout (23, 24). In this study, more than half of those who attempted suicide were unemployed or housewives. We believe that being employed has a protective effect against suicide attempts through self-esteem, self-efficacy, socioeconomic status and social relationships. The rate of previous suicide attempts among farmers was 42.9%, which was significantly higher than in the other occupational groups.

The lethality of suicide methods is determined by the time between the initiation of the suicidal act and the probable expected death. A long duration of this period may reduce lethality by increasing the likelihood that the person will change their mind and seek medical help (5). In various studies carried out in our country, the most common method of attempted suicide (82.5%-83.6%) is drug overdose (25, 26). In studies conducted abroad, 80.0%-95.9% of suicide attempts were due to drug intoxication (13, 22). In this study, the most common methods of suicide were drug intoxication (92.6%), cutting and hanging. We believe that easy access to drugs and poisonous substances and the fact that most of the attempted suicides were female led to a preference for this method, which is less likely to be fatal than other methods.

In several studies conducted in Türkiye, the most common reasons for suicide attempts were domestic discord and problems with the opposite sex (25, 26). In a study conducted by Polat et al, 57.5% were accompanied by psychiatric disorders (25). It was found that about two thirds of suicide attempts were accompanied by psychiatric disorders, the most common of which were mood changes (54%) (13). In the present study, family problems (31.3%), no reason given and mental illness were in the first three ranks of the distribution of reasons for attempted suicide. In addition, the fact that the fourth most common reason among men was economic reasons (6.5%) is striking in terms of the impact of the pandemic on society. The fact that family problems are so high compared to other reasons shows that there are serious problems in family communication. In addition, the fact that family problems are considered taboo in Turkish society means that outside intervention is not welcomed and is a serious obstacle to seeking professional help.

The fact that a person has attempted suicide before is an important risk factor for attempting suicide again. This is particularly important in the first year after the suicide attempt (15, 22). In a study by Fountoulakis et al, approximately half of the suicide attempters attempted suicide within the same year and 75% attempted suicide again within two years (22). In a study conducted in Türkiye, the rate of previous suicide attempts was 12.5% (25). In this study, about a fifth of the participants (21.1%) had previously attempted suicide. We believe that failure to address the conditions that led to a previous suicide attempt, failure to provide appropriate follow-up and treatment, and crossing an important psychological threshold in this regard facilitate a reattempt.

A family history of suicide attempts is an important risk factor (18). The rate of suicidal ideation was 2.09 times higher in patients with a family history of suicide attempts (27). In the study by Deveci et al, this rate was 8.8% (28). The rate of previous suicide attempts in the families of the study participants was 4.9%. In this study, a statistically significant correlation was observed between the presence of previous suicide attempts in the family and previous suicide attempts in the individual. We believe that the presence of suicide attempts in the family history sets a bad example for family members.

In the literature, several studies have reported that the presence of psychiatric disorders (such as major depressive disorder, conduct disorder, attention-deficit/hyperactivity disorder) is an important risk factor for suicide attempt (25). The most common psychiatric disorder associated with suicide attempts is depression (18). In the study by Ünlü et al, 65.6% of suicide attempters were found to have a psychiatric disorder, whereas in our study this rate was 24.2% (26). The most common psychiatric diagnoses were depression, anxiety and bipolar disorder. It is thought that psychiatric disorders negatively affect self-perception and self-efficacy, increase social anxiety and promote suicide attempts by increasing impulsivity.

In a study conducted in Norway, it was observed that those who had completed suicidal behaviour had inadequate risk assessment compared with those who had attempted suicide. Patients who had attempted suicide were found to have received only medication, whereas completed suicides were found to have received both medication and psychotherapy (29). In this study, similar to the literature, about one third of the

patients who attempted suicide had received drug treatment only. It is emphasised that those receiving psychiatric drug treatment should be subjected to a risk assessment for suicide attempt.

Requesting a psychiatric consultation may reduce the risk of recurrent suicide attempts (30). In different studies conducted in Türkiye, the rates of patients who attempted suicide in the emergency department without requesting psychiatric consultation ranged from 46.5% to 80.0% (25, 31). Considering that suicide attempts are usually not aimed at death, but rather a call for help, it is unfortunate that psychiatric consultation was requested in only 11.5% of the patients who attempted suicide in this study. Patients admitted to the emergency departments of hospitals following a suicide attempt are typically directed towards medical or surgical treatments, depending on the type of suicide attempt. Psychiatric consultations that should have been carried out after these treatments could not be carried out sufficiently due to a lack of sufficient consultant physicians (there are no psychiatrists in district hospitals), organisational failures, and patients' unwillingness to undergo psychiatric examination after acute medical and/or surgical treatment.

In this study, 69.5% of patients had a single visit, 23.6% were referred to psychiatry and only 1.6% were referred for follow-up. It has been shown in the literature that recurrent suicide attempts decreased in patients who were followed up, but it was noted that there was a serious lack of follow-up (32). Increasing the rate of referral to outpatient psychiatric services at case closure will increase the number of people who are included in follow-up.

Among the topics taught in the 6th year family medicine clerkship at various medical schools in our country are the definition of suicide risk and referral indications in depressed patients, family dynamics and domestic violence. (33). The psychiatry rotation of the Family Medicine Residency training programme encompasses a range of key areas, including the application of a biopsychosocial approach, the screening and treatment of individuals at risk, psychiatric interviewing, mental status assessment, the management of psychiatric emergencies and diseases, the referral and consultation process, and the approach to psychiatric patients and their families. Additionally, the training provides an in-depth understanding of the medical and psychological support skills required in this field. (34). It is our contention that family physicians who have undergone these training programmes will be better placed to respond effectively to instances of attempted suicide.

Limitations of the study include the presence of various deficiencies in the forms completed in emergency departments and the lack of follow-up information after the suicide attempt.

Conclusion

In conclusion, the majority of those who attempted suicide were adolescents and young people, unemployed, female, illiterate and primary school graduates. The most common reasons and methods were family problems and drug and toxic substance use.

Based on this picture, it is important to inform and offer solutions to people who attempt suicide, their families and society. In addition, it is necessary to ensure that all attempted suicides have access to psychiatric services. In regions where access to psychiatric services is difficult, appropriate coordination should be ensured. To this end, it is important to plan the necessary arrangements, starting with the emergency services.

In addition, as family physicians work in primary care, they have a critical role to play in the identification and appropriate management of patients who are or may be at risk of attempting suicide. Therefore, it is important for family physicians to implement practices that ensure continuity of care and treatment of the patient by a team consisting of a psychiatrist, psychologist and/or social worker following a suicide attempt.

Ethical Approval

In order to conduct the research, permission was obtained from the ethics committee of a Uşak university, dated 21 September 2023 and numbered 176-176-09. All principles of the Declaration of Helsinki were complied with throughout the study.

Conflict of Interest:

The authors declare that there is no conflict of interest.

Financial Disclosure:

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ORIGINAL ARTICLE

Evaluation of the Frequency of Blood Ammonia Test Requests in Clinic of Pediatrics Before and After the Establishment of the Department of Pediatric Metabolism

Pediatri Kliniklerinde Kan Amonyak Tetkiki İstenme Sıklığının Çocuk Metabolizma Bölümü Açılması Öncesinde ve Sonrasında Değerlendirilmesi

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ABSTRACT

Background/Aims: Hyperammonemia causes severe mortality and morbidity when left unnoticed. We aimed to compare the number of ammonia test requests before and after establishing the Department of Pediatric Metabolism (DPM) in a clinic of pediatrics.
Methods: The study was conducted retrospectively between 15/11/2022-16/11/2023. Study data were evaluated before (pre-group) and after (post-group) the establishment of DPM.
Results: Two hundred eighty-five admissions were assessed in the study. There were 99 admissions in the pre-group and 186 in the post-group. There were 17 admissions for different reasons in the pre-group and 29 in the post-group. The most common reasons for admission were elevated transaminases, seizures, vomiting and metabolic acidosis. Definitive diagnosis was made in 16 (17.6%) patients admitted in the pre-group and 39 (23.8%) in the post-group. The most common diagnoses were genetic syndromes, mitochondrial diseases and organic acidemias. Twenty-one patients were diagnosed with inherited metabolic diseases (IMDs). Mitochondrial diseases were the most commonly diagnosed IMD (8(38%)). From the 15 pediatric subunits, ammonia test was requested from 8 in the pre-group and 13 in the post-group. In the pre-group, the pediatric subunit where ammonia was requested the most was the Pediatric Neurology Polyclinic (n=25 (25.3%)). In the post-group, the subunit that required the highest number of ammonia tests was the DPM (68(23.9%)). In the ROC analysis conducted for the predictive power of the initial ammonia level in requesting a control ammonia test, the area under the curve is 0.927, and the p-value is 0.001. For the cut-off value of 60.3 µmol/l, the sensitivity was 90.9%, and the specificity was 88.6%.
Conclusion: After DPM was established, there was an increase in ammonia test requests, in the diversity of reasons for requesting ammonia testing from admissions, and in IMD diagnosis. DPM had a positive effect on pediatricians' awareness of hyperammonemia.

Keywords: Hyperammonemia, Ammonia, Inherited metabolic diseases, Pediatrics

ÖZ

Amaç: Hiperamonyemi, fark edilmediğinde ciddi mortalite ve morbiditelere neden olur. Bir pediatri kliniğinde, Çocuk Metabolizma Hastalıkları kliniği (ÇMHK) açılmadan öncesi ve sonrası amonyak istem sayılarının karşılaştırılmasını amaçladık.
Yöntem: Çalışma, 15/11/2022-16/11/2023 tarihleri arasında retrospektif olarak gerçekleştirildi. ÇMHK kurulmasına göre öncesi ve sonrası olarak çalışma verileri değerlendirildi.
Bulgular: Çalışmada 285 başvuru değerlendirildi. Öncesi grupta 99, sonrası grupta 186 başvuru vardı. Öncesi grupta 17, sonrası grupta 29 farklı nedenle başvuru oldu. En sık başvuru nedenleri; transaminaz yüksekliği, nöbet, kusma ve metabolik asidozdu. Öncesi grupta başvuran hastaların 16 (%17,6)'sına, sonrası gruptaysa 39 (%23,8)'una tanı konuldu. En sık tanılar; genetik sendromlar, mitokondriyal hastalıklar ve organik asidemilerdi. 21 hastaya kalıtsal metabolik hastalık (KMH) tanısı konuldu. En çok tanı konulan KMH, mitokondriyal hastalıktı (8 (%38)'i). 15 pediatri alt biriminin öncesi grupta 8, sonrası grupta 13'ünden amonyak tetkiki istendi. Öncesi grupta en çok amonyak istenen pediatri alt birimi Çocuk Nöroloji Polikliniğiydi (n=25 (%25,3)). Sonrası grupta en fazla amonyak istenen alt birim ÇMHK'ydi (68(%23,9)). İlk amonyak düzeyinin kontrol amonyak tetkiki istemedeki kestirim gücü için yapılan ROC analizinde eğri altında kalan alan 0,927, p değeri 0,001'dir. Kestirim değeri 60,3 µmol/l için duyarlılık %90,9, özgüllük %88,6 saptandı.
Sonuç: ÇMHK kurulduktan sonra, amonyak testi istemlerinde, amonyak testi istenen başvurulardaki çeşitlilikte ve KMH tanılarında artış saptandı. ÇMHK, pediatristlerin hiperamonyemi farkındalığı üzerine olumlu etkiye sahipti.

Anahtar kelimeler: Hiperamonyemi, amonyak, kalıtsal metabolik hastalıklar, pediatri

Introduction

Ammonia is a neurotoxic molecule formed due to the breakdown of amino acids in the protein structure and is also produced by bacteria in the intestinal flora (1). Ninety percent of the ammonia produced in the body is transported to the periportal hepatocytes by the portal circulation, where it is converted to urea via the urea cycle pathway and excreted in the urine (1). Ten percent of ammonia, a water-insoluble molecule

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that does not enter the urea cycle, is transported to perivenous hepatocytes and converted from glutamate to glutamine by the enzyme glutamine synthase (2). Glutamine is used as energy or excreted in urine (2). In the case of hyperammonemia, which develops due to increased production or decreased elimination of ammonia, ammonia passes from the portal circulation to the systemic circulation (3). It reaches the brain, causing severe neurological findings with its neurotoxic effect (3).

Hyperammonemia is defined as the ammonia level above 80 µmol/L in infancy and 55 µmol/L in older children (4). However, there are different threshold values in different sources (5). Clinical findings of hyperammonemia are nausea, vomiting, anorexia, growth retardation, neuropsychiatric symptoms, headache, ataxia, dysarthria, behavioral changes, neurodevelopmental retardation, hypotonia, seizure, changes in consciousness, coma and central hyperventilation (1). It may present with sepsis-like clinical conditions, especially in the neonatal period (1). The ammonia level should be checked in cases that exhibit a wide range of clinical findings and in every child with undiagnosed neurological findings (3,4).

Hyperammonemia is caused by inherited metabolic diseases (IMDs) caused by enzyme deficiency and genetic disorders (urea cycle disorders, organic acidemias, lysinuric protein intolerance, carbonic anhydrase VA deficiency, pyruvate carboxylase deficiency, fatty acid oxidation defects), acute or chronic liver diseases, medications (valproic acid, cyclophosphamide), portosystemic shunt and conditions that lead to protein catabolism (5).

In addition to various diseases in the etiology of hyperammonemia, false positive results are also high due to pre-analytical situations (6). A study in the literature found that 48% of 1880 ammonia measurements from 479 patients had false positive high results (6). Conditions that cause false positive ammonia levels: It is the release of ammonia from the lysis of erythrocytes after blood collection, the formation of ammonia as a result of the deamination of amino acids in the plasma, the tourniquet applied during blood sample collection and the transport temperature of the sample (6-8). Such false positive results may also negatively influence clinicians' orders for ammonia testing.

While the majority of the causes of hyperammonemia in adults are cirrhotic liver diseases, in children, IMDs, especially urea cycle disorders and organic acidemias, come to the fore (9-11). Although IMDs are prominent in the etiology of hyperammonemia in children, diseases in this group are still considered among the "rare diseases." The incidence of urea cycle disorders is reported as 1/35,000, organic acidemias are 1/3000 and fatty acid oxidation defects are 1/9000 (11-12). Although the incidence of an IMD may seem "rare" when viewed individually, the number of IMDs identified by developing genetic studies is increasing yearly (13). Considering all IMDs, the incidence of being diagnosed with a metabolic disease is between 1/800 and 1/2500 and is not rare (13).

For this reason, these diseases do not often come to mind in clinical practice, except for Pediatric Metabolism specialists and other specialists specifically interested in IMDs. However, there are still many admissions to all clinic of pediatrics with symptoms of hyperammonemia (nausea, vomiting, loss of appetite, growth retardation, neuropsychiatric symptoms, headache, ataxia, dysarthria, behavioral changes, neurodevelopmental retardation, hypotonia, seizures, changes in consciousness).

This study aims to compare the number of ammonia test requests from patients admitted to clinic of pediatrics for the period of six months before and after the Department of Pediatric Metabolism (DPM) was established in a university hospital. This comparison was planned to reveal the hyperammonemia awareness level in the clinic of pediatrics and the characteristics of the patient groups whose ammonia levels were measured.

Material and Methods

Study design and settings

This study was conducted retrospectively with second-grade students within the scope of the Selçuk University Faculty of Medicine, Evidence-Based Medical Practices program. It was started after receiving ethics committee approval (Selçuk University Faculty of Medicine Local Ethics Committee; No: 2023/591, Date: 19/12/2023). The study was carried out using the hospital automation system records and patient file information. Patients under the age of 18 whose blood ammonia level was requested in the polyclinics and inpatient services under the Department of Pediatrics between November 15, 2022, and November 16, 2023 were included in the study. Patients over the age of 18, pregnant women, and patients requiring ammonia in internal and surgical medicine branches other than pediatrics were excluded from the study. Since the Department of Pediatric Metabolism was established in May 2023 and patient admission started on May 16, 2023, six months before the establishment of the Department of Pediatric Metabolism (November 15, 2022-May 15, 2023) was considered as the "pre-group" in the study. The six months after the clinic's establishment (May 16, 2023-November 16, 2023) was defined as the "post-group". In addition, all polyclinics and inpatient service units within the Department of Pediatrics were examined under 15 headings. These units were evaluated in 4 categories: polyclinic, inpatient services, intensive care units, and emergency department according to the medical care the patients received as outpatient or inpatient. The number of ammonia requests, ammonia levels, sample rejection numbers, the number of control ammonia requests from the same patient, demographic characteristics, reasons for admission and final diagnoses of the patients were recorded in the data collection form as study data.

Statistical analysis

Statistical analysis was performed using SPSS 26.0 for

Windows. Descriptive criteria, mean and standard deviation, median and minimum and maximum values were presented as percentage distribution. The suitability of the data for normal distribution was checked with the Kolmogorov-Smirnov test. Student-t-test was used to compare continuous variables and chi-square analysis was used to compare distributions. ROC analysis was employed to examine the significance of the first ammonia test result in predicting the second test intake. The significance level was taken as $p<0.05$.

Results

The study included 285 admissions among 255 patients who met the criteria and requested ammonia testing. One hundred forty-six (51.2%) of all admissions were male; the mean age was 67.2±69.7 months (Table 1).

Table 1. Comparison of study data before and after the establishment of the Department of Pediatric Metabolism

	Pre-group	Post-group	Total	
	Mean ± Standard Deviation (mean±SD)	Mean ± Standard Deviation (mean±SD)	Mean ± Standard Deviation (mean±SD)	p value
Age (month)	71.9±76.8	64.7±65.7	67.2±69.7	0.403*
Ammonia level (µmol/l)	46.49±51.18	47.36±36.92	47.06±42.33	0.869*
Presence of sample rejection	0.05±0.22	0.07±0.38	0.06±0.33	0.935**
	Number (Percentage) n (%)	Number (Percentage) n (%)	Number (Percentage) n (%)	
Gender				
Male	64 (64.6)	82(44.1)	146 (51.2)	0.001***
Female	35(35.4)	104(55.9)	139 (48.8)	
Ammonia level (µmol/l)				
Ammonia level <60 µmol/l	84 (84.8)	151 (81.2)	235 (82.5)	0.439***
Ammonia level >60 µmol/l	15 (15.2)	35 (18.8)	50 (17.5)	
Treatment Place				
Polyclinic	56 (56.6)	108 (58.1)	164 (57.5)	0.075***
Service	11 (11.1)	35 (18.8)	46 (16.1)	
Intensive Care Unit	13 (13.1)	25 (13.4)	38 (13.3)	
Emergency Service	19 (19.2)	18 (9.7)	37 (13.1)	
Sample rejection				
Number of sample rejection	5 (5.1)	9 (4.8)	14 (4.9)	0.937***

* Student t-test,**Mann Whitney-U test, ***Chi-Square test

When all admissions were evaluated, 99 (34.7%) ammonia test requests were in the pre-group, 186 (65.3%) were in the post-group, and 68 (23.9%) were requested from the DPM in the post-group (Figure 1).

The mean value for ammonia in all admissions was 47.06 ± 42.33 µmol/l. There was no statistically significant difference detected between the groups for mean ammonia values (p=0.869) distribution of patients according to inpatient or outpatient treatment services (p=0.075), presence of sample rejection (p=0.935), and the number of sample rejections (p=0.937). The high ammonia value (>60 µmol/l) was detected in 15.2% of the pre-group and 18.8% of the post-group (Table 1).

The distribution of the patient's reasons for admission in the pre-group and post-group is shown in Figure 2. It was determined that they were admitted for 17 different reasons in the before group and for 29 different reasons in the post group. The four most common reasons for admission were elevated transaminase (37 [37.4%] in the pre-group, 53 [28.5%] in the post-group), seizure (12 [12.1%] in the pre-group, 26 [14%] in the post-group), vomiting (11 [11%] of the pre-group, 10 [5.4%] of the post-group) and metabolic acidosis (3 [3%] of the pre-group, 13 [7%] of the post-group).

A definitive diagnosis was made in 16 (17.6%) of the patients admitted in the pre-group and in 39 (23.8%) in the post-group. The most common diagnoses were genetic syndromes [2 (2.2%) of the patients in the pre-group, 7 (4.3%) in the post-group], mitochondrial diseases [2 (2.2%) of the patients in the pre-group, 6 (%3.7) in the post group] and organic acidemias [7 (4.3%) of the patients admitted in the post-group]. At the same time, it was not detected in the pre-group) (Figure 3a). A total of 21 patients were diagnosed with IMD. Mitochondrial diseases were the most commonly diagnosed IMD (8 [38%]). All organic acidemias were diagnosed in the post-group, and it was the second most diagnosed IMD (7 [33.8%]). There was one patient diagnosed with hereditary fructose intolerance and congenital glutamine deficiency, and they were diagnosed in the post-group (Figure 3b).

The distribution of admissions requiring ammonia testing in the pre-group and post-group from the pediatric subunits is shown in Figure 4. There were 15 subunits under the roof of the Department of Pediatrics. Ammonia tests were requested from 8 of the 15 pediatric subunits in the pre-group and 13 in the post-group. In the pre-group, the pediatric subunit where ammonia tests were requested most frequently was the Pediatric Neurology polyclinic (n=25 [25.3%]). Pediatric Metabolism polyclinic was the subunit with the highest number of ammonia test requests in the post-group (68 [23.9%]). While there was no ammonia request in the pre-group from the General Pediatrics service, there were 11 ammonia requests in the post-group. In addition, it was observed that there was an approximately two-fold increase in the number of ammonia test requests in the Pediatric Gastroenterology service and Pediatric Intensive Care subunits in the post-group.

There were 50 admissions with an initial ammonia value >60 µmol/l. The mean ammonia level of these admissions was 109.2 ± 69.9 µmol/l (min: 60.4 µmol/l, max: 413.5 µmol/l). A repeat ammonia test was requested from 20 of 50 admissions (40%) whose initial ammonia value was found to be over 60 µmol/l. Even though the first value was above 60 µmol/l in 30 (60%), a repeat ammonia test was not requested. Of the 50 admissions whose first ammonia value was over 60 µmol/l, a second ammonia test was requested from 9, a third from 5, a fourth from 5, and a fifth from 1. The mean time to request a second repeat ammonia test was 43.1 ± 60.2 hours (min: 1.5 max: 228.0).

The ROC analysis was conducted to determine the predictive power of the initial ammonia level in requesting a control ammonia test, which had an area under the curve of 0.927 and a p-value of 0.001. When the cut-off value was taken above 60.3 µmol/l, the sensitivity was found as 90.9%, and the specificity was 88.6% (Figure 5).

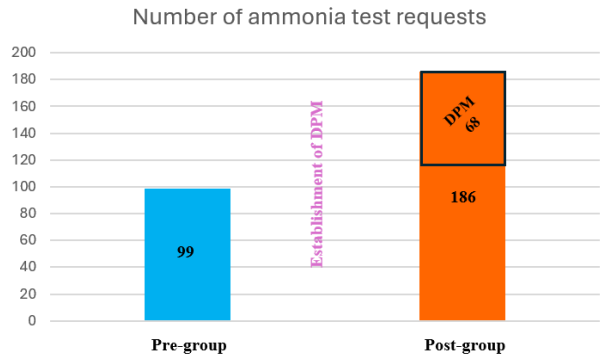

Figure 1. Comparison of ammonia test request numbers in groups before and after the establishment of DPM.

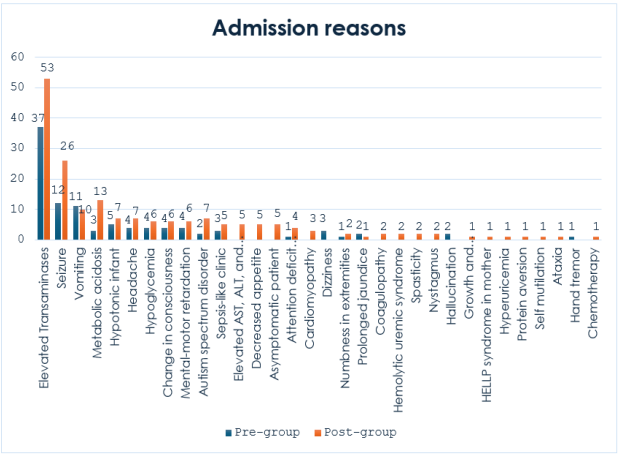

Figure 2. Comparison of admission reasons in groups before and after the establishment of DPM.

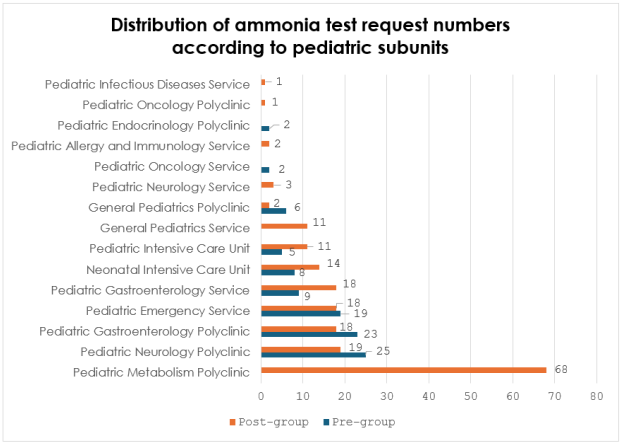

Figure 4. Distribution of ammonia test request numbers according to pediatric subunits

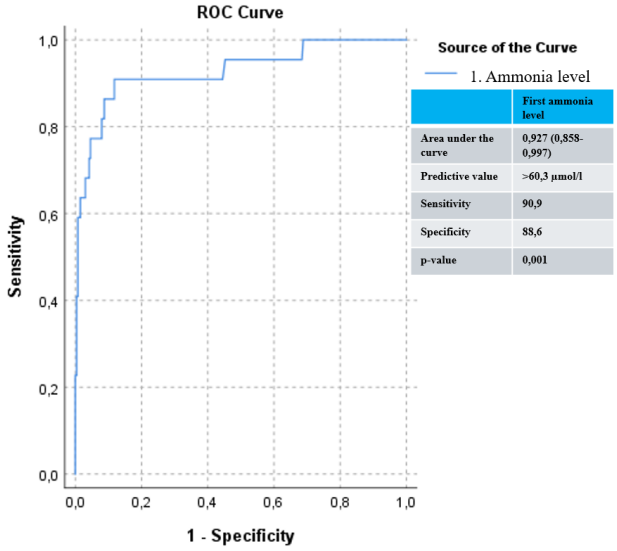

Figure 5. The ROC analysis to determine the predictive power of the initial ammonia level in requesting a control ammonia test.

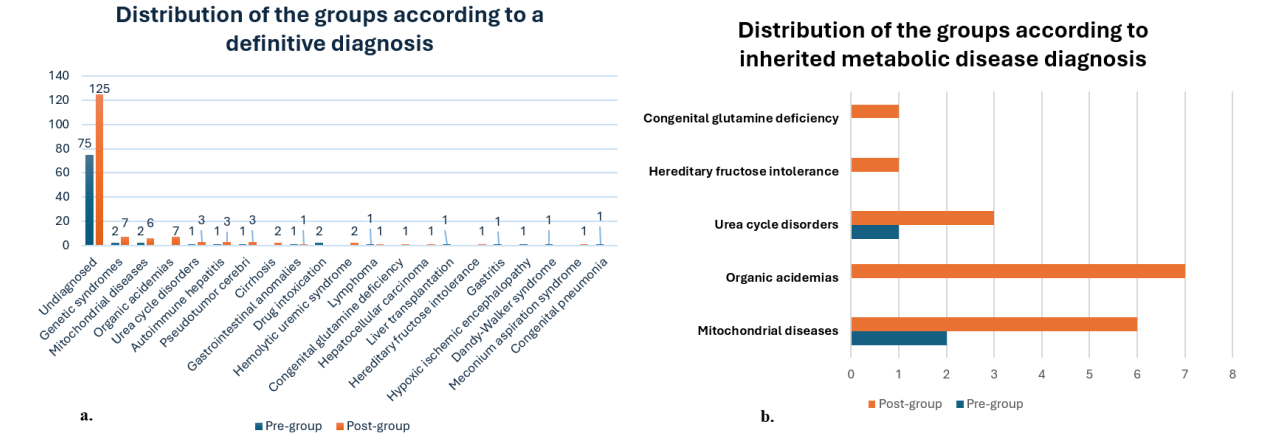

Figure 3. Distribution of definitive diagnosis and inherited metabolic diseases diagnosis between groups. a; distribution of the groups according to a definitive diagnosis, b; distribution of the groups according to inherited metabolic disease diagnosis.

Discussion

IMDs are mostly inherited as autosomal recessive and can be diagnosed at any age from the neonatal period to adulthood (14-16). Studies have shown that in the diagnosis of IMDs, it is essential to determine the clinical and biochemical phenotypes of the cases (rhabdomyolysis, hyperammonemia, myelopathy, etc.) and then to associate the phenotype in the cases with specific IMD and that suspecting the disease is vital in the diagnosis, and that it is beneficial to consult a metabolism specialist after a preliminary diagnosis is made. (15,16). As IMDs have begun to be diagnosed more frequently in our country and around the world, there is a need for physicians specialized in this field, which leads to the emergence of a DPM that deals with these diseases (16). Our study evaluated the period before and after the DPM in terms of hyperammonemia. We investigated the effect of this branch of science on pediatricians' awareness of hyperammonemia.

In our study, it was found that after the establishment of the DPM, more ammonia tests were requested, more ammonia tests were requested for different reasons at admissions, more patients were diagnosed, and more patients were diagnosed with IMD. It is mentioned in the literature that physicians lack knowledge and experience about IMDs and avoid the diagnosis and treatment process of these diseases such as hyperammonemia and metabolic acidosis, which should be considered in the differential diagnosis (16). In our study, the increase in the diversity of hyperammonemia admissions and the increase in ammonia requests and diagnosed patients showed that the awareness of hyperammonemia among pediatricians has increased. The DPM may not only raise awareness of rare diseases in other pediatric subunits but also alleviate the hesitation of pediatricians in the diagnosis and follow-up of IMD.

Our study found that patients admitted to pediatric subunits had 29 different signs and symptoms of hyperammonemia. The most common reasons for admission were elevated transaminases, seizures, vomiting and metabolic acidosis, respectively. It has been reported in the literature that hyperammonemia does not have specific signs and symptoms and can present with a wide variety of clinical conditions such as unexplained vomiting, seizures and unexplained neurological findings (17-19). It was similar to the literature that patients applied for many different reasons and that admissions were due to seizures, vomiting and metabolic acidosis. However, the fact that elevated transaminase levels is the most common reason for admission in more than 1/3 of the patients is different from the literature. Hyperammonemia and elevated transaminase levels coexistence is more common in cirrhosis (17). This may be because pediatric gastroenterology polyclinics and service units are among the pediatric subunits most frequently requiring ammonia tests after pediatric metabolism polyclinics.

The etiology of hyperammonemia, a symptom of many congenital and acquired disorders due to hepatic or nonhepatic reasons, is very diverse (11,17,20,21). Its etiology includes urea cycle defects, including enzymatic defects, organic acidemias, congenital lactic acidosis, mitochondrial fatty acid oxidation defects, and dibasic amino acid deficiencies, as well as other disorders such as transient hyperammonemia of the newborn, neonatal Herpes simplex virus (HSV) infection, cirrhosis, malignancy, and severe perinatal asphyxia. (17,22). This situation may have caused more than one clinic to evaluate the patient together, thus requiring more ammonia tests in service patients during the diagnosis and treatment. In our study, the fact that genetic syndromes, mitochondrial diseases, organic acidemias, and urea cycle defects were the most common diagnoses in patients presenting with signs and symptoms of hyperammonemia shows that although IMDs are defined as rare diseases, they are not very rare and should be considered in the differential diagnosis of hyperammonemia.

The limited number of sample rejections in both periods in the study showed that laboratory and healthcare workers were aware of situations that could cause erroneous results in the ammonia test, such as blood collection by tightening with a tourniquet, not transporting the sample at optimal temperature (with an ice tray), and running the test late because the reliability of ammonia testing requires strict standardization from blood collection to transportation to the laboratory and the process of working in the laboratory (23).

Hyperammonemia is a severe clinical condition that causes mortality and morbidity in patients (20). Therefore, in treating acute hyperammonemia, reducing the ammonia level and controlling specific complications such as cerebral edema and intracranial hypertension are the most critical issues (17). To reduce circulating ammonia, protein intake is stopped, and calories are provided with glucose infusions (17). Hemodialysis should be considered in cases where ammonia must be removed rapidly (24,25). Additionally, sodium benzoate and phenylacetate compounds, which convert nitrogenous residues into non-urea components, are used in IMDs (25). Oral non-absorbable disaccharides (such as lactulose) are used for hepatic encephalopathy secondary to hyperammonemia. These sugars reduce the production and absorption of ammonia in the intestine (26). The patient's clinical findings and control ammonia levels should be closely monitored to evaluate the response to treatment (11,17,20,22,24).

In our study, out of 50 admissions whose first ammonia value was found over 60 µmol/l, an ammonia test was requested from 9 of them for the 2nd time, 5 of them for the 3rd time, 5 of them for the 4th time, and 1 of them for the 5th time. In addition, when the predictive value of the initial ammonia level for requesting a control ammonia test was taken above 60.3 µmol/l, the sensitivity was 90.9%, and the specificity was 88.6%. This revealed that pediatricians closely monitor the

ammonia level higher than 60.3 µmol/l in patients presenting with hyperammonemia, both in diagnosis and treatment follow-up and request a control ammonia test above this value.

There were some limitations in our study. A limitation is that the study is retrospective and conducted as an archive scan. Another limitation is that we did not evaluate the clinical outcomes of the patients. Although this is an issue we did not address because our study was not a mortality study, it prevented us from commenting on the relationship between ammonia levels and clinical outcomes. Since the study was not conducted prospectively, we cannot discuss standardization or what criteria physicians consider when ordering ammonia tests. In this case, it is an important limitation as it will prevent the randomization of the study.

Conclusion

In our study, we found that after the DPM was established, ammonia tests were requested by pediatricians from more patients who came for different reasons, more patients were diagnosed, and the number of patients diagnosed with IMD increased. Our study revealed that pediatricians should pay attention to the ammonia level of 60.3 µmol/l when requesting a control ammonia test to diagnose and follow up hyperammonemia. All these indicators showed that the Department of Pediatric Metabolism positively impacted pediatricians' awareness of hyperammonemia.

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Ethical Approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Selçuk University Faculty of Medicine Local Ethics Committee (Decision No: 2023/591, Date: 19/12/2023).

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ORIGINAL ARTICLE

Surgical Techniques for the Treatment of Proximal Humerus Fractures in Elderly Patients: A Comparative Analysis

Yaşlı Hastalarda Proksimal Humerus Kırıklarının Tedavisinde Cerrahi Teknikler: Karşılaştırmalı Bir Analiz

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ABSTRACT

Aim: It is common for the elderly, mostly due to osteoporosis and falls, to suffer proximal humerus fractures. This study aims to compare the efficacy of reverse total shoulder arthroplasty (rTSA) and open reduction with internal fixation (ORIF) in the treatment of these fractures with a focus on functional outcomes and patient satisfaction.
Methods: In this retrospective study, 65-85-year-old patients who underwent rTSA or ORIF for displaced proximal humerus fractures between January 1, 2021 and January 1, 2022 were analyzed. Sixty patients participated in this study; they were divided into two groups as follows: Group 1 (rTSA, n=30) and Group 2 (ORIF, n=30). Constant and Oxford shoulder scores were used to evaluate outcomes while complications and patient satisfaction were also recorded. Statistical analysis involved t-tests and Chi-square tests whereby the p-value <0.05 indicated significance.
Results: There was considerable improvement in various categories: Group 1 (rTSA), the constant score improved from preoperative stage of 35 ±8 to postoperatively of 75±10; oxford score ranged from preoperative level of 25±6 to postoperative level of 80±9 respectively p<0.05 for both cases Group II (ORIF), the constant score improved from preoperative stage of33±7 to postoperatively of65±12; oxford score ranged from preoperative level24±5 to postoperative level70±11respectively(p<0.05 for both). Patients who underwent rTSA were more satisfied than those who underwent ORIF; 66.7% versus 54.5%.Several complications occurred more frequently in the ORIF group including delayed union (18.2% vs3.3%) and infection (22.7 vs6.7%).
Conclusion: rTSA is associated with better functional outcomes, higher patient satisfaction, and fewer complications compared to ORIF for proximal humerus fractures in the elderly. These findings suggest that rTSA may be a more favourable surgical option for this population of patients. Moreover, future studies should involve larger samples and look at longer follow-up periods to ascertain these results.

Keywords: Proximal humerus fractures, reverse total shoulder arthroplasty, open reduction internal fixation

ÖZ

Amaçlar: Yaşlılarda proksimal humerus kırıkları, düşmeler ve osteoporoz nedeniyle yaygındır. Bu çalışmanın amacı, bu kırıkların tedavisinde ters total omuz artroplastisi (rTSA) ve açık redüksiyon ve internal tespiti (ORIF) etkinliğini karşılaştırmak, fonksiyonel sonuçlar ve hasta memnuniyetine odaklanmaktır.
Yöntemler: Bu retrospektif çalışma, 1 Ocak 2021 ile 1 Ocak 2022 tarihleri arasında yer değiştirmiş proksimal humerus kırıkları nedeniyle rTSA veya ORIF uygulanan 65-85 yaş arası hastaları analiz etti. Çalışmaya toplam 60 hasta dahil edildi, iki gruba ayrıldı: Grup 1 (rTSA, n=30) ve Grup 2 (ORIF, n=30). Sonuçlar Constant ve Oxford Omuz Skorları kullanılarak değerlendirildi ve komplikasyonlar ile hasta memnuniyeti de kaydedildi. İstatistiksel analizlerde t-testleri ve Ki-kare testleri kullanıldı, p-değerleri <0.05 anlamlı kabul edildi.
Bulgular: Grup 1'de (rTSA) Constant Skorları preoperatif olarak 35 ± 8'den postoperatif olarak 75 ± 10'a, Oxford Skorları ise 25 ± 6'dan 80 ± 9'a anlamlı şekilde iyileşme gösterdi (her ikisi de p < 0.05). Grup 2'de (ORIF) Constant Skorları 33 ± 7'den 65 ± 12'ye, Oxford Skorları ise 24 ± 5'ten 70 ± 11'e iyileşti (her ikisi de p < 0.05). rTSA hastaları, %66.7 çok memnuniyet oranı ile ORIF grubundaki %54.5'ten daha yüksek memnuniyet bildirdi. ORIF grubunda gecikmiş kaynama (%18.2'ye karşı %3.3) ve enfeksiyon (%22.7'ye karşı %6.7) gibi komplikasyonlar daha yaygındı.
Sonuçlar: rTSA, yaşlılarda proksimal humerus kırıkları için ORIF'e kıyasla daha iyi fonksiyonel sonuçlar, daha yüksek hasta memnuniyeti ve daha az komplikasyon ile ilişkilidir. Bu bulgular, rTSA'nın bu hasta popülasyonunda tercih edilebilir bir cerrahi seçenek olabileceğini göstermektedir. Bu sonuçları doğrulamak için daha büyük örneklemli ve uzun takip süreli gelecekteki çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Proksimal humerus kırıkları, Ters total omuz artroplastisi, Açık redüksiyon internal tespit

Introduction

The high rate of proximal humerus fractures among the elderly is often due to their vulnerability to falls and osteoporosis. Various patterns of fractures, comorbidities, and intricate shoulder joints make managing this type of disability in the elderly challenging for orthopaedic surgeons (1). Based on factors such as functional demand or other health conditions, there is surgical treatment that depends on whether it is nonsurgical or not (2). Reverse total shoulder arthroplasty (TSA) with stable angular plates or open reduction with internal fixation (ORIF) are two widely known surgical approaches to displaced proximal humerus fractures (3). Both methods are compared in this article (4). When proximal humerus fractures are not

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properly treated, it means destabilising morbidity, as well as improving aspects of quality of life in addition to functioning during treatment (5, 6); thus, more patients should be able to receive attention once affected by this condition due to a reason that requires surgical advancement. These soft tissue envelope that require special handling but have complex features as a result, unlike the disease of the upper arm itself (7). Preservation of age-appropriate autonomy through repair rather than fracture surgery only ensures function restoration before incapacitating injury.

Instead of conservative treatments, some new complex surgical methods have recently been recommended to treat proximal humerus fractures in many cases. The development of sophisticated surgical techniques and prosthetic designs, together with the accumulated knowledge about long-term biomechanics, has resulted in this progress in surgical processes now (8, 9). Nonsurgical treatment generally works well for undispaced/minimally displaced fractures (10). However, after elbow surgery, all complicated and displaced fractures must undergo an operative intervention aimed at optimising the general postoperative health status (9). The nature (size), the number of bone density, and the combined regularity depend on whether the TSA or ORIF approach will be used to treat them (11).

The complexity of fractures is also one reason why reverse total shoulder arthroplasty is increasingly becoming the preferred option, especially when there are limitations in reconstruction options due to poor quality bones (12). Changes in TSA deficits, altered bone quality, and complications pertaining to the union process. However, there are invasiveness issues within the country as well as prosthetic agreements, nerve marriages, etc. within the country. Another category of complements includes (13). On the other hand, ORIF preserves key anatomy with minimal invasion; however, this requires sufficient bone to achieve resolution, so malunion as well as hardware problems can develop (14).

This retrospective study was based on the hypothesis that surgical technique has a significant impact on the prognosis of the treatment of proximal humerus fractures in older people. By doing this study, surgeons are assisted because differences in functional outcomes between TSA and ORIF and patient satisfaction rates can be explained to them. Much can be gained from broad clinical data in retrospective studies.

In short, the treatment of proximal humeral fractures in geriatric patients presents many challenges to clinicians. Additionally, this study aims to compare TSA with ORIF approaches based on maximisation of patient outcomes while providing recommendations based on evidence-based practice on the surgeries to utilise; thus, orthopaedic surgeons for this examination will continue to grow as they could diagnose cases related to proximal humerus fractures using clinical evaluations leading to better patient care.

Methods

To analyse the results of patients with proximal humeral fractures aged 65 to 85 years who underwent traditional ORIF or rTSA among a cohort, this study used two different surgical techniques. It commemorates the ethical principles of the Declaration of Helsinki and it was approved by the local Ethics Committee under Decision number 2673 on 22 June 22, 2022. Research carried out after the signed informed consent of the participants were obtained. The medical records of 67 patients who were treated between January 01, 2021, and January 01, 2022 were retrospectively reviewed. Seven patients (four dead) did not meet the inclusion criteria: Three cases were affected with incomplete preoperative or postoperative data, which resulted in the participation of 60 respondents. Therefore, patients were divided into two groups applying the two different methods of surgery; TSA and ORIF (Group I; n=30), (Group II; n=30) (Fig. 1).

Some of the studies that can be accessed are those about OTA/AO-11-B2 & C2 fragmented proximal humeral fractures of OTA / AO-11-B2 & C2 resulting from OTA / AO-11-B2 & C2 among people aged 65 to 86 years. Additionally, the lack of data files for certain cases, such as multiple traumatic injuries (beyond exclusion criteria) and untreated shoulder area surgeries, including pathological fractures and unrelated past surgeries, may be one of the reasons why we excluded some patients. The records indicated that the names of the Delta X, Exceed and Latitude product names were together with those of Group I(rTSA) supplies and if cemented/uncemented options were used or not. In addition, surgery was only one approach that was deltopectoral, while cemented / uncemented implantation was determined by bone quality, which was examined by an anaesthesiologist intraoperatively. In Group II subjects (ORIF), we recorded details such as the angular stable plate type used (LCP or PHILOS), the number of screws applied, the deltopectoral approach mode.

The most crucial was the result of pain and the range of movements that the joint allowed, which are prerequisites for leading the daily activity of the patient. Furthermore, OSS and radiographs were used to assess the quality of treatment and quality of life in patients with operatively managed prostate humeral fracture, respectively. Second, the complications of the patients and the satisfaction levels were also noted. Patients were followed for 2 years after surgery at regular postoperative intervals: 6 months 12 months, and 24 months. Some of the timelines for follow-up were changed during the analysis to ensure consistency of the data. This was not allowed to happen in observation during evaluation by surgeons who cannot be blind but because they are surgical skill surgeons instead of type of surgery the assessors did not know which kind, and hence bias could not be brought in.

Power analysis was carried out to determine the right sample size. Previous studies have shown that a

minimum of 25 patients per group are needed with a power of 80% at an alpha level of 0. 5 to carry out the study and to find a statistically significant difference in constant and Oxford shoulder scores. We can still manage, given that the final calculated sample size is larger than this requirement for 30 patients in each group. The effect size is approximately 0. 1. The evaluation of the effectiveness of the intervention was limited by the calculated estimate of the results, which was based on the marked differences between the two groups in the outcome measures. SPSS software was used for data analysis. Categorical variables are shown as n (%) and continuous data are presented as means ± SD. The normal test was performed using the Shapiro-Wilk test. Differences in continuous variables having a normal distribution will be assessed using the t test or the Mann-Whitney U test if they are non-parametric. The Chi-square test was used to compare categorical variables. All p-values <0. 05 indicated statistical significance.

Results

The study period was such that it included 52 individuals. The patients consisted of two groups determined by the type of treatment they received due to fractures in their proximal humerus. Thirty patients in group one (rTSA) had a mean age age of 72 ± 5 years, while twenty-two patients constituted group two (ORIF) with a mean age of 70 ± 6 years. There was a similarity in gender distribution in both groups, where women made up 60% and 59% in groups one and two, respectively. Right-sided fractures were predominantly reported, which were 53.3 % and 54.5% for group one and two consecutively. These studies showed that type B2, which was also known as type II-B2, represented 67% among other types for Group1; However, in Group A, Type C2 is represented by 33%, while in Group B this same fracture makes up 36%. Osteoporosis existed in 73% of all these comorbidities followed by diabetes mellitus and hypertension found in each case with a frequency of 27%, respectively, and somewhere this condition existed at least 60% in either way (Table1).

The surgical details showed a distinction between the groups where three different implants were used, namely Delta X (33%), Exceed (40% Latitude (26%). For example, cementing occurred only six of ten reverse shoulder arthroplasties performed by our team, but their practice relied mainly on the use of LCP plates (54,5% ORIF cases), few PHILOS plates (44,5%) with the majority using more than five screws per joint, that is, 63% (Table2).

Group One (rTSA) had significant improvements in constant scores from the preoperative period of 35 ± 8 to the postoperative period of 75 ± 10, which is +40 ± 5 ($p < 0.05$). In the same group, the Oxford scores increased from 25 ± 6 to 80 ± 9, indicating a change of +55 ± 4 ($p < 0.05$). Patients in Group Two (ORIF) had Constant Scores that improved from 33 ± 7 before operation to 65 ± 12 post-operations (+32 ± 6, $p < 0.05$), and Oxford shoulder scores that ranged between 24 ± 5 and 70 ± 11, with a difference of +46 ± 5 ($p < 0.05$). These results clearly demonstrate the functional improvements observed in both groups, with rTSA showing greater improvement in both Constant and Oxford scores compared to ORIF (Figure 2, Figure 3, Table3).

Regarding patient experience, it was 66. Of the 14 people in Group 1 (rTSA), 7 (50%) were very happy, while in Group 2 (surgery), only 54% (4 out of 7 patients) reported being very satisfied and 5% in Group 2 (ORIF). Additionally, Only 7% of 26 discharged from the TSA hospital were satisfied, while the figure was seen as. 3% of 27 ORIF patients. Six people felt neither sadness nor happiness; 7% of patients with rTSA and 9. 1% of patients with ORIF. In Operative stabilization, Internal Fixation Group (ORIF) there was 4. Among the 5% of dissatisfied patients, there were 4 others. 5% were very unhappy, while no patients in the TSA group were unhappy or very unhappy (Table 4).

Table 1: Baseline Characteristics of Patients

Characteristics	Group 1 (TSA) (n=30)	Group 2 (ORIF) (n=22)	p-value
Age (mean ± SD)	72 ± 5	70 ± 6	0.15 (t-test)
Gender			0.85 (Chi-square)
- Female	18 (60%)	13 (59%)	
- Male	12 (40%)	9 (41%)	
Fracture Side			0.92 (Chi-square)
- Left	14 (46.7%)	10 (45.5%)	
- Right	16 (53.3%)	12 (54.5%)	
Fracture Type			0.72 (Chi-square)
- 11-B2	20 (67%)	14 (64%)	
- 11-C2	10 (33%)	8 (36%)	
Comorbidities			
- Osteoporosis	22 (73%)	16 (73%)	0.99 (Chi-square)
- Diabetes	8 (27%)	6 (27%)	0.99 (Chi-square)
- Hypertension	18 (60%)	13 (59%)	0.94 (Chi-square)

Table 2: Surgical Details

Characteristics	Group 1 (TSA) (n=30)	Group 2 (ORIF) (n=22)	p-value
Prosthesis Type			
- Delta X	10 (33.3%)	N/A	
- Exceed	12 (40%)	N/A	
- Latitude	8 (26.7%)	N/A	
Fixation Type			
- Cemented	18 (60%)	N/A	
- Uncemented	12 (40%)	N/A	
Plate Type	N/A		
- LCP	N/A	12 (54.5%)	
- PHILOS	N/A	10 (45.5%)	
Number of Fasteners	N/A		0.45 (Chi-square)
- ≤5	N/A	8 (36.4%)	
- >5	N/A	14 (63.6%)	

Table 3: Functional Outcomes - Constant and Oxford Shoulder Scores

Outcome Measure	**Preoperative (mean ± SD)**	**Postoperative (mean ± SD)**	**Change in Score (mean ± SD)**	**p-value (Paired t-test)**
Group 1 (rTSA) Constant Score	35 ± 8	75 ± 10	+40 ± 5	< 0.001
Group 1 (rTSA) Oxford Score	25 ± 6	80 ± 9	+55 ± 4	< 0.001
Group 2 (ORIF) Constant Score	33 ± 7	65 ± 12	+32 ± 6	< 0.001
Group 2 (ORIF) Oxford Score	24 ± 5	70 ± 11	+46 ± 5	< 0.001

Table 4: Patient Satisfaction

Satisfaction Level	Group 1 (TSA) (n=30)	Group 2 (ORIF) (n=22)	p-value (Chi-square)
Very Satisfied	20 (66.7%)	12 (54.5%)	0.45
Satisfied	8 (26.7%)	6 (27.3%)	
Neutral	2 (6.7%)	2 (9.1%)	
Unsatisfied	0 (0%)	1 (4.5%)	
Very Unsatisfied	0 (0%)	1 (4.5%)	

Table 5: Complications

Complication Type	Group 1 (TSA) (n=30)	Group 2 (ORIF) (n=22)	p-value (Chi-square)
Delayed Union	1 (3.3%)	4 (18.2%)	0.07
Infection	2 (6.7%)	5 (22.7%)	0.11
Hemorrhage	0 (0%)	3 (13.6%)	0.04
Hardware Failure	N/A	2 (9.1%)	
Prosthesis Loosening	3 (10%)	N/A	
Nerve Injury	1 (3.3%)	1 (4.5%)	0.99

Complication rates were different in these two groups. Furthermore, the ORIF group was statistically more likely to have delayed union than those treated conservatively, with complications rates differing between the groups, and delayed union occurring in 3. 3% of patients in Group 1 (rTSA) and Group 2 (ORIF) represented 2% of the patients. The study detected 6 cases of infections. 7% of the TSA group and 7% of the people who had ORIF. The haemorrhage occurred in 13. Intraoperative failure occurred in only 6% of those who received ORIF treatment, but was not observed in the TSA group. Hardware failure was recorded in 9 cases. 1% of ORIF and 10% of rTSA showed adverse events (loss of the prosthesis). The rate of nerve injury was mild and similar in both groups, occurring at 3% of patients with rTSA and 4% of 20 ORIF patients (Table5).

The findings of this study revealed that rTSA performed better, offering greater patient satisfaction and fewer complications compared to ORIF in the management of proximal humerus fractures among the elderly. This research indicates that rTSA could be a better surgical option for the treatment of these fractures in this group of patients.

Discussion

It is difficult to treat proximal humerus fractures in elderly patients. These fractures are complicated and are found in people with weak bones. Reverse total shoulder arthroplasty (RTSA) or open reduction internal fixation (ORIF) are some of the surgical options that have their own pros and cons. This analysis is necessary to

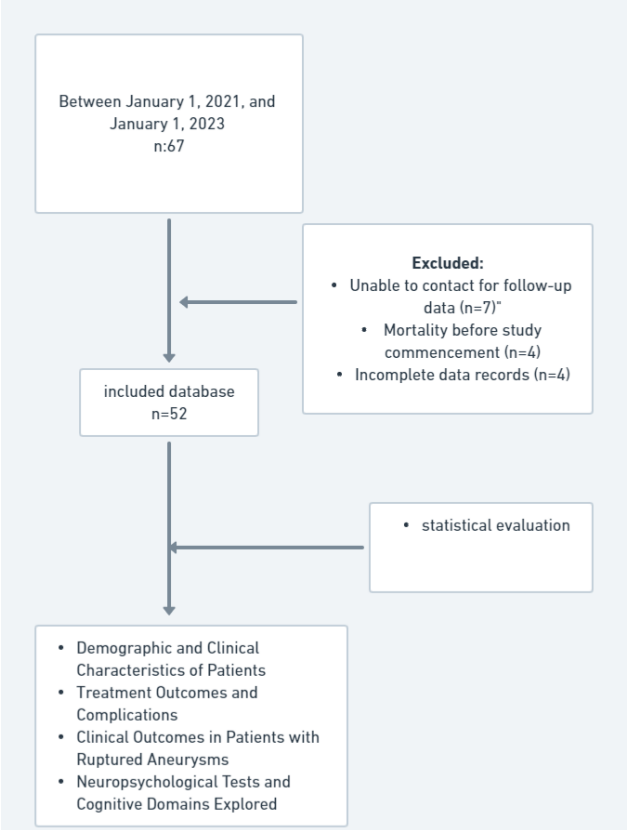

Figure 1

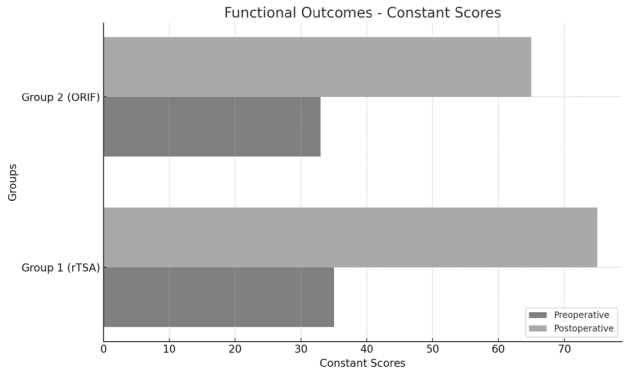

Figure 2

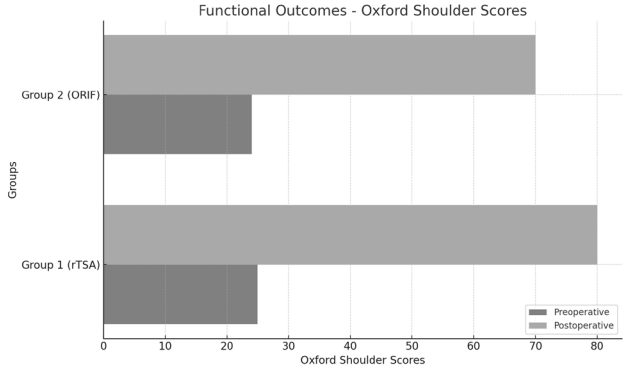

Figure 3

choose the most effective ways of treatment that can improve clinical outcomes, minimize complications, and increase patient satisfaction. Quality of life, as well as general health in older patients, is greatly affected by proximal humerus fractures. They cause long-term pain that also results in reduced mobility and functional limitations; All of these lead to loss of independence, among other things that makes them rely more on caregivers. The surgical method chosen may affect the healing process and the lifelong health of these patients (15). To provide optimal care to patients with proximal humerus fractures, it is important that clinicians know all the clinical conditions that exist with respect to this disease, among others. They include, but are not limited to; severity of fracture, bone quality, patient comorbidities, functional demands, etc. Compared to ORIF, RTSA has shown superior functional outcomes and low complication rates, making it a suitable option for elderly patients with complex fractures and poor bone quality (16).

Previous research carried out on the demographic characteristics related to this study confirms its findings. According to Garrigues et al. (2012), there was a mean age of 75 years of respondents in the study that involved 23 patients treated with hemiarthroplasty or RTSA, revealing no significant differences in distribution according to sex and type of fracture between groups (17). Similarly, Grubhofer et al. (2016) studied 52 shoulders from 51 subjects with an average age of 77 years supporting the demography of this study, finding that the mean ages for Group I (TSA) and Group II (ORIF) were 72 ± 5 and 70 ± 6 respectively. These studies confirm that elderly people have similar demographic profiles when it comes to the surgical management of proximal humerus fractures (18).

According to the present study, different implants and surgical techniques had different results. In rTSA, cementation was performed in some cases while Delta X, Exceed, and Latitude were also used as three types of implants. Similarly, in ORIF cases LCP and PHILOS plates were applied. These results are corroborated by the literature in which RTSA has been shown to lead to significant improvements in shoulder function and patient satisfaction after failure of ORIF. Grubhofer et al. (2017) demonstrated that RTSA showed significant improvements in constant scores with low revision rates leading to high patient satisfaction; thus, confirming its efficacy as a salvage procedure (19). Furthermore, Hussey et al. (2015) found that RSA resulted in a significant improvement in shoulder scores and pain reduction despite a complication rate even when considered as a salvage procedure (20). Current studies confirm these findings that implant choice and surgical technique play a significant role in the outcomes of the treatment of proximal humerus fractures among elderly patients.

The preoperatively constant scores were 35 ± 8 and 75 ± 10 postoperatively in which the study presents findings that Group 1 (TSA) showed significant improvements, and for the Oxford shoulder scores they changed from 25 ± 6 to 80 ± 9. This is consistent with previous research. Shannon et al. (2016) found that primary reverse total shoulder arthroplasty (RTSA) results in substantial improvements in constant scores and overall shoulder function among patients with proximal humerus fractures, supporting the better results recorded in the TSA group in our study from this article (21). Furthermore, Heo et al. (2023) conducted a systematic review and meta-analysis showing that RTSA had higher Constant-Murley and Oxford Shoulder scores compared to open reduction internal fixation (ORIF), thus confirming the better functional results and reduced complication rates observed between Group 1 (TSA) of our study compared to those of Group 2 (ORIF) (22). These comparisons demonstrate the effectiveness of RTSA in improving shoulder functioning and patient satisfaction among older adults with complicated proximal humeral fractures.

The finding of the present study demostrates that 66.7% of patients in Group 1 (TSA) were very satisfied compared to 54.5% of Group 2 (ORIF), and it is consistent with previous studies. Compared to ORIF and HA, RTSA reported better patient-reported results and higher satisfaction scores, as well as a better functional score in patients with RTSA who reported the highest satisfaction rates (Chalmers et al., 2014) (23). Similarly, Garca-Fernandez et al. (2018) revealed significant improvements in shoulder function and patient satisfaction after RTSA for failed ORIF, where most patients rated their outcome as excellent or good. The results of this study confirm that RTSA is associated with considerably greater patient satisfaction compared to ORIF (24).

A recent investigation found that the ORIF group had more complications, such as delayed bone healing, infection, and defective equipment compared to the TSA group. This discovery is consistent with previous studies. In another study by Klug et al. (2019), it was reported that the overall rates of complication for ORIF and RTSA were 37.8% and 22%. In addition, there are higher rates of revision surgery for the ORIF group due to persistent motion deficits. The results support the observation of an increased risk of complications in patients treated with ORIF (25). Similarly, Shannon et al. (2016) also found that RTSA had lower complication rates compared to ORIF, with fewer cases of infection, hardware failure, and delayed union in the RTSA group, which supports our findings (26).

More research can be conducted on the long-term follow-up of patients who have undergone TSA and ORIF. However, more studies are needed to investigate the risks associated with delayed complications and the durability of the prosthesis, as well as the effects of ageing on surgical outcomes after surgery (27, 28).

Although much research provides useful information, it is not without flaws. In one respect, retrospective designs could be good for probing the effects on interventions in real life situations, but on the other hand, they are prejudiced and cannot establish causality. Furthermore, although the sample size was large enough to achieve the objectives of this study, its generalizability to others is limited. Future researchers in this area might find it useful to include more participants and conduct multicenter prospective studies that will validate these conclusions within a different population and health care context. Furthermore, further analyses must be performed continuously to determine whether these findings continue to apply in surgical settings, as there are ongoing changes in surgical procedures and implant types.

Conclusion

The present study suggests that reverse total shoulder

arthroplasty (rTSA) presents a better trend in function after the operation, a higher patient satisfaction rate and a lower complication rate than open reduction and internal fixation (ORIF) for the treatment of proximal humerus fractures in the elderly. Such advantages as early function restoration, less trauma to the remaining bones, and the possibility of faster and better recovery make rTSA a more preferable surgical procedure, especially in situations with multiple fractures or poor bone condition. However, future research studies with larger samples and long-term follow-up are needed to confirm these findings and determine the potential risks and the long-term effect of the prosthesis.

List of abbreviations: rTSA: Reverse total shoulder arthroplasty, ORIF: Open reduction with internal fixation, OTA/AO: Orthopaedic Trauma Association / Arbeitsgemeinschaft für Osteosynthesefragen, SD: Standard Deviation, VAS: Visual analogue scale, SPSS: Statistical package for the Social Sciences, IRB: Institutional Review Board, LCP: Locking Compression Plate, PHILOS: Proximal Humeral Internal Locking System

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Data availability: Data used in this study can be provided on reasonable request.

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ORIGINAL ARTICLE

Evaluation of Sociodemographic and Clinical Characteristics of Forensic Cases Referred to a University Hospital

Bir Üniversite Hastanesine Sevk Edilen Adli Olguların Sosyodemografik ve Klinik Özelliklerinin Değerlendirilmesi

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ABSTRACT

Objective: Judicial authorities may refer forensic cases to the child and adolescent psychiatry outpatient clinic for different evaluations when deemed necessary. Both children who are dragged into crime and children who are victims of crime are evaluated and a medical opinion is formed in order to prepare the reports requested by the judicial authorities. In this context, it was aimed to evaluate the sociodemographic and clinical characteristics of forensic cases referred to the child and adolescent psychiatry outpatient clinic by judicial authorities in 2023.
Material and Methods: In 2023, the files of forensic cases referred to the child and adolescent psychiatry outpatient clinic by judicial authorities were examined retrospectively and sociodemographic characteristics such as age, gender, family status, education level, parental education level, and whether they were diagnosed as a result of psychiatric evaluation were analyzed.
Results: The files of 96 cases between the ages of 2-17 years were evaluated. Seventy-two (75%) of the cases were boys and 24 (25%) were girls and the mean age was 13.60±2.04 years. The most common reasons for the referral of the forensic cases were "to determine whether they comprehend the legal meaning and importance of the crime alleged to have been committed and whether they have developed the ability to direct their behavior" (n=66, 68%) and "to determine whether they can defend themselves physically or mentally" (n=18, 18%), respectively. It was determined that cases with a psychiatric disorder had significantly more repeated offenses. In addition, it was found that repeat offenses were significantly lower in children living with both parents compared to children living with a single parent or without parents.
Conclusion: It was observed that having a psychiatric disorder and not living with both parents may provide important data on recidivism in forensic cases referred to our clinic. In this sense, it was thought that treatment of psychiatric disorder and social service interventions for risky groups may be important in terms of preventive medicine.

Keywords: Child, Adolescent, Forensic psychiatry, Psychiatric comorbidity

ÖZ

Amaç: Adli makamlar gerekli gördüğü durumlarda çocuk ve ergen psikiyatri polikliniğine adli olguları farklı değerlendirmeler için yönlendirebilmektedir. Hem suça sürüklenen çocuklar hem de suç mağduru çocuklar adli makamların istediği raporların düzenlenmesi amacı ile değerlendirilmekte ve tıbbi kanaat oluşturulmaktadır. Bu bağlamda adli makamlar tarafından 2023 yılı içinde çocuk ve ergen psikiyatri polikliniğine yönlendirilen adli olguların sosyodemografik ve klinik özelliklerinin değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntem: 2023 yılında çocuk ve ergen psikiyatri polikliniğine adli makamlarca yönlendirilmiş adli olguların dosyaları geriye dönük olarak incelenmiş ve yaş, cinsiyet, aile durumu, eğitim düzeyi, ebeveyn eğitim düzeyi gibi sosyodemografik özelliklerin yanı sıra psikiyatrik değerlendirme sonucunda tanı alıp almadıkları gibi veriler incelenmiştir.
Bulgular: 2-17 yaş aralığında 96 olgunun dosyası değerlendirilmiştir. Olguların 72'si (%75) erkek, 24'ü (%25) kız olup ortalama yaş 13.60±2.04 bulunmuştur. Adli olguların en sık yönlendirilme sebepleri sırası ile "işlendiği iddia olunan suçun hukuki anlam ve önemini kavrayıp kavramadığı ve davranışlarını yönlendirme yeteneğinin gelişip gelişmediğinin tespiti" (n=66, %68), "beden veya ruh bakımından kendisini savunup savunamayacağının tespiti" (n=18, %18) olmuştur. Psikiyatrik bir bozukluğa sahip olguların anlamlı düzeyde daha fazla suç tekrarına sahip olduğu belirlenmiştir. Ayrıca her iki ebeveyni ile yaşayan çocuklarda tek ebeveynle/ebeveynsiz yaşayan çocuklara kıyasla suç tekrarının anlamlı düzeyde daha az olduğu saptanmıştır.
Sonuç: Kliniğimize yönlendirilen adli olgularda psikiyatrik bozukluğa sahip olmanın ve her iki ebeveynle birlikte yaşamıyor olmanın suç tekrarına ilişkin önemli veriler sağlayabileceği görülmüştür. Bu anlamda psikiyatrik bozukluğun tedavisi ve riskli gruplara yönelik sosyal hizmet müdahalelerinin koruyucu hekimlik açısından önemli olabileceği düşünülmüştür.

Anahtar kelimeler: Çocuk, ergen, adli psikiyatri, psikiyatrik komorbidite

Introduction

Behaviors that threaten the security and order of society or violate the rights of other individuals are considered crimes under certain legal regulations and are punished according to the penalties prescribed by law. Statutory offenses include crimes defined in criminal laws such as murder, theft, sexual abuse and assault, and often require some form of sanction such as imprisonment or a fine as a result of a judicial trial. Legal offenses also apply to children (1). According to a 2010 Canadian study, 37% of children in 7th and 9th grades were dragged into crime and 50% of these children committed their first crime before the age of 12 (2). According to data from the Turkish Statistical Institute, the number of incidents involving children who

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came to or were brought to security units increased by 20.5% in 2022 compared to 2021 and reached 601,754. Two hundred six thousand eight hundred fifty-three of these incidents occurred due to being dragged into crime (3). Of the crimes charged, 37.8% were wounding, 25.2% were theft, 4.5% were using, selling or buying drugs or stimulants, 4.2% were crimes against the passport law and 4.1% were threat crimes.

The penalties to be imposed by judicial authorities are defined by specific legal regulations. Article 31/2 of the Turkish Penal Code (TPC) states that children who have completed the age of 12 but have not completed the age of 15 should be evaluated whether their ability to perceive the legal meaning and consequences of the act committed or to direct their behavior in relation to this act has developed sufficiently, or Article 32 of the TPC states that due to mental illness, the ability to perceive the legal meaning and consequences of the act committed or to direct their behavior in relation to this act has decreased or significantly decreased (1). In this context, children who are referred to child and adolescent psychiatry outpatient clinics for the evaluation of their ability to perceive the legal meaning and consequences of the act committed or to direct their behavior in relation to this act, to determine whether they can defend themselves physically or mentally, and for the presence of any psychopathology, should be examined at the direction of the court. At the same time, Article 124/2 of the Turkish Civil Code states that judges may authorize the marriage of boys and girls who have reached the age of 16 in extraordinary circumstances and for a very important reason (4). Children who are victims of crime and children who want to marry before reaching the age of majority are also referred to the child and adolescent psychiatry department. These children are also evaluated on the reliability of their declaration and their suitability for marriage. In a study conducted in Sakarya in 2012, the presence of a psychopathology was found in 71% of abuse cases, 56.9% of children dragged into crime (CDC) and 11.5% of children who applied for marriage (5). In addition, when children who were dragged into crime were examined, repeated offenses were associated with having negative family relations (6), dropping out of school, having friends who were dragged into crime (7), having low- and middle-income level socioeconomically (8) and having more siblings (9). At the same time, it has been statistically revealed that children with comorbid psychopathology constitute the majority of CDC.

The number of referred forensic cases is increasing every year (3). In the evaluation of these referred cases, it is important to determine the risk factors for being dragged into crime and to identify the determinants of the possibility of repeat offences. Therefore, we have two aims. Our first aim is to determine the sociodemographic characteristics of forensic cases. Our second aim is to determine the relationship between psychiatric disorder and being dragged into crime. Our hypothesis is that if children dragged to crime have psychiatric disorders, the rate of repeat offences will increase.

Material and Methods

The sample of this study consists of children referred to the Child and Adolescent Psychiatry Outpatient Clinic of Selçuk University, Faculty of Medicine Hospital by judicial authorities between January 1 and December 31, 2023. Forensic cases referred to our clinic are interviewed under the supervision of the responsible faculty member, the reason for the referral, the forensic file is examined and detailed diagnostic interviews are conducted with the family and the child based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (10). In addition, the Wechsler Intelligence Scale for Children (WISC-R) is administered to determine cognitive characteristics in cases with clinically suspected Intellectual Disability (ID). The data to be used in this study were obtained by file screening method.

Ethics committee approval of the study was obtained from Selcuk University, Faculty of Medicine Local Ethics Committee with protocol number 2024/103. The data of the study were obtained retrospectively by file scanning method. Statistical analyses were performed using SPSS version 22. Continuous variables were expressed as mean ± standard deviation while categorical variables were summarized as frequencies and percentages. The Kolmogorov-Smirnov test was used to check the normality of the data. Before conducting the analysis, kurtosis and skewness values were evaluated to ensure the normality assumption, with coefficients falling within the acceptable range of -1 to +1 (11). Participants were divided into two groups based on family status (intact or separated) and presence or absence of psychiatric disorders. Differences in age, gender, and recidivism rates between the two groups were analyzed using Student's t-test and Chi-square tests. A significance level of $p < 0.05$ was adopted for all tests.

Results

The study included 96 children between the ages of 2-17 years, and the mean age of the children was 13.60±2.04 years. 25% of the children were girls (n=24) and 75% were boys (n=72). 2.1% (n=2) of the children had not yet reached school starting age, 22.9% (n=22) had dropped out of school, and 75% (n=72) were attending school.

In 30.2% (n=29) of the children, parents were divorced while 69.8% (n=67) had preserved family unity. When parental education status was analyzed, the mother of 13.5% (n=13) was illiterate and the father of 4.2% (n=4) was illiterate. None of the parents of the participants included in the study were university graduates. 97.9% (n=94) of the children lived in rural areas and 2.1% (n=2) lived in urban areas. 71.9% (n=69) of the children were referred to us because of damage to property and person, 12.5% (n=12) because of theft, and 10.4% (n=10) because of underage marriage. As a result of detailed diagnostic interviews with the

children, it was determined that 67.7% (n=65) had no psychiatric disorder, 24.9% (n=24) had attention deficit and hyperactivity disorder (ADHD) and 16.7% (n=16) had ID. (these data are shown in table 1.)

Table 1. Characteristics of participants

Participant characteristics (N=96)	%/M (SD)
Gender	
Female	25 (n= 24)
Male	75 (n= 72)
Age	13.60 (2.04)
Educational level of children	
Under school age	2.1
Drop out of school	22.9
Attending school	75
Educational level of the mother	
Illiterate	13.5
Primary School	56.3
Secondary school	21.9
High school	8.3
Educational level of the father	
Illiterate	4.2
Primary School	63.5
Secondary school	7.3
High school	25
Living Space	
Rural	97.9
Urban	2.1
Having a Psychiatric Disorder	
No	67.7
Yes	32.3
Reasons for referral	
Damage to property and person	71.9
Theft	12.5
Underage marriage	10.4
Other	5.2

When the reasons for referral of forensic cases were examined, the most common reasons for referral were "to determine whether the patient comprehends the legal meaning and importance of the crime alleged to have been committed and whether his/her ability to direct his/her behaviors has developed" (n=66, 68%) and "to determine whether he/she can defend himself/herself physically or mentally" (n=18, 18%). 79.2% (n=76) of the children were referred to us for the first offense and 20.8% (n=20) were referred to us for repeated offenses. When children who committed repeated offenses were analyzed, it was found that the tendency to commit repeated offenses was statistically higher among children living in separated families and those with psychiatric disorders (These data are shown in table 2,3.).

Table 2. Comparison of repeated offense rates according to family status

Participant characteristics (N=96)	Intact Family	Separated Family	p	$x^{2^\wedge}/t^*$
Gender				
Female	n=14	n=12	0.135	4.006^
Male	n=53	n=17		
Age	13.2 ± 3.5	12.8 ± 3.7	0.629	0,485*
Repeated Offense				
Present	n=50	n=8	0.007	7.365^
Absent	n=17	n=21		

^Chi-square test was applied

* Student's t-test was applied

Results with statistically significant differences are in bold.

Table 3. Comparison of repeated offense rates according to psychiatric comorbidity

Participant characteristics (N=96)	Having a Psychiatric Disorder	Not Having a Psychiatric Disorder	p	$x^{2^\wedge}/t^*$
Gender				
Female	n=6	n=18	0.512	1.337^
Male	n=25	n=47		
Age	12.5 ± 3.2	13.8 ± 3.4	0.212	1.256*
Repeated Offense				
Present	n=13	n=7	<0.001	12.362^
Absent	n=18	n=58		

^Chi-square test was applied

* Student's t-test was applied

Results with statistically significant differences are in bold.

Discussion

The study aimed to comprehensively examine the sociodemographic and clinical characteristics of pediatric cases referred to the Child and Adolescent Psychiatry Outpatient Clinic of Selçuk University, Faculty of Medicine Hospital by judicial authorities. Although the findings are largely consistent with previous studies in this field, they include some differences and unique contributions. As a result of the study, living in a separated family and having a psychiatric disorder were found as the factors that increased the likelihood of repeated offenses.

ADHD was detected in 24.9% of the cases in the study, and 16.7% of the cases had ID. These findings are consistent with the results of Bilginer et al. (2020) who reported that a large proportion of CDC had a previous psychiatric diagnosis. The prevalence of ADHD explains the difficulties these children experience in impulse control and adaptation to social norms. The relationship between ADHD and criminal behavior has been widely documented in the literature; it is known that individuals with ADHD are at higher risk of being dragged into crime due to their attention deficits and impulsivity (13). In this context, it can be concluded that it may be in the best interest of the children to conduct comprehensive psychiatric examinations of CDC and to closely monitor children with psychiatric diagnoses, especially in terms of the risk of being dragged into crime.

When children who have committed repeated offenses are examined more closely, it is also investigated which factors may predispose them to reoffending. In this context, it was determined that CDC living in broken families were significantly more likely to reoffend compared to children living in nuclear and/or extended families. One of the factors affecting the tendency of those living in broken families to reoffend may be poor social support. Tunceroğlu's (2015) study shows that family disharmony increases the risk of juvenile delinquency. Having a fragmented family structure may cause children to not receive sufficient emotional and social support, leading to an increase in criminal behavior. In this sense, it may be important to follow children who have been dragged into crime once and live in a broken family more closely to prevent them from being dragged into crime again.

In the Child Protection Law published in the Official Gazette in 2005, there are cautionary decisions defined for CDCs. These cautionary decisions are of great importance in closely monitoring CDCs and providing them with the necessary support (12).

Another factor found to be significant in the study on recidivism is having a psychiatric disorder. In our study, it was found that individuals with psychiatric disorders were significantly more likely to be dragged into repeated offenses. Although this finding does not mean that every child with a psychiatric diagnosis will be dragged into crime, it has been concluded that it may be appropriate to follow up children who have been dragged into crime and have a psychiatric disorder in order to prevent them from being dragged into crime again and to evaluate them in terms of the measures specified in the Child Protection Law (12). However, longitudinal studies with a larger sample on this subject are important to confirm the results emphasizes the prevalence and the role of comorbidity. In particular, it is known that neurodevelopmental disorders such as ADHD and ID can negatively affect children's social adaptation skills and problem-solving abilities and may predispose them to criminal behavior (14).

Limitations

Our study has some limitations. For example, sampling from only one university hospital and the relatively small sample size limit the generalizability of the results. In addition, the retrospective collection of the data used in our study may cause some information gaps. Therefore, it is recommended that future studies be conducted on larger sample groups and with different methods.

Conclusion

As a result, this study may provide an opportunity to comment on the fact that mental disorders are present in a significant number of children referred by judicial authorities and that family structure may have a determining effect on being dragged into crime. It emphasizes the importance of comprehensively assessing and supporting the mental and social needs of children involved in judicial processes. In order to support the healthy development of children and reduce the risk of children being dragged into crime, effective cooperation between families, educational institutions and judicial authorities should be ensured in order to strengthen family relationships and increase social support. These recommendations may show the necessity of multidisciplinary and coordinated work in terms of both preventing children from being dragged into crime and preventing CDC from being dragged into crime again. More multidisciplinary studies with larger samples are important to confirm the results of our study.

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