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ORIGINAL ARTICLE

Self-Management Perceptions and Death Anxiety of Patients with Diabetes Mellitus

Diyabetes Mellitus'lu Hastaların Öz Yönetim Algıları ve Ölüm Kaygıları

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ABSTRACT

Aims: In the present study, it was aimed to determine the death anxiety and diabetes self-management perceptions of diabetes mellitus (DM) patients.
Methods: The descriptive and correlational study was conducted on 351 DM patients who visited the internal medicine outpatient clinic of a government hospital between 20.02.2022 and 20.05.2022. The Patient Identification Form (PIF), Death Anxiety Scale (DAS), and Diabetes Self-Management Perception Scale (DSMS) were used as data collection tools. The descriptive statistics, Mann-Witney U, Kruskall-Wallis, and Spearman correlation tests were used to evaluate the data. In the study, $p<0.05$ was considered significant
Results: It was determined that 39.3% of DM patients participating in the study experienced fear of death. It was determined that the average score of the patients on the death anxiety scale was 9.24±3.70, and the average score on the diabetes self-management perception scale was 24.84±3.28. It has been determined that the self-management skills of patients who are primary school graduates and patients who develop acute complications due to DM are higher. In terms of death anxiety scale scores, it was determined that women had higher death anxiety levels than men and patients with DM-related fear of death compared to others. There was no significant relationship between the Death Anxiety Scale Total Score and the Diabetes Self-Management Scale Total Score ($p>0.05$).
Conclusion: In the study, it was determined that patients experienced more severe death anxiety and moderate death anxiety. Additionally, the self-management of DM patients was found to be above average. No relationship was found between the patients' Death Anxiety Scale and Diabetes Self-Management Perception Scale score averages. The mean Diabetes Self-Management Perception Scale scores of primary school graduates and patients with DM-related complications are significantly higher than others

Keywords: Death anxiety, diabetes mellitus, patient, perception, self-management

ÖZ

Amaç: Bu çalışmada diabetes mellitus (DM) hastalarının ölüm kaygısı ve diyabet öz yönetim algılarının belirlenmesi amaçlanmıştır.
Yöntem: Tanımlayıcı ve ilişki arayıcı tipteki çalışma, 20.02.2022-20.05.2022 tarihleri arasında bir Devlet Hastanesinin Dahiliye polikliniğine başvuran 351 DM hastası ile yapılmıştır. Araştırmada veri toplama aracı olarak; Hasta Tanılama Formu, Ölüm Kaygısı Ölçeği (ÖKÖ) ve Diyabet Öz-Yönetim Algısı Ölçeği (DÖYAS) kullanılmıştır. Verilerin değerlendirilmesinde; tanımlayıcı istatistikler, Mann-Witney U, Kruskall-Wallis ve Spearman Korelasyon testleri kullanılmıştır. Çalışmada $p<0.05$ anlamlı olarak kabul edilmiştir.
Bulgular: Araştırmaya katılan DM hastalarının %39,3'ünün ölüm korkusu yaşadığı belirlenmiştir. Hastaların ölüm kaygısı ölçeğinden aldıkları puan ortalamasının 9,24±3,70, diyabet öz yönetim algısı ölçeğinden aldıkları puan ortalamasının ise 24,84±3,28 olduğu belirlenmiştir. İlkokul mezunu hastalar ile diyabete bağlı akut komplikasyon gelişen hastaların özyönetim becerilerinin daha yüksek olduğu saptanmıştır. Ölüm kaygısı ölçeği puanları açısından kadınların erkeklere göre, diyabete bağlı ölüm korkusu olan hastaların ise diğerlerine göre ölüm kaygısı düzeylerinin daha yüksek olduğu belirlenmiştir. Ölüm Kaygısı Ölçeği Toplam Puanı ile Diyabet Öz Yönetim Ölçeği Toplam Puanı arasında anlamlı bir ilişki bulunmamıştır ($p>0.05$).
Sonuç: Araştırmada hastaların daha çok şiddetli ölüm kaygısı ve orta düzeyde ölüm kaygısı yaşadığı belirlenmiştir. Ayrıca DM hastalarının öz yönetimlerinin ortalamanın üzerinde olduğu saptanmıştır. Hastaların Ölüm Kaygısı Ölçeği ve Diyabet Öz-Yönetim Algısı Ölçeği puan ortalamaları arasında ilişki bulunamamıştır. İlköğretim mezunlarının ve DM' ye bağlı komplikasyonu olan hastaların DSMS puan ortalamaları diğerlerine göre anlamlı derecede yüksektir.

Anahtar Sözcükler: Algı, hasta, ölüm kaygısı, öz-yönetim, şeker hastası

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease that requires constant medical care in which the organism cannot benefit sufficiently from carbohydrates, fats, and proteins due to insulin deficiency or problems in the effect of insulin (1). Today, Type 1 and Type 2 DM have become a very important health problem affecting millions of people worldwide, and their incidence in childhood is increasing and is increasing much faster than expected (2). Type 2 DM is the most common form of DM (3).

Since DM is a chronic disease and patients see a healthcare professional only a few times a year, the rest of the time, patients need to self-manage

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their disease by controlling all these problems themselves. Self-management is defined as the active participation of patients in their treatment (4), and self-management medical management includes processes such as taking medication and following dietary recommendations, adopting new behaviors and emotional management in the context of chronic disease, and coping with feelings of disappointment, fear, and helplessness associated with chronic disease (5).

DM self-management practices include nutrition planning, self-monitoring of blood sugar, metabolic control, proper exercise, avoiding risky behavior, prevention of acute and chronic complications, and good problem-solving skills (6). Complications seen in individuals with DM cause individuals to experience sadness, anger, anxiety, self-sufficiency, social isolation, helplessness, hopelessness, anxiety, stress, fear and anxiety of death, and weakening of their self-management (6-9). Individuals show different reactions to death anxiety. These reactions may tend to increase or decrease health-promoting behaviors. When individuals' health becomes critical, factors such as death anxiety levels, social supports, and self-management perceptions may affect their illness self-management (10, 11). Thus, effective DM self-management becomes important in reducing DM-related complications and death anxiety by ensuring that the DM patient complies with the treatment and care programs (6).

Studies on death anxiety show that cancer cases are the most common chronic diseases. Nefs et al. (2019) stated that individuals with DM experience intense psychological problems and cannot manage their self-care well (12). It is thought that in a disease with a better prognosis, such as DM, there is a need for study results on self-care management and attitude toward death (13, 14). When the literature is examined, it is seen that there are different results regarding death anxiety in patients. Based on the literature, it is reported that death anxiety is high in women with Type II DM. In a study on spiritual development and death attitude in women with Type II DM, it is reported that the spiritual development of women is significantly related to some elements of attitude profiles towards death, and DM patients with depression have high death anxiety (10, 15). Therefore, this study aimed to determine DM patients' death anxiety and diabetes self-management perceptions.

Research Questions

1. What are the death anxiety and self-management perception levels of DM patients?

2. Is there a relationship between self-management perceptions and death anxiety of individuals with DM?

3. What are the variables affecting the death anxiety and self-management perceptions of individuals with DM?

Methods

Study Design: This research is a descriptive and correlational study. The STROBE Checklist directive was followed in the study.

Setting and Sample: The research was carried out between 20.02.2022 and 20.05.2022 in Akşehir State Hospital Internal Medicine Polyclinic with DM patients who met the research criteria and volunteered to participate in the research. The population of the study consisted of 680 Type I and Type II DM patients registered in the Internal Medicine Polyclinic in the last year. The required minimum sample size universe was calculated using the known sample calculation and the formula n= Nt2pq/d2(N-1)+pq. The minimum sample size was determined as 246 with a 95% confidence interval and a 5% margin of error. A total of 351 patients constituted the sample of our study. Of the 351 patients with DM, 43 are patients with Type I DM and 308 are patients with Type II DM. Patients admitted to the DM polyclinic for examination met the inclusion criteria and volunteered to be referred to the researchers by the physician. The researchers gave information about the research to the patients and asked them to fill out the data collection form after obtaining verbal and written consent. Patients who were able to fill out the data collection form filled it out themselves. Patients who could not fill it out were asked questions by the researchers.

The inclusion criteria consisted of the following: Being 18 years of age or older, having been diagnosed with DM at least one year ago, not having a communication problem, agreeing to participate in the study, being a DM patient admitted to the internal medicine clinic on the dates of the study. However, the exclusion criteria were as follows: Not being under 18 years of age, and communication problems such as vision and hearing. Those who were illiterate and did not want to participate in the study were also excluded.

The Data Collection

The Patient Identification Form (PIF), Death Anxiety

Scale (DAS), and Diabetes Self-Management Perception Scale (DSMS) were used as data collection tools in the study.

The Patient Identification Form (PIF)

The form consisting of two parts includes questions about the sociodemographic and disease characteristics of the patients, such as age, gender, marital status, educational status, place of residence, employment status, income status, smoking and alcohol use, number of people living at home, duration of DM disease, duration of insulin use, duration of oral antidiabetic drug use, development of acute and chronic complications due to DM, experiencing death anxiety due to DM, type of DM.

The Death Anxiety Scale (DAS)

It was developed by Templer (1970) and its validity and reliability study in our country was carried out by Şenol 1989 (16). It is a 15-question scale that measures the anxiety and fears of the person's death and the danger of death answered as true or false. The scale consists of 15 items and is arranged as a true-false binary Likert scale. Correct answers are given 1 point, while incorrect answers are not scored. In the test, whose score range is between 0-15, it is interpreted that there is an increase in death anxiety as the scores increase in this range, and those who score 7 and above are considered to have anxiety. "1" for each "yes" answer given to the first 9 questions in the scale (for example: "I am very afraid of dying"), "0" for "no" answers, and "0" for each of the other 6 items (for example: "I am not afraid of dying at all"). A score of "1" is given for a "no" answer and a "0" for a "yes" answer. The sum of the scores obtained from the scale reports the death anxiety score. The maximum score taken from the scale is 15. 0-4 points are considered as "mild", 5-9 points as "moderate", 10-14 points as "severe", and 15 points as "panic" as "death anxiety". Şenol (1989) found Cronbach's Alpha coefficient to be 0.86 in his validity and reliability study. The Cronbach's Alpha coefficient for this study was found to be 0.83

The Diabetes Self-Management Perception Scale (DSMS):

DSMS is a scale prepared by Wallston et al., (2007) colleagues, taking into account the Perceived Competence Health Scale (PHCS) developed by Smith et al., (1995). The scale was adapted to Turkish by Bayındır Çevik (2010). The scale consists of one dimension and 8 items. It is scored as strongly disagree 1, disagree 2, undecided 3, agree 4, strongly agree 5. The minimum score that can be obtained from the scale is 8, and the maximum score is 40. A high total score on the scale indicates that the individual's awareness of diabetes management is very good. DSMS was studied to be adapted to Turkish society and its Cronbach's Alpha value was found to be 0.83 (17). The Cronbach's Alpha coefficient for this study was found to be 0.72.

Implementation of the research

Consent was obtained from patients who met the inclusion criteria. Then the patients were asked to fill in the scales. The research was carried out between February and May 2022. Data collection took approximately 20-25 minutes per patient and data were collected from 351 patients. Data from 29 patients were excluded from the sample due to missing data on the data collection form. The study was completed with 351 patients. Data were collected by the same researcher.

Data analysis

IBM SPSS 24.0 and SigmaStat 3.5 statistical programs were used to evaluate the data. Summary statistics are given as the number of units (n), percent (%), mean ± standard deviation, median, and percentile. The distribution of numerical variables was evaluated with the normality test. Mann-Witney U test was used in the comparison of two groups, the Kruskall-Wallis test was used in the evaluation of more than two measurements, and the Spearman correlation analysis was used in the comparison of the scales used with each other. In the study, $p < 0.05$ was accepted as significant

Ethical consideration

Ethical permission (2022/59), necessary institutional permissions, and verbal consent from the patients to participate in the study were obtained from the non-interventional ethics committee of the university to implement the study and collect data. Permission for the scale work was obtained from the relevant persons via e-mail. All principles of the Declaration of Helsinki were complied with in the study.

Results

Half of the DM patients participating in the study were between the ages of 36-64, 67.0% were women, 49.0% were primary school graduates, 83.2% lived with their families, and 60.1% were housewives. It was

determined that 51.6% had income (Table 1).

Table 1. Distribution of patients with DM by socio-demographical and disease characteristics (n=351)

Variables	n	%
Age (years)		
18-35	19	5.4
36-64	176	50.2
65 years and older	156	44.4
Gender		
Female	235	67.0
Male	116	33.0
Marital status		
Married	303	86.3
Single	48	13.7
Educational Status		
Illiterate	80	22.8
Primary education	172	49.0
Secondary education	65	18.5
High education	34	9.7
Person living with		
Alone	45	12.8
Family	292	83.2
Relative	20	4.0
Employment Status		
Housewife	211	60.1
Office	19	5.4
Employed	33	9.4
Unemployed	88	25.1
Income status		
Income less than expenses	181	51.6
Income equal to expenses	158	45.0
Income more than expenses	12	3.4
Smoking status		
Yes	12	3.4
No	332	94.6
I quit	7	2.0
Alcohol Use		
Yes	12	12.8
No	332	81.5
I quit	7	5.7
DM disease duration (years) ($\bar{X}$ ±SD)	11.47±8.41	
Duration of insulin use (years) ($\bar{X}$ ±SD)	8.44±7.40	
Oral antidiabetic drug use duration (years) ($\bar{X}$ ±SD)	10.96±7.90	

DM: Diabetes mellitus, SD: Standard deviation

In Table 2, DAS and DSMS mean scores of DM patients, minimum (min) and maximum (Max), Cronbach Alpha values are included. In the study, it was determined that 53.8 % of the patients had severe (Min: 10, Max: 14) death anxiety, and 32.5% had moderate (Min: 5, Max: 9) death anxiety. It was determined that the DAS mean score of DM patients was 9.24±3.70 points above the mean score (Min: 0, Max: 15), and the DSMS mean score was 24.84±3.28 above the mean (Min: 8, Max: 40) (Table 2).

Table 3 shows the relationship between DAS and DSMS mean scores of patients with DM who participated in the study. It was determined that there was no significant relationship between death anxiety and self-management perceptions of DM patients (r=-0.077, p=0.149).

Table 3. Correlation between death anxiety and self-management perceptions of individuals with DM

Scales	DSMS	
	r	p
DAS	-0.077	0.149

DAS: Death anxiety scale, DM: Diabetes mellitus, DSMS: Diabetes self-management perception scale

Table 4 shows the distribution of mean scores of DM patients participating in the study according to variables affecting their perception of death anxiety and diabetes self-management. In the study, it was determined that women's DAS score averages were significantly higher than men's. It was found that the average DAS score of those who had a fear of death due to DM was higher. According to education level, the mean DSMS scores of primary school graduates and patients with DM-related complications were found to be significantly higher than others (Table 4)

Discussion

DM consists of self-management; it is required to

Table 2. Mean Scores of the DAS and the DSMS (N=351)

	N	%	$\bar{x}$ ±SS	Min	Max	Cronbach Alpha
DAS (Min: 0, Max: 15)	351	100.0		0	15	
Mild death anxiety	35	12.8		0	4	
Moderate death anxiety	114	32.5	9.24±3.70	5	9	0.831
Severe death anxiety	189	53.8		10	14	
Panic-level death anxiety	3	0.9		-	15	
DSMS (Min: 8, Max: 40)	351	100.0	24.84±3.28	8	40	0.720

*Min: Minimum, Max: Maximum, $\bar{X}$ ±SD: Mean±Standard deviation. DAS: Death anxiety scale, DSMS: Diabetes self-management perception scale

Table 4. Comparison of death anxiety and self-management perceptions of individuals with DM with some sociodemographic and disease characteristics **(N=351)**

Variables	n	%	DAS $\bar{X}$ ±SS	DSMS $\bar{X}$ ±SS
Gender				
Woman	235	67.0	9.57±3.53	24.73±3.14
Male	116	33.0	8.56±3.96	25.06±3.55
z /p			z=-2.160, **p = 0.031**	z = -1.173, p = 0.241
Educational Status				
Illiterate	80	22.8	10.11±3.17	24.20±2.84 [c]
Primary education	172	49.0	9.02±3.60	25.25±3.24 [a]
Secondary education	65	18.5	9.10±4.03	24.89± [3.78b]
High education	34	9.7	8.52±4.42	24.20±3.20 [d]
KW /p			KW=5.429, p=0.143	KW =8.943, **p=0.030**
Complication development status due to DM				
Yes	250	71.2	9.36±3.51	24.63±3.24
No	101	28.8	8.95±4.13	25.36±3.33
z /p			z=-0.489, p = 0.625	z = -2.036, **p = 0.042**
Fear of death due to DM				
Yes	138	39.3	11.13±2.82	24.56±3.24
No	213	60.7	8.01±3.69	25.02±3.30
z /p			z =-7.917, **p = 0.000**	z = -1.527, p=0.127

Min: Minimum, Max: Maximum, *In the comparison of two independent groups not showing normal distribution; z: Mann - Whitney U test ** In the comparison of three independent groups; KW: Kruskal - Wallis Test, $\bar{X}$ ±SD: Mean±Standard Deviation. DAS: Death anxiety scale, DM: Diabetes mellitus, DSMS: Diabetes self-management perception scale

prevent acute and chronic complications in DM (10). It is emphasized that the self-management skills of DM patients are an important factor that increases the chance of success in treatment (9). In the literature, it is stated that death anxiety aggravates the conical disease state and affects self-management because it is a multidimensional concept that includes the fear of death (18-20). In this study, death anxiety and self-management perceptions of patients with DM were discussed in the literature.

In the study, it was found that 53.8% of the patients experienced severe death anxiety and 32.5% experienced moderate death anxiety. It was determined that the mean Death Anxiety Scale score of DM patients was 9.24±3.70 points above the mean score. Thinking about death is also one of the concerns of DM patients (21). It is stated that the prevalence of anxiety and depression is high in patients with Type 2 DM (15), and if the necessary interventions are not made, the patient's self-management is negatively affected, the risk of complications increases, and they experience death anxiety over time (15, 21). When the literature is examined, it is seen that there are a limited number of studies examining the levels of death anxiety and fear in DM patients (7, 20, 22). In a study comparing the self-concept and death anxiety of Type II DM and healthy women, it was stated that death anxiety in women with Type II DM was significantly higher at 44.41±8.44 (7). In a study conducted on spiritual development and death attitude in women with Type II DM, it was observed that women's spiritual development was significantly associated with some elements of their attitude towards death profiles (11). In the study of DM patients with depression, it was found that the death anxiety scores of the patients were significantly higher than the pre-test and post-test before training (15). However, it is also seen in the literature that there are studies addressing death anxiety in different chronic diseases with similar results to our study findings (23). One of the reasons why the death anxiety scores of patients with DM were moderate and severe in our study may be the large number of individuals aged 65 and over. In a study conducted with patients with DM; It has been stated that the patients' age and high

level of religiosity may have reduced their anxiety, and for these reasons, they experienced less death anxiety (24). The results of this study suggest that the death anxiety levels of individuals with chronic diseases such as DM should be determined at an early stage and their disease self-management perceptions should be positively strengthened.

It was found that the mean score of Diabetes Self-Management Perception was significantly lower in patients who developed acute complications due to DM compared to those who did not, and their awareness of diabetes management was poor. In a study conducted to determine the relationship between Self-Management Perceptions and the Health status of individuals with DM; DSMS scale scores of DM patients were determined as 30.69±2.65. In a study conducted with 110 DM patients, it was emphasized that cognitive fusion and distortion were among the variables that predicted death anxiety in patients (25). When the literature is examined, it is emphasized that the self-management skills of patients with DM are weak, with similar results to our study findings, and that self-management perceptions and skills should be increased with training programs (9). The results of this study made us think that it is important to increase the disease self-management perceptions of DM patients through training and turn them into positive behavioral changes.

The results of this study made us think that it is important to increase the self-management perceptions of patients with DM who develop complications by supporting them with regular education programs.

Limitations of the Study

The data are limited to DM patients who came to the hospital's outpatient clinic at the time of the study. The data are based on self-report and cannot be generalized to all DM patients. Another limitation is that the study was conducted in a mixed age group rather than a specific age group. Conducting the study during the COVID-19 pandemic period, requiring compliance with masks, distance, and hygiene rules, causing a decrease in the number of patients participating in the study, and affecting possible death anxiety levels and self-management perceptions can be counted among the limitations.

Conclusions and Recommendations

It was determined that nearly half of the DM patients participating in the study experienced moderate death anxiety, more than half experienced severe death anxiety, and their diabetes management perceptions were above average. In addition, it was determined that the average DAS score of women was significantly higher than that of men, and the average DAS score of those who had a fear of death due to DM was higher. According to education level, the mean DSMS scores of primary school graduates and patients with DM-related complications were found to be significantly higher than others. Diabetic patients can be supported to manage their disease better by reducing their death anxiety by giving training at regular intervals and providing psychological support. It is recommended to increase the self-management perceptions of patients with DM through self-management programs.

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Conflict of Interest

The author declares that there is no conflict of interest.

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ORIGINAL ARTICLE

Red Blood Cell Distribution width: A Reliable Marker in Patients with Multiple Sclerosis?

Kırmızı Kan Hücresi Dağılım Genişliği: Multipl Sklerozlu Hastalarda Güvenilir Bir Belirteç mi?

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ABSTRACT

Objective: The red blood cell distribution width (RDW) is a prognostic marker in patients with active or chronic inflammation, cardiovascular, and other autoimmune diseases. Therefore, this study aimed to evaluate levels of RDW in patients with multiple sclerosis (MS), disease subtypes, and attacked groups.
Material and Methods: MS patients and healthy controls were included in the study. Demographic characteristics of MS and controls, types of MS, MS attacks or no attacks, and laboratory parameters analysis were evaluated. RDW was calculated according to the following formula: RDW = (Coefficie t of Variability of RBC ÷ mean MCV) × 100. All groups and subgroups were compared according to the RDW value.
Results: The study was conducted on 105 MS patients, 74 (70.5%) females, and 31 (29.5%) males, with a mean of 38 (20-64) years of age. RDW values in the MS group were 13.8 (12.1-27.1), whereas in the control group, the values were 13.4 (12.1-17.4) (p=0.007). Receiver operating characteristic (ROC) analysis revealed that using a cut-off point of 13.55, RDW predicts MS with a sensitivity of 59% and specificity of 54.2%. There was no statistically significant difference among the MS subgroups and attacked groups according to RDW value (p=0.41, p=0.92).
Conclusion: RDW would be a novel, low-cost-effective, widely and immediately available biomarker for patients with MS.

Keywords: Red blood cell distribution width, Multiple sclerosis, Biomarker,Inflammatio

ÖZ

Amaç: Eritrosit dağılım genişliği (RDW), aktif veya kronik inflamasyonu olan, kardiyovasküler ve diğer otoimmun hastalıkları olan hastalarda prognostik bir belirteçtir. Bu çalışmanın amacı multiple skleroz hastalarında, hastalık alt tiplerinde ve atak gruplarında RDW düzeylerini değerlendirmektir.
Gereç ve Yöntem: Çalışmaya multiple skleroz (MS) hastaları ve sağlıklı bireyler dahil edildi. MS ve kontrol grubunun demografik özellikleri, MS tipleri, MS atağı olup olmadığı ve laboratuvar parametrelerinin analizi değerlendirildi. RDW şu formüle göre hesaplandı: RDW = (RBC Değişkenlik Katsayısı ÷ ortalama MCV) × 100. Tüm gruplar ve alt gruplar RDW değerine göre karşılaştırıldı.
Bulgular: Çalışma, yaş ortalaması 38 (20-64) yıl olan, 74'ü (%70,5) kadın ve 31'i (%29,5) erkek olmak üzere 105 MS hastası üzerinde gerçekleştirildi. MS grubunda RDW değerleri 13,8 (12,1-27,1), kontrol grubunda ise 13,4 (12,1-17,4) idi (p=0,007). Alıcı işlem karakteristikleri (ROC) analizi, RDW'nin 13,55 kesme noktası kullanıldığında hastalığı %59 duyarlılık ve %54,2 özgüllükle tahmin ettiğini ortaya çıkardı. MS alt grupları ve atak grupları arasında RDW değerine göre istatistiksel olarak anlamlı fark yoktu (p=0,41, p=0,92).
Sonuç: RDW, MS hastalarına yönelik yeni, düşük maliyetli, yaygın olarak ve hemen bulunabilen bir biyobelirteç olabilecektir.

Anahtar kelimeler: Eritrosit dağılım genişliği, Multiple skleroz, Biyobelirteç, İnflamasyo

Introduction

Red blood cell distribution width (RDW) is a routinely reported parameter in the complete blood cell count test and refle ts variation in red blood cell size or red blood cell volume (1). Recent studies have shown that RDW is an inflammatory biomarker. Furthermore, the complete blood cell count test reported a positive correlation between RDW and the severity of inflammation (2). RDW is a prognostic biomarker in patients with cardiovascular diseases, COVID-19, brain injury, active or chronic inflammation, and other autoimmune diseases (3-8).

It is well-known that autoimmune diseases develop because of chronic inflammation. Multiple Sclerosis (MS) is an autoimmune disease associated with the activation of the immune system, leading to demyelination of the central nervous system (9).

MS is divided into 4 main groups according to the clinical course of the disease. The most common MS subtype is the relapsing-remitting MS variant (RRMS), in which the disease presents with relapses. In this disease group, separate attacks that can last from days to weeks are observed. Clinical stability is observed between attacks. Complete recovery is expected after the first attacks. However, the attacks start to leave disability after a while. In the following periods, some patients with RRMS have fewer attacks, but clinically significant progression

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is observed. This group is called secondary progressive MS (SPMS). There is also a type of MS in which clinical progression is observed from the beginning of the disease with no attacks. This group is called primary progressive MS. The least common MS variant is progressive relapsing MS (PRMS), in which progression continues, with occasional attacks. Although this variant has similarities with primary progressive MS, it is distinguished by occasional attacks (10).

The pathologic mechanisms in MS types are not fully understood. However, inflammation is always present with active demyelination and neurodegeneration occurs in all forms of MS (11). The pathological mechanism of MS types has yet to be sufficiently clarified. However, inflammation always coexists with active demyelination and neurodegeneration occurs in all forms of MS. In some cases, MS can be complicated to diagnose.

A hemogram is a straightforward and widely available test. Our first aim in this study was to evaluate the RDW level and its correlation in patients with MS. With correlation, it is thought to be a helpful and simple biomarker for the diagnosis of MS. Our second aim is to examine the RDW levels between attacks and also MS subtypes.

Methods

In our retrospective study, we included patients admitted to the Department of Neurology, Selcuk University Faculty of Medicine Hospital, who were diagnosed with MS according to the 2017 McDonald criteria, and who had been followed up in our department for at least 1 year (12-15). The study was approved by the Selcuk University Local Ethics Committee (Reg. number: 2018/24, Decision number: 2018/437). Between November 2017 and December 2018, 105 MS patients (patient group) and 59 healthy individuals (control group) were included in the study. MS and control groups were matched in terms of age and gender. The medical records of the patients were obtained retrospectively through the hospital automation system. Demographic characteristics, MS subtypes, attack positive/non-attack positive groups, and laboratory parameters were recorded. Patient records were reviewed and the diagnosis of the disease and the specified MS subtype were recorded. Patients were not retrospectively diagnosed with MS subtype. MS patients were analyzed in 3 subtypes: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS). Progressive relapsing MS patients were also included in the PPMS group. Patients with clinically isolated syndrome or radiologic isolated syndrome were not included in the study.

RDW level was analyzed in the study. Since we aimed to examine the correlation that can only be understood with a simple test, such as a hemogram, other parameters were not included in the study. The RDW level in the first hemogram test performed on the hospital automation system when the patient came for follow-up or was admitted to the hospital was recorded.

Patients with comorbidities that might affect RDW levels were not included in the study. Therefore, patients with a history of rheumatologic diseases, active or chronic infections, hematologic diseases, hypertension, diabetes, cardiovascular diseases, malignancies, and renal or hepatic insufficiency were excluded. RDW was calculated according to the formula RDW = (RBC Coefficient of Variation ÷ mean MCV) × 100. The RDW reference range in our laboratory is between 1 and 15.0%.

This study was conducted under the national regulations and the Declaration of Helsinki. Ethics committee approval was obtained from the Ethics Committee of the Faculty of Medicine at Selcuk University.

Statistical analysis

The data in this study were analyzed with Statistical Package for the Social Sciences (SPSS), version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The Shapiro-Wilk test was used for data distribution analysis. Categorical variables were summarized as numbers and percentages; continuous variables were presented as standard deviation if normally distributed, otherwise as median (minimum-maximum). The groups were compared using an independent sample t-test or Mann-Whitney U test for continuous variables and chi-square tests for categorical variables according to the distribution of the data. Kruskal-Wallis analysis was used to compare the three groups. An additional evaluation was performed to determine cut-off points for RDW in MS using receiver operating characteristic (ROC) curve analysis. A p-value of <0.05 was considered statistically significant

Results

The study was conducted patients with 105 MS patients, 74 (70.5%) females, and 31 (29.5%) males,

with a mean age of 38 (20-64) years. Fifty-nine patients were included in the control group, 35 (59.3%) were female and 24 (40.7%) were male, with a mean age of 34 (26-55) years. There was no statistically significant difference between the groups according to age or gender (p=0.2, p=0.2). The RDW values were higher in the MS group. As shown in Table 1, the RDW values were 13.8 (12.1-27.1) in the MS group and 13.4 (12.1-17.4) in the control group (p=0.007). Using a cut-off point of 13.55, ROC analysis revealed that RDW predicted MS with 59% sensitivity and 54.2% specificity (Figure 1). The area under the curve for this association was 0.627 and the 95% CI was 0.541-0.713 (p=0.007).

Table 1. The red blood cell distribution width (RDW) in patients with multiple sclerosis and control group

	MS (n=105)	Control (n=59)	*P* value
Age (median, mean-maximum)	38 (20-64)	34 (26-55)	0.2
Gender (n, %) Male Female	31 (29.5%) 74 (70.5%)	24 (40.7%) 35 (59.3%)	0.2
RDW (%) (median, mean-maximum)	13.8 (12.1-27.1)	13.4 (12.1-17.4)	0.007*

*Statistically significant value, MS: Multiple sclerosis, n: number, RDW: Red blood cell distribution width

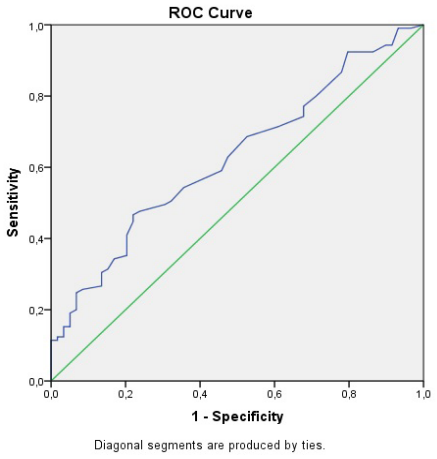

Figure 1. The red blood cell distribution width (RDW) in MS with receiver operating characteristic (ROC) curve analysis

The RDW ratio was not statistically different in patients with and without MS attacks (14.7±2.5% vs. 14.7±2.8%, *P*=0.92) (see Table 2). Eighty-five patients (80.9%) were diagnosed with RRMS, seven patients (6.7%) with PPMS, and 13 patients (12.4%) with SPMS. There was no statistically significant difference in RDW values between the groups (p=0.41) (see Table 3). RDW at diagnosis was found to be an independent predictor for the diagnosis of the disease in patients with MS.

Table 2. The red blood cell distribution width (RDW) according to attacks groups in patients with multiple sclerosis

	Attack (n=68)	No Attack (n=37)	*P* value
Age (mean SD)	38.8±12.1	38.6±9.6	0.95
Gender (n, %) Male Female	19 (%27.9) 49 (%72.1)	12 (%32.4) 25 (%67.6)	0.8
RDW (%) (mean SD)	14.7±2.5	14.7±2.8	0.92

RDW: Red blood cell distribution width, n: Number, SD: Standard deviation

Table 3. The red blood cell distribution width (RDW) according to disease subgroups in patients with multiple sclerosis

	RRMS (n=85)	PPMS (n=7)	SPMS (n=13)	*P* Value
Age (mean SD)	37.9±11.5	34.6±8.2	46.1±8.2	0.02*
Gender (n, %) Male Female	21 (%24.7) 64 (%75.3)	5 (%71.4) 2 (%28.6)	5 (%38.5) 8 (%61.5)	0.02
RDW (%) (mean SD)	14.8±2.7	13.8±1.2	14.7±2.7	0.41

Discussion

It has been shown that inflammation can cause changes in red blood cell maturation. RDW is a parameter refl cting the greater degree of red blood cell volume distribution and can also be used as an indicator of inflammation. Studies on atherosclerosis have revealed that a high RDW level is a marker for atherosclerotic diseases and also indicates an increased risk of the progression of atherosclerosis. Furthermore, many diseases have shown that an increased RDW level can predict severe morbidity and mortality. In addition, RDW may reflect subclinical inflammation and is associated with poor functional status among the elderly (16-19). It is known that RDW increases with age. In our study, the groups and subgroups were middle-aged. RDW values were not at very high levels. High RDW levels can be detected in numerous diseases, including hematologic diseases, hypertension, diabetes mellitus, cardiovascular diseases, malignancies, renal or hepatic disorders, and other inflammatory diseases. Therefore, we excluded these diseases from our study.

The pathogenesis of MS is multifactorial, but it is considered an autoimmune disease. Most MS research has focused on the pathologic involvement of B and T lymphocytes. However, there is also some research on erythrocytes, which may play an important role in MS pathology. Erythrocytes have antioxidant enzymes and

structural proteins. The impaired antioxidant capacity of erythrocytes can lead to oxidative stress. Oxidative stress may be associated with inflammation. In one study, advanced oxidation protein products (AOPP), malondialdehyde (MDA), and superoxide dismutase (SOD) activity in erythrocytes were significantly correlated with clinical severity, radiological findings (gadolinium uptake lesion volume) and disease duration in RRMS. Neuroinflammation in MS is associated with altered oxidative status and this may have effects on erythrocytes. We examined this inflammatory effect not at the enzyme level but as a more gross change in RDW (20).

RRMS patients have been shown to have increased RDW levels compared to healthy controls. They also revealed that increased RDW levels were positively correlated with EDSS scores (20). In our study, it is surprising that no change was found in RDW values in patients with and without attacks. This may be related to immunosuppressive or immunomodulatory treatments. However, we did not evaluate the relationship between disease, RDW, and treatment options in this study.

Many studies have shown that increased RDW level is associated with poor prognosis and morbidity (20-23). In our study, we did not evaluate in terms of prognosis or clinical severity, but it is obvious that there is a certain disease progression and morbidity in patients with MS, since a comparison was made with the control group. Our study showed that despite increased RDW levels in all patients with MS, there was no significant difference between MS subtypes. This may also be related to immunosuppressive or immunomodulatory therapies. Therefore, RDW is not a parameter to be used to determine prognosis and subtypes in patients with MS.

Conclusion

RDW will be a new, suitable, low-cost-effective, widespread, and available biomarker for MS patients. Although the exact mechanism is unknown, it may reflect the inflammatory status of MS. However, RDW is not a parameter to be used for determining prognosis and relapse in MS. Our study has some limitations. The MS patients were relatively small, and the study was conducted in a single center. In addition, immunosuppressive or immunomodulatory treatment options were not evaluated.

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Conflicts of interest

Authors have no conflicts of interest to disclose

Ethical standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Presentation in congress

This study was presented as an oral presentation at the International Turkish World Multiple Sclerosis Congress on 14-17 February 2019.

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ORIGINAL ARTICLE

The Relationship of Pregnancy Planning Status with Perception of Risk and Anxiety During Pregnancy: A Cross-Sectional Study

Gebeliğin Planlı Olma Durumunun Gebelikte Risk Algısı ve Anksiyete İle İlişkisi: Kesitsel Bir Çalışma

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ABSTRACT

Aims: The objective of this study was to determine the relationship of pregnancy planning status with perception of risk and anxiety during pregnancy.
Material and Methods: The sample for the cross-sectional study formed from 268 pregnant women applied to a hospital in eastern Turkey between April 1 and April 20, 2022. The data were obtained using the "Personal Information Form," the "London Measure of Unplanned Pregnancy (LMUP)," the "Perception of Pregnancy Risk Scale (PPRS)," and the "Pregnancy-Related Anxiety Scale-Revision-2 (PRAS-R2)." In statistical analysis, the percentage distribution, arithmetic mean, standard deviation, Cronbach's alpha, t test in independent groups, and Pearson correlation analysis were utilized.
Results: The proportion of women who planned to have a baby was found to be 77.2%. The mean total PPRS and PRAS-R2 scores of the women with planned pregnancies were 30.21±16.63 and 27.79±7.72, respectively, and the difference between the groups was determined to be significant (p=0.000). The mean total PPRS and PRAS-R2 scores of the women who had an unplanned pregnancy were 40.71±11.80 and 32.49±5.59, respectively, and the difference between the groups was determined to be significant (p=0.000). According to the correlation analysis, there was a weakly significant positive correlation between the mean total scores of women with planned and unplanned pregnancies on the GRAS and GAS-R2, and as the level of perceived risk of pregnancy increased, so did the level of pregnancy-related anxiety.
Conclusion: It was found that women with unplanned pregnancies had a higher degree of risk perception and anxiety during pregnancy, and that the level of pregnancy-related anxiety rose as the level of risk perception increased.

Keywords: Anxiety, Pregnancy, Planned pregnancy, Unplanned pregnancy, Perception of risk.

ÖZ

Amaç: Bu araştırmada, gebeliğin planlı olma durumunun gebelikte risk algısı ve anksiyete ile ilişkisini belirlemek amaçlanmıştır.
Gereç ve Yöntemler: Kesitsel nitelikte yapılan araştırmanın örneklemini Türkiye'nin doğusunda bulunan bir hastaneye 1-20 Nisan 2022 tarihleri arasında başvuran 268 gebe oluşturmuştur. Veriler, "Kişisel Tanıtım Formu", "Londra Plansız Gebeliği Belirleme Ölçeği (LPGBÖ)", "Gebelikte Risk Algısı Ölçeği (GRAÖ)" ve "Gebelikle İlişkili Anksiyete Ölçeği-Revizyon-2 (GAÖ-R2)" ile toplanmıştır. İstatistiksel değerlendirmede; yüzdelik dağılım, aritmetik ortalama, standart sapma, Cronbach's alfa, bağımsız gruplarda t testi ve pearson korelasyon analizi kullanılmıştır.
Bulgular: Planlı gebelik yaşayan kadınların oranı %77.2 olarak saptandı. Planlı gebelik yaşayan kadınların GRAÖ ve GAÖ-R2 toplam puan ortalamalarının sırasıyla 30.21±16.63, 27.79±7.72 olduğu ve gruplar arasındaki farkın anlamlı olduğu belirlendi (p=0.000). Plansız gebelik yaşayan kadınların GRAÖ ve GAÖ-R2 toplam puan ortalamalarının sırasıyla 40.71±11.80, 32.49±5.59 olduğu ve gruplar arasındaki farkın anlamlı olduğu saptandı (p=0.000). Yapılan korelasyon analizi sonucunda planlı ve plansız gebelik yaşayan kadınların GRAÖ ve GAÖ-R2'nden aldıkları toplam puan ortalamaları arasında pozitif yönde zayıf düzeyde anlamlı ilişki olduğu ve gebeliğin riskli algılanma düzeyi arttıkça gebelikle ilişkili anksiyete düzeyinin de arttığı belirlendi.
Sonuç: Gebelikteki risk algısı ve anksiyete düzeyinin plansız gebelik yaşayan kadınlarda daha yüksek olduğu ve gebeliğin riskli algılanma düzeyi arttıkça gebelikle ilişkili anksiyete düzeyinin de arttığı belirlendi.

Anahtar Sözcükler: Anksiyete, Gebe, Planlı gebelik, Plansız gebelik, Risk algısı

Introduction

A planned pregnancy is a personal decision made by women and couples to choose their own pregnancy aims and timing. It also involves assumptions about what it means to be prepared to have a baby (1). Planned pregnancy is a complicated circumstance that involves not only components of desire and purpose, but also contraceptive behavior and proper personal situations in marriage (1, 2). Having children has always been seen as one of the primary goals of marriage (3). The idea of "no marriage without children" in Turkish culture favorably influences the attitude toward planned pregnancy and parenting in our nation. Indeed, whereas the planned pregnancy rate was 68% in 2013, it jumped to 75% in 2018 according to TNSA 2013 data (4,5). According to the research review, age, marital relationships, living with a partner, having had a prior pregnancy, and having experienced abortion or miscarriage were all positively connected

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to pregnancy planning (6).

In addition to emotions of delight and excitement, pregnant moms begin to face the bodily load of pregnancy, anxiety, and a strong sense of responsibility (7). In addition to these scenarios, it has been found that the frequency of feeling bad mood rises with the influence of rising progesterone hormone (8). Although pregnancy has a beneficial impact on women's lives, it is a time when women confront several hazards in the prenatal and intranatal processes. The attitude of danger among pregnant women towards themselves originates precisely here (9). The idea of risk perception in pregnant women is unique and subjective (10). The idea of risk comprises perceptions about the probability of damage to the mother or infant, as well as the severity of the risk scenario. In addition to the cognitive capacity to comprehend a personal danger scenario, the physical state of pregnancy is critical. The perception of danger in pregnancy impacts the woman's mental state and is effective in decision making in all pregnancy and delivery settings (11). Situations such as caesarean section, the fear of dying during pregnancy, preterm birth, congenital problems in the infant or the need to be hospitalized in the neonatal intensive care unit, and worries regarding the site of birth may all be considered as perceived risks during pregnancy (12). All of these perceived concerns might induce anxiety and concern in pregnant mothers.

Anxiety is a troubling sensation of concern and dread that each human feels from time to time in different stages of life, and it is often accompanied by bodily symptoms that are dangerous or regarded as threatening to life (13). Anxiety during pregnancy has been demonstrated to be a greater and frequently more constant predictor of infant-related illnesses and/or delivery than general psychological distress (14). Anxiety in pregnancy may emerge in a variety of ways and be connected with a variety of anxiety disorders as well as pregnancy-specific anxieties and concerns (15). Pregnancy anxiety refers to pregnancy-specific anxieties or anguish, such as the health of the growing baby, changes in the woman's personal appearance, loss of labor force, and parental issues in future periods with delivery (14, 16, 18). According to this viewpoint, evaluating the anxiety experienced/might be encountered during pregnancy and offering support systems by healthcare experts would help women to live a more pleasant life throughout pregnancy and post-pregnancy processes.

The fact that planned pregnancies may secure the long-term well-being of mothers and their newborns by increasing the capacity to manage perceived risk and anxiety issues will also promote the successful completion of the complete pregnancy process. The purpose of this study was to evaluate the connection between pregnancy planning status and perceived risk and anxiety throughout pregnancy.

Material And Method

The purpose of this cross-sectional research was to examine the connection between pregnancy planning status and perceptions of risk and anxiety throughout pregnancy. The research was carried out at an eastern Turkish hospital between April 1 and April 20, 2022. Pregnant women who applied to the hospital where the research was performed made up the study's population. All pregnant women who applied to the hospital on the study day, agreed to participate in the research, had no communication difficulties, and had no psychiatric disorders were included in the study. While calculating the sample of the study, G*Power 3.1.9.2 program was used and the study "Anxiety during the pregnancy and affecting factors: a cross-sectional study" was taken as reference (19). Accordingly, Effect size (Cohen's D) was taken as 0.730 and it was determined that a total of at least 10 pregnancies should be reached, at least 50 planned and 50 unplanned, with a 95% confidence interval and 95% power. The study was completed with 268 pregnant women (planned pregnant:207 ; unplanned pregnant:61) who met the inclusion criteria.

Data Collection Tools

The information was gathered using the "Personal Information Form," the "London Measure of Unplanned Pregnancy (LMUP)," the "Perception of Pregnancy Risk Scale (PPRS)," and the "Pregnancy-Related Anxiety Scale-Revision-2 (PRAS-R2)."

Personal Introduction Form

There are a total of 18 questions in the personal introduction form prepared by the researchers in accordance with the literature, including 11 questions about socio-demographic characteristics of pregnant women (age, educational status, employment status, economic status, etc.) and 7 questions about obstetric characteristics (gestational week, baby gender, low curettage status, etc.) (20-23).

London Measure of Unplanned Pregnancy Measure (LMUP)

Barrett et al. (22) created the London Measure of Unplanned Pregnancy (LMUP), which is a psychometric assessment of unplanned pregnancy. Altiparmak et al. (21) assessed its Turkish validity and reliability. The scale consists of 5 items. 0-3 points can be divided into 3 groups as unplanned, 4-7 points as undecided, 8 and above points as planned pregnancy or ≤7 can be divided into two groups as unplanned and ≥8 as planned pregnancy. The scale's Cronbach Alpha reliability coefficient was determined to be 0.90. Cronbach Alpha reliability coefficient was reported to be 0.86 in this study.

Perception of Pregnancy Risk Scale (PPRS)

Heaman and Gupton created a 9-item measure to assess pregnant women's perceptions of risk (23). Evcili et al. performed a Turkish validity and reliability research on the scale, which is a visual analogue type assessment instrument. It is divided into two subdimensions: "pregnant woman's risk perception towards the baby" and "pregnant woman's risk perception towards herself."

- The sub-dimension "perception of risk of the pregnant woman towards the baby" consists of 5 questions, numbered 2, 6, 7, 8, and 9.

- The "perception of risk of the pregnant woman towards herself" sub-dimension is made up of four items, which are numbered 1, 3, 4, and 5.

Under each item on the scale, there is a 0-100 mm linear line with the expressions "no risk at all" and "extremely high risk" used to answer the questions. The scale's total score is computed by adding the scores for each of the nine components and dividing the total score by 9. A score for the scale's sub-dimensions is calculated by summing the scores of the appropriate sub-dimensions and dividing the result by the number of items. The measure has no cut-off point, and a rise in the scale's score is interpreted as an increase in the pregnant woman's sense of danger associated to herself and her baby. The scale's Cronbach Alpha reliability coefficient was calculated to be 0.84 (8). The Cronbach Alpha reliability coefficient was determined to be 0.86 in this investigation.

Pregnancy-Related Anxiety Scale-Revision 2 (PRAS-R2)

Van den Bergh created the Pregnancy-Related Anxiety Scale in 1990. Aksoy Derya et al. performed the Turkish validity and reliability research of the scale, which was amended by Huizink et al. in 2016 so that it may be responded by all pregnant women regardless of parity (24-26). The scale includes 11 items and three sub-dimensions, including "fear of childbirth (items 1, 2, 6, and 8)," "fear of having a disabled child (items 4, 9, 10, and 11)," and "concerns about physical appearance (items 3, 5, and 7)." The scale's eighth item is for women who have never given birth previously and does not apply to multiparous women. Items on the 5-point Likert-type scale are scored between 1 and 5, with primiparous women scoring 11-55 and multiparous women scoring 10-50. All of the items on the scale are positive, and the higher the score, the more anxiety during pregnancy is tolerated. There is no cut-off point on the scale. The scale's Cronbach Alpha reliability value was 0.94 for the primiparous group and 0.93 for the multiparous group (26). Cronbach Alpha reliability coefficient was determined to be 0.83 in this study.

Data Collection

The researcher collected study data from pregnant women who applied to a hospital in eastern Turkey through face-to-face interviews. Data gathering takes around 15-20 minutes on average.

Data Evaluation

The data was coded and analyzed in a computer setting using the SPSS 20.0 package application. In statistical analysis, the percentage distribution, arithmetic mean, standard deviation, and t test in separate groups were utilized. The data were analyzed at the 95% confidence interval and at the $p<0.05$ level of significance

Ethical Considerations in Research

The appropriate local ethics committee (Decision No: 2022/3295) and the management of the institution where the research was performed provided written consent. Before beginning the trial, all pregnant women completed an informed consent form. While gathering study data, the Declaration of Helsinki was followed.

Results

Table 1 shows the comparison of women with planned and unplanned pregnancies according to their demographic characteristics. Among the groups, age, gestational period, spouse's education status, place of residence, family type, relationship status with

Table 1. Distribution of descriptive characteristics of pregnant women (n=268)

Descriptive Characteristics	Planned Pregnancy (n=207)		Unplanned Pregnancy (n=61)		Test and p value
	Mean±SD (min-max)		Mean±SD (min-max)		
Age (years)	28.03±4.40 (19-41)		29.59±5.73 (18-42)		t=43.219 p=0.009
Spouse Age (years)	31.85±5.11 (19-45)		33.68±6.72 (22-55)		x^2=51.407 p=0.003*
Gestation Period (weeks)	31.72±9.04 (4-41)		33.34±8.39 (5-41)		x^2=24.157 p=0.934
	n	%	n	%	
Employment Status					
Working	60	29.0	10	16.4	x^2=3.871 p=0.049**
Not working	147	71.0	51	83.6	
Education Status					
Primary school graduate	15	7.7	15	24.6	
Secondary school graduate	30	14.5	12	19.7	x^2=19.687 **p=0.001***
High school graduate	61	29.5	20	32.8	
University and above	100	48.3	14	23.0	
Spouse Employment Status					
Working	200	96.6	56	91.8	x^2=2.554 p=0.110
Not working	7	3.4	5	8.2	
Spouse Education Status Primary school graduate	8	3.9	9	14.7	
Secondary school graduate	32	15.4	12	19.7	x^2=15.679 **p=0.003***
High school graduate	64	30.9	22	36.1	
University and above	103	49.8	18	29.5	
Place of Residence					
Province	143	69.1	36	59.0	x^2=2.864 p=0.239
District	46	22.2	20	32.8	
Village	18	8.7	5	8.2	
Income Status Income more than expenditure	34	16.4	5	8.2	
Income equals expenditure	139	67.2	33	54.1	x^2=13.474 **p=0.001***
Income less than expenditure	34	16.4	23	37.7	
Family Type Nuclear family	177	85.5	53	86.9	x^2=0.074 p=0.786
Extended family	30	14.5	8	13.1	
Spouse Relationship Status Positive	200	93.2	53	86.9	
Neither Positive nor Negative	14	6.8	5	8.2	x^2=18.476 **p=0.001***
Negative	-	-	3	4.9	
Family/Environmental Relationship Status Positive	199	96.2	54	88.8	
Neither Positive nor Negative	8	3.8	6	9.6	x^2=7.199 p=0.066
Negative	-	-	1	1.6	

Number of Pregnancy Primiparous	106	51.2	17	27.9	x^2=10.335 **p=0.001***
Multipara	101	48.8	44	72.1	
Pregnancy Type Healthy Pregnancy	187	90.3	51	83.6	x^2=2.148 p=0.143
Risky Pregnancy	20	9.7	10	16.4	
Baby Gender Girl	97	46.9	32	52.5	x^2=1.138 p=0.566
Male	88	52.5	25	41.0	
I don't know	22	10.6	4	6.5	
Low Living Status Yes	36	17.4	12	19.7	x^2=0.047 p=0.828
No	171	82.6	49	80.3	
Experience of Abortion Yes	25	12.1	8	13.1	x^2=0.167 p=0.683
No	182	87.9	53	86.9	
Stillbirth Status Yes	6	2.9	3	4.9	x^2=0.592 p=0.442
No	201	97.1	58	95.1	

SD:Standard Deviation * p<0.001 **p<0.05

t:Independent Sample T Test x2:Chi-Square Test

family/environment, pregnancy type, baby gender, low living status, experience of abortion and stillbirth status was homogeneous (p > 0.05, Table 1), and the groups were similar in terms of some demographic characteristics. It was determined that there was a significant difference between the groups in terms of employment status, spouse age, spouse employment status, income level, relationship with spouse, and number of pregnancies in favor of unplanned pregnancy.

Table 2. Women's status of experiencing unplanned pregnancy according to London Measure of Unplanned Pregnancy cut-off score (n=268)

London Measure of Unplanned Pregnancy	Cut-off score	n	%
Unplanned Pregnancy	≤ 7	61	22.8
Planned Pregnancy	≥8	207	77.2

The unplanned pregnancy status of women according to the cut-off score of the London scale for determining unplanned pregnancy is given in Table 2. The proportion of pregnant women who had an unplanned pregnancy with a score of 7 points or less was 22.8%, while the proportion of pregnant women who had a planned pregnancy with a score of 8 points or more was 77.2%.

The distribution of the lowest-highest scores that can be obtained by pregnant women on the PPRS and PRAS-R2 and the distribution of the lowest-highest scores obtained by the pregnant women who participated in the study are given in Table 3. The lowest and highest scores of women with planned pregnancies obtained from PPRS were found to be 10.00-88.89, and the lowest and highest scores of women with unplanned pregnancies for PPRS were found to be 20.00-83.33. In addition, the lowest and highest scores of women with planned pregnancies obtained from PRAS-R2 were determined to be 11-55, and the lowest and highest scores of women with unplanned pregnancies for PRAS-R2 were found to be 24-49.

The comparison of the mean total scores of the women according to the planning status of their pregnancies from the subscales of PPRS and PRAS-R2 is given in Table 4 3. It was determined that the mean total score of Perception of risk in Pregnancy Scale was 30.21±16.63 and the mean total score of Pregnancy-Related Anxiety Scale was 27.79±7.72 and the difference between the groups was significant (p=0.000). The mean total score of Perception of risk in Pregnancy Scale was 40.71±11.80, the mean total score of Pregnancy-Related Anxiety Scale was 32.49±5.59 and the difference between the groups was determined to be significant (p=0.000). As a result of the statistical evaluation, it was found that the mean total scores of the Perception of Pregnancy Risk Scale and Pregnancy-Related Anxiety Scale were

Table 3. Comparison of the mean total scores of women according to their pregnancy planning status on the subscales of PPRS and PRAS-R2 (n=268)

Scales	Planned Pregnancy (n=207)	Unplanned Pregnancy (n=61)	Test* and p value	
	Mean±SD	Mean±SD	T	p
PPRS	30.21±16.63 10.00-88.89 (min-max)	40.71±11.80 20.00-83.33 (min-max)	4.597	0.000
Perception of Risk of The Pregnant Woman Towards The Baby	15.07±10.16	13.35±9.25	-1.185	0.277
Perception of Risk of The Pregnant Woman Towards Herself	14.55±7.92	15.24±8.41	0.588	0.503
PRAS-R2	27.79±7.72 11-55 (min-max)	32.49±5.59 24-49 (min-max)	4.414	0.000
Fear of Childbirth	13.72±3.67	15.71±2.82	2.697	0.078
Fear of Having A Disabled Child	10.52±3.88	12.90±3.31	4.341	0.248
Concerns About Physical Appearances	7.53±3.06	8.67±2.52	2.644	0.051

*Independent samples t test SD:Standard Deviation

PPR Perception of Pregnancy Risk GPA-R2: Pregnancy-Related Anxiety Scale-Revision-2

statistically higher in women who had unplanned pregnancies (p<0.05).

Discussion

The outcomes of the research done to assess the association of pregnancy planning status with perception of risk and anxiety during pregnancy are addressed in this part along with related literature.

It was observed that the majority (77.2%) of the women participating in the research had planned pregnancies. This scenario might be attributed to the fact that family planning (FP) techniques are well understood and widely practiced. When the TNSA 2018 data is analyzed, it is seen that 75% of the pregnancies of women who gave birth were desired-planned pregnancies, and our conclusion represents the culture in which the survey was performed. In the same research, it was determined that family planning techniques were widely understood, and 70% of women utilized any FP method (4). Although it is seen that the planned pregnancy rates of women in the eastern region of Turkey (66.1%), where the study was conducted, are similar to our study, the reason why the pregnancies of women living in this region are planned is; It is thought to be related to the values placed on having children (4) . Having a child in the Eastern Anatolia Region, where the traditional family structure is dominant; It is seen as important for a woman to feel valuable and to position herself in an important place in the family (27, 28). Based on this fact, it can be concluded that most women's voluntary pregnancy is connected to the widespread use of family planning techniques. Indeed, when the literature is examined, according to the TNSA (2018) data, it was determined that the vast majority of women living in the east and in rural areas are knowledgeable about family planning methods and the majority of them use any FP method (4, 29). When the studies were analyzed, it was found that the majority of the women had planned pregnancies, and the relevant literature was consistent with the findings of this study (1, 8, 18, 20, 27-39 30-40). When the reasons for this situation are examined, it can be concluded that the FP methods are well known and frequently used in today's society, the educational level of women has increased (48.3% in this study were university and above), the status of women in society has increased and, in addition to entering the working life, life in the city has increased, and the trainings given by midwives and other health professionals in the pre-pregnancy period have increased (4, 28, 40 30, 41). In addition, the analysis conducted within the scope of this study found that an increase in the number of pregnancies was more significant in favor of women who had unplanned pregnancies. When the literature

was examined, it was determined that this finding was consistent, and that low education level, not working in any job, low income level and an increase in the number of pregnancies brought about unplanned pregnancies (42-44).

The mean total score of the GRAS of women with planned pregnancy was 30.21±16.63, while the mean total score of women with unplanned pregnancy was 40.71±11.80, and the perception of risk of women with unplanned pregnancy was shown to be greater than that of women with planned pregnancy. However, no research assessing the connection of pregnancy planning status with risk perception was found in the literature. According to the findings of Şahin et al. (2022), the majority of pregnant women planned their pregnancy, and the mean total score of the pregnant women was 42.6±29.38. However, the association between pregnancy planning status and perception of risk throughout pregnancy was not investigated in this study (37 38).

In this study, the mean total GAS-R2 score of women with planned pregnancy was 27.79±7.72, whereas the mean total GAS-R2 score of women with unplanned pregnancy was 32.49±5.59. According to these findings, women who had unexpected pregnancies reported greater levels of anxiety than those who had planned pregnancies. While the pregnancy process is stressful for women even when it is planned, the shock and uncertainty that comes with an unforeseen pregnancy enhances the woman's anxiety (33, 41,42 34, 45, 46). When the literature was examined, it was found that there was a positive relationship between unplanned pregnancy and anxiety, as in our study, and that women's unplanned pregnancy increased their anxiety (1, 43-49 48-54). This data might be interpreted as women seeing unexpected pregnancies as a risk factor in pregnancy, increasing their level of anxiety.

Limitations

The limitation of the study is that the participants were recruited from pregnant women in a public hospital in Turkey. Since it was conducted in a single center, the results of the research cannot be generalized to the whole population.

Conclusions And Recommendations

This study found that women who had an unplanned pregnancy had greater levels of risk perception and anxiety throughout pregnancy than women who had a planned pregnancy. Based on these findings, it is advised that prenatal care begin with the planning stage, that the pregnancy continue in a healthy manner, and that the delivery go off without a hitch. Midwives and other health providers should emphasize that planned pregnancy and support from husband, family, and friends throughout pregnancy will assist women's adaptation to pregnancy and positive perspective of pregnancy. Midwives should give pre-pregnancy training to help reduce unplanned pregnancies. Women and partners should be advised that unexpected pregnancies might harm mother-child health, and couples should be educated on family planning.

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Author(s) contribution(s)

Conception: SA, YAD; Design: SA, YAD; Supervision: SA, YAD; Data Collection and/or Processing: ET, NMK, KA, ŞKB; Analysis- Interpretation: SA; Literature Review: ET, NMK, KA, ŞKB; Writing: SA, ET, NMK, KA, ŞKB; Critical Review: SA, YAD.

Conflict of interest

The authors have no conflicts of interest to disclose

Ethical approval

Prior to the study, written permission was obtained from the institutions in which the study was conducted, and ethical approval was obtained from the Scientific Research and Publication Ethics Committee of the Malatya Inonu University of Health Sciences in Turkey on (No.2022/3295).

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ORIGINAL ARTICLE

Evaluation of Treatment Outcomes in Orthopaedic Firearm Injuries: A Review of 52 Cases

Ortopedik Ateşli Silah Yaralanmalarında Tedavi Sonuçlarının Değerlendirilmesi: 52 Olgunun İncelenmesi

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ABSTRACT

Background/Aims: The prevalence of firearm-related fractures (FAF) among public has increased in many countries. The management of these injuries is challenging for physicians. The aim of this study was to evaluate the clinical outcomes of the patients treated for FAF.
Materials and Methods: The study included adults treated in orthopaedic clinics for long bone shaft fractures of the extremities caused by civilian firearm injuries between 2015 and 2020. The medical records of the patients were retrospectively reviewed in this double-center study. Age, gender, fracture bone name, fracture type, treatment type, time to union, presence of permanent sequelae, presence of deep or superficial infection, presence of neurovascular injury, presence of mal-union and follow-up time were analysed.
Results: This study was performed in 52 cases with a mean age of 43 years. Fifty patients were males, and two were females. 22 tibia, 20 femur, four humerus, four ulna, and two radius fractures were included. In total, 11 patients were treated with conservative method, 15 patients with plate-screw fixation, nine patients with intramedullary nails and 17 patients with external fixators. Permanent sequelae occurred in 13 (25%) patients following treatment. Seven (13.5%) infections were diagnosed during the treatment phase, and four (7.7%) were superficial and three (5.8%) were deep infections. In cases treated with external fixator, infection occurred in five (29.4%) patients, four of them were superficial infections. The mean follow-up period for all patients was 37.5 (25-60) months. While the mean time to union was 6.6 (1.5-15) months in all patients, this time was shorter with a mean of 2.5 months in patients treated with conservative treatment ($p < 0.001$).
Conclusion: From admission to the emergency department to the finalisation of treatment, FAFs are challenging forensic cases for physicians. In addition to fractures, they may cause vascular, nerve and soft tissue injuries and may leave a high rate of sequelae. In addition to modern surgical techniques, conservative treatment is successfully used in appropriate cases.

Keywords: Firearm-related fracture, orthopaedics, surgery

ÖZ

Amaç: Siviller arasında ateşli silah yaralanmaları (ASY) sebebiyle oluşan kırıkların yaygınlığı birçok ülkede artmıştır. Bu yaralanmaların yönetimi hekimler için zorlayıcıdır. Bu çalışmanın amacı, ASY nedeniyle ortopedi kliniğinde tedavi edilen hastaların sonuçlarını değerlendirmektir.
Gereç ve Yöntem: Çalışmaya 2015-2020 yılları arasında, ekstremitelerin uzun kemiklerinde sivil ASY'ye bağlı şaft kırığı nedeniyle ortopedi kliniğinde tedavi edilen yetişkinler dahil edildi. İki merkezli çalışmada hastaların tıbbi kayıtları retrospektif olarak incelendi. Yaş, cinsiyet, kırık kemik adı, kırık tipi, tedavi tipi, kaynamaya kadar geçen süre, kalıcı sekel varlığı, yüzeyel veya derin doku enfeksiyon varlığı, nörovasküler yaralanma varlığı, malunion varlığı ve takip süresi analiz edildi.
Bulgular: Bu çalışma yaş ortalaması 43 olan 52 olguda gerçekleştirildi. Elli hasta erkek, iki hasta kadındı. Çalışmaya 22 tibia, 20 femur, dört humerus, dört ulna ve iki radius kırığı dahil edildi. Toplam 11 hasta konservatif tedavi, 15 hasta plak-vida tespiti, dokuz hasta intramedüller çivi ve 17 hasta eksternal fiksatör ile tedavi edildi. Tedavi sonrası 13 (%25) hastada kalıcı sekel meydana geldi. Tedavi sırasında yedi (%13,5) enfeksiyon tanısı kondu; bunların dördü (%7,7) yüzeyel, üçü (%5,8) derin enfeksiyondu. Eksternal fiksatör ile tedavi edilen olgularda, dördü yüzeysel enfeksiyon olmak üzere beş (%29,4) hastada enfeksiyon ortaya çıkmıştır. Tüm hastalar için ortalama takip süresi 37.5 (25-60) aydı. Kaynama süresi tüm hastalarda ortalama 6.6 (1.5-15) ay iken, konservatif tedavi ile tedavi edilen hastalarda bu süre ortalama 2.5 ay ile daha kısaydı ($p < 0.001$).
Sonuç: Acil servise başvurudan tedavinin sonuçlanmasına kadar, ASY hekimler için zorlu adli vakalardır. Kırıklara ek olarak damar, sinir ve yumuşak doku yaralanmalarına neden olabilirler ve yüksek oranda sekel bırakabilirler. Modern cerrahi tekniklerin yanı sıra uygun vakalarda konservatif tedavi de başarıyla uygulanmaktadır.

Anahtar Kelimeler: Ateşli silah yaralanması, cerrahi, ortopedi

Introduction

The prevalence of firearm-associated fractures (FAFs) among civilians has increased in numerous nations, as a result of an increase in private armament (1-3). The degree of tissue damage caused by a bullet depends on numerous factors, including the type of bullet, its diameter, the kind of tissue affected, the angle of entry, and its course within the body (4-6). Firearm-associated fractures primarily affect the spine, femur, tibia-fibula, hand and forearm bones, and can result in amputation or death (7). In addition, compartment syndrome, neurovascular damage, and soft tissue injury may result (4). The spectrum of soft tissue injuries induced by FAF ranges from a single bullet hole to extensive soft tissue defects (8,9). In addition, FAF is

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associated with an increased likelihood of infection, since the bullet or its fragments create an opening through which bacteria from the skin flora, clothing, or other intermediate targets may enter the wound (4,10,11). Many of these factors make treatment of FAFs challenging (3,9,12). Although various methods have been described for fractures, the treatment of FAFs is still controversial (3,9,12-17). Therefore, the aim of this study was to evaluate the outcomes of patients treated in an orthopaedic clinic for FAFs.

Material and Method

This study was retrospective and bicentral. Ethics committee approval was obtained. The study was conducted in adult patients treated for long bone shaft fractures caused by FAFs in an orthopaedic clinic between 2015 and 2020.

The medical records of the patients were analysed. Patients with comprehensive evaluation data in their medical records and a follow-up period of at least two years were included in the study. The cases with complete information including age, gender, fractured bone, fracture type, treatment type, time to union, presence of permanent sequelae, presence of deep-superficial infection, presence of neurovascular injury, presence of mal-union, time to complete union and follow-up period were included in the study. Patients with less than two years of follow-up or missing evaluation criteria were excluded from the study. The study was conducted with 52 patients who fully met the criteria out of 67 patients treated in both clinics. Informed consent was obtained from the patients admitted for follow-up. Fractures healed with limb length discrepancy and deformity were considered as permanent sequelae (12). In anterior-posterior and lateral radiographs, union was determined by the presence of callus in three of the four cortices (13). The fractures were classifie based on the Gustilo-Anderson classification (GAC) (8)

Sterile dressing was applied to the wounds in the emergency room. The wounds of patients that underwent fracture stabilization procedures were debrided (3,16). Bullets and gunshot fragments that were superficial or encountered during surgery were removed, but no extra investigation was undertaken to remove other bullets or fragments (4). Primary closure of wounds was not performed. Closed reduction and plaster cast was applied to the patients who were planned to be treated conservatively (CT). These patients were followed up with daily dressings for the first week after debridement in the emergency department and intermittent dressings thereafter. Then weekly follow-ups were performed. Intramedullary nailing (IM), plate screw fixation (PS) or external fixation (EF) methods were used in the patients for whom operation had been planned. Before and after surgery, intravenous antibiotics were administered to all patients. Intravenous antibiotic treatment (first generation cephalosporin, gentamicin and metronidazole) was administered to all patients for at least five days from the first day. Antibiotic treatment was then regulated according to the culture results. In addition, vascular injuries were treated with dissection and end-to-end anastomosis in the same session. In case of nerve injury, the nerve was dissected and repaired, if necessary, in operated patients. In the mobilization of lower extremity fractures, patients treated with IM were allowed to bear weight as much as they could tolerate in the early postoperative period. In patients who received EF, PS and CT treatments, X-ray evaluations were made at the end of the 6th week and weight bearing was started as tolerated. Weekly or monthly follow-ups were performed after discharge.

Statistical Analysis

Categorical variables were expressed as numbers (%) and continuous variables were expressed as median (range). Conformity of continuous variables to normal distribution was evaluated with Kolmogorov-Smirnov and Shapiro-Wilk tests. Since the quantitative variables did not display normal distributions, more than two independent groups were compared using the Kruskal-Wallis test and two groups were compared using the Mann–Whitney U-test. The Chi-square test and Fisher Exact test were used, where appropriate, to compare the proportions in different groups. Pairwise comparisons of proportions were evaluated with the Bonferroni method in more than two groups. A p-value below 0.05 was considered as statistically significant. The Statistical Package for Social Sciences for Windows, version 26.0 (SPSS, IBM Corp., Armonk, N.Y., USA) was used to calculate the statistics.

Results

This study was performed in 52 cases with a mean age of 43 years. Fifty patients were males, and two were females. In total, 11 patients were treated with CT, 15 patients with PS, nine patients with IM surgery and 17 patients with EF.

There were 22 tibia, 20 femur, four humerus, four

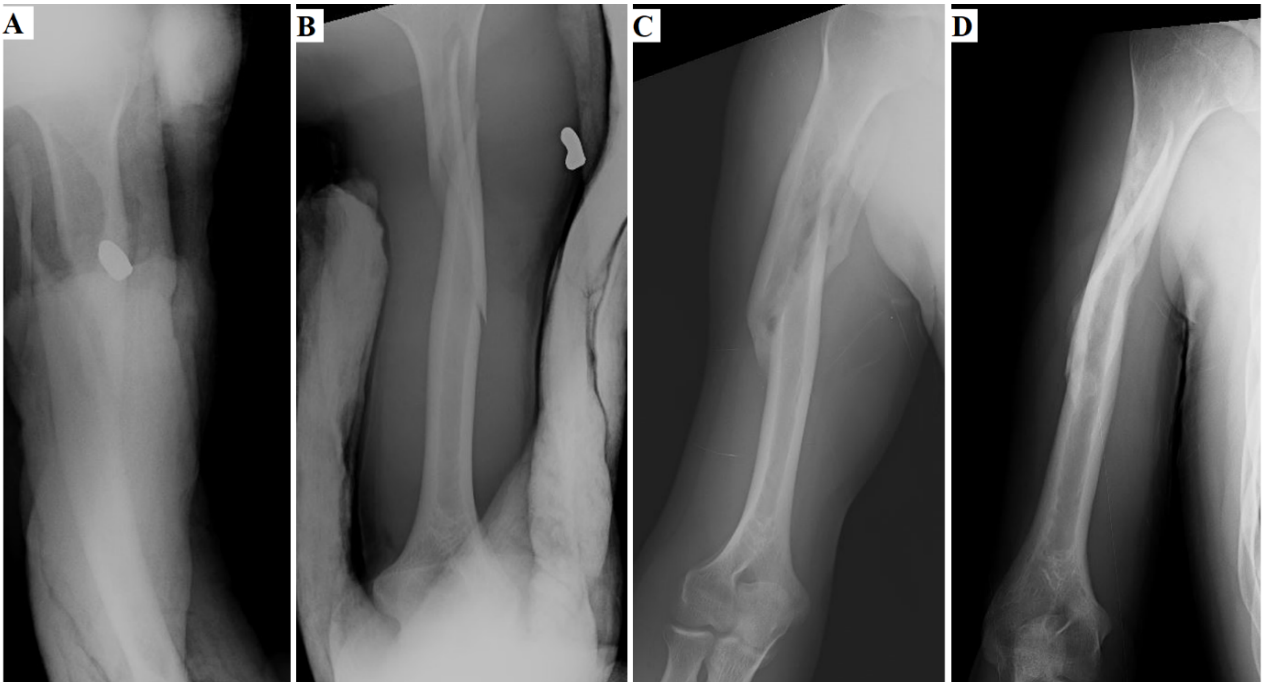

Figure 1. Fracture of the diaphysis of the humerus treated with conservative treatment (A,B: radiography images with splints, C,D: radiography images after union)

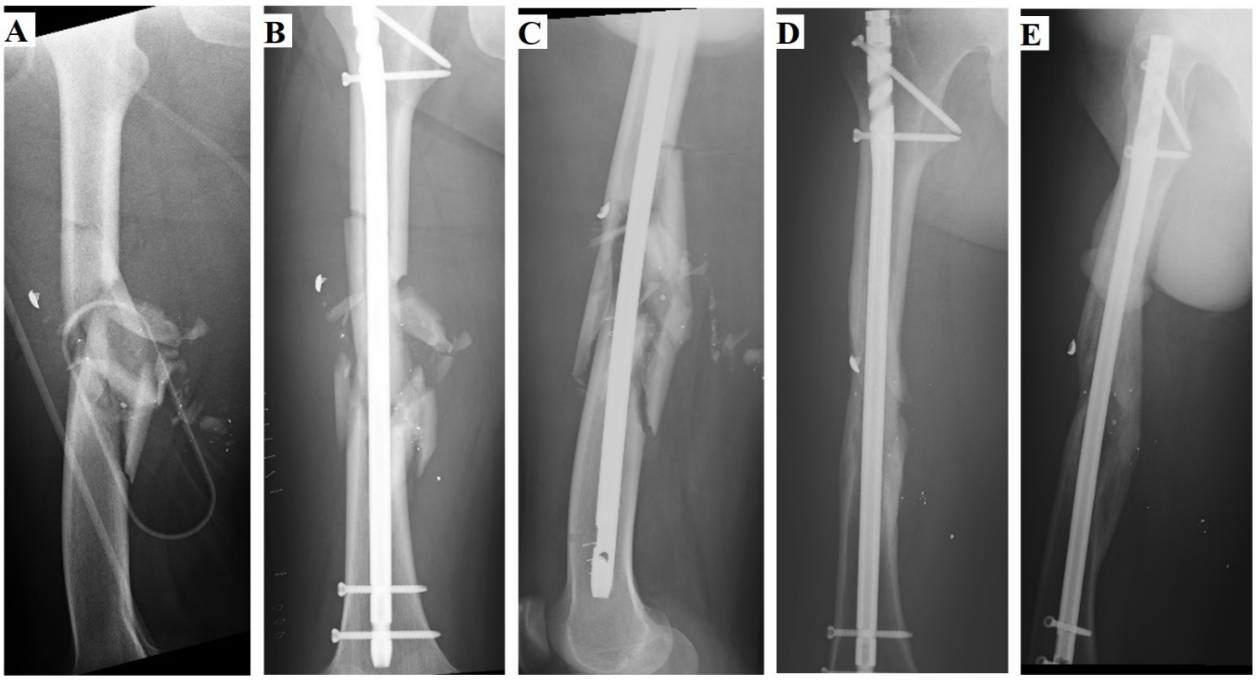

Figure 2. Internal fixation with intramedullary nail fixation in femoral diaphysis fracture (A: The first radiography image, B: Anterior-posterior radiography image after surgery, C: lateral radiography image after surgery, D: Anterior-posterior radiography image after union, E: Lateral radiography image after union)

ulna, and two radius fractures. Permanent sequelae occurred in 13 (25%) patients following treatment. The mean length of antibiotic use was 15 (5-45) days. Seven (13.5%) infections emerged during the treatment phase, and four (7.7%) were superficial, and three (5.8%) were deep infections. In cases treated with EF, infection occurred in five (29.4%) patients, four of them being superficial infections.

Deep infection occurred in two patients (22.2%) treated with IM. Vascular injury was observed in three and nerve injury in eight patients. According to the GAC, fractures of 37 patients were classified as type 3A, 12 as type 3B, and three as type 3C open fractures.

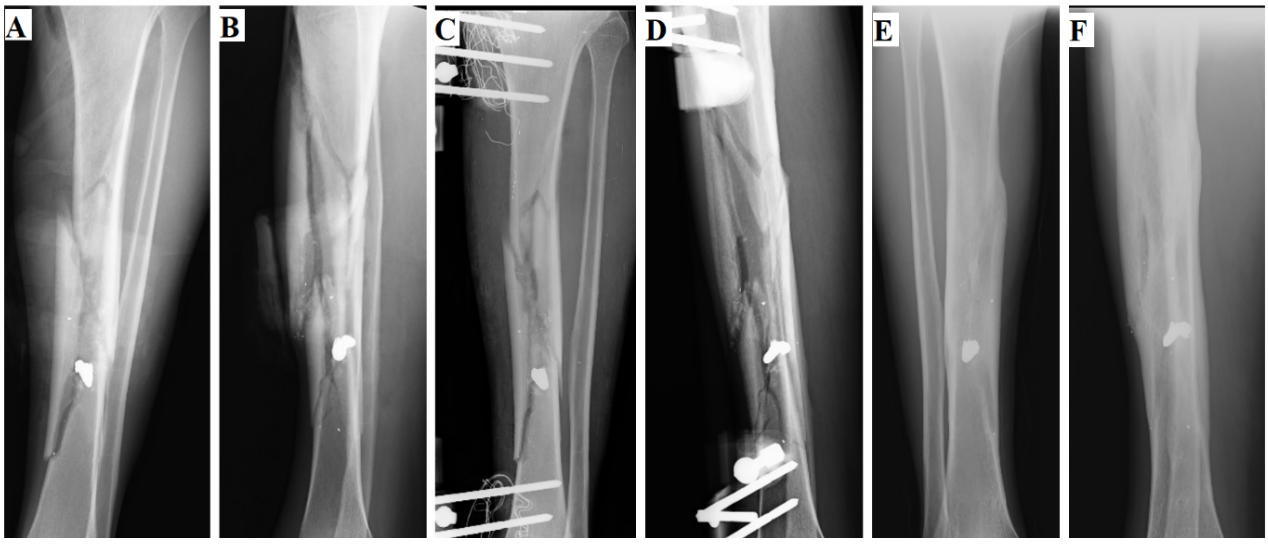

Figure 3. External fixation in tibia diaphysis fracture (A: The first anterior-posterior radiography image, B: The first lateral radiography image C: Anterior-posterior radiography image after surgery, D: Lateral radiography image after surgery , E: Anterior-posterior radiography image after union, F: Lateral radiography image after union)

Table 1 shows the overall characteristics of patients included in the study.

Table I. General characteristics of patients included in the study.

Characteristic	**n (%)**
Age (*Min-Max*) (years)	43 (15-73)
Gender	
Male	50 (96.2)
Female	2 (3.8)
Type of Treatment	
Conservative	11 (21.2)
Plate – Screw	15 (28.8)
Intramedullary	9 (17.3)
External Fixator	17 (32.7)
Fractured Bone	
Femur	20 (38.5)
Tibia	22 (42.3)
Humerus	4 (7.7)
Ulna	4 (7.7)
Radius	2 (3.8)
Gustilo-Anderson classification(%	
3 A	37(71,2)
3 B	12(23)
3 C	3(5.8)
Additional Injury or Complication	
Deep Infection	3 (5.8)
Superficial Infectio	4 (7.7)
Vascular Injury	3 (5.8)
Nerve Damage	8 (15.4)
Malunion	6 (11.5)
Sequela(*shortness, osteomyelitis, limitation of movement and atrophy*)	13 (25)

The mean follow-up period for all patients was 37.5 (25-60) months. While the mean time to union was 6.6 (1.5-15) months in all patients, this time was shorter with a mean of 2.5 months in patients treated with CT ($p<0.001$). Figure 4 shows the distribution of union time according to treatment type as a box plot.

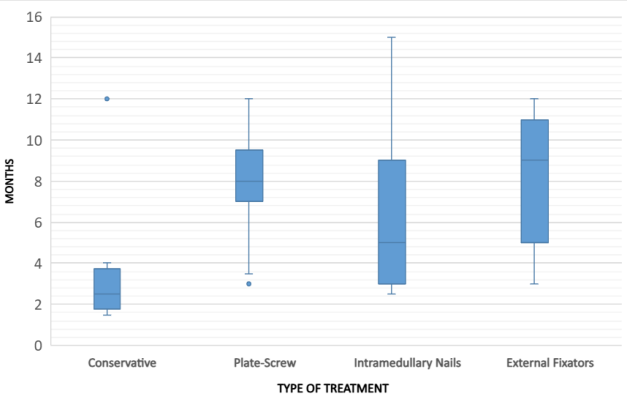

Figure 4. The distribution of union time and time to full function according to treatment type as represented in a box plot

When four treatment types were compared, no significant difference was found between the GAC fracture types. All patients undergoing CT were GAC type 3A fractures. One patient with vascular damage was treated with PS and two with EF, while one patient with nerve damage was treated with PS, four with IM and three with EF. No malunion was observed in any of the patients undergoing IM surgery. Four cases of malunion were observed in patients treated with EF. Table 2 shows the comparison of treatment types.

The distribution of permanent sequelae (shortness,

Table 2. Comparison of treatment types

	Conservative	Plate - Screw	Intramedullary	External Fixator	p
Age(*Min-Max*) (Years)	28 (15-62)	47 (23-73)	33 (23-47)	46 (32-56)	**0.020**
Fusion time (*Min-Max*) (Months)	2,5 (1.5-12)	8 (3-12)	5(2.5-15)	9(3-12)	**0.001**
Number of surgical procedures(*Min-Max*)	0	1 (1-3)	1 (1-3)	1 (1-4)	0.205
Gustilo-Anderson classification (%)					0.129
3 A	11(100)	11 (73.3)	5 (55.6)	10(58.8)	
3 B	0	3(20)	4(44.4)	5(29.4)	
3 C	0	1(6.7)	0	2(11.8)	
Sequela (%)	1 (9.1)	4 (26.7)	1 (11.1)	7 (41.2)	0.225
Infection(%)	0	0	2 (22.2)	5 (29.4)	0.026
Malunion(%)	1 (9.1)	1 (6.7)	0	4 (23.5)	0.408

osteomyelitis, limitation of movement and atrophy) according to the bones was seen in five (22.7%) tibia fractures, five (25%) femur fractures, one (25%) humerus fracture and two (50%) ulna fractures. Vascular injury was observed in 2(9.1%) of tibia fractures and 1(50%) of radius fractures. Nerve injury was observed in three (13.6%) tibia fractures, one (5%) femur fracture, two (50%) humerus fractures, one (25%) ulna fracture and one (50%) radius fracture. Deep infection developed in two (9.1%) tibia fractures and one (5%) femur fracture. Superficial infection developed in two (9.1%) tibia, one (25%) ulna and one (5%) femur fractures.

Discussion

Permanent sequelae were observed in 25% of the cases in our study, indicating the severity of FAFs injuries. In addition, the treatment of these fractures is difficult due to infection, vascular injury, nerve injury and soft tissue injury (9). There is limited data regarding the treatment of this injury (3,9).

The majority of patients in our study were men, with a rate of 96.2%. It is suggested that men are impacted by FAFs more than women because they have easier access to firearms and are more likely to engage in criminal activities (18,19). In several research, the mean age of FAFs was reported to be between 26.3 and 33.6 years; however, our study determined it to be 43 (13,18-22). The higher mean age compared to the literature may have caused a difference in the results of the study in terms of fracture union time or complications compared to the literature.

In our study, we observed that 80.8% of all long bone fractures in FAFs occurred in the lower extremities. In a study of FAFs patients admitted to the emergency room, the lower extremities were reported as the most frequently injured location with a rate of 41.3% (18). A similar study reported the frequency of FAFs in upper extremity as 55.7% and the lower extremity was 43% (20). The femur has previously been reported as the most commonly fractured long bone in FAFs (7). In our study, tibia fractures were the most common (42.3%), while femoral fractures were the second most common (38.5%). We observed that these two bones had a relatively similar damage rate.

Superficial infection was observed in 7.7% of cases and deep infection in 5.8%. In a study evaluating FAFs, the rate of deep and superficial infections was reported as 5.7% and 15.1% respectively, and deep infection was not detected in patients treated non-operatively (22). Infection rates in IM procedures performed on FAFs have been found to be significantly variable in investigations, ranging from 0% to 2.5%, 26.1%, 28.2%, and 31% (21-24). In a trial where IM was performed on tibial FAFs, profound infection was observed in 6.5% and 17.4% of the groups with and without irrigation and debridement, respectively (21). In another trial comparing EF and IM treatment, there was no statistically significant difference between the two groups, but the infection rate in the IM group was reported as being 5.2% (9). A study evaluating the use of PS in the humeral fractures demonstared that 1.6% of patients had deep infection (19).

In our study involving different bones in different extremities, it is not possible to make a definite judgement between treatment types. However, when the treatment groups were compared in general, no

significant difference was found between EF and IM groups in terms of infection. The infection rate was statistically higher in the IM and EF groups compared to the CT and PS groups (p=0.026). All superficial infections were observed in the EF group in our cases. The infection rates in our study are comparable to those reported in literature, despite the fact that the results are often highly variable. In the CT group, no GAC type 3B and 3C fractures were observed, while all were in class 3A. In addition, 73.3% of the PS group was type 3A, while 55.6% in the IM group and 58.8% in the EF group were type 3A. The incidence of type 3B and 3C fractures was found to be relatively higher in the IM and EF groups. This may help explain the higher infection rates in the IM and EF groups.

Despite the high probability of infection during FAFs treatment, there is no consensus on the usage of antibiotics (4,11). Although many physicians consider extensive debridement and complete removal of bullet from the body to be necessary, debridement and bullet excision can lead to additional complications (4,17). As suggested in literature, we only removed the fragments or bullet that were observed during surgery and no additional intervention was conducted for fragments located in deep tissues or that weren't visualized.

Several studies have assessed nonunion criterion (9,13,14,19). Since the predicted union time of each bone is different, we did not determine a specific nonunion time in our study involving multiple bones. In a study of femoral fractures after FAFs, union time was compared between the EF (mean 5.8 months) and IM (mean 3.1 months) groups and the authors found that the IM group required considerably less time to heal (mean union time: 5.8 and 3.1 months, respectively) (9). In the same study, no difference was observed between groups in terms of evaluation of union (9). In a study of femur fractures caused by high-speed FAFs treated with EF and delayed IM, the mean union time was determined to be 24 weeks (14). In our study, we observed a mean time of 8.59 months, which was longer than the time reported in literature. There was no significant difference when we compared treatment types. In our study, it was observed that CT can be successfully applied together with advanced surgical techniques in appropriate fracture cases. However, it should be kept in mind that patients treated with CT are selected from fractures with adequate fracture alignment and relatively less soft tissue damage. None of the patients treated with CT had major soft tissue damage or neurovascular injury. This may explain why, in some respects, CT has fewer complications or more successful outcomes compared to surgical treatments. Additionally, it is known that there are many factors that affect fracture union positively or negatively (25-28).

Malunion rates after IM treatment of bone fractures caused by FAFs have been reported between 0% and 1.1% 15,29. In our study, this rate was found to be 11.5% in the general analysis of all treatment types. While malunion was not observed in patients treated with IM treatment, it was observed in 23.5% in EF treatment. Therefore, bone alignment follow-up should be performed well in EF treatment.

In FAFs, nerves may be damaged directly, indirectly, or through mechanisms related to transient cavitation (30,31). Direct injury is caused by direct contact between the object and a nerve. Indirect injury, on the other hand, is caused by compartment syndrome that results from the shock wave or transient cavitation generated by the object (30,31). The management of peripheral nerve damage in FAFs remains controversial 30. Of the treatment protocols, none have been established as the standard (32). In our study, nerves of patients who underwent open surgery were examined and, if necessary, repaired. In the event of a vascular damage, surgical intervention was conducted as a matter of urgency. Tokyay et al. reported the incidence of vascular and nerve injuries as 5.5% and 11.1%, respectively (33). In another study examining low-energy lower extremity FAFs cases, vascular injury and nerve injury were 6.1% and 1.4%, respectively (34). In a civilian upper extremity FAFs study, the rate of nerve injury in fractured patients was reported to be 43.1% 35. In our study, the rate of nerve injury was 15.4% and the rate of vascular injury was 5.8% in all extremities.

Limitations

The research is a retrospective and descriptive study. Since it included different clinics, the treatments were performed by different surgeons. Since the study included bone fractures in all extremities, no standardisation can be made for the results of treatment types. Due to the wide variety of treatment options, larger studies are needed to determine the ideal treatment of FAFs.

Conclusion

FAFs is an important injury with a 25% permanent

sequelae rate in the extremities. From admission to the emergency room to the conclusion of treatment, FAFs are challenging forensic cases for physicians. In addition to fractures, vascular and nerve injuries and soft tissue evaluation are important in the initial examination of patients. Treatment types are highly variable and far from standardized. CT, PS, IM, and EF therapies are effective in treating FAF-related long bone shaft fractures. In addition to modern surgical procedures, CT is still an important treatment option due to its shorter mean union time and low infection rate when conducted under the appropriate conditions.

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ORIGINAL ARTICLE

Comparison of the Symmetric-Tip vs Split-Tip Tunneled Hemodialysis Catheter: A Retrospective Study

Simetrik Uçlu ve Ayrık Uçlu Tünelli Hemodiyaliz Kateterinin Karşılaştırılması: Retrospektif Bir Çalışma

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ABSTRACT

Background: Despite not being the primary choice for vascular access in hemodialysis patients, permanent tunneled catheters are commonly utilized, but exhibit elevated rates of complications and dysfunction. This study retrospectively compares the dysfunction durations of symmetric and asymmetric-tipped permanent hemodialysis catheters.
Materials and Methods: A total of 307 patients, undergoing the placement of either symmetric or asymmetric-tipped permanent tunneled catheters at our interventional radiology clinic between 2021 and 2023, were included. Therefore, the present study aimed to examine the dysfunction rates associated with each type of catheter.
Results: Among the included patients, 157 were male (51.1%), and 150 were female (48.9%), with an average age of 64.2±12.2 years. The catheters were predominantly placed in the right jugular in 242 patients (78.8%), followed by the left jugular in 59 patients (19.2%), and femoral placement in 6 patients (2%). Symmetric-tipped catheters were employed in 161 patients (52.4%), while asymmetric-tipped catheters were utilized in 146 patients (47.6%). During follow-up, the catheter dysfunction rate was significantly higher in split-tip catheters than in symmetrical-tip catheters (p <0.0001).
Conclusion: The study revealed a statistically significant increase in catheter dysfunction for the asymmetric-tipped catheter type.

Keywords: Hemodialysis, Split tip, Symmetric tip, Tunneled catheter

ÖZ

Amaç: Hemodiyaliz hastalarının vasküler erişim yolu için kalıcı tünelli kateterler birinci seçenek olmamakla birlikte oldukça sık kullanılmaktadır. Bununla birlikte, komplikasyonları ve disfonksiyon oranları da oldukça yüksektir. Kalıcı hemodiyaliz kateterlerinin farklı tipleri mevcuttur. Bu çalışmamızda simetrik ve ayrık uçlu kateterlerin disfonksyione olma sürelerini retrospektif karşılaştırdık.
Gereç ve Yöntem: Girişimsel radyoloji kliniğimizde 2021-2023 yılları içerisinde, simetrik ve ayrık uçlu kalıcı tünelli kateter yerleştirilen toplam 307 hasta dahil edildi ve kateterlerin disfonksiyon oranlarına bakıldı.
Bulgular: Hastaların 157'si erkek (%51,1), 150'si (%48,9) kadındı. Hastaların yaş ortalaması 65,2±12,2 idi. Katater 242 hastada (%78,8) sağ juguler, 59hastada (%19,2) sol juguler, 6 hastada (%2) femoral yerleşimli idi. 161 hastada (%52,4) simetrik uçlu kateter, 146 hastada (%47,6) ayrık uçlu kateter yerleştirilmişti. Takiplerde kateter disfonksiyon oranı ayrık uçlu kateterde simetrik uçlu kateterlere göre anlamlı şekilde daha fazlaydı (P< 0,0001).
Sonuç: Kateter disfonksiyonu ayrık uçlu kateter tipinde anlamlı şekilde fazla bulundu.

Anahtar Kelimeler: Ayrık uç, Hemodiyaliz, Simetrik uç, Tünelli kateter

Introduction

Many patients needing dialysis rely on large-bore double-lumen permanent venous catheters as their vascular access route. Permanent dialysis catheters are placed into a central vein and tunneled subcutaneously. When arteriovenous fistulas or interposition grafts fail, permanent access routes are utilized in chronic hemodialysis (1). The ease of placement compared to fistula operations allows some patient groups to compete with fistulas (2). Additionally, permanent tunneled catheters are frequently preferred during the maturation process of fistulas (3). Furthermore, permanent tunneled catheters are preferred over AV fistulas in patients with comorbid conditions such as heart disease or respiratory failure. If catheterization is required for more than three weeks, fistula formation is not feasible, and life expectancy is short, a permanent tunneled catheter is recommended (4).

Among the advantages of tunneled catheters are ease of placement, immediate readiness for use, avoidance of percutaneous cannulation in each treatment, and lower risk of re-circulation (5). Many early and late complications can cause catheter dysfunction. Thrombosis, infection, formation of fibrin sheath, and central venous stenosis are among the most prominent complications over time, encompassing both early and

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late complications of the catheter (6-8). Development of fibrin sheath associated with hemodialysis catheters is widespread. Thrombus formation around the sheath is also frequent and among the most common causes of catheter malfunction. Therefore, due to early and late complications, the lifespan of permanent tunneled catheters is indicated to be within a wide range of 2-16 months in the literature (9,10). Mechanisms of fibrin sheath and thrombus formation are distinct. Fibrin sheath forms outside throughout the entire length of the catheter, leading to a flap valve effect. While fibrin sheath formation can occur within the first seven days, the formation mechanism is based on contact between fibrinogen and coagulation factors converting albumin to fibrin. Thrombus, on the other hand, can form both inside and outside the catheter tip, although the exact underlying mechanism of this formation is not yet precise; some contributing factors have been suggested, including recurrent vascular access, platelet and endothelial dysfunction, inflammation, and abnormalities in coagulation (8)

Numerous variables related to the catheter and the patient can be considered in catheter dysfunction. Regarding patient-related variables, age and gender, along with comorbidities such as hypertension (HT), diabetes mellitus (DM), high body mass index (BMI), anemia, and thrombotic genetic predispositions, can have an impact. Particularly, female gender and hypertension have been reported as prominent factors in the literature (10).

Various variables related to the catheter can contribute to dysfunction due to thrombosis and fibrin sheath formation. These include vascular calibration, secondary central venous stenosis, vascular access site traumas, catheter tip position, tunnel length, symmetry of catheter tips (symmetric, stepped, or split), angulation, straightness of the catheter, and the vessel into which the catheter is inserted (8,11).

Different approaches are available for revising catheters dysfunctional due to thrombosis or fibrin sheath. Treatment options for catheter dysfunction caused by fibrin sheaths or thrombi include catheter-directed thrombolysis, catheter replacement, balloon angioplasty, or stripping the fibrin sheath with a snare. Catheter-directed thrombolysis, where a thrombolytic agent is trapped within the catheter, is the simplest treatment method and provides a solution in two-thirds of cases. In the past, urokinase was used for this purpose, but nowadays, it has been replaced by alteplase. However, for underlying fibrin sheath-based dysfunctions, balloon angioplasty is recommended to break down the fibrin sheath, thus resolving the issue (5, 12). Additionally, numerous lumen and tip designs have been developed to prevent dysfunction due to catheter-related factors. In our study, the dysfunction rates and reasons of patients presenting to our clinic with catheter dysfunction were compared retrospectively based on whether their catheters had symmetric or split tips.

Materials and Methods

The study was approved by the Ethics Committee. A total of 307 patients with permanent tunneled catheters placed in our interventional radiology clinic between 2021 and 2023 were included. Of these patients, 157 were male (51.1%), and 150 were female (48.9%). The mean age of the patients was 65.2±12.2 years. Catheters were placed in the right jugular vein in 242 patients (78.8%), in the left jugular vein in 59 patients (19.2%), and in the femoral vein in 6 patients (2%). Symmetric-tip catheters were placed in 161 patients (52.4%), while split-tip catheters were placed in 146 patients (47.6%). Catheter dysfunction was accepted as the patient's inability to enter dialysis without any problems due to thrombosis or fibrin sheath. Causes of patient-related dysfunction, such as spontaneous extrusion of the catheter, were excluded. A total of 85 patients (27.6%) developed catheter dysfunction. The hospital system retrospectively evaluated the data of these patients by interventional radiologists.

Statistical Analysis

MedCalc (version 12, Ostend, Belgium) was used for statistical analysis. Descriptive statistics were presented as median (minimum-maximum) and mean±standard deviation. Categorical variables were expressed as frequencies and percentages. Fisher's exact test, Pearson chi-square test, and the corrected Yates version of Pearson chi-square test were used for comparing categorical variables. Independent sample t-test was used for comparing continuous variables with normal distribution, while Mann-Whitney U test was used for data that did not follow a normal distribution according to the Kolmogorov-Smirnov test. Kaplan-Meier analysis was used to evaluate catheter durability. A p-value <0.05 was considered statistically significant

Results

One hundred and fifty-seven patients were male (51.1%), and 150 patients were female (48.9%), with

an average age of 64.2±12.2 years. The catheters were predominantly placed in the right jugular in 242 patients (78.8%), followed by the left jugular in 59 patients (19.2%), and femoral placement in 6 patients (2%). Symmetric-tipped catheters were employed in 161 patients (52.4%), while asymmetric-tipped catheters were utilized in 146 patients (47.6%). 51.5% of the patients had HT, and 33.7% had DM, and there was no statistical difference between the groups.

There was no significant difference observed between symmetric-tip and split-tip catheters in terms of age (p=0.573) and gender (p=0.138). However, the rate of catheter dysfunction was significantly higher in the split-tip catheter group (p <0.0001) (Table 1).

Table 1. Patients' characteristics and comparison of the dysfunction of symmetrical-tip and split-tip catheters

	Symmetric Tip	Split Tip	*p*
Age (years) (mean)	64.1	64.3	0.573
Gender (M/F)	89/72	68/78	0.138
Hypertension (%)	52.3	50.8	0.813
Diabetes Mellitus (%)	34.9	32.5	0.698
Catheter Dysfunction (%)	9.3	47.9	< 0.0001

DM: Diabetes mellitus, HT: Hypertension

The Kaplan-Meier analysis revealed a median patency duration of 10 months with a patency rate of 71.3%. The patency duration (11 months) and patency rate (89.7%) of the symmetric-tip catheter were significantly higher compared to the split-tip catheter, which had a patency duration of nine months and a patency rate of 71.3% (p=0.0042) (Figure 1).

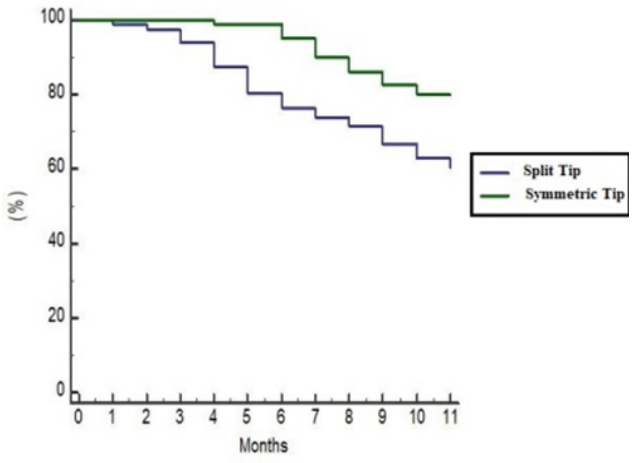

Figure 1. Survival curves obtained by the Kaplan-Meier analysis for symmetric-tipped and split-tipped catheter patency examined with a 95% confidence interva

Discussion

The National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) recommends arteriovenous (AV) fistula as the preferred vascular access for dialysis patients. However, using permanent tunneled catheters is quite common in dialysis treatments (13). Dysfunction of permanent tunneled dialysis catheters leads to additional costs and interventions, prompting the development of various catheter types to prevent dysfunction. Some involve modifying the shape of the catheter tip, while others aim to extend functional durability by changing the material from which the catheter is made. In a study by Özdemir et al. (14), it was shown that dialysis catheters with symmetric tips made from heparin-coated materials exhibited less fibrin sheath formation compared to non-heparin-coated ones, and they had longer patency durations. Unfortunately, an ideal hemodialysis catheter has not yet been established. Each type of catheter has its advantages and disadvantages (15).

NKF-KDOQI defines dysfunction as the inability to sustain the necessary blood flow for adequate hemodialysis without prolonging the prescribed hemodialysis treatment. Effective blood flow, recirculation, and arterial-venous pressure data are determinants during dysfunction. However, reversing the bloodlines without intervention may significantly increase catheter recirculation (16). In a study by Tal on pigs, symmetric-tip catheters showed minimal recirculation compared to split-tip and stepped-tip catheters when the bloodlines were reversed without intervention (17).

The flow rate of the catheter is also a variable in the dysfunction process. In a study by O'Dwyer et al., they compared split-tip catheters with stepped-tip catheters. Split-tip catheters were found to allow increased flow rates during hemodialysis, but these increased flow rates were not statistically significant. However, they emphasized that split-tip catheters were more prone to minor complications, especially dislodgement and kinking (18).

One of the most critical variables in the dysfunction process is the recirculation rate. In a study conducted by Ash, it was found that split-tip catheters had a higher pullout force compared to symmetric-tip catheters, but the recirculation rate was lower (19). Hwang et al., in their study, reported that symmetric-tip and stepped-tip catheters provided adequate hemodialysis doses. However, they stated that symmetric-tip catheters

had advantages over stepped-tip catheters in terms of lower incidence of catheter dysfunction, maintenance of hemodialysis with reversed bloodlines without intervention, and higher short-term catheter survival rate (16).

In another similar study, Jean et al. compared the dysfunction rates of symmetric-tip and split-tip catheters in 87 hemodialysis patients. It was demonstrated that the symmetric-tip catheter had a lower dysfunction rate than the split-tip catheter, and fibrin sheath formation was also less common in the symmetric-tip catheter. Based on their experience, it was considered that the symmetric-tip catheter is a more suitable option for providing longer-term vascular access for chronic hemodialysis patients (20). In our study, the catheter patency durations of 307 patients were retrospectively evaluated, and similar results were obtained with a larger number of patients.

In the literature, these studies highlight symmetric-tip catheters associated with better dialysis adequacy and slower progression of the dysfunction process. Nadolski et al. compared symmetric-tip catheters from two brands and found their 90-day primary patency rates to be significantly similar (21)

As for the limitations of our study, it should be noted that besides age and gender, the relationship between patients' additional comorbidities and the vascular site where the catheter is placed was disregarded, and only the catheter type and dysfunction durations were evaluated. This might have influenced the results. Another limitation is the small and non-homogeneous sample size.

Conclusion

Our study demonstrated that symmetric-tip catheters can provide the expected blood flow for dialysis longer than split-tip catheters. These results are consistent with other studies in the literature comparing dysfunction durations of catheter types and show that symmetric-tip catheters have longer durations before dysfunction occurs.

Ethical Approval

The study was approved by the Ethics Committee of the Sakarya University Faculty of Medicine, (Number:330155_05 Date: 30.01.2024), and performed by Helsinki Declaration.

Conflict of Interest

The authors declare that they have no conflict of interest.

Informed Consent

Informed consent was obtained from all patients before the procedure.

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ORIGINAL ARTICLE

Impact of Foot Problems on Physical Activity, Balance, and Musculoskeletal Pain

Ayak Sorunlarının Fiziksel Aktivite, Denge ve Kas-İskelet Ağrısı Üzerindeki Etkisi

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ABSTRACT

Background/Aims: Foot problems are common in society and can frequently occur during daily life activities. This study aims to investigate common foot problems among healthy young adults and to determine the effects of these problems on physical activity, balance, and musculoskeletal pain.
Methods: Demographic data were recorded. Physical activity levels were evaluated using the International Physical Activity Questionnaire short form (IPAQ). Musculoskeletal disorders were assessed using the Extended Nordic Musculoskeletal Questionnaire (NMQ-E). The Foot Function Index (FFI) was utilized for foot function assessment. Balance was assessed using the Single Leg Standing Test. The navicular drop test was conducted for pes planus evaluation, and hallux valgus was assessed using the Manchester Scale and goniometric assessment.
Results: Data from 480 participants were analyzed (hallux valgus: 81, pes planus: 204, control: 195). A comparison of balance, FFI, and IPAQ scores revealed that the balance time of participants with pes planus decreased significantly compared to the control group ($p<0.05$). Significant differences in body pain were found among the groups for the lower back, hip/thigh, and ankle areas ($p<0.05$). No significant differences were observed among other sub-parameters ($p>0.05$). In the lower back region, pain was reported by 29 individuals in the hallux valgus group, 163 in the pes planus group, and 13 in the control group ($p<0.05$).
Conclusions: Foot deformities can negatively impact an individual's foot functionality and balance, leading to pain in various body regions.

Keywords: Balance, Hallux valgus, Pes planus, Physical activity, Pain

ÖZ

Giriş/Amaç: Ayak problemleri toplumda yaygındır ve günlük yaşam aktiviteleri sırasında sıkça ortaya çıkabilir. Bu çalışma, sağlıklı genç yetişkinler arasında yaygın ayak problemlerini araştırmayı ve bu problemlerin fiziksel aktivite, denge ve kas iskelet sistemi ağrısı üzerindeki etkilerini belirlemeyi amaçlamaktadır.
Yöntemler: Katılımcıların demografik verileri kaydedildi. Fiziksel aktivite düzeyleri Uluslararası Fiziksel Aktivite Anketi (IPAQ) kısa formu ile değerlendirildi. Kas-iskelet sistemi rahatsızlıkları Genişletilmiş Nordic Kas-İskelet Anketi (NMQ-E) ile değerlendirildi.. Ayak fonksiyonu değerlendirmesi için Ayak Fonksiyon İndeksi (FFI) kullanıldı. Denge, Tek Ayak Üzerinde Durma Testi ile değerlendirildi. Pes planus değerlendirmesi için naviküler düşme testi yapıldı, halluks valgus ise Manchester Skalası ve gonyometrik ölçümle değerlendirildi.
Bulgular: Toplam 480 katılımcının verileri analiz edildi (halluks valgus:81, pes planus:204, kontrol:195). Denge, FFI ve IPAQ skorlarının karşılaştırılmasında pes planus olan katılımcıların denge süresinin kontrol grubuna göre anlamlı ölçüde azaldığı görüldü ($p<0.05$). Alt sırt, kalça/üst bacak ve ayak bileği bölgelerindeki vücut ağrısı açısından gruplar arasında anlamlı farklar bulundu ($p<0.05$). Diğer alt parametrelerde anlamlı bir fark gözlenmedi. ($p>0.05$). Alt sırt bölgesinde halluks valgus grubunda 29 kişi, pes planus grubunda 163 kişi ve kontrol grubunda 13 kişi ağrı bildirdi ($p<0.05$).
Tartışma: Ayak deformiteleri, ayakların fonksiyonelliği ve durumu olumsuz olabilir. Ayrıca deformite varlığı çeşitli vücut bölgelerinde ağrıya yol açabilir.

Anahtar Kelimeler: Ağrı, denge, Fiziksel aktivite, Halluks valgus, Pes planus

Introduction

The foot carries body weight, lowers the gravity line on a narrow support surface, provides stability, and absorbs shocks during daily activities such as walking and running. Genetic structure, trauma, muscle weakness, ligament laxity, fall of the talar head, paralysis, high heels, and inappropriate shoe choices can cause many foot problems by disrupting foot structure and function (1).

Foot problems are common in society and can occur commonly during our daily living activities. Foot varus and valgus deformities, pes planus, pes cavus, and hallux valgus are among the most common foot problems (2). It has been stated that approximately 70-80% of the people in developed countries have several types of foot problems and complain of foot pain, and in a field study, foot pain or feeling of stiffness ranges from 18-63% (3, 4). Deformities caused by foot problems lead to loss of labor force, decreased quality of life, depression, and deterioration of mental health in young individuals (5).

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The foot, together with the ankle, knee, and hip joints, forms the lower limb kinematic chain that adjusts the body balance in an upright posture. Any change in the integrity of body biomechanics can negatively affect all body segments starting from the foot. Deformities in the arch height, flexibility, or strength of the foot impair its function and standing balance. Deformities, muscle weakness, decreased motor or sensory control, balance problems, as well as gait cycles can negatively affect the gait cycle and cause gait disturbance (6).

Physical activity (PA) levels have decreased significantly among young people, especially adolescents. Inadequate PA and sedentary behaviors are among the major lifestyle problems seen in young people in recent years (7). In a study examining the relationship between body composition, PA profile and the occurrence of knee and foot posture changes in young healthy adults, it was reported that PA level was negatively associated with knee and foot deformities (8).

Although it is known that foot problems lead to pain, balance problems, falls, physical inactivity, and difficulty walking in older ages, there are very few comprehensive studies on the youth period when the foot develops rapidly and is prone to deformity development (9, 10). This study aimed to investigate common foot problems among healthy young people studying in health departments and to determine the effects of these problems on PA, balance, and musculoskeletal pain.

Material and Method

This study is a case-control investigation conducted between October and December 2023. The research protocol received approval from the local ethics committee of Selcuk University Medical School Non-Interventional Clinical Researches Ethics Committee (approval number: 2023/483). The study adhered to the principles outlined in the Declaration of Helsinki and the guidelines of the International Council for Harmonization of Good Clinical Practice. The study included voluntary individuals aged between 18-30 years old.

In this study, the inclusion criteria were as follows: Healthy young adults between the ages of 18 and 35 were included. Participants were required to have no systemic diseases or chronic health conditions and no serious health problems that could limit PA. Individuals diagnosed with hallux valgus or pes planus were included, as well as those without any foot deformities who served as the control group. Additionally, all participants were required to provide informed consent and voluntarily agree to participate in the study. Only those who could independently perform daily activities and had no restrictions on PA were selected.

Exclusion criteria were based on participants' medical histories and health conditions. Individuals with serious orthopedic or neurological disorders that could significantly affect balance or walking ability, such as stroke or multiple sclerosis, were excluded. Similarly, participants with inflammatory or autoimmune diseases, such as rheumatoid arthritis or lupus, as well as those who were pregnant, were not included in the study. Participants who had experienced trauma or undergone surgery on the lower extremities within the past six months were also excluded. Those receiving active treatment or physical therapy for hallux valgus or pes planus deformities were not eligible for participation. Additionally, individuals with cognitive or psychiatric disorders that would prevent them from fully understanding or participating in the study were excluded.

In this study, individuals with concurrent diagnoses of both pes planus and hallux valgus were also excluded to ensure clearer differentiation between the two deformities and their respective impacts. This exclusion criterion was implemented to avoid potential confounding effects that might arise from the coexistence of these two conditions.

The demographic characteristics, PA levels, and musculoskeletal pain of all participants were assessed using a standardized form. Demographic data such as age (years), height (cm), weight (kg), body mass index (kg/m2) were recorded. Additionally, the patient was questioned whether she had any other foot problems. PA level was evaluated using the International Physical Activity Questionnaire short form (IPAQ) (11), and musculoskeletal disorders were assessed using the Extended Nordic Musculoskeletal Questionnaire (NMQ-E) (12). The Foot Function Index (FFI) (5) was used for foot function assessment. Balance assessment was performed using the single-leg standing test. The navicular drop test was conducted for pes planus evaluation. Hallux valgus was assessed using the Manchester Scale and goniometric assessment.

The Foot Function Index (FFI)

The Foot Function Index (FFI) was used to assess the foot function of the volunteers. Turkish adaptation was done by Yalıman et al (5). The FFI measures foot pain that affects a person's daily activities. Participants are asked to most accurately describe the condition of their feet over the past week and rate each question from 0 (no pain or difficulty at all) to 10 (most severe pain or too difficult to do). Participants are asked to read all the questions and mark their chosen number with an X. If right and left foot complaints are different, they are asked to write a score in separate boxes.

FFI is a 23-item scale with 3 subscales: pain, disability, and activity limitation. The pain subscale contains 9 items and measures the level of foot pain in various situations. The disability subscale contains 9 items and determines how much difficulty the person has during functional activities due to foot problems. The activity limitation subscale contains 5 items and assesses activity limitations caused by foot problems.

The Expanded Nordic Musculoskeletal Questionnaire (NMQ-E)

The Expanded Nordic Musculoskeletal Questionnaire (NMQ-E), developed by Dawson et al. (12), was used to assess musculoskeletal disorders. The NMQ-E is a self-administered questionnaire that provides reliable information on the onset, prevalence, and outcome of musculoskeletal pain in nine body regions (neck, shoulders, back, elbows, wrists/hands, lower back, hips/thighs, knees, ankles/feet). The questionnaire is a scale used to examine musculoskeletal pain and related conditions in workers and/or the general population. The NMQ-E asks yes/no questions about the presence or absence of pain, soreness, or discomfort in nine body parts at any time, in the last 12 months, in the last four weeks, and on the day of the assessment.

The International Physical Activity Questionnaire Short Form (IPAQ)

To determine the level of PA, the IPAQ, which was developed by Craig et al. (11), and the Turkish validity and reliability study conducted by Sağlam et al. were used. (13) This form can be self-administered and consists of seven questions related to activities performed in the "last seven days" to assess the level of PA. The questionnaire provides information on time spent sitting, walking, moderately vigorous activities, and vigorous activities. A score is obtained by multiplying minutes, days, and metabolic equivalent values. The Metabolic Equivalent of Task (MET) calculations of the participants were computed as follows (14);

Vigorous Activity: Number of Days × Minutes per day × 8

Moderate Activity: Number of Days × Minutes per day × 4

Walking: Number of Days × Minutes per day × 3.3

Total PA: Vigorous Activity + Moderate Activity + Walking

Balance Assessment

Single Leg Stance Assessment

During the single-leg stance test, the person is asked to stand on one leg for thirty seconds, focusing his/her eyes on a fixed point on the wall in front of him/her and keeping his/her balance. The test is performed on the right and left foot separately for eyes open and eyes closed. Each test is repeated three times and the average of the standing times of the individuals in each trial is taken and recorded. Standing times on the right and left foot are measured with a stopwatch. The test is terminated when the foot is lowered to the ground, the foot moves, or the eyes are closed during the test (15).

Assessment for Pes Planus

The arch of the foot is evaluated in both sitting and standing conditions. Feiss line (16) was used to assess arch height. It was checked whether the medial malleolus, navicular tubercle, and the head of the first metatarsal were on the same line. For the navicular drop test (17), the distance between the navicular tubercle and the ground was measured in the sitting position with no load on the foot and then the navicular-ground distance was measured bilaterally in millimeters in the bipedal standing position. The difference between loaded and unloaded conditions was considered normal if 5-9 mm, pronation if 10 mm or more, and supination if 4 mm or less.

Assessment for Hallux Valgus

Hallux valgus angle measurement is performed in three repetitions using a goniometer. The hallux valgus angle is the angle between the longitudinal plane of the proximal phalanx bone of the thumb and the longitudinal plane of the first metatarsal bone. Normal limits are usually between 5° and 15°. Angulations below 0° are considered hallux varus or adducts (18).

The Manchester Scale

The Manchester Scale, developed by Garrow (19) was used to determine the degree of hallux valgus deformity. In this scale, hallux valgus deformity is assessed with a clinical tool including photographs of the foot and classified into 4 levels: none-1, mild-2, moderate-3, severe-4. According to the scale;

• At the none-1 level, the first phalanx has a normal appearance,

• At the mild-2 level, there is minimal medial translation of the first metatarsal bone and lateral translation of the first phalanx

• At the moderate-3 level, the translation of the first metatarsal bone is increased and the bony prominence of the distal end of the first metatarsal bone is prominent, and the first phalanx is translated under the second phalanx,

• At the severe-4 level, ossification at the distal end of the first metatarsal bone is completely prominent and the first phalanx is completely translated under the second phalanx.

The Turkish validity and reliability study of the scale was conducted in 2016 (20). According to the evaluation of the scale, those at the level of none-1 are included in the group without hallux valgus, and those with a value of 2 and above are included in the hallux valgus group.

Table 1. Demographic data of the participants

		Hallux Valgus (n=81)	Pes Planus (n=204)	Controls (n=195)	x^2	p
		(Group 1)	(Group 2)	(Group 3)		
		X±SD	X±SD	X±SD		
Age (years)		21.78±6.66	21.16±5.92	21.17±5.76	0.349	0.706
Height (cm)		165.64±8.55	165.04±8.13	166.66±8.46	1.903	0.150
Body Weight (kg)		59.63±12.06	60.56±13.71	63.10±13.89	2.617	0.074
BMI (kg/m²)		21.64±3.42	22.11±4.19	22.63±4.10	1.888	0.153
		n (%)	n (%)	n (%)		
Gender	**Female**	69 (85.19)	169 (82.84)	153 (78.46)	2.167	0.339
	Male	12 (14.81)	35 (17.16)	42 (21.54)		
Dominant Hand	**Right**	71 (87.65)	182 (89.22)	176 (90.26)	3.731	0.734
	Left	10 (12.35)	22 (10.78)	19 (9.74)		
Smoking	**Yes**	20 (24.69)	40 (19.61)	47 (24.1)	1.487	0.476
	No	61 (75.31)	164 (80.39)	148 (75.9)		

n: Number of participants, X: Mean, SD: Standard deviation, p <0,05

Statistical analysis

Statistical analysis of the study was performed using the Statistical Package for Social Sciences program for Windows, Version 22.0 (IBM, SPSS Statistics IBM Corp., Armonk, New York, USA). The normality distribution of continuous variables was examined using histogram plots, skewness and kurtosis coefficients, Shapiro-Wilk test, coefficient of variance analysis, and normal Q-Q plots without trend. The chi-square test was used to compare categorical variables. For intergroup comparisons of continuous variables, one-way ANOVA (Analysis of Variance) was used when the assumption of bivariate normal distribution was met, otherwise, the Kruskal-Wallis test was used. An overall p-value below 0.05 was considered statistically significant

Results

The study included 81 participants with hallux valgus, 204 with pes planus, and 195 in the control group. The mean age of the participants was 21.78 ± 6.66 years in Group 1, 21.16 ± 5.92 years in Group 2, and 21.17 ± 5.76 years in Group 3. There were no statistically significant differences among the groups in terms of participants' ages (p=0.706), heights (p=0.150), weights (p=0.074), and other demographic variables (BMI (p=0.153), dominant hand (p=0.734), smoking (p=0.476)). In the hallux valgus group, there were 69 females and 12 males, in the pes planus group, there were 169 females and 35 males, and in the control group, there were 153 females and 42 males. The demographic information of the participants is summarized in Table 1.

When balance, FFI, and IPAQ scores were compared, it was concluded that the balance time of pes planus patients statistically significantly decreased compared to the control group. However, the balance time in

the group with hallux valgus statistically significantly increased compared to the control group. Significant differences were also found between the groups in FFI subheadings. The pain was significantly higher in pes planus and hallux valgus patients compared to the control group. However, the groups showed similar results in the IPAQ total score and other sub-parameters except for IPAQ severity and sitting (Table 2).

When comparing participants' body pains, significant differences were found in the groups for the lower back, hip/thigh, and ankle areas. There were no significant differences among the other sub-parameters. In the lower back region, there were 29 individuals with pain in the hallux valgus group, 163 in the pes planus group, and 13 in the control group. In the hip/thigh region, there were 15 individuals with pain in the hallux valgus group, 63 in the pes planus group, and 35 in the control

Table 2. Comparison of participants' balance, foot function, and physical activity scores

	Hallux Valgus (Group 1) X±SD	Pes planus (Group 2) X±SD	Controls (Group 3) X±SD	F, x^2	p	Groups
SLSA						
Right Eyes Open	23.14±9.99	18.81±10.36	22.45±9.61	8.778	<0.001	1.2 2.3
Left Eyes Open	22.83±9.96	19.73±10.57	21.62±9.85	3.263	0.039	1.2
Right Eyes Closed	8.68±6.88	6.67±5.40	7.82±6.60	3.585	0.028	1.2
Left Eyes Closed	8.04±6.00	5.750±5.24	7.59±6.33	6.903	0.001	1.2 2.3
FFI						
Pain Right	11.51±12.80	12.68±13.19	9.14±9.12	4.892	0.028	2.3
Pain Left	11.3±12.52	12.16±12.43	9.47±9.13	6.41	0.002	2.3
Disability Right	10.23±12.26	10.67±10.99	9.08±9.33	8.404	<0.001	1.3 2.3
Disability Left	10.19±12.43	10.44±11.36	9.29±9.18	15.727	<0.001	1.3 2.3
Activity Limitation Right	2.08±3.71	2.32±3.49	1.74±3.56	5.85	0.003	2.3
Activity Limitation Left	1.93±3.37	2.19±3.34	1.89±3.58	20.386	<0.001	1.3 2.3
Total Right	23.76±26.11	25.79±25.45	19.96±18.80	10.653	<0.001	1.3 2.3
Total Left	23.7±26.57	24.86±24.92	20.67±18.85	22.269	<0.001	1.3 2.3
IPAQ						
Vigorous	1349.14±5524.87	240.86±1160.25	893.54±3967.21	3.49	0.031	1.2
Moderate	643.70±1941.12	347.31±1157.97	395.84±1309.01	1.38	0.253	-
Walking	1698.69±2272.64	2074.47±2934.72	1885.76±2582.76	0.619	0.539	-
Sitting	316.30±411.23	230±212.16	312.67±357.01	4.142	0.016	2.3
Total	4007.83±7340.74	2892.65±4199.31	3487.81±5870.07	1.326	0.266	-

FFI: Foot Function Index, IPAQ: International Physical Activity Questionnaire, SLSA: Single Leg Stance Assessment, SD: Standart deviation, X: Mean

group. The comparison of participants' body pains is shown in Table 3.

Table 3. Body pain regions of participants according to groups

		Hallux Valgus (n=81) (Group 1)		Pes Planus (n=204) (Group 2)		Controls (n=195) (Group 3)		x^2	P
		n	%	n	%	n	%		
Neck	Yes	43	53.09	121	59.31	123	63.08	7.581	0.108
	No	38	46.91	83	40.69	72	36.92		
Shoulder	Yes	29	35.8	87	42.65	87	44.62	7.104	0.131
	No	52	64.2	117	57.35	108	55.38		
Upper Back	Yes	27	33.33	84	41.18	68	34.87	2.348	0.309
	No	54	66.67	120	58.82	127	65.13		
Elbows	Yes	2	2.47	11	5.39	16	8.21	3.581	0.167
	No	79	97.53	193	94.61	179	91.79		
Wrists Hands	Yes	13	16.05	46	22.55	39	20	1.543	0.462
	No	68	83.95	158	77.45	156	80		
Waist	Yes	29	35.8	163	79.9	13	6.67	252.975	<0.001
	No	52	64.2	41	20.1	182	93.33		
Hip Thighs	Yes	15	18.52	63	30.89	35	17.95	30.103	<0.001
	No	66	81.48	141	69.11	160	82.05		
Knee	Yes	43	53.09	81	39.71	87	44.62	4.271	0.118
	No	38	46.91	123	60.29	108	55.38		
Ankles	Yes	45	55.56	89	43.63	68	34.87	55.967	<0.001
	No	36	44.44	115	56.37	127	65.13		

n: Number of participants, x^2: Chi square test, $p < 0.05$

Discussion

When comparing groups, differences were observed in the open and closed-eye balance comparisons, with individuals in the pes planus group having the worst balance. Similarly, differences were found in the FFI comparison among groups, indicating poorer foot function in the pes planus group. In the comparison of PA (except sitting), it was concluded that groups had similar characteristics. Regarding the evaluation of body pains among groups, it was noted that participants in the pes planus group experienced more pain in the lower back, hip/thigh, and ankle regions.

Foot deformities can lead to differences in joint mobility and contact with the ground surface, which in turn can affect balance (21). In a study conducted on individuals with and without pes planus, it was observed that individuals with pes planus experienced an average decrease of 10% in balance duration with eyes open and a 20% decrease with eyes closed compared to those without pes planus (22). Studies on balance in individuals with Hallux valgus are controversial. In a study conducted by Taş et al., no change in balance parameters was observed between individuals with and without hallux valgus (23). However, Hurn et al. concluded that individuals with mild to moderate hallux valgus did not experience balance changes, whereas those with severe deformities experienced balance loss (20). In our study, it was observed that individuals with hallux valgus had better balance compared to the control group. The lack of consensus in the literature may be due to studies being conducted on different populations (20, 23). We also believe that the decrease in balance in the pes planus group may be due to the biomechanics of the foot intrinsic muscles and foot proprioception being affected by pes planus (20). The increase in balance duration in the hallux valgus group may be attributed to the population being young, having a low BMI, and exhibiting mild to moderate hallux valgus.

The impairment of foot function due to foot deformities is an inevitable consequence. In a study, it was indicated that as the severity of hallux valgus increases, foot functions are negatively affected (24). Talu et al. compared functionality with FFI scores in individuals with Hallux valgus in their study and found the highest

score in pain and the lowest score in activity limitation (25). In our study, similar to the literature, we also found the highest score in the pain subcategory of the FFI while the lowest score was observed in activity limitation. Similarly, individuals with pes planus also experience a negative impact on foot function (26). In a study conducted by Dikici et al., foot function was evaluated using the FFI. It was concluded that the FFI subparameters and total score were high in the pes planus group (27). In this study, we also observed that the FFI total score and subcategory scores of individuals with pes planus were higher compared to the control group. Additionally, similar to hallux valgus, it was found that the highest impairment was in the pain subcategory in the pes planus group. We believe that the impairment of functionality in both the hallux valgus and pes planus groups is due to disrupted foot biomechanics, which leads to pain and reduced functionality.

The pain caused by foot deformities and the resulting impairment in foot function can negatively affect individuals' physical activities. It has been noted in the literature that individuals with pes planus may struggle with activities such as prolonged standing and walking (28). In another study, it was found that individuals with pes planus experience negative effects on physical fitness parameters, with a decrease in stair climbing speed observed among individuals with pes planus (29). In this study, it was concluded that the total PA score showed similar characteristics among the groups. We believe that this may be due to the inclusion of individuals with mild to moderate hallux valgus complaints in the study and the fact that the study was conducted on young adults, who are one of the populations with the highest PA levels.

Foot deformities can lead to instability, which may result in pain not only in the foot but also in areas beyond the foot, such as the ankle, knee, or lower back. In a study, it was reported that individuals with unilateral pes planus deformity experienced pain in the thoracic region, while those with bilateral pes planus deformities had complaints of pain in the thoracolumbar and lumbar regions (30). Some researchers have also suggested that pes planus can lead to pain in the heel, knee, hip, and back (31). In another study, it was concluded that pes planus increases pelvic inclination, leading to the development of lower back pain (32). In our study, we also concluded that participants with pes planus experienced pain in the lower back, hips, and feet. The presence of pain in the lower back and hips may be attributed to changes in weight distribution and stabilization due to limitations in foot physical function and the development of pain.

This study has several limitations. Firstly, balance was not evaluated using computer-assisted devices. Similarly, foot functionality was assessed only through surveys, and specific clinical evaluation parameters were not utilized. Additionally, our study only included young adults. There is a need for studies that include populations from different age groups.

In conclusion, foot deformities can negatively affect an individual's foot functionality and balance, and may lead to pain in various parts of the body beyond the foot. Our study conducted on young adults has enabled us to conclude that these effects can be observed even in the early stages. We believe that addressing foot deformities in the early stages is crucial to preventing these effects and associated secondary complications in older age groups.

Ethics Committee Approval

Ethical approval for this study was obtained from the Selcuk University Medical School Non-Interventional Clinical Research Ethics Committee (approval number: 2023/483). All authors declared that they follow the rules of Research and Publication Ethics.

Conflict of Interest

The authors declare that they have no conflict of interest.

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Authors' Contributions

All authors contributed to the conception, design of the study, data collection, data analysis, and assembly. The manuscript was written and approved by all authors.

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ORIGINAL ARTICLE

Does the Stroop effect decrease with imagery?

Stroop etkisi imgeleme ile azalır mı?

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ABSTRACT

Background/Aims: The present study examines the impact of imagery on the Stroop effect, which is a measure of interference effects on attention.
Methods: The Stroop task requires participants to identify the color of a word while disregarding its meaning. The study group consisted of 40 participants undergoing 14 weeks of imagery sessions, each lasting 90 minutes. The data were analyzed using the Statistical Package for Social Sciences, version 25.0 software. Statistical tests, including the Mann-Whitney U Test and the Wilcoxon Signed Rank Test, were also employed to compare the pre-test and post-test results.
Results: The results indicate that imagery has a beneficial impact on reducing the Stroop effect
Conclusion: The findings suggest that imagery has a positive effect on reducing the Stroop effect. The results indicate a notable impact on the Stroop effect, assessing the influence of imagery on attention and cognitive interference. Nevertheless, further research is recommended to validate these results.

Keywords: Attention, imagery, Stroop effect, Stroop test

ÖZ

Arka Plan/Amaçlar: Bu çalışma, imgelemenin dikkat üzerindeki girişim etkilerinin bir ölçüsü olan Stroop etkisi üzerindeki etkisini incelemektedir.
Metodoloji: Stroop görevi, katılımcıların bir kelimenin anlamını göz ardı ederken rengini tanımlamalarını gerektirir. Çalışma grubu, her biri 90 dakika süren 14 haftalık imgeleme seanslarına tabi tutulan 40 katılımcıdan oluşmuştur. Veriler SPSS 25 yazılımı kullanılarak analiz edilmiş ve ön test ve son test sonuçlarını karşılaştırmak için Mann-Whitney U Testi ve Wilcoxon İşaretli Sıra Testi gibi istatistiksel testler kullanılmıştır.
Bulgular: Sonuçlar, imgelemenin Stroop etkisini azaltmada faydalı bir etkiye sahip olduğunu göstermektedir.
Sonuç: Bulgular, imgelemenin Stroop etkisini azaltmada olumlu bir etkiye sahip olduğunu göstermektedir. Sonuçlar, imgelemenin dikkat ve bilişsel müdahale üzerindeki etkisini değerlendiren Stroop etkisi üzerinde kayda değer bir etkiye işaret etmektedir. Bununla birlikte, bu sonuçları doğrulamak için daha fazla araştırma yapılması önerilmektedir.

Anahtar Kelimeler: Dikkat, imgeleme, Stroop Etkisi, Stroop Testi

Introduction

The Stroop paradigm is a widely used test to assess attentional bias (1). Although similar to the traditional Stroop task, the emotional Stroop paradigm uses words with emotional content (2). When a person tries to name the color of an incongruently spelled color word, the response time (RT) is prolonged due to the distraction of emotional words (3). This can be explained by the person's attention being diverted towards disorder-related or personal issues. The Stroop effect is generally weaker compared to the effects in the traditional Stroop task. This test is a tool used to elicit and examine attentional biases in individuals with mental disorders (4).

A fundamental feature of the human cognitive system is the ability to attend to and utilize goal-directed stimuli while ignoring environmental distractions (5). The Stroop task provides a means of assessing selective attention (6). This task requires participants to name the displayed color of words presented while ignoring the meaning of the words (7). In the field of psychology, the

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Stroop effect refers to the observed delay in reaction time between stimuli (8). that are congruent and those that are incongruent (9). The Stroop effect has been employed in the construction of psychological tests, most notably the Stroop test (10). A fundamental example of this phenomenon can be observed when there is a discrepancy between the designation of a color (e.g. "blue," "green," or "red") and the color in which it is presented (such as the word "red" printed in blue ink instead of red ink). When respondents are asked to identify the color of a word, they tend to require a longer RT and are more prone to error when the color of the ink does not correspond to the name of the color (11). The Stroop task provides evidence for the automaticity of reading (12). The fastest responses are observed in congruent trials, where the meaning of the presented word is congruent with its displayed color (e.g. "RED" shown in red), followed by neutral trials, where the meaning of the given words is unrelated to the colors (e.g., "LOT" shown in red) (13). The slowest RTs are observed on incongruent trials, wherein the color displayed and the meaning of the words are incongruent (e.g. red shown in blue). The efficacy of the task can be evaluated by calculating the differences in RTs between the aforementioned imagery-applied flood conditions (7). The Stroop effect is sufficiently pronounced to capture attention, and a considerable number of individuals report experiencing cognitive dissonance during an incongruent trial (14). The Stroop effect persists despite prolonged training and is resistant to conscious strategies employed in imagery (1). The methods that result in reduced Stroop effects all entail the manipulation of the stimulus context (e.g., the coloring of a single letter instead of all letters or the reduction of the response-stimulus interval) to provide external support for imagery mechanisms. Consequently, these methods are unlikely to be the result of deliberate, top-down imagery. Financial incentives, provided to enhance motivation and performance, are unlikely to influence reaction times, except perhaps to accelerate them across all trial types, or to reduce the Stroop effect to a minimal extent (15).

Cognitive processes are typically classified as automatic. Automatic processes are either involuntary at birth or become so through extensive practice. It is proposed that some processes are innate and automatic, whereas others become automatic through practice. To illustrate, reading words is a pseudo-automatic process for proficient readers. Consequently, the Stroop effect is regarded as the "gold standard" of automatized performance (16). The act of reading words is regarded as an automatic process. Although explicit instructions are provided for competent readers to focus on the color in which words are printed, the tendency to access the meaning of the word remains.

Imagery is a state of consciousness that involves focused attention (selective attention/selective inattention hypothesis) (17), reduced environmental awareness, and an enhanced capacity to respond to suggestions (18). While it is widely acknowledged that imagery can influence cognitive processes, the precise extent to which imaginative suggestions contribute to this phenomenon remains a topic of contention (19). There is a plethora of theories about the nature of imagery. Imagery is regarded as an altered state of mind, characterized by a distinct level of awareness that differs from the typical state of consciousness (20). Imagery may also be conceptualized as a placebo effect (21), a redefi ition of the therapeutic interaction (22), or a form of imaginary role-playing (23). It is posited that during the process of imagery, an individual's focus and concentration are enhanced, and their responsiveness to suggestion is optimized (24). Imagery commences with a hypnotic induction, which encompasses a series of preliminary instructions and suggestions. The application of imagery for therapeutic purposes is referred to as "hypnotherapy." The extant research evidence indicates that hypnotizing a person can facilitate the formation of false memories and that the use of imagery does not enhance the accuracy of memory recall (25).

The majority of imagery theories concur that responding to a hypnotic suggestion entails top-down cognitive imagery processes and that the sensation of involuntariness, which is the hallmark of the hypnotic phenomenon is exclusively attributable to impaired or relinquished metacognition (26). The most straightforward imagery theory is cold imagery, which makes few assumptions and regards reduced metacognition as the fundamental process underlying the hypnotic response. In particular, this theory suggests that hypnotic responding is achieved through the use of deliberate imagery. Subjects deliberately engage in perceptual or cognitive strategies to create the imagery applied to the imagery described in the suggestion, while simultaneously altering the monitoring of their intentions and convincing themselves that they are not acting intentionally

(27). The theory is based on higher-order theories of thought consciousness, which posit that a mental state becomes conscious as a result of being referred to by a higher state (28). Under the tenets of cold imagery, responding to a suggestion entails the deployment of a strategy to generate the imagery delineated in the suggestion, without the subject being aware of the strategic nature of their actions. This assumption leads to the conclusion that the only distinction between a hypnotic and a non-hypnotic response is the form of the accompanying second-order state. It can thus be inferred that if the Stroop interference effect can be reduced by responding to the suggestion of blindness, it should also be possible to do so through a voluntary non-hypnotic strategy that employs the same approach as that used in response to the suggestion. Identifying such a strategy is pivotal to imagery theory and straightforward, metacognitive explanations of imagery. This is because the absence of a clear explanation involving intentional actions invites more complex theories to address the issue of blindness suggestion (29).

Bressler and Rossman (30) were other pioneers of the imagery method, and their work contributed to the widespread use of the method in psychological treatments by defining how it should be used. It is typically employed as a supplementary approach. In a study conducted by Campbell-Gillies (31), positive mental imagery was employed in conjunction with music for individuals diagnosed with breast cancer. The findings indicated that participants exhibited a reduction in stress, anxiety, and depressive symptoms during their chemotherapy treatment, which spanned six sessions. In this study, we tried to determine whether imagery can reduce Stroop interference. The Stroop effect can be significantly reduced or eliminated in certain contexts (12). Research has shown that responses obtained during imagery can occur after imagery (22, 32, 33). If the Stroop effect can be modulated simply without initiating imagery, it may have broader effects than previously believed. To date, no experimental study on the Stroop effect of imagery has been conducted in Turkey. Accordingly, the present study sought to ascertain whether the use of imagery affects adversely the Stroop effect.

The hypotheses of the present study are organized as follows;

H1: The use of imagery has a significant effect on the Stroop effect.

H2: There is no significant effect on the Stroop effect between the experimental group using imagery and the control group not using imagery.

Materials and Method

This study was designed in a quasi-experimental design to examine the effect of imagery on the Stroop effect. Experimental and control groups were formed from homogeneous groups (34). The main purpose is to test the cause-and-effect relationships between the independent variable and the dependent variable (35).

Participants

The study group of this research was formed in the 2022-2023 academic year in Beyoglu, in the province of Istanbul. Forty participants were admitted to a private health center in the district; therefore, a total of 40 participants were included in the study, 20 in the imagery group and 20 in the non-imagery group. Three participants in each group were included in the study as a backup in case of data loss. In quasi-experimental studies, the sample size can be as low as 15 subjects (36). The research was conducted in the psychology room of a private health center. The research was conducted by obtaining the necessary permissions from the health center. In addition, the study group was informed about the purpose of the research and the process by using the Voluntary Consent Form and permission was obtained for the study group to participate in the research voluntarily. The study group was conducted at different times so that the experimental and control groups were not affected by each other's performances.

Fig 1

Ethics

Written informed consent was signed by all participants before data collection. The study was approved by the Ethics Committee of Istanbul Gelisim University with the number (2023-08-57) and was conducted under the 1961 Declaration of Helsinki and its later amendments.

Inclusion and Exclusion Criteria

Individuals who met any of the following criteria were excluded from participation in the study: (a) individuals with disabilities who required special accommodations, (b) individuals with a lifetime history of organic mental disorder, psychotic disorder, bipolar disorder, or substance abuse, and (c) individuals with severe axis II psychopathology, as defined by the

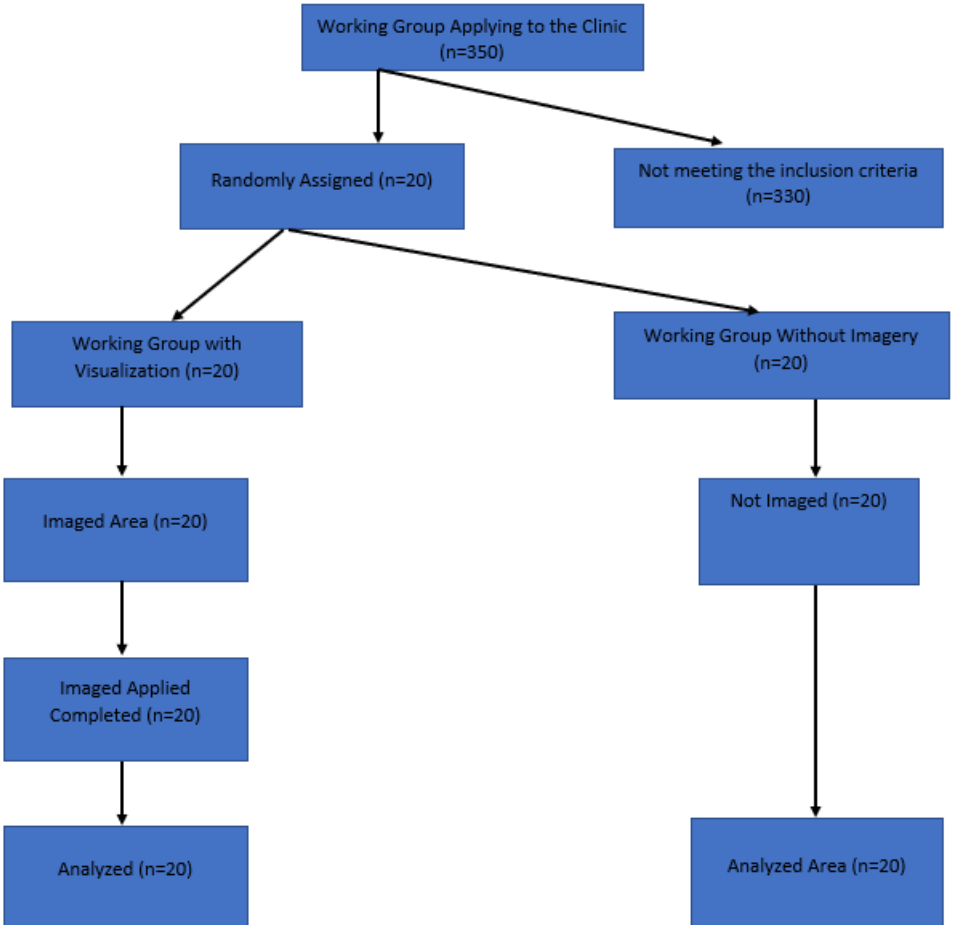

Figure 1. Flow Chart of the Study Group

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, Text Revision (DSM-IV-TR), including cluster personality disorders, antisocial personality disorder, non-voluntary individuals, and borderline personality disorder.

Data Collection Tools and Techniques

The Personal Information Form (PIF)

In the study, eight questions were prepared in the Personal Information Form developed to determine the sociodemographic information of the study group. The form included demographic information such as gender, age, income, education level, and whether the study group had a psychiatric diagnosis.

The Stroop Test

There are many single Stroop Tests in the literature (37). In the Stroop Test, it is asked to say color names printed using a color different from the color. There is a Turkish form called BILNOT Battery (38). The original Stroop Test consists of the Victoria Form. In this form, the Stroop Test TBAG (Scientific and Technical Research Council of Turkey) Form consists of four white cards with a size of 14.0 x 21.5 cm and each card has 6 lines of 4 items arranged on it. These cards are the "stimulus" items of the test and the reactions that the subject should give to these stimuli, i.e. the "tasks" that the subject should fulfill, constitute the sections of the test. The basic scores of the test are scored separately for these sections (38).

The TBAG Form of the Stroop Test includes the colors blue, green, red, and yellow, and the names of these colors used in the Victoria Form as follows: Card 1 has color names printed in black on a white background, showing a feature of the original Stroop Test; the card has color names printed in different colors, but the color used to print each word is different from the color that the word expresses, i.e. the word "red" is printed in "yellow" and is the main stimulus, and the most critical part of all Stroop tests. The control of reading speed and color utterance is done for control purposes. Even so, card 3 is printed in different colors,

0.4 cm in diameter, and is taken from the Victoria Form; in the original Stroop Test, these stimuli are presented as squares. Card 4 contains neutral words printed in different colors (the words "as much, weak, if, medium") and is available in the Victoria Form (38).

The four stimulus cards and related tasks in the TBAG Form of the Stroop Test include all of the cards and tasks leading to the three factors obtained for the Stroop Effect in Jensen's (39) study. In the study (39), where completion time scores were used, Factor 1, color naming, required a card with colored circles (card 3 in the present study) and a card with color names written in white on a black background (card 1 in the present study); Factor 2, interference effect, required a card with color names (card 2 in the present study) and a card with colored circles (the card 3); and finally, Factor 3, speed, required a card with color names written in white (card 1 in the present study). Three types of scores were calculated from each of the four cards in the Stroop Test TBAG Form. These were the time elapsed from the time the subject was given the "Go" command until the last item of the card was read/spoken, the number of errors, and the number of corrected responses. The duration and error scores were also found in previous Stroop tests. The number of correction scores was used for the first time in the Stroop Test TBAG Form.

There are two critical sections in the Stroop test. This section is Section 5, where the 2nd card colors are said. The other sections are control sections in which the basic levels of reading and color naming are determined. Card 1, with color names printed in black, shows the basic level of reading speed; Card 3, with colored shapes, and Card 4, with neutral words printed in color, show the basic level of color naming speed (38).

Practising Imagery

The study group received 14 weekly sessions of 90 minutes each. The imagery method involves the use of imagination for therapeutic purposes to reduce stress in people. Mental images are stimulated by a therapist to visualize the images in the mind (40). The imagery method works by using the special connection between the nervous system and the visual cortex and has similar features to the imagery method. The client is made to focus on whatever the symptom is. Thus, the unconscious mind uses that imagery to allow the mind to replace negative things with more positive thoughts. In the research, imagery was used for the symptoms of the participants and it was replaced with a more positive situation with the power of the mind (41). Sessions with each participant were conducted at different times. No participant was negatively affected by the imagery method. Some participants wanted the sessions to be used for different problems. These participants were referred to a different specialist.

The flow chart of the application is shown below

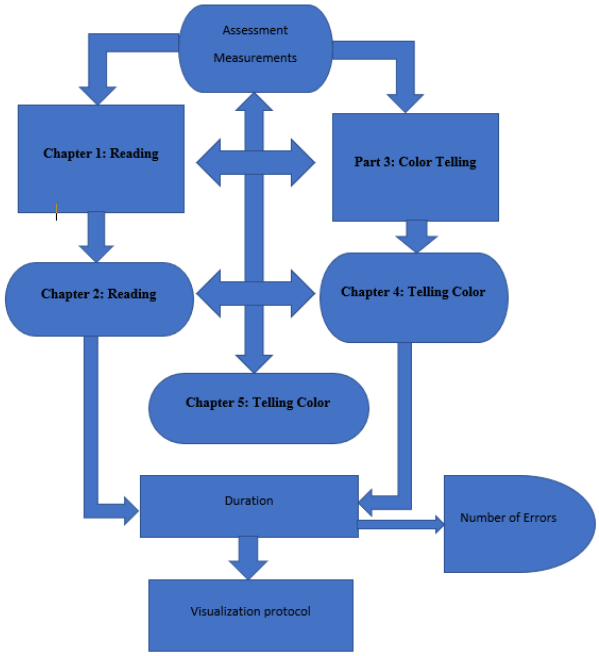

Figure 2. Imagery and the Stroop Flowchart

Data Analysis

In the data analysis phase of the study, to decide which tests were appropriate, the values obtained from the pre-test applications were examined whether they met the parametric or nonparametric basic assumptions, and it was concluded that the data were not a homogeneous and normally distributed group. In line with the data obtained from the homogeneity and normality tests, it was decided that nonparametric tests could be used in the study, aiming to examine the effect of imagery on the Stroop effect. In the study, there are two groups: Experimental and control groups. In terms of measurements, there are intra-group, inter-individual, and intra-individual measurements. The Mann-Whitney U Test was used to determine the difference between the pre-test and post-test of the groups, and the Wilcoxon Signed Rank Test was used to evaluate the pre-test and post-test differences between the groups. The data were analyzed on the computer using SPSS 25.

Results

Table 1. Mann Whitney U Test and results of the analysis of the Stroop Test scores of the pretest imagery applied and imagery not applied groups

Part 3: Color Singing, Part 4: There was no significant difference (p>.0.05) between the scores before and after Color Singing, Part 2: Reading, Section 5: Color Singing Duration and Number of Errors before and after scores show that there is a significant difference

Table 1. Mann Whitney U Test and results of the analysis of the Stroop Test scores of the pretest imagery applied and imagery not applied groups

Variables	Groups	n	Mean Rank	Sum of Ranks	U	P
Section 1: Reading	**Imagery Applied**	20	20,80	416,00		
	Imagery Not Applied	20	20,20	404,00	194,000	,865
	Total	40				
Section 2: Reading	**Imagery Applied**	20	20,83	416,50		
	Imagery Not Applied	20	20,18	403,50	193,500	,854
	Total	40				
Section 3: Colour Telling	**Imagery Applied**	20	20,43	408,50		
	Imagery Not Applied	20	20,58	411,50	198,500	,965
	Total	40				
Section 4: Colour Telling	**Imagery Applied**	20	21,43	428,50		
	Imagery Not Applied	20	19,58	391,50	181,500	,608
	Total	40				
Section 5: Colour Telling	**Imagery Applied**	20	19,88	397,50		
	Imagery Not Applied	20	21,13	422,50	187,500	,724
	Total	40				
Duration	**Imagery Applied**	20	22,43	448,50		
	Imagery Not Applied	20	18,58	371,50	161,500	,271
	Total	40				
Number of Errors	**Imagery Applied**	20	20,75	415,00		
	Imagery Not Applied	20	20,25	405,00	195,000	,885
	Total	40				

As seen in Table 1, the pretest Stroop of the study group in the Imagery Applied and Non-Imagery Applied group; Part 1: Reading, Section 2: Reading, Part 3: Saying Color, Part 4: Saying Color, Section 5: Color Saying, Duration and Number of Errors, no statistically significant difference was found between the scores, supporting the hypothesis of the study (p.0.05). This can be accepted as an indication that there was no difference between the groups in terms of Stroop scores before the imagery study. This finding will show the change in the effect in the imagery group according to the starting point for each section

The results of the analysis show that the study group participating in the research was able to measure the Stroop effect of imagery in Chapter 1: Reading, (p<.0.05). Significant effect in Stroop test 2: Reading, Chapter 5: Reading, Section 5: Color Saying Duration and Number of Errors, and these variables show a significant decrease. In this context, the hypothesis of the study was supported by finding a statistically significant difference in the Stroop scores of the study group in favor of the post-test. This finding indicates that the imagery study influenced reducing the Stroop effect.

Discussion

The general aim of this study is to investigate the effect of imagery on the Stroop effect. For this purpose, 20 participants in the imagery group and 20 participants without imagery were included in the study. In the

Table 2. Wilcoxon Matched Pairs Signed Test analysis results of pretest-posttest experimental and control groups of the Stroop Test Data

Groups			N	Mean rank	Sum of ranks	z	p
Imagery Applied	Section 1: Reading	Negative ranks	11	5,74	165,50	1,507	932
		Positive ranks	8	5,50	155,50		
		Ties	1				
		Total	20				
	Section 2: Reading	Negative ranks	14	5,00	15,00	-2,926[c]	011
		Positive ranks	4	9,86	138,00		
		Ties	2				
		Total	20				
	Section 3: Colour Telling	Negative ranks	12	10,00	190,00	1,099	344
		Positive ranks	7	,00	,00		
		Ties	1[i]				
		Total	20				
	Section 4: Colour Telling	Negative ranks	12[j]	9,25	196,50	1,099	090
		Positive ranks	8	10,75	193,50		
		Ties	0[l]				
		Total	20				
	Section 5: Colour Telling	Negative ranks	16	8,50	25,50	2,001	001
		Positive ranks	4[n]	9,11	127,50		
		Ties	0				
		Total	20				
	Duration	Negative ranks	19	,00	,00	1,232	003
		Positive ranks	1	10,50	210,00		
		Ties	0				
		Total	20				
	Number of Errors	Negative ranks	17	2,79	54,50	1,566	034
		Positive ranks	3	4,70	73,50		
		Ties	0				
		Total	20				
Imagery Not Applied	Section 1: Reading	Negative ranks	11	11,38	182,00	2,11	877
		Positive ranks	9	12,67	188,00		
		Ties	0				
		Total	20				
	Section 2: Reading	Negative ranks	10	7,33	122,00	2,455	766
		Positive ranks	10	9,93	149,00		
		Ties	0				
		Total	20				
	Section 3: Colour Telling	Negative ranks	9	9,50	171,00	1,122	433
		Positive ranks	11	9,00	,00		
		Ties	0[i]				
		Total	20				
	Section 4: Colour Telling	Negative ranks	3[j]	6,67	20,00	1,999	122
		Positive ranks	15[k]	10,07	151,00		
		Ties	2[l]				
		Total	20				
	Section 5: Colour Telling	Negative ranks	8[m]	9,44	75,50	2,444	666
		Positive ranks	10[n]	9,55	95,50		
		Ties	2[o]				
		Total	20				
	Duration	Negative ranks	1[p]	4,50	4,50	1,339	322
		Positive ranks	18[q]	10,31	185,50		
		Ties	1[r]				
		Total	20				
	Number of Errors	Negative ranks	6[s]	5,75	34,50	1,555	090
		Positive ranks	4[t]	5,13	20,50		
		Ties	10[u]				
		Total	20				

study, the groups were compared with one another both before and after the application. The data obtained from the study indicated that imagery was an effective method for reducing the Stroop effect. In other words, the Stroop effect was found to be reduced by the use of imagery. In this context, it is evident that the use of imagery can effectively reduce and even eliminate the need for Stroop intervention (16). This indicates that cognitive processes that have become automatized through practice can be removed from automaticity and brought under conscious control. This finding shifts the focus of research on the effect of imagery on the Stroop effect from the field of altered consciousness to the field of cognitive neuroscience

One of the few exceptions to the robustness of the Stroop effect is that it can be achieved by word blindness after hypnotic suggestion (18). The suggestion of word blindness, defined as the ability to see words as nonsense or meaningless characters during a Stroop task, was given to highly hypnotizable subjects. The results demonstrated a significant reduction in the Stroop effect compared to standard, unimagined subjects (42). The Stroop effect refers to the finding that, in comparison to a baseline condition, participants required a longer RT to indicate the font color in which a word was presented when the color of the word was incongruent with the font color. Raz, Shapiro, Fan, and Posner (43) demonstrated that the Stroop effect was markedly diminished when subjects were led to perceive words as meaningless. Moreover, electroencephalogram (EEG) data recorded during the Stroop task demonstrated a notable increase in frontal theta and frontal beta power among participants who were influenced by post-imagery suggestion (44). These findings indicate that post-imagery suggestions are effective methods for eliciting top-down processes (45). The EEG findings may be interpreted as evidence that this is due to the provision of additional cognitive control (46).

Concerning the characteristics of individuals who are predisposed to imagery, Casiglia et al. (47) observed a reduction in the hemodynamic response and the Stroop effect during hypnotic suggestion. The hemodynamic response is defined as the cardiological response of the circulatory system to external stimuli perceived as stressors. The dominant response is more pronounced when the word is read in a context that is perceived as stressful. In contrast, the impact of word blindness on the facilitatory component of the Stroop effect (neutral RT minus congruent RT) appears to be more nuanced. (29). The question of whether it is possible to regain in individuals with imagery is rarely posed, yet it has been observed that this process can reduce or even eliminate the Stroop intervention in highly imagery-prone individuals. In conclusion, the Stroop effect is markedly diminished in individuals who engage in imagery.

Some studies have used hypnosis to influence the Stroop effect (48). Two main approaches are used in these studies. The first is to apply a period of hypnosis with post-hypnotic instruction. However, these strategies have been found to have little effect on Stroop interference. The other approach is to tell hypnotized participants that a language with meaningless words is used during hypnosis. This approach reduces the Stroop effect post-hypnotically, but the effect is still present. It should be noted that the post-hypnotic sessions are the second session and the order of testing is shuffled. It was observed that Stroop task performance increased after hypnosis and post-hypnotic anxiety levels decreased (49). It is thought that participants with decreased anxiety levels can use inhibition strategies more easily (50). In the experiments conducted under different conditions, no interaction of hypnosis on the Stroop task was found (48).

Post-hypnotic suggestions designed to impede access to word meaning demonstrated consistent and persistent effects on cognitive control processes engaged during the Stroop task (51). The impact of post-hypnotic suggestions was most pronounced in the significantly shorter reaction times observed on incongruent trials relative to the non-hypnotic condition. However, reaction times remained unaltered on neutral trials. This may be attributed to the elimination of interference between word meaning and color naming, either through the prevention of automatic word activation during reading or the enhancement of conflict resolution processes (29). The specific location of the effects of post-imagery suggestions on information processing remains a topic for future research.

Several studies on the Stroop effect have yielded insights into the neural processes underlying this phenomenon (24). The available evidence indicates that the Stroop effect is associated with forebrain regions (52). However, no consensus regarding the specific brain hemisphere is affected. However, given that attention function is a task of the forebrain (53), it can be postulated that imagery reduces the Stroop effect by affecting cognitive skills (54). In light of these

findings, it can be posited that the impact of imagery on Stroop is a natural phenomenon.

Conclusion

It is crucial to gain a comprehensive understanding of the underlying mechanisms that underpin the remarkable cognitive and behavioral effects of imagery. It has been demonstrated that the Stroop interference effect can be reduced through the use of imagery. This effect is acknowledged as a component of pre-executive functions (55). An illustrative example of the reduction of Stroop interference is the phenomenon of word blindness observed in post-hypnotic suggestion (i.e., a suggestion to perceive words as meaningless during the Stroop task). When this suggestion is provided to individuals with a proclivity for imagery, it has been demonstrated to reduce Stroop interference by half (29).

In this context, participants who were particularly responsive to imagery may have blurred their vision, perceiving only the color of the letter (56). The results indicated that the suggestion to interpret words as meaningless scribbles significantly reduced the Stroop effect in highly suggestible individuals. This effect was attributed to imagery. A potential limitation of the present study is that examining the brain mechanisms of individuals prone to imagery may elucidate top-down effects. Nevertheless, additional factors, such as the expectancy effect and placebo, may also contribute to a more comprehensive understanding of this process.

Consequently, the imagery method has been demonstrated to reduce the Stroop effect. Nevertheless, it is advised that this study be repeated, given the limited number of participants and the necessity for a different sample group. While there are international studies on the brain-based Stroop effect, it would be beneficial to conduct national brain-based studies to further support this research.

Ethical approval

The research has the Istanbul Gelisim University Ethics Committee Approval Decision NO: 2023-08-57 Date: 04.11.2022

All procedures performed in studies involving hu\man 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.

Conflict of interest

The author has no conflict of interest

Informed consent

Consent was obtained from all participants included in the study.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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ORIGINAL ARTICLE

Investigation of The Efficacy and Safety of An Ultrasonography-guided Percutaneous Pigtail Drainage Catheter

Ultrasonografi Kılavuzluğunda Perkütan Pigtail Drenaj Kateterinin Etkinliği ve Güvenliğinin Araştırılması

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ABSTRACT

Background/Aims: This study aimed to evaluate the effectiveness, reliability, and complications of percutaneous pigtail catheter drainage guided by ultrasound (USG) in the treatment of pleural effusion.
Materials and Methods: This retrospective study analyzed patients aged 18 years and older treated with percutaneous pigtail catheter placement under USG guidance between January 1st, 2019, and January 1st, 2023. Clinical, laboratory, and radiological characteristics of the patients, etiological causes of pleural fluid, biochemical properties of the pleural fluid, and success rates of percutaneous pigtail catheter drainage were analyzed.
Results: A total of 77 patients were included in the study. 59.7% of the patients were male. Exudative effusion was detected in 61% of the patients, with a mean age of 52.8±17.7 years in this group. Most effusions in both exudative and transudative groups were on the right side, observed in 55.3% and 56.6% of cases, respectively. Bilateral pleural effusion was present in 2.12% of the exudative group and 23.3% of the transudative group. The mean pleural fluid depth was 58 mm in the exudative group and 54 mm in the transudative group. The mean drainage duration was 6.5 days in the exudative group and 4.5 days in the transudative group. Comorbidities such as hypertension (76.6%), diabetes mellitus (53.3%), and coronary artery disease (36.6%) were more prevalent in the transudative group. Metastasis (32%) and lung cancer (26%) were the most common causes of exudative effusions, while heart failure (46.6%) and liver failure (30%) were the predominant causes of transudative effusions. The success rate of percutaneous pigtail catheter drainage was 90.5% in exudative effusions and 93% in transudative effusions.
Conclusion: Our study concludes that percutaneous pigtail catheter drainage guided by USG is an effective and reliable method with high success rates and low complication rates for the treatment of both exudative and transudative pleural effusions.

Keywords: Pigtail catheter, Pleural drainage, Pleural effusion, Ultrasonography

ÖZ

Amaç: Bu çalışmada plevral efüzyon tedavisinde USG kılavuzluğunda perkütan pigtail drenaj kateterinin etkinliği, güvenilirliği ve komplikasyonlarının değerlendirilmesi amaçlanmıştır.
Materyal ve Metod: Bu çalışma 01.01.2019 ile 01.01.2023 tarihleri arasında USG kılavuzluğunda perkütan pigtail drenaj kateteri yerleştirilerek tedavi edilen 18 yaş ve üzeri hastalar analiz edilerek retrospektif olarak yapılmıştır. Hastaların klinik,laboratuar ve radyolojik özellikleri, plevral sıvının etyolojik nedenleri, plevral sıvının biyokimyasal özellikleri, perkütan pigtail drenaj kateter tedavisinin başarı yüzdesi analiz edilmiştir.
Bulgular: Çalışmada 77 hasta analiz edildi. Hastaların %59.7'si erkekti. Hastaların %61'inde eksüdatif efüzyon tespit edildi ve eksüdatif efüzyonu olan hastaların yaş ortalaması 52.8±17.7 idi. Hem eksüdatif hem de transüdatif grupta efüzyonların çoğu sağ tarafta olup eksüdatif grupta %55.3, transüdatif grupta %56.6 hastada efüzyonlar sağ tarafta izlenmiştir. Eksüdatif grupta %2.12, transüdatif grupta %23.3 hastada bilateral plevral efüzyon izlendi. Ortalama plevral sıvı derinlikleri eksüdatif grupta 58 mm, transüdatif grupta 54 mm olarak hesaplandı. Ortalama drenaj süresi eksüdatif grupta 6,5 gün, transüdatif grupta 4,5 gün idi. Komorbid hastalıklardan hipertansiyon (%76.6), diabetes mellitus (%53.3) ve koroner arter hastalığı (%36.6) transüdatif grupta daha fazla görüldü. Eksüdatif efüzyonların en sık nedeni metastaz (%32) ve akciğer kanseri (%26), transüdatif efüzyonların en sık nedeni kalp (%46.6) ve karaciğer (%30) yetersizliği idi. Perkütan pigtail drenaj kateterinin başarı yüzdesi eksüdatif efüzyonalarda %90.5, transüdatif efüzyonlarda %93 olarak saptandı.
Sonuç: Çalışmamızda hem eksüdatif hem de transüdatif plevral efüzyonların tedavisinde, USG kılavuzluğunda yerleştirilen pigtail kateter drenajının yüksek başarı ve düşük komplikasyon oranları ile etkin ve güvenilir bir yöntem olduğu sonucuna varılmıştır.

Anahtar Kelimeler: Plevral drenaj, Plevral efüzyon, Pigtail kateter, Ultrasonografi

Introduction

Pleural effusion arises from an imbalance between the secretion and absorption of pleural fluid, attributed to various etiologies such as congestive heart failure (CHF), malignancy, liver and kidney failure, and pneumonia (1-4). Recent studies have suggested that using smaller caliber pigtail drainage catheters under ultrasonography (USG) guidance is effective, reliable, and better tolerated by patients compared to larger chest tubes in treating pleural effusion or pneumothorax (5-7). Smaller catheters are less invasive, easier to place, and associated with lower complication rates. Ultrasound-guided placement is particularly suitable. This study aimed to evaluate the efficacy, reliability,

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and complications of percutaneous pigtail drainage catheters in the management of pleural effusion.

Materials and Methods

This retrospective study utilized data from patients who underwent percutaneous pleural effusion drainage catheter placement under USG guidance at the Radiology Department of Iğdır Dr. Nevruz Erez State Hospital between January 2019 and January 2023. Informed consent was obtained from all patients or their families in cases where patients were unable to provide consent. The study was approved by the Iğdır University Non-Interventional Clinical Research Ethics Committee on 28/02/2024 (approval number: 3), and there are no conflicts of interest among the authors

Patients included in the study were those aged 18 and above with pleural effusion who were treated with a USG-guided percutaneous pigtail drainage catheter. Patients who had undergone pleural drainage catheter placement under USG guidance but for whom clinical, laboratory, and USG parameters were unavailable, and those who underwent surgical chest tube placement as initial treatment, were excluded. Demographic data, diagnoses, clinical, laboratory, and USG parameters of included patients were recorded. Cytological, biochemical, and microbiological properties of pleural fluid were documented. Light's criteria (8) were used to distinguish exudative from transudative effusions.

Routine procedures performed in our clinic for patients undergoing pleural effusion drainage were as follows:

The Pre-procedural evaluation: The guide proposed by Colice et al. (9) was used for draining parapneumonic effusions and empyemas. Patients with decompensated heart, liver, and kidney failure with massive transudative pleural effusion, despite adequate medical treatment, underwent pleural effusion drainage via percutaneous pigtail drainage catheter. For traumatic hemothorax patients, the indications for drainage catheter placement were guided by Adrales (10). Using USG examination, the depth of intrapleural fluid measurement and the craniocaudal extent of effusion between both pleural layers were routinely recorded. Pre-procedural evaluation of patients' laboratory findings indicated that procedures were performed on patients with platelet counts >50.000 and INR <1.5. Procedures were conducted under local anesthesia with 5-10 mL of 2% lidocaine for intensive care unit patients and difficult to-transfer patients, and in all other patients, in the interventional radiology unit.

The procedure under USG guidance: After determining the appropriate insertion site under USG guidance, catheters were placed using the modified Seldinger technique. Pigtail catheters (GEOTEK Medical, Ankara, Turkey), with a diameter of 8-14 French (F) and a length of 25 cm, were used. After securing the catheters to the skin, they were connected to drainage bags and left for free drainage. The drainage procedure was considered successful if imaging and/or clinical symptoms related to pleural disease improved without requiring additional intervention. Cases without improvement in imaging and/or clinical and laboratory symptoms, necessitating large-bore chest tube/surgical intervention for drainage, were considered unsuccessful.

Statistical evaluation: Statistical analysis was performed using the SPSS package program. Categorical data were presented as numbers (%), and continuous numerical data as mean ± standard deviation. Independent t-tests were used for continuous numerical data and chi-square tests for categorical data. Correlation and variance analyses were applied to demonstrate relationships between numerical data. P <0.005 was considered statistically significant

Results

Seventy-seven patients with pleural effusion were included in the study. Of these, 46 (59.7%) were male and 31 (40.3%) were female. Forty-seven patients (61%) had exudative effusions, and thirty patients (39%) had transudative effusions. The mean age was 52.8 ± 17.7 years for patients with exudative effusion and 66.2 ± 16.5 years for those with transudative effusion. In both groups, there were more male patients (exudative: 29, 61.7%; transudative: 17, 56.6%). Most effusions requiring drainage were on the right side in both groups (p=0.002), with 26 (55.3%) in the exudative group and 17 (56.6%) in the transudative group. Bilateral pleural effusions were observed in one patient (2.12%) in the exudative group and seven patients (23.3%) in the transudative group. The mean depths of pleural fluid were 58 mm in the exudative group and 54 mm in the transudative group. Post-catheterization drainage times varied from one to 17 days. The average drainage time was 6.5 days for patients with exudative effusion and 4.5 days for those with transudative effusion (p>0.005). The

median drainage time for the entire study group was 5.5 days (Table 1).

Table 1. Demographic data of the patients undergoing pleural drainage catheter placement under USG guidance, characteristics of effusion, pleural fluid depths, and drainage times

	Exudate (n=47) n (61%)	Transudate (n=30) n (39%)	*p*-value
Gender			
Male	29 (61.7)	17 (56.6)	>0.005
Female	18 (38.3)	13 (43.4)	>0.005
Hemithorax			
Right	26 (55.3)	17 (56.6)	**0.002**
Left	20 (42.5)	6 (20)	>0.005
Bilateral	1 (2.12)	7 (23.3)	>0.005
Pleural fluid depth (mm)	58	54	>0.005
Drainage duration (days)	6.5	4.5	>0.005

When comparing the comorbid disease histories of patients, hypertension (p<0.001), diabetes mellitus (p=0.001), and coronary artery disease (p=0.003) were more prevalent in patients with transudative effusion, whereas the smoking history was similar in both groups (n=8, 17% and n=6, 20%, respectively). Hypertension was found in 23 patients (76.6%) in the transudative group, diabetes mellitus in 16 patients (53.3%), and coronary artery disease in 11 patients (36.6%). In patients with exudative effusion, hypertension was found in 17 patients (36.1%), diabetes mellitus in 11 patients (23.4%), and coronary artery disease in six patients (12.7%) (Table 2).

Table 2. Comparison of comorbid diseases

	Comorbid Diseases			
	DM (n=27) (35%)	**HT (n=40) (51.9%)**	**CAD (n=17) (22%)**	**Smoking (n=14) (18.2%)**
Exudate (n=47)	11 (40.7)	17 (42.5)	6 (35.2)	8 (57.1)
Transudate (n=30)	16 (59.3)	23 (57.5)	11 64.8)	6 (42.9)
***p*-value**	**0.001**	**<0.001**	**0.003**	>0.005

CAD: Coronary artery disease, DM: Diabetes mellitus, HT: Hypertension,

The most common indications for pleural drainage catheter placement were massive transudative effusions (n=29, 37.6%), malignant pleural effusions (n=27, 35%), and infectious pleural effusions (n=10, 12.9%). The most common causes of exudative effusions were metastasis (n=15, 32%) and lung cancer (n=12, 26%), while the primary causes of transudative effusions were heart (n=14, 46.6%) and liver failure (n=9, 30%) (Table 2). Breast cancer metastasis accounted for 26% (n=4) of metastatic pleural effusions. Non-specific exudative effusion classifications included pulmonary embolism, drug reaction, and trauma patients. Chylothorax was observed in one patient with non-specific transudative effusion

The success rate of drainage catheters in treating all effusion causes was 91.5%. The success rate was 90.5% in exudative effusions and 93% in transudative effusions. The success rate of drainage catheters was higher when used to treat malignant pleural effusions (93.8%) and massive transudative effusions (93.4%). It was lower when used for hemothorax treatment (77%) and pleural infection/parapneumonic effusion treatment (84%) (Table 3).

Table 3. Etiology of pleural effusion and success rates of percutaneous pigtail catheter placement guided by ultrasound

Diagnosis	Number (n)	Percentage (%)	Success Rate (%)
Exudate	47	61	90.5
Metastatic	15	32	89
Lung cancer	12	26	100
Pleural infection	10	12.9	84
Inflammator	2	4.2	90.5
Traumatic	1	2.1	77
Non-specifi	7	14.8	88.6
Transudate	30	39	93
Heart Failure	14	46.6	94.7
Liver Failure	9	30	93
Kidney Failure	6	20	89
Non-specifi	1	3.3	93.2

Complications were detected in 7 out of 77 patients (9%) in our study. One patient (1.3%) with liver failure in the transudative group developed empyema, which was treated by placing a 14 F drainage catheter under ultrasound guidance. Methicillin-resistant S. aureus was identified as the responsible pathogen

in the laboratory evaluation sample. Four patients (5.1%) developed minor complications related to the procedure that did not have clinical significance (catheter occlusion and dislocation). Additionally, two patients (2.6%) experienced pain at the procedure site requiring simple analgesics. Pneumothorax, luminal organ perforation, and procedure-related mortality were not observed.

Discussion

Our study demonstrates that the placement of small-bore catheters under ultrasound guidance for the treatment of pleural effusion has shown high treatment success rates with low complication rates. While some researchers have suggested that small-bore (≤ 14F) drainage catheters may not provide effective drainage, our study has proven it to be an effective and reliable procedure (11-14). The British Thoracic Society currently recommends small-bore (10-14F) drainage catheters for pneumothorax, parapneumonic effusion, and malignant effusion (15).

In our study, the drainage duration ranged from one to 17 days (median 5.5 days) across all study groups. It was found that there is a statistically significant need for longer drainage durations in the exudative effusion group. When compared with similar studies, no significant differences were found in drainage durations; Jayakrishnan et al. reported an average drainage duration of five days in their study. Similarly, they reported that more than three days of drainage were needed in 76.1% of patients with exudative effusion, suggesting a longer duration required for drainage in patients with exudative effusion (16). Jain et al. reported an average drainage duration of seven days in their study (17), while Parulekar et al. reported six days (18).

In our study, the success rate of drainage catheters was highest when used to treat malignant pleural effusions (93.8%). Cafarotti et al. reported a similar success rate of 93.8% in their retrospective study involving 324 small-bore drainage catheters in malignant effusions (19). Jayakrishnan et al. reported success rates ranging from 90% to 100% in drainage catheter procedures for metastatic and lung malignancies (16). Similarly, our study resulted in high success rates, such as 89% in the metastatic group and 100% in the primary lung cancer group. Currently, pleurodesis is known as the definitive treatment for recurrent symptomatic malignant pleural effusions. However, the use of pleural drainage catheters is increasing due to their potential to produce symptomatic relief in addition to pleurodesis.

In advanced decompensated stages of heart, liver, and kidney failure, massive transudative effusions can sometimes develop. When there is no symptomatic improvement despite appropriate and adequate medical treatment, drainage may be necessary (20,21). In our study, drainage procedures in patients with massive transudative effusions resulted in a high success rate of 93.4%. Specifically, we recorded success rates of 94.7% in patients with heart failure and bilateral transudative pleural effusion, 93% in those with liver failure, and 89% in those with kidney failure. Liang et al. reported that in a broad sample of critically ill patients, pigtail drainage catheters were effective in draining massive transudative pleural effusions, albeit with longer drainage durations and potentially higher infection rates (12%).

In our study, one patient with hepatic hydrothorax developed empyema following drainage. Liang et al. reported success rates ranging from 42% to 80% when using pigtail catheters for empyema treatment in a group of critically ill patients in the ICU (22). Nevertheless, as a conclusion of their study, they recommended the use of pigtail catheters without imaging evidence of loculations due to their ease of procedure, safety, and less invasive nature. Jayakrishnan et al. reported a success rate of 83.3% in pleural infections/parapneumonic effusions (16), whereas we achieved a slightly lower but still high success rate of 84% in our study compared to other groups.

Studies have reported rare but serious complications such as pneumothorax, left ventricular penetration, subclavian artery laceration, and cerebral air embolism secondary to pigtail catheter placement (23,24). In our study, pneumothorax, luminal organ perforation, and procedure-related mortality were not observed. Various studies have reported pneumothorax incidences ranging from 2.8% to 31%. Jayakrishnan et al. reported a pneumothorax incidence of 2.8%, Sabry et al. reported 3.3%, and Morrison et al. reported 19-31% pneumothorax rates (16,25,26). Jain et al. reported a pneumothorax rate of 20% in their study, suggesting that small pneumothoraces may occur due to air entry during the procedure (17).

In our study, a complication rate of 9% (7/77) was observed. However, the majority of these were minor

complications related to the procedure that did not have clinical significance. Catheter obstruction and dislodgement occurred in four patients (5.1%). The obstruction rates of small-bore catheters have been reported between 3.9% and 15% in studies (11,17,27). It has been reported that catheters are particularly prone to obstruction in cases of empyema, and in our study, it was found that two patients (2.6%) who developed catheter obstruction were diagnosed with empyema (28). Pain at the procedure site may vary depending on the catheter size, placement technique, use of analgesics, and patients' pain sensitivity. In our study, simple analgesics were required in two patients (2.6%) due to pain at the procedure site.

In a patient with liver failure in the transudative group who underwent 14 days of drainage, empyema developed, which was drained by percutaneous placement of a 14F drainage catheter under ultrasound guidance. We believe this occurred due to the prolonged drainage duration seen in massive transudative effusions, as indicated in previous studies.

Our study has some limitations. Firstly, being retrospective, documentation of minor complications and possible minimal pneumothoraces may not have been recorded. Secondly, no comparison was made with traditional chest tubes. Thirdly, although early success rates of the procedure were measured, it is unknown whether additional interventions were performed on patients in the long term.

Conclusion

Ultrasound-guided pigtail catheter drainage for pleural effusion has shown high treatment success with low complication rates. When indicated, it should be considered as the initial intervention for draining a pleural effusion.

Data Availability

The data sets generated during or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflict of Interest Statement

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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All authors have made substantive contributions to the study, and all authors endorse the data and conclusions.

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ORIGINAL ARTICLE

Comparison of Conventional vs. Modified Seldinger Technique in Percutaneous Cholecystostomy and Evaluation of Procedural Efficiency and Safety

Perkütan Kolesistostomide Konvansiyonel ve Modifiye Seldinger Tekniklerinin Karşılaştırılması ve Prosedürel Etkinlik ve Güvenlik Değerlendirmesi

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ABSTRACT

Background/Aims: To assess the effectiveness and safety of a modified Seldinger technique (MST), bypassing consecutive dilatation steps, versus the conventional Seldinger technique (CST) in percutaneous cholecystostomy (PC).
Material and Methods: We conducted a retrospective cohort study at a tertiary healthcare facility in Turkey, analyzing de-identified data from January 2021 to January 2023. The study included 152 patients undergoing PC, comparing procedural times, complication rates, and pain scores between MST and CST groups. Statistical analyses included t-tests for continuous variables and chi-square tests for categorical variables, with significance set at $p < 0.05$
Results: No significant differences were found regarding demographic, clinical, or laboratory characteristics between the CST and MST groups, indicating comparable patient profiles. The clinical efficacy rates were comparable between the CST and MST groups (85% and 88.5%, respectively; $p = 0.547$). The MST group had significantly shorter procedural time compared to the CST (4.24±1.52 vs. 2.85±1.31, $p=0.001$). Safety profiles were similar between groups ($p=0.486$), with minor bleeding resolving spontaneously in one patient per group and no major complications observed. Pain during the CST procedure was significantly higher than in the MST group, though this difference did not persist at the 12-hour follow-up ($p=0.01$ and 0.6, respectively).
Conclusion: The utilization of the MST technique for PC demonstrated comparable efficacy and safety to the CST. However, MST was found to be associated with a lower incidence of complications related to the procedure, and required less time to perform, when compared to the CST.

Keywords: Bypass, percutaneous cholecystostomy, Seldinger technique

ÖZ

Amaç: Modifiye Seldinger tekniğinin (MST) ardışık dilatasyon aşamalarını atlayarak perkütan kolesistostomi (PC) üzerindeki etkinliği ve güvenliğini konvansiyonel Seldinger tekniği (CST) ile karşılaştırmak.
Materyal ve Yöntem: Türkiye'deki bir üçüncü basamak sağlık merkezinde retrospektif bir kohort çalışması gerçekleştirdik ve Ocak 2021 ile Ocak 2023 arasındaki anonimleştirilmiş verileri analiz ettik. Çalışmaya PC uygulanan 152 hasta dahil edildi ve MST ile CST grupları arasında işlem süreleri, komplikasyon oranları ve ağrı skorları karşılaştırıldı. İstatistiksel analizlerde sürekli değişkenler için t-testleri, kategorik değişkenler için ki-kare testleri kullanıldı ve anlamlılık düzeyi $p < 0.05$ olarak belirlendi.
Bulgular: CST ve MST grupları arasında demografik, klinik veya laboratuvar özellikleri açısından anlamlı bir fark bulunmadı, bu da hasta profillerinin benzer olduğunu gösterdi. Klinik etkinlik oranları CST ve MST grupları arasında benzerdi (%85 ve %88,5; p=0,547). MST grubunda işlem süresi CST'ye kıyasla anlamlı derecede daha kısaydı (4.24±1.52 dakikaya karşın 2.85±1.31 dakika, p=0.001). Güvenlik profilleri gruplar arasında benzerdi (p=0.486); her iki grupta birer hastada görülen hafif kanama kendiliğinden düzeldi ve ciddi bir komplikasyon gözlenmedi. CST prosedürü sırasında MST grubuna göre ağrı anlamlı derecede daha yüksekti, ancak bu fark 12 saatlik takipte ortadan kalktı (p=0,01 ve 0.6, sırasıyla).
Sonuç: PC için MST tekniğinin etkinlik ve güvenliğinin CST ile karşılaştırılabilir olduğu gösterilmiştir. Ancak, MST'nin prosedüre bağlı komplikasyonların daha düşük görülmesi ve daha kısa sürede tamamlanması ile ilişkilendirildiği bulunmuştur.

Anahtar Kelimeler: Baypas, perkütan kolesistostomi, Seldinger tekniği

Introduction

Acute cholecystitis (AC) is an inflammatory condition of the gallbladder that poses significant risks for morbidity and mortality (1). It is a frequently encountered emergency admission in surgical practice. The majority of AC cases, over 90%, are linked to gallstones and cholecystectomy is the established and widely accepted treatment for circumstances where the patient is deemed suitable for surgery (2).

Early laparoscopic cholecystectomy is a safe and cost-effective method for AC treatment (3). However, emergency cholecystectomy mortality rates might reach 30% for patients with major comorbidities (4, 5). Therefore, high-risk patients may benefit from nonoperative treatment with systemic antibiotics,

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either with or without decompression, to prevent perioperative morbidity (6).

Percutaneous cholecystostomy (PC) is a minimally invasive procedure that aims to decompress the gallbladder by draining. This method helps prevent the gallbladder from perforating and developing sepsis. PC can be used as an interim measure before surgery until the inflammation has reduced. However, it has also been proposed as a permanent treatment for AC in patients who are not suitable for surgery or for most patients with acute acalculous cholecystitis (2).

PC can be carried out utilizing the Seldinger technique, which has notable benefits and drawbacks. The Seldinger procedure is widely regarded as safe due to the use of a small-caliber 21-gauge needle for the first entry. This needle creates a little defect, hence minimizing the risk of harm to surrounding structures, particularly the liver and bowel, in the event of an accidental puncture. Although the treatment may typically be done with the help of ultrasound (US) to save time, many European institutions opt to complete the remaining phases of the process, consecutive dilations, with fluoroscopic guidance in the angiography suite for enhanced safety. However, while doing consecutive dilations bile leakage and peritonism may occur. Also, more post-interventional pain could be seen due to the nature of the CST (7).

To prevent bile leakage and peritonism and reduce post-operative pain, we propose a modification by bypassing the consecutive dilatation step and inserting the catheter directly through the guidewire to the gallbladder for the Seldinger technique. Therefore, we aimed to compare the efficacy and safety of the modified and conventional Seldinger technique in the paper.

Material and Methods

Study design

This retrospective analysis was conducted to include patients who underwent PC at a tertiary university hospital. The study was conducted in compliance with the Declaration of Helsinki. After obtaining approval from the institutional board, informed consent was acquired from all patients following a thorough explanation of the risks and advantages associated with the treatment.

Study sample

The study included all patients who underwent PC within 24 months from January 1st, 2021, to January 1st, 2023. The diagnosis of AC was made by considering the patient's medical history, clinical symptoms, and signs (including fever, pain in the upper right quadrant, and the presence of Murphy's sign), as well as the results of laboratory tests (such as elevated levels of inflammatory markers like C-reactive protein (CRP), white blood cell count (WBC), and bilirubin levels), and imaging findings from ultrasound (US) or computed tomography (CT) scans. Both US and CT scans were consistently conducted to verify the suspected diagnosis and aid in the planning of the intervention.

The indications for PC were determined through a collaborative decision-making process involving surgeons and interventional radiologists. The study collected data on the basic demographic characteristics of the participants, as well as their comorbidities such as cardiac diseases, and malignancies. The presence of gallstones, potential gallbladder perforation at the time of diagnosis, and the possible coexistence of ascites were also recorded. Additionally, information on the imaging method used for diagnosis assessment, procedural details, and follow-up information was documented.

All patients in need of PC, regardless of the underlying cause, were eligible to be included in the study. Patients who had an international normalized ratio (INR) value below 2 and a platelet count of 50,000 cells/mm3 or greater were included in the study. Coagulation disorders that could not be corrected before the procedure (patients with an INR >2 or platelet count <50.000 cells/mm^3) and patients with prior PC, gallbladder surgery, or other invasive gallbladder procedures were excluded from the study. Requisite actions, such as transfusions before the procedure, were carried out to rectify any abnormalities in the coagulation profile if needed. Nevertheless, PC was administered to patients suffering from acute sepsis, even when the aforementioned targets could not be reached even after receiving proper therapy.

Procedure

Before the procedure, all patients were administered antibiotic prophylaxis (ceftriaxone of 1000 mg) as determined by the attending physician. Two interventional radiologists, each possessing over two years of expertise in conducting the US-guided Seldinger method for PC, carried out the procedures. The patient was positioned in a supine or semi-lateral posture for transhepatic, subcostal catheter placement. When appropriate, a transperitoneal approach, intercostal approach, or a combination of both techniques were utilized.

In the group following the standard Seldinger procedure, the placement of the PC catheter was carried out under the administration of local anesthetic. The initial entry was achieved under the

guidance of the US. After inserting the 21-gauge, 15-cm needle and establishing bile drainage, the gallbladder was decompressed and a sample was collected for examination. Thereafter, a small amount of contrast medium (maximum 2 mL) was given to demonstrate the gallbladder and help position the guidewire (a 0.035-inch stiff guidewire (Amplatz Super Stiff Guidewire, Boston Scientific), as described in a previous study (8). Thereafter, over-the-wire dilations were carried out using a 6 and 8-French dilator, and an 8-French pigtail catheter was placed over the wire with the aid of continuous fluoroscopic guidance. However, in the MST group, we omitted the dilatation phase and instead placed the pigtail directly using the guidewire. Technical success was defined as the confirmation of catheter placement into the gallbladder through imaging verification, followed by the aspiration of bile (8), while clinical success was determined by the steady decline of indicators such as signs, symptoms, and increased levels of inflammatory markers (9). Pain experienced during PC and at 12-h follow-up was assessed by visual analog score (0-10 points).

Statistical Analysis

Discrete variables are represented by count and percentage values, while continuous variables are represented by the median (interquartile range [the range between the 25th and 75th percentiles]) or mean (± standard deviation) values if they pass the normality test. The Kolmogorov-Smirnov test was employed to ascertain whether continuous data originated from normal distributions. If the variables passed the normality test, the unpaired t-test was used to determine the significance of the difference. However, for qualitative variables and continuous variables that did fit into normal distributions, the Mann-Whitney test was used for nonparametric testing. A chi-square test of independence or Fisher's exact test was used to compare the proportions of different diagnostic methods between the two groups. The statistical analysis was conducted using the DATAtab online statistical program (DATAtab: Online Statistics Calculator. DATAtab e.U. Graz, Austria. URL https://datatab.net).

Results

PC was successfully conducted on all 152 patients who participated in the trial. Of them, 74 patients were in the CST group and 78 patients were in the MST group. Table 1 shows the demographics and clinical features of patients who had a PC procedure using either the CST or MST. No statistically significant differences were observed regarding sex, age, and the prevalence of diabetes mellitus, cardiac disease, hypertension, end-stage renal disease, cerebrovascular disease, malignant disease, and calculous or acalculous cholecystitis between CST and MST groups. In addition, no statistically significant differences were observed in INR, WBC, or PLT count.

Table 1. Demographic and clinical characteristics of patients who had percutaneous cholecystostomy (PC) using either the conventional (CST) or modified Seldinger technique (MST).

Characteristic	CST (n=74)	MST (n=78)	p
Sex			
Male	37 (50)	37 (47.4)	0.081*
Female	37 (50)	41 (52.6)	
Age (years), mean±SD	75.16±12.56	74.91±11.84	0.126[a]
Comorbidity			
Diabetes mellitus	32 (43.2)	33 (42.3)	0.380[a]
Cardiac disease	21 (28.3)	25 (33.8)	0.768[a]
Hypertension	43 (58.1)	39 (50)	0.383[a]
End-stage renal disease	7 (9.4)	9 (11.5)	0.176[a]
Cerebrovascular disease	24 (32.4)	26 (33.3)	0.139[a]
Malignant disease	13 (17.5)	15 (19.2)	0.065[a]
Cholecystitis			
Calculous	68 (92)	71 (91)	0.101[a]
Acalculous	6 (8)	7 (9)	
Gallbladder rupture	12 (16.2)	14 (17.9)	0.083[a]
Ascites	4 (5.4)	6 (7.6)	0.590[a]
Diagnostic imaging technique			
US	62 (83.7)	61 (78.2)	0.430[a]
CT	30 (40.5)	35 (44.8)	0.355[a]
Laboratory			
INR, mean±SD	1.21±0.15	1.20±0.19	0.370[a]
WBC, mean±SD	15.400±4410	15.850±3860	0.680[a]
PLT, mean±SD	201.000±74.000	205.000±71.000	0.340[a]

*chi-square test, a two-sample t-test, CST: Conventional Seldinger technique, CT: Computed tomography, INR: International normalized ratio, MST: Modified Seldinger technique, PC: Percutaneous cholecystostomy, PLT: Platelet, SD: Standard deviation, US: Ultrasound, WBC: White blood cell

Technical success was 100% for both groups and no need for a second effort to puncture was required in both groups. The average procedure time was significantly shorter in the MST group compared to the CST group (2.85±1.31 vs. 4.24±1.52 minutes; p=0.001). The CST group exhibited a higher incidence of procedure-related complications compared to the MST group (p=0.486). Within the CST group, one patient had minor bleeding, three patients experienced a bile leak, and one patient had a gallbladder rupture. Imaging

verified all complications. There were no instances of significant bleeding observed in either research group, however, one case of minor bleeding occurred in the CST and MST groups. There were no deaths due to the procedures All procedures in our cohort were conducted using the subcostal technique, primarily through the transhepatic route. The mean pain during the CST procedure was significantly higher than in the MST group, although at 12-h follow-up no significant difference was observed. (Table 2).

Table 2. Comparison of Procedural Details for the Use of Conventional and Modified Techniques in Percutaneous Cholecystostomy

	CST (n=74)	MST (n=78)	*p*
Approach			
Transhepatic	62 (83.8)	70 (89.7)	0.279*
Transperitoneal	12 (16.2)	8 (10.3)	
Duration (min), mean ±sd	4.24±1.52	2.85 ± 1.31	0.001[α]
Clinically successful			
Yes	63 (85)	69 (88.5)	0.547*
No	11 (15)	9 (11.5)	
Pain score, mean ±sd			
During procedure	4.4±1.66	3.2±1.9	**0.01**[α]
At 12 h of follow-up	2.4±1.35	2.6±1.21	0.6[α]
Complications			
Minor bleeding	1	1	1[β]
Major bleeding	0	0	N/A
Bile leak	3	1	0.356[β]
Abscess formation	0	0	N/A
Bowel perforation	0	0	N/A
Gallbladder rupture	1	1	1[β]
Pneumothorax	0	0	N/A
Death	0	0	N/A

*Chi-square test, α T-test, β Fischer's- exact test, N/A: Not applicable, CST: Conventional Seldinger technique, MST: Modified Seldinger technique

The clinical success rate was comparable between the two trial groups, with 88.5% for the MST group and 85% for the CST group (p=0.547). A comparable proportion of patients in both study groups experienced mortality either during their hospital stay or within the 3-month follow-up period. Specifically, 11 out of 74 patients (14.8%) in the CST group and 14 out of 78 patients (18%) in the MST group died (p=0.666).

Discussion

The potential for morbidity and mortality of AC continues to pose a significant challenge in surgical practice, frequently requiring emergent intervention. Although cholecystectomy is the standard treatment for eligible patients, high-risk individuals may benefit from nonoperative methods, such as PC. The objective of this investigation was to evaluate the safety and efficacy of the CST and the MST for PC. The study results demonstrate that our proposed model, which modifies the usual Seldinger procedure, achieved comparable levels of safety and efficacy. Furthermore, it resulted in a reduced number of complications and operation time, while maintaining equivalent rates of technical and clinical success.

The trocar or Seldinger technique is the primary method used to perform PC. The pigtail drainage catheters that are inserted into the gallbladder are typically 8 or 10 French in diameter, but they may be larger if necessary due to the viscosity of the contents, according to either technique. During the performance of PC using the trocar approach, the complete trocar system is inserted into the gallbladder while real-time image guidance is provided using US. The system consists of the needle, which is enclosed within the stylet, which is then covered by the pigtail drainage catheter. Once the US has verified the exact positioning of the trocar system in the gallbladder lumen, the needle is removed, and the pigtail drainage catheter is advanced over the stylet while keeping it still(10). On the other hand, the Seldinger approach involves using a smaller needle (typically 18 gauge) to gain initial access into the gallbladder lumen, with the guidance of real-time US imaging. Once the needle is confirmed to be correctly inserted into the gallbladder and bile is observed flowing through it, the contents of the gallbladder are suctioned and a sample is collected for culture and analysis. Subsequently, under the continued oversight of the US, a 0.035-inch guidewire is inserted through the needle and guided to form loops within the gallbladder. After removing the needle, the guidewire is utilized to advance pigtail drainage catheter placement with serial dilations (11). However, serial dilations can lead to bile spills and peritonism, which can prolong the procedural duration, while the trocar technique enables the entire system to be inserted into the gallbladder using US guidance in one phase, without the need for dilations and over-the-wire exchanges. This makes the trocar procedure faster and easier to perform. In this study, therefore, we drew inspiration from the Trocar technique to adapt the MST. Our hypothesis posited that circumventing serial dilations would lead to a reduction in procedure duration and complications.

In the literature, technical success rates of the Seldinger technique are aligned with our findings (95.8-100%) (7, 12, 13). Our findings indicate that both MST and CST achieved technical success in all cases, with no notable disparity. Our findings indicate that the modified technique, which skips consecutive dilation phases and directly inserts the catheter through

the guidewire, is equally effective as the traditional method in accomplishing gallbladder decompression. Furthermore, the fact that there was no requirement for a second attempt to puncture in both groups highlights the practicality and dependability of both approaches.

Reppas et al. demonstrate that the mean procedural time for the Seldinger technique in patients requiring PC was 4.88±2.68 (13). Similarly, in the TROSELC II trial, the mean time to perform PC with the Seldinger technique was 4.41±2.68. (7) Although our results align with the literature regarding the Seldinger technique (4.24±1.52), the variance in procedure duration between the two techniques was one of the most significant findings of our investigation. The MST group had an average procedure time that was significantly shorter than that of the CST group (2.85±1.31). This decrease in procedure time with MST can be attributed to the omission of consecutive dilatation stages, which simplifies the procedure. In our study, both CST and MST were performed under local anesthesia, which is generally well-tolerated by patients and avoids the risks associated with general anesthesia. However, it is important to note that in some centers, percutaneous cholecystostomy (PC) is performed under general anesthesia, which may increase the procedural risks, especially in high-risk patients with significant comorbidities

A key factor in assessing PC safety is procedure-related complications. While not statistically significant, our analysis revealed a tendency toward fewer problems in the MST group as opposed to the CST group. Remarkably, there was a greater frequency of complications in the CST group, including gallbladder rupture, bile leak, and mild hemorrhage which is similar to the literature(7, 12, 13). These complications highlight the possible hazards connected with the traditional method even though they were handled without major negative effects. On the other hand, the modified approach demonstrated encouraging safety outcomes; no cases of major bleeding and a lower incidence of bile leak were noted.

In a study by Arkoudis et al., the clinical success rate was 92% with the Seldinger technique for PC (7). In another study, it was 95.7% (12). Although the clinical efficacy, as measured by the remission of symptoms and inflammatory markers, was similar in both groups in our study, our results were lower compared to the literatüre (85-88%). This could be attributed to patient population differences, sample size, and the experience and skill of the practitioners. However, this finding implies that the modified method does not undermine the clinical results of PC. Moreover, the death rates during the hospital stay and the 3-month follow-up period were comparable across the MST and CST groups, suggesting that the modified strategy does not pose any extra risks in terms of patient survival.

An intrinsic limitation of our study is its retrospective design, which has the potential to introduce biases and confounding factors. Furthermore, the limited sample size may restrict the applicability of our findings, and additional studies with larger groups of participants are necessary to confirm the validity of our results. Additionally, collecting data on the long-term outcomes of patients who underwent PC utilizing the improved approach beyond the first 3-month period would offer useful insights into the sustainability of these results.

Our study concludes that the MST for PC is a safe and efficient substitute for the traditional method. The updated approach eliminates the need for sequential dilatation phases, which can lower the risk of complications associated with the procedure while still achieving similar therapeutic outcomes. Further prospective studies are necessary to validate these findings and clarify the long-term advantages of the modified method in the treatment of AC

Conflict of Interest Statement

The authors declare no conflicts of interest

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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ORIGINAL ARTICLE

Evaluation of the Causative Microorganisms and Antibiogram Results in Women with Vaginal Swab Cultures Through Prediagnosis of Vaginitis

Vajinit Ön Tanısı ile Vajinal Sürüntü Kültürü Alınan Kadınlarda Etken Mikroorganizmaların ve Antibiyogram Sonuçlarının Değerlendirilmesi

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ABSTRACT

Objective: Bacterial vaginosis is a common cause of vaginitis worldwide and is associated with serious diseases such as increased risk of preterm birth, sexually transmitted infections, and pelvic inflammatory disease. In this study, we aimed to evaluate the demographic data, growth of pathogenic microorganisms, and antibiotic susceptibility of women who underwent vaginal swab cultures with a preliminary diagnosis of vaginitis.
Methods: Vaginal swab samples from 314 women admitted to the Department of Obstetrics and Gynecology of Kafkas University were included in the study. Women with immunosuppressive diseases, gynecologic malignancies, and the use of intrauterine devices (IUD) were excluded from the study. Vaginal swab samples were sent to the Medical Microbiology laboratory immediately after collection with a transport swab. When the specimens arrived at the laboratory, they were Gram stained without waiting, inoculated on 5% sheep blood, eosin methylene blue, Sabouraud dextrose agar, and Chukulatamsi media, and incubated at 37 °C for 24-48 hours. Microorganisms were identified using conventional and biochemical methods, and antibiotic susceptibility tests were performed using the Kirby-Bauer disk diffusion method, according to the EUCAST guidelines.
Results: The median age of 314 women included in this study was 39 years (20-69). In total, 73.6% (n=231) were premenopausal, 24.5% (n=77) were postmenopausal and 1.9% (n=6) were pregnant. The most common complaint was abdominal/pelvic pain (142 patients; 45.2%). A total of 123 women (39.1%) grew different microorganisms in vaginal cultures. The most common causative microorganism was Escherichia coli (41.5%). According to the antibiogram results, gentamicin was the most sensitive antibiotic and ampicillin was the most resistant antibiotic in both gram (+) and gram (-) groups.
Conclusion: Rapid and accurate identification of etiological microorganisms for proper treatment will significantly reduce the incidence of both sexually transmitted diseases and neonatal infections.

Keywords: Bacterial infection, Candidiosis, Gentamicin, Vaginitis

ÖZ

Amaç: Bakteriyel vajinoz, dünya çapında vajinitin yaygın bir nedenidir ve erken doğum riskinin artması, cinsel yolla bulaşan enfeksiyonlar ve pelvik inflamatuar hastalık gibi ciddi hastalıklarla ilişkilidir. Bu çalışmada, vajinit ön tanısıyla vajinal sürüntü kültürü alınan kadınların demografik verilerinin, üreyen patojen mikroorganizmaların ve antibiyotik duyarlılık sonuçlarının değerlendirilmesi amaçlanmıştır.
Method: Kafkas Üniversitesi Kadın Hastalıkları ve Doğum Anabilim Dalına başvuran 314 kadının vajinal sürüntü örnekleri çalışmaya dahil edildi. İmmunsupresif hastalığı olanlar, jinekolojik malignitesi olanlar ve RİA kullananlar çalışma dışı bırakıldı. Vajinal sürüntü örnekleri transport swab ile alındıktan hemen sonra Tıbbi Mikrobiyoloji laboratuvarına gönderildi. Örnekler laboratuvara ulaştığında bekletilmeden Gram boyamaları yapıldı ve %5 koyun kanlı, Eosin Methylen Blue, Sabouraud Dekstroze agar ve Çukulatamsı besiyerlerine ekimleri yapıldı ve 37° C'de 24-48 saat inkübe edildi. Mikroorganizmalar konvansiyonel ve biyokimyasal yöntemler kullanılarak tanımlandı ve antibiyotik duyarlılık testleri EUCAST kılavuzlarına göre Kirby-Bauer disk difüzyon yöntemi kullanılarak gerçekleştirildi.
Bulgular: Bu çalışmaya dahil edilen 314 kadının ortanca yaşı 39 (20-69) idi. Toplamda %73,6'sı (n=231) premenopozal, %24,5'i (n=77) postmenopozal ve %1,9'u (n=6) gebeydi. En yaygın şikayet karın/pelvik ağrıydı (142, %45,2). 123 kadından (%39,1) alınan vajinal kültürlerde farklı mikroorganizmalar üremiştir. En yaygın etken mikroorganizma Escherichia coli (%41,5) idi. Antibiyogram sonuçlarına göre hem gram (+) hem de gram (-) grupta en duyarlı antibiyotik gentamisin, en dirençli antibiyotik ise ampisilin idi.
Sonuç: Doğru tedavi için etiyolojide yer alan mikroorganizmaların hızlı ve doğru bir şekilde tanımlanması hem cinsel yolla bulaşan hastalıkların hem de yenidoğan enfeksiyonlarının görülme sıklığını önemli derecede düşürecektir.

Anahtar Kelimeler: Bakteriyel enfeksiyon, Candidiozis, Gentamisin, Vajinit

Introduction

The main problem in vaginitis, inflammation of the mucosa lining the inner surface of the vagina, is a disorder of the vaginal flora (1, 2). Intrauterine devices (IUD), smoking, multipartners, cosmetics (use of soap, vaginal deodorant-perfume, etc.), vaginal cleaning with antiseptics, vaginal douching, textile materials, detergents used in underwear, antibiotic use, hormonal changes occurring during menopause, pregnancy, and adolescence are risk factors that disrupt the vaginal flora (1, 3, 4, 5)

The vaginal flora is an aerobic environment with different characteristics depending on the secretions,

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enzymes, and microorganisms it contains. The normal flora includes Lactobacilli, Bacteroides, S. epidermidis, group B and D streptococci, Chorinobacteria, Peptostreptococci, E. coli, Gardnerella vaginalis, Trichomonas vaginalis and a small amount of Candida albicans (6,7). Only aerobic lactobacilli were detected in the vagina during the first few weeks of the neonatal period. During puberty, Streptococci, Staphylococci, Diphtheroids, and E. coli bacteria are added to the flora, and the pH acidifies. During the sexually active period, Candida species and Trichomonas vaginalis can be considered causative agents. After menopause, lactobacilli decrease again and mixed flora emerge (6,7)

In healthy women of reproductive age, the flora has an acidic pH in the range of 3.8-4.2 due to the effect of estrogen. Estrogen stores glycogen in vaginal epithelial cells. Lactic acid is formed as a result of the destruction of glycogen by enzymatic reactions and lactobacilli create an acidic environment (1, 2). Epithelial proliferation decreases, epithelium becomes thinner, and pH rises to 6-8 with a decrease in estrogen levels in the pre-puberty and menopausal periods. Decreased epithelial proliferation makes the vagina more sensitive to trauma and infections, and lactobacilli are replaced by a mixed flora composed of pathogenic cocci (6-8).

The first presenting complaint was itching due to irritation caused by increased vaginal discharge. Other complaints include changes in the odor, color, and consistency of the discharge, feeling of restlessness, burning during urination, pain during sexual intercourse, redness, and edema in the vulvar region (1,9,10). This study aimed to evaluate the culture and antibiogram results of women who underwent vaginal cultures for vaginitis.

Materials and Methods

Patients and Data Collection

This study included 314 women who underwent vaginal culture at the Department of Obstetrics and Gynecology of the Kafkas University Application and Research Center between January 2023 and December 2023. Patients with IUD use, gynecologic malignancies, and immunosuppressive diseases were excluded from the study.

Demographic data such as age, pregnancy, parity, abortion, smoking history, comorbidity, drug use, history of surgery, presenting complaint, and premenopausal/ pregnancy/postmenopausal period were obtained retrospectively from medical records. Microorganism growth in vaginal cultures and antibiogram results were recorded.

Vaginal discharge or vaginal swab samples sent with sterile swabs were Gram stained, sown on 5% sheep blood agar, eosin methylene blue agar, Sabouraud dextrose agar, and Chukulatamsi agar, and incubated at 37°C for 24-48 hours. Leukocyte and clue cell status was evaluated by Gram staining. The microorganisms produced after the incubation period were identified using conventional (oxidase, catalase, and coagulase) and biochemical methods (IMVIC test). Antibiotic susceptibility tests of the identified isolates were performed using the Kirby-Bauer disk diffusion method as recommended by the EUCAST guidelines, and the results were evaluated according to the most recent EUCAST guidelines.

Ethics Committee Approval

This study was approved by the Non-Interventional Clinical Research Ethics Committee of the Kafkas University Faculty of Medicine (26/06/2024, 80576354-050-99/ 498). The study complied with the recommendations of the Declaration of Helsinki for human biomedical research.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows, version 24.0 (SPSS Inc., Chicago, IL, USA). Categorical variables are shown as numbers with corresponding percentages. Continuous variables are shown as mean ± standard deviation or median (minimum-maximum), depending on their distribution, as determined using the Kolmogorov-Smirnov test. Categorical variables were assessed using the chi-square test or Fisher's exact test when appropriate, whereas continuous variables were assessed using the Mann-Whitney U test. The level used to determine statistical significance was set at $p < 0.05$.

Results

Demographic Data of the Patient

The median age of the 314 women included in this study was 39 (20-69) years. The median gravida was two (0-14), median parity was one (0-10), and median abortion was zero (0-8). A total of 1.3% (n=4) of women were smokers. Different comorbidities were present in 17.2% (n=54) of the patients, most commonly diabetes mellitus (DM) (n = 21, 6.7%). Among women, 11.1 % (n = 35) were taking medications. Overall, 73.6% (n=231) were premenopausal, 24.5% (n=77) were postmenopausal, and 1.9% (n=6) were pregnant. The most common complaint was abdominal/pelvic pain (142 patients; 45.2%). Vaginal cultures from 123 women (39.1%) showed the growth of different microorganisms. The detailed data are presented in

Table 1.

Table 1. Demographic Data of the Patient

	Total Cohort n=314 (%)
Age (Median (Min-Max))	39 (20-69)
Gravida (Median (Min-Max))	2 (0-14)
Parity (Median (Min-Max))	1 (0-10)
Abortion (Median (Min-Max))	0 (0-8)
Smoking (n, %)	4 (%1.3)
Presenting Complaint (n, %)	
Abdominal/Pelvic Pain	142 (45.2)
Vaginal Discharge	97 (30.9)
Vaginal Itching	39 (12.4)
Vaginal Bleeding	30 (9.6)
Dysuria	37 (11.8)
Dyspareunia	7 (2.2)
Prolapse	3 (1.0)
Comorbidity (n, %)	54 (17.2)
Asthma	2 (0.6)
Crohn's disease	1 (0.3)
Diabetes Mellitus	21 (6.7)
Epilepsy	2 (0.6)
Hypertension	18 (5.7)
Hypothyroidism	13 (4.1)
Congenital Heart Disease	5 (1.6)
Migraine	1 (0.3)
Polycystic ovary syndrome	2 (0.6)
Systemic lupus erythematosus	1 (0.3)
Thrombophilia	1 (0.3)
Medication (n, %)	35 (11.1)
Period (n, %)	
Premenopausal	231 (73.6)
Pregnancy	6 (1.9)
Postmenopausal	77 (24.5)
Microorganism (n, %)	
No Growth	191 (60.9)
Reproduction	123 (39.1)

Comparison of Patients with and without Vaginal Culture Growth

The median age of patients with vaginal culture growth was 36 (21-69) years, and the median age of those without vaginal culture growth was 43 (20-66) years. Abdominal/pelvic pain (53.7% vs. 39.8%) was significantly higher in patients with culture growth (p=0.016). Other presenting complaints, gravida, parity, number of abortions, comorbidities, drug use, smoking, and premenopausal, pregnancy, and postmenopausal periods were similar between the two groups. DM (11.4% vs. 3.7%) was significantly higher in patients with culture growth (0.015). The detailed data are presented in Table 2.

Table 2. Comparison of Patients with and without Vaginal Culture Growth

	Vaginal Culture Growth (+) n=123 (%)	Vaginal Culture Growth (-) n=191 (%)	*p*
Age (Median (Min-Max))	36 (21-69)	43 (20-66)	0.051
Presenting Complaint (n, %)			
Abdominal/Pelvic Pain	66 (53.7)	76 (39.8)	0.016
Vaginal Discharge	38 (30.9)	59 (30.9)	0.999
Vaginal Itching	17 (13.8)	22 (11.5)	0.668
Dysuria	14 (11.4)	23 (12)	1.0
Vaginal Bleeding	4 (3.3)	26 (13.6)	0.004
Dyspareunia	2 (1.6)	5 (2.6)	0.709
Gravida (Median (Min-Max)	1 (0-10)	2 (0-14)	0.248
Parity (Median (Min-Max))	0 (0-10)	1 (0-10)	0.103
Abortion (Median (Min-Max)	0 (0-3)	0 (0-8)	0.103
Smoking (n, %)	3 (2.4)	1 (0.5)	0.304
Comorbidity (n, %)	19 (15.4)	35 (18.3)	0.613
Diabetes Mellitus	14 (11.4)	7 (3.7)	0.015
Hypertension	3 (2.4)	15 (7.9)	0.077
Polycystic ovary syndrome	2 (1.6)	0 (0)	0.077
Hypothyroidism	2 (1.6)	11 (5.8)	0.132
Crohn's disease	1 (0.8)	0 (0)	0.212
Migraine	1 (0.8)	0 (0)	0.212
Epilepsy	1 (0.8)	1 (0.5)	0.753
Thrombophilia	0 (0)	1 (0.5)	0.422
Systemic Lupus Erythematosus	0 (0)	1 (0.5)	0.422
Asthma	0 (0)	2 (1)	0.255
Congestive Heart Disease	0 (0)	5 (2.6)	0.161
Medication (n, %)	10 (8.1)	25 (13.1)	0.238
Period (n, %)			
Premenopausal	92 (74.8)	139 (72.8)	0.744
Pregnancy	28 (22.8)	3 (1.6)	0.744
Postmenopausal	3 (2.8)	49 (25.7)	0.744

Results of Microorganism Growth in Vaginal Culture

The most common causative microorganism was Escherichia coli (41.5%). Other pathogens were Candida albicans (24.4%), Klebsiella pneumoniae (10.6%), Candida glabrata (8.9%), and Enterococcus spp. (8.9%), methicillin-resistant Staphylococcus aureus (MRSA) (6.5%), Proteus mirabilis (3.3%), and Enterobacter spp. (2.4%), Acinetobacter (1.6%), Pseudomonas Aureginosa (0.8%), Serratia marcescens (0.8%), Candida kefyr (0.8%), and methicillin-sensitive Staphylococcus aureus (MSSA) (1.1%) (Table 3).

Table 3. Results of Microorganism Growth in Vaginal Culture

	Vaginal Culture Growth (+) n=123 (%)
Microorganism Agent (n, %)	
Escherichia coli	51 (41.5)
Candida albicans	30 (24.4)
Klebsiella Pneumonia	13 (10.6)
Candida glabrata	11 (%8.9)
Enterococcus spp.	11 (8.9)
Methicillin-resistant Staphylococcus aureus (MRSA)	8 (6.5)
Proteus Mirabilis	4 (3.3)
Enterobacter spp.	3 (2.4)
Acinetobacter	2 (1.6)
Pseudomonas Aeruginosa	1 (0.8)
Serratia Marcescens	1 (0.8)
Methicillin-sensitive Staphylococcus aureus (MSSA)	1 (0.8)
Candida kefyr	1 (0.8)

Comparison of Gram (+) and Gram (-) Antibiogram Data (Susceptible and Resistant Antibiotics)

Table 4. Comparison of Gram (+) and Gram (-) Antibiogram Data (Susceptible and Resistant to Antibiotics)

	Gram (-) n=75 (%)	Gram (+) n=20 (%)	p
Antibiogram			
Sensitive (n, %)			
Gentamicin	66 (88)	15 (75)	0.194
Trimethoprim-Sulfamethoxazole	39 (52)	9 (45)	0.761
Ampicillin	15 (20)	8 (40)	0.080
Levofloxaci	61 (81.3)	7 (35)	**<0.001**
Ciprofloxaci	50 (66.7)	6 (30)	**0.007**
Rifampicin	1 (1.3)	4 (20)	**0.007**
Penicillin	1 (1.3)	2 (10)	**0.049**
Tetracycline	1 (1.3)	2 (10)	**0.049**
Moxifloxaci	0 (0)	1 (5)	0.475
Resistant (n, %)			
Ampicillin	54 (72)	11 (55)	0.237
Penicillin	14 (18.7)	3 (15)	1.0
Gentamicin	3 (4)	3 (15)	0.105
Tetracycline	0 (0)	2 (10)	**0.006**
Levofloxaci	5 (6.7)	2 (10)	0.636
Ciprofloxaci	6 (8)	2 (10)	0.673
Moxifloxaci	1 (1.3)	0 (0)	1.0
Trimethoprim-Sulfamethoxazole	5 (6.7)	0 (0)	0.580

In both gram-negative and gram-positive groups, the most sensitive antibiotic was gentamicin ((n=66, 88% vs. n=15, 75%); p=0.194)) and the most resistant antibiotic was ampicillin ((n=54, 72% vs. n=11, 55%); p=0.237)). The detailed data are presented in Table 4.

Discussion

In this study, the demographic data, culture, and antibiogram results of 314 women who underwent vaginal culture between January 2023 and December 2023 in the Department of Obstetrics and Gynecology of the Kafkas University Application and Research Center were analyzed.

In our study, bacteria and/or fungi were isolated as causative agents in 39.1% of vaginal culture samples. Vaginal discharge is the most common cause of hospital admission for vaginitis. Bacterial vaginosis is the most common cause of abnormal vaginal discharges. It was first described in 1955; however, its etiology remains unknown (11-13). With the decrease in lactobacilli, which constitute 90%-95% of healthy vaginal flora, they are mostly replaced by anaerobic opportunistic bacteria such as gram-positive cocci and gram-negative bacilli (11,14-16). Its prevalence was found to be 58.3% in sub-Saharan South Africa, 30.3% in Zimbabwe, 14.2% in Nigeria, 23.2% in Bangladesh, 32% in Chile, 29.2% in the USA, 4.7% in Australia, and 8.6% in Finland (17-23). Low socioeconomic status, poor hygiene, and malnutrition are considered to increase its incidence.

The diagnosis can be made using the Amsel criteria or Gram staining techniques, but different degrees of accuracy occur between the two diagnostic methods (13,14). Vaginal swab culture is the gold standard for diagnosing most bacterial infections. However, since it is difficult to produce microorganisms in bacterial vaginosis, culture is not the gold standard method. Gram staining is an inexpensive, short-term, and readily accessible laboratory method. In previous studies, the sensitivity and specificity of Gram staining for the diagnosis of bacterial vaginosis ranged between 89-93% and 70-83%, respectively (24). Compared with Gram staining, diagnosis can be made with 70-90% sensitivity and 90-94% specificity according to the Amsel criteria (25).

Studies have shown that the number of lifetime sex partners, sex between women, use of sex toys, early coitus, frequency of vaginal sex, recent change of partners, oral sex, anal sex, intravaginal practices such as vaginal cleansing and/or vaginal douching increase the risk of vaginitis, which in turn increases the risk of sexually transmitted agents such as HIV, Neisseria gonorrhoeae, Chlamydia Trachomatis, Trichomonas Vaginalis and Herpes Simplex virus-2 (11,13,26,27). Some studies have shown that the use of an IUD increases risk (28), whereas others have shown that it decreases risk (29). Women using IUDs were excluded

from our study.

The Centers for Disease Control and Prevention (CDC) treatment guidelines recommend treating only symptomatic women (30). This leads to a higher recurrence rate among asymptomatic women. According to previous studies, the recurrence rate in the first year can vary between 15%-80% (16,31). It has been shown that treatment of asymptomatic women significantly reduces sexually transmitted disease agents (32).

75% of adult women experience at least one episode of vulvovaginal candidiasis in their lifetime and 45% experience at least two episodes each year. Candida albicans is the causative agent in 85%-90% of cases. Other Candida species have also been observed in immunosuppressed, postmenopausal, and diabetic women (33,34). BV is the second most common cause of vaginitis, worldwide. In studies conducted in our country, the rate of Candida growth in vaginal swab cultures was found–16-39.8% (35-37). Its frequency increases in pregnant women, obese women, patients with immune dysfunction, and those with a recent history of antibiotic use. As it causes chronic, recurrent, and resistant infections, it may lead to sexual dysfunction and impaired quality of life in women (35). In our study, 24.4% of Candida albicans, 8.9% of Candida glabrata, and 0.8% of Candida kefyr were found to be causative agents. In the premenopausal period, 11.7% (n=27), 33.3% (n=2), and 1.3 % (n = 1) of the participants were postmenopausal (p=0.004). This may be explained by the higher frequency of estrogenic and sexual activity.

As the estrogen level decreases, the vaginal epithelium becomes thinner and a condition called atrophic vaginitis occurs. The vagina is dry, there is usually no odor or discharge, and dyspareunia is the most common complaint. It is one of the most common complaints during the postmenopausal period (36,38). In the present study, 22.8% (n=28) of women were postmenopausal, and different microorganisms were found in 36.4 % (n = 28) of the cultures.

Although many microorganisms are found in balance in the aerobic vaginal flora, the most important factor contributing to this is lactobacilli, which constitute 90%. In addition, commensal agents include C. albicans, S. aureus, and S. agalactiae (38). Aerobic vaginitis is characterized by a decrease in the predominance of lactobacilli in the flora and a predominance of commensal pathogens, with more inflammatory changes compared to bacterial vaginosis. It was found to be 5-24% in patients presenting with vaginal discharge and 8-11% in pregnant women (38). In a study of 610 vaginal swab cultures, the causative microorganisms isolated were E. coli (24.92%), K. pneumoniae (23.5%), S. aureus (16.52%), and Enterococcus spp. (8.40%) and coagulase-negative staphylococci (6.44%) in order of frequency. The growth rate of these bacteria was higher in non-pregnant women and in those between 25-40 years of age (39). Among the gram-negative bacteria isolated in the literature, E. coli is the most common, with a rate of 69.3%-76% (35,36). The agents isolated in our study were as follows; 41.5% E.coli, 10.6% Klebsiella Pneumoniae, 8.9% Enterococcus spp., 6.5% MRSA, 3.3% Proteus mirabilis, 2.4% Enterobacter spp., 1.6% Acinetobacter, 0.8% Pseudomonas Aureginosa, 0.8% Serratia Marcescens and 1.1% MSSA.

The limitations of our study include the small number of cases and the retrospective nature of the study. Vaginitis constitutes an important part of admissions to Gynecology and Obstetrics Outpatient Clinics in all age groups. Failure to provide treatment for the causative agent may result in pelvic inflammatory disease, infertility, and serious complications, such as meningitis and sepsis, in newborns. It can cause deterioration in the quality of life of women due to complaints such as vaginal discharge, bad odor, bleeding, and dyspareunia, and in advanced stages, it can cause serious psychological problems. Therefore, it remains an important health problem. Therefore, it is important to treat asymptomatic women in contrast to CDC recommendations to prevent possible complications. Therefore, it is important to quickly and accurately identify microorganisms involved in the etiology of the correct treatment.

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ORIGINAL ARTICLE

Development of Electric Vehicle Accidents Attitude Scale in Cognitive, Affective and Behavioral Dimensions: A Reliability and Validity Study

Elektrikli Araç Kazaları Tutum Ölçeğinin Bilişsel, Duygusal ve Davranışsal Boyutlarda Geliştirilmesi: Bir Güvenilirlik ve Geçerlilik Çalışması

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ABSTRACT

Background/ Objective: The knowledge, attitudes, and behaviors of healthcare professionals are directly related to mortality and morbidity due to road traffic crashes. It has become important to investigate the causes of various injuries in electric vehicle accidents. These issues are indirectly the responsibility of forensic medicine. This study aimed to develop an Electric Vehicle Accidents Attitude Scale (EVAAS) regarding cognitive, affective, and behavioral dimensions to determine the attitudes of healthcare professionals toward electric vehicle accidents.
Materials and Methods: The sample group of the study consisted of 386 physicians and other health professionals, working in the emergency services and 112 units (emergency health services in Türkiye) of hospitals in Türkiye. The Delphi technique was performed in the development of EVAAS, and validity/reliability analyses were conducted after a focus group study and a pilot application.
Results: The 26-item EVAAS scale was grouped into three-dimensional factors (cognitive, affective, and behavioral), which explained 65.257% of the total variance. Cronbach's alpha coefficient for EVAAS was 0.859, retest reliability was 0.781, and the test-retest reliability was calculated as 0.766.
Conclusion: A valid and reliable EVAAS scale consisting of 26 items in three dimensions (cognitive, affective, and behavioral) was developed in the study.

Keywords: Attitude scale, Electric vehicle accidents, Emergency medicine, Forensic medicine, Health care professionals

ÖZ

Arka Plan/Amaç: Sağlık çalışanlarının bilgi, tutum ve davranışları, doğrudan karayolu trafik kazalarından kaynaklanan mortalite ve morbidite ile ilişkilidir. Elektrikli araç kazalarında çeşitli yaralanmaların nedenlerini araştırmak önemli hale gelmiştir. Bu konular dolaylı olarak adli tıbbın sorumluluğundadır. Bu çalışmanın amacı, sağlık çalışanlarının elektrikli araç kazalarına yönelik tutumlarını belirlemek için bilişsel, duygusal ve davranışsal boyutlara ilişkin bir Elektrikli Araç Kazaları Tutum Ölçeği (EAKTÖ) geliştirmektir.
Materyal ve Yöntem: Çalışmanın örneklem grubu, Türkiye'deki hastanelerin acil servislerinde ve 112 birimlerinde (Türkiye'deki acil sağlık hizmetleri) çalışan 386 hekim ve diğer sağlık çalışanından oluşmuştur. EAKTÖ'nün geliştirilmesinde Delphi tekniği uygulanmış ve odak grup çalışması ve pilot uygulama sonrasında geçerlilik/güvenilirlik analizleri yapılmıştır.
Bulgular: 26 maddelik EAKTÖ üç boyutlu faktörlere (bilişsel, duygusal ve davranışsal) ayrıldı ve toplam varyansın %65,257'sini açıkladı. EAKTÖ için Cronbach alfa katsayısı 0,859, tekrar test güvenilirliği 0,781 ve test-tekrar test güvenilirliği 0,766 olarak hesaplandı.
Sonuç: Çalışmada bilişsel, duygusal ve davranışsal olmak üzere üç boyutta 26 maddeden oluşan geçerli ve güvenilir bir EAKTÖ ölçeği geliştirildi.

Anahtar kelimeler: Acil tıp, adli tıp, Elektrikli araç kazaları, tutum ölçeği, sağlık çalışanları

Introduction

One of the most important factors related to public health is road traffic accidents. The knowledge, attitudes, and behaviors of health professionals are important dimensions affecting the mortality and morbidity caused by accidents. This issue directly and/ or indirectly concerns forensic medicine specialists, who play an important role in the assessment of injuries and the determination of the cause of death (1). The majority of clinical forensic practice involves cases of injury and death related to road traffic accidents. Determining the cause of death when investigating the nature and severity of traffic accident injuries and determining whether death occurred as a result of a traffic accident are among the responsibilities of forensic medicine specialists (2). Although forensic medical specialists are not involved in the initial stages of the process, emergency medical services are among the first responders at the scene of an accident. Accurate and rapid first medical response is one of the most important factors in reducing the mortality rate in road traffic accidents (3). The training status (professional training) and the attitudes of the emergency medical response team toward the types of accidents play a key role in the effectiveness of the first medical response

In recent years, the frequency of electric vehicles (EVs) in traffic has been increasing day by day with the

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rapid development of new technology (3). Although EVs are similar to other fossil fuel vehicles in terms of driving and mobility, they have significant technical differences. In particular, the batteries that store energy can cause injuries and fatalities that do not occur in other traffic accidents. The most important of these are spontaneous and unquenchable fires (4), skin and tissue burns (5), blast injuries from explosions (6), poisoning from the release of toxic gases (7), and injuries from electric current (8). Spontaneous combustion of electric vehicles and the inability to extinguish fires have been in the news recently. The cognitive, affective, and behavioral attitudes of first responders to an incident regarding the knowledge, recognition, and management of these injuries are critical to providing an accurate, rapid, and effective response to the incident and to ensuring occupational health and safety. It is possible that both the early recognition and emergency intervention with the injury and the protection of the emergency healthcare professionals from injury, experience, and emotional and behavioral basis about these accidents will contribute to reducing the number of deaths and injuries.

Attitudes, including cognitive, affective, and behavioral dimensions, are defined as the tendency to have a positive or negative learned response to an event, situation, institution, or person (9). The cognitive parameter of an attitude consists of an individual's beliefs, knowledge, and thoughts about the object of the attitude. The affective parameter consists of the individual's feelings and evaluations about the attitude object, and the behavioral parameter consists of the individual's behavior toward a situation (10). Therefore, attitude scales have been developed in various fields to enable individuals to clearly express their opinions in a broad framework.

In recent years, many studies on electric vehicle accidents have taken their place in the literature. However, most of the studies are technical and aim to increase the efficiency of the vehicles and to identify risks. In terms of attitudes, there are no studies on attitudes towards accidents, except for studies on electric vehicle preference. The establishment of an attitude scale for the teams dealing with accidents involving these vehicles, which present many different risks, will undoubtedly contribute to remedying this deficiency

In the framework of the above information, this research aims to develop an Electric Vehicle Accidents Attitude Scale (EVAAS) in cognitive, affective, and behavioral dimensions to determine the attitudes of healthcare professionals towards electric vehicle accidents. The EVAAS will be a significant contribution to the literature on the subject, as no such scale for the same purpose has been found in the literature.

Materials and Methods

The study used a survey, which is one of the data collection techniques including EVAAS. The Delphi technique was used to develop the attitude scale. The Delphi technique was developed by two researchers, Norman Dalkey and Olaf Helmer, in the 1950s in the USA. According to Dalkey and Helmer (11), the main purpose of using this technique is to obtain the most reliable consensus from a group of expert opinions through an intensive series of questionnaires in such a way that controlled feedback can be obtained. In short, the Delphi technique is used to obtain the common views of a group of independent and uninformed experts through a rational and written approach, and thus to plan programs, develop policies, predict events and trends, and develop standards.

Within the framework of the above information, a comprehensive literature review was first carried out for the study, and three dimensions (subscale, factor), namely cognitive, affective, and behavioral, were taken into consideration, as in the attitude scales used in many studies (12-15). The procedure regarding the stages of the Delphi technique used in the study is as follows:

Statement of the problem: To determine the cognitive, affective, and behavioral attitudes of healthcare workers regarding electric vehicle accidents,

Selection of panel members: Twenty professionals with a certain level of knowledge, experience, research, and training on the subject were selected as panelists. Accordingly, 10 panelists consisting of three forensic specialists, two emergency physicians, two paramedics, one emergency medical technician, one psychologist, and one biostatistician were selected as panelists.

The first Delphi survey (Round I): The dimensions (cognitive, emotional, behavioral) defined by the problem of the study were sent to the panelists and a pool of 60 items was created by asking the panelists to write "items that can measure the attitudes of health care workers towards electric vehicle accidents". At

the end of this round, 48 items were included in the pool by combining similar suggestions.

The second Delphi survey (Round II): The 48 items ranked under the identified factors were then presented to the panel members again and given a 3-point scale for the appropriateness of the items (appropriate, partially appropriate, and not appropriate). The data obtained at the end of the round were analyzed to generate median, interquartile, and range (q3-q1) statistics. As a result of the analysis, the pool was reduced to 40 items.

The third Delphi Survey (Round III): The medians, quartiles, and ranges calculated for the item pool were sent to the panelists, and three options (appropriate, partially appropriate, not appropriate) were again presented to reach a consensus on which items should be included in the pool. The 32-item EVAAS was constructed as a result of the Delphi rounds within the framework of the data obtained.

In the following process, the comprehensibility of the 32 items in EVAAS was reduced to 29 items by removing three items as a result of a focus group study consisting of 15 health professionals (paramedics, emergency medical technicians, forensic specialists, and emergency medicine specialists). In addition, the final scale was reduced to 27 items by removing 2 items as a result of the validity and reliability analysis of the data obtained with a pilot study of 30 people. A total of 27 items (12 items for the cognitive dimension, eight items for the affective dimension, and seven items for the behavioral dimension) were presented to the health workers. Each item of the EVAAS was subjected to a 5-point Likert-type rating, scored as 1=strongly agree, 2=agree, 3=neutral, 4=disagree, 5=strongly disagree.

The population of this study consists of physicians, paramedics, emergency medical technicians, and ambulance drivers working in 112 units (Emergency Health Service in Türkiye) and emergency departments of public state and university hospitals in Turkey. Due to constraints such as time, cost, and distance, the convenience sampling method, which was preferred by the participants in this study (16), was used for selection. The study used the n=s2.Za2/d2 formula (17), which is recommended for large populations and quantitative research, to calculate the minimum sample size. Accordingly, using the data obtained as a result of the pilot study with 30 participants, standard deviation s = 1, effect size d = 0.1, and Z0.05 = 1.96 (for significance level a= 0.05), the minimum sample size was calculated as 384. In this framework, 391 health workers from 16 provinces in different regions of Turkey formed the sample group (17, 18).

Exploratory factor analysis (EFA) with varimax rotation was used in the study to determine the construct validity of the 27-item EVAAS. Reliability and internal consistency statistics of the scale and subscales (factors and dimensions) were measured by corrected item-total correlation, Cronbach's alpha when items were deleted, and Cronbach's alpha coefficient. The correlation between the two variables was calculated for test-retest reliability. In addition, a confirmatory factor analysis (CFA) was applied to the data obtained with different samples of 291 people to test the factor structure. LISREL 8.71 was used for CFA, and SPSS 21.0 for Windows (SPSS, Inc., Chicago) was used to analyze other data in the study.

The study was approved by the Ethics Committee for Non-Interventional Clinical Research of xxx University, decision number 2023/26.

Results

The results of the exploratory factor analysis (EFA) and reliability analysis of EVAAS, including three dimensions (cognitive, affective, and behavioral), are shown in Table 1. According to the factor analysis results, Bartlett's test of sphericity and Kaiser-Meyer-Olkin measure of sampling adequacy verify the factorability of the data (Bartlett's test of sphericity= 4383.103; $p<0.001$ and KMO=0.808). The 26-item EVAAS was grouped into three dimensions or factors (cognitive, affective, and behavioral), which explained 65.257% of the total variance.

The cognitive dimension, consisting of 11 items and explaining 29.432% of the total variance, constituted the first factor of the scale, followed by the affective/emotional (22.444%) and behavioral (13.381%) dimensions. The factor loadings of all items were found to be above 0.40, except for the 10th item (factor loading is 0.342) in the cognitive dimension. Cronbach's alpha coefficients for reliability analysis were calculated as 0.821 for the cognitive dimension, 0.853 for the affective/emotional dimension, and 0.831 for the behavioral dimension. As a result of the confirmatory factor analysis (CFA) applied in the study, the coefficient of the 10th item in the cognitive dimension was found to be quite low (0.17). However, the CFA goodness of fit indices (RMSEA, NFI, SRMR, AGFI, and $\chi 2/DF$) were at acceptable levels. Under

Table 1. Results of Exploratory Factor Analysis (EFA) and Reliability Analysis for EVAAS

	Factors and Items	Factor Loading	Corrected Item-Total Correlation	Cronbach's Alpha (α) if Item Deleted	Cronbach's Alpha (α)
F1: Cognitive dimension -Eigenvalues (% of Variance) = 5.896 (29.432)					
1	Accident types and risks in traffic accidents vary depending on vehicle fuel types.	0.800	0.428	0.860	0.821
2	I don't think electric vehicle accidents are different from other traffic accidents. (R)	0.650	0.418	0.862	
3	I have sufficient knowledge about the working system of electric vehicles (battery, current, voltage, etc.).	0.732	0.583	0.852	
4	I recognize that a vehicle involved in an accident is electric by its make, model, logo, etc.	0.609	0.493	0.857	
5	I have sufficient knowledge about the electrical components of electric vehicles (batteries, wiring points, etc.).	0.861	0.661	0.849	
6	I have sufficient knowledge about electric vehicle accidents and risk factors.	0.834	0.686	0.847	
7	I know the precautions to be taken against electric vehicle accidents.	0.819	0.628	0.850	
8	Battery-caused fires in electric vehicle accidents are very difficult to extinguish	0.612	0.584	0.852	
9	I know that toxic gases (methane, cyanide, carbon monoxide, carbon monoxide hydrogen fluoride, etc.) originating from batteries cause poisoning in electric vehicle accidents.	0.644	0.689	0.845	
10	Battery-induced explosive injuries can develop in electric vehicle accidents.	0.342	0.421	0.827	
11	Battery-induced electric shock or thermal injuries can occur in electric vehicle accidents.	0.841	0.673	0.847	
12	Standard equipment for the response to electric vehicle accidents needs to be developed.	0.568	0.591	0.851	
F2: Affective dimension-Eigenvalues (% of Variance) = 4.496 (22.444)					
13	I feel psychologically prepared for electric vehicle accidents.	0.807	0.759	0.833	0.853
14	The knowledge I have about electric vehicle accidents gives me peace of mind.	0.772	0.664	0.840	
15	I have the necessary attention and concentration when faced with the high risks of electric vehicle accidents.	0.845	0.716	0.836	
16	Electric vehicle accidents generally scare me. (R)	0.800	0.445	0.866	
17	I hesitate to intervene in electric vehicle accidents. (R)	0.819	0.424	0.862	
18	My lack of knowledge about electric vehicle accidents disturbs me. (R)	0.805	0.504	0.857	
19	Non-extinguishable fires in electric vehicle accidents scare me. (R	0.781	0.575	0.852	
20	I am concerned about battery-induced explosions, toxic gas, and thermal injuries in electric vehicle accidents. (R)	0.698	0.430	0.860	
F3: Behavioral dimension -Eigenvalues (% of Variance) =2.681 (13.381)					
21	I pay attention to the fuel type of the vehicle when responding to those injured in traffic accidents	0.637	0.481	0.857	0.831*
22	I attend training meetings on electric vehicle accidents and injuries.	0.585	0.656	0.847	
23	I do not intervene in electric vehicle accidents before the rescue team-fire brigade arrives.	0.650	0.492	0.857	
24	I use protective equipment (gloves, shoes, etc.) when responding to electric vehicle accidents due to electric shock and thermal injuries.	0.731	0.590	0.846	
25	I use a gas mask when responding to electric vehicle accidents to avoid any possible toxic gas releases from batteries.	0.661	0.431	0.862	
26	I take precautions for myself or the injured when responding to electric vehicle accidents.	0.613	0.547	0.849	
27	Since electric vehicles operate quietly and are difficult to detect, I approach the vehicle from the side in case it moves suddenly in an accident.	0.548	0.513	0.850	
General scale Explanation rate of total variance = % 65.257					

Note: The 10th item in the cognitive dimension was excluded from the evaluation due to its negative effect on total variance and Cronbach's alpha.

the EFA and CFA results, it was decided to remove the 10th item in the cognitive dimension from the scale.

Table 2. Test, Retest, and Test-Retest Reliability

Reliability	Value
Test reliability	Cronbach's Alpha (a)=0.859
Retest reliability	Cronbach's Alpha (a)=0.781
Test-retest reliability	Correlation (r)=0.766

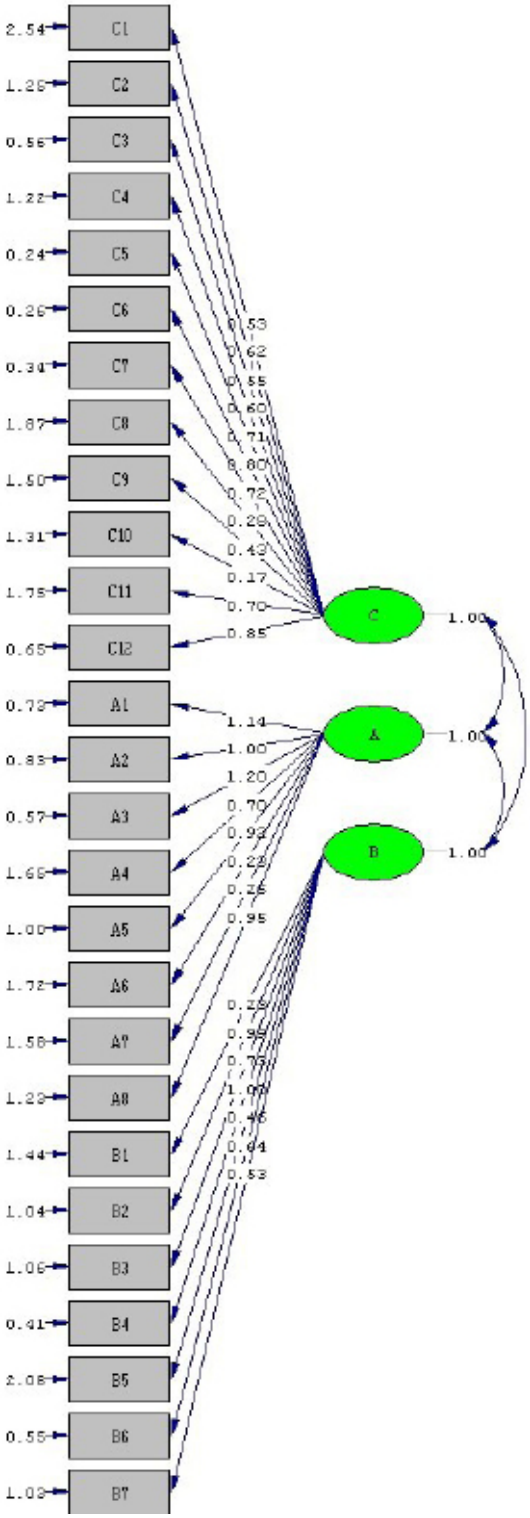

Table 3. Model fit indices of the scal

Fit Indexes	Good Fit	Acceptable Fit	Model	Results
RMSEA	0<RMSEA<0.05	0.05<RMSEA<0.08	0.08	Acceptable
NFI	0.95≤NFI≤1	0.90≤NFI≤0.95	0.90	Acceptable
SRMR	0≤SRMR≤0.05	0.05≤SRMR≤0.10	0.09	Acceptable
AGFI	0.90≤GFI≤1	0.85≤AGFI≤0.90	0.86	Acceptable
χ2/DF	<3	<5	3.42	Acceptable

AGFI: Adjusted goodness of fit index, DF: Degree free, NFI: Normal fit index, RMSEA: Root-mean-square error of approximation, SRMR: Standardized root mean square residual, χ2: Chi-square

Discussion

In the study, following the focus group study and pilot application processes as proposed and recommended in the literature for scaling, a scale consisting of 26 items in the cognitive, affective, and behavioral dimensions was developed using the Delphi technique to determine the attitudes of healthcare professionals towards electric vehicle (EV) accidents. A new scale (EVAAS) consisting of 26 items dealing with three dimensions (cognitive, affective, behavioral) was developed in the study after relevant literature, the Delphi technique, focus group study, and pilot application processes to determine the attitudes of healthcare workers towards electric vehicle (EV) accidents. This scale structure was based on the ABCs of attitudes (affective, behavioral, and cognitive) [10]. The 8-item affective dimension consists of items measuring an individual's emotional outlook (emotion, happiness, fear, anxiety, etc.). The 7-item behavioral dimension includes items related to behavioral responses to electric vehicle accidents. The 11-item cognitive dimension includes items that express individuals' opinions as well as some basic information. According to the EFA results, 26 items in the three dimensions explained about two-thirds of the total variance in the study. The Cronbach's alpha coefficients of the scale and subscales were above the critical value of 0.70 (19). The EFA, CFA, Cronbach's alpha and adjusted item-total correlation results confirmed the validity and reliability of the EVAAS without removing any items (20). Considering the number of injuries and deaths associated with road traffic crashes, they are among the most significant public health problems. While millions of people are reported to die annually, many more are injured and disabled (21-23). In addition, road traffic crashes result in loss of time + loss of work intensity for many professional groups involved in medical first aid,

treatment and rehabilitation, and the ensuing legal processes. Traffic crashes primarily affect firefighters search and rescue personnel, emergency medical technicians, traffic police officers, vehicle assistance officers, hospital emergency personnel, and other medical specialists and health care professionals. Medical examiners are responsible for providing forensic reports on basic issues such as the severity of victims' injuries and determining the cause of death in fatal cases. Secondarily, the workload of judicial officials (prosecutors, judges, lawyers, etc.) is affected. The fact that the number of deaths and injuries can be prevented shows the importance of efforts to prevent and reduce traffic accidents. The fact that fossil fuel vehicles (gasoline, diesel, and LPG) have been on the road for a long time and that society has learned the characteristics of the vehicles suggests that attitudinal evaluations of vehicles will be futile. However, when we look at electric vehicles, which are a new technology product both in terms of their different operating systems and the risks they pose, the importance of attitudes in responding to these vehicle accidents becomes apparent.

Determining the attitudes of healthcare workers toward EV accidents is valuable in several ways. First and foremost, it will ensure that healthcare workers can approach victims appropriately and that their positive and negative perceptions of these vehicles do not lead to delays in intervention or even incorrect early intervention. In addition, responders who do not have sufficient knowledge about the risks of EVs can be prevented from having occupational injuries. In addition, delayed or incorrect intervention can lead to medical malpractice claims. Determining the attitudes of healthcare workers will contribute to the processes that may develop in the coming years.

Other attitudinal assessments have been examined, and in the study conducted by Kaya et al. in 2017, it was found that as the level of encountering risk factors and knowledge of healthcare workers increased, their awareness of screening increased, and the rate of regular cancer screening was high in this group (24). This study shows that the behaviors of people who have achieved cognitive competence are properly manifested. Similarly, the study "Nursing students' knowledge, willingness, and attitudes toward first aid behavior as bystanders in traffic accident trauma: A cross-sectional survey," conducted by Pei et al. in 2019, claims that first aid behavior was stronger in traffic accidents that occurred immediately after first aid training (25). Both studies show the importance of training, especially in ensuring the correct development of behavior in healthcare professionals. In the review of Demiralp's 2023 study, which examined nurses' attitudes toward CBRN incidents, the importance of training long before accidents or attacks was mentioned (26). All of these studies have shown the need for appropriate and adequate training to achieve the desired behaviors, and the need for training has been determined by studies using attitude scales.

Conclusion

EVs are becoming more and more common, and the number of accidents is increasing with this increase. Different approaches, materials, and mental equipment are required in emergency intervention due to their potential to cause non-extinguishable fires, explosions, and poisoning, which are different from the classical fossil-fuelled vehicles. Our study will be an important contribution to reveal the awareness of emergency health workers towards these accidents and to provide the necessary educational and managerial solutions.

Although the EVAAS scale is designed for healthcare professionals, it can be applied to firefighters traffic police, vehicle assistance technicians, and especially to EV users and passengers with minor modifications. Thus, the study will make a significant contribution to determining the educational status of the risk group on the subject of safety measures regarding EV accidents and to develop awareness and subsequently reduce possible deaths, occupational accidents, and injuries.

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ORIGINAL ARTICLE

Evaluation of Systemic Inflammatory Marker in Patients with Laryngopharyngeal Reflux

Larengofaringeal Reflüsü Olan Hastalarda Sistemik İnflamatuar Belirteçlerin Değerlendirilmesi

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ABSTRACT

Aim: It was aimed to investigate whether systemic inflammation markers have diagnostic value in laryngopharyngeal reflux disease
Materials and Methods: This retrospective study was conducted including 32 patients with laryngopharyngeal reflux and 27 subjects with vocal cord nodules. Patients with laryngopharyngeal reflux were evaluated as Group 1, and subjects with vocal cord nodules as Group 2. Patient files were scanned. Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and systemic inflammation index values were calculated. In addition, the previously filled Reflux symptom index and the Reflux sign scores performed by videoendoscopic examination were noted.
Results: While the mean age was 43.21±13.26 years in Group 1, it was 38.04±10.39 years in Group 2. While there were 12 male and 20 female patients in Group 1, there were 12 male and 15 female patients in Group 2. When Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and systemic inflammation index values were examined, no statistically significant difference was found between Group 1 and Group 2 ($p>0.05$). Reflux symptom index and Reflux sign scores were significantly higher in Group 1 ($p<0.05$). There was a significant positive correlation between the Reflux symptom index and Reflux sign scores
Conclusion: In our study, no significant difference was found in the Neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, and systemic inflammation index values used in the follow-up of many diseases compared to the control group in laryngopharyngeal reflux patients and had no diagnostic value. While the Reflux symptom index and Reflux sign scores were found to be significantly higher in laryngopharyngeal reflux patients compared to the control group, they were significantly positively correlated with each other

Keywords: Laryngopharyngeal Reflux, Lymphocyte, Neutrophil, Reflux Symptom Index, Reflux Finding Score

ÖZ

Amaç: Laringofaringeal reflü hastalığında sistemik inflamasyon belirteçlerinin tanısal değeri olup olmadığının araştırılması amaçlandı.
Gereç ve Yöntemler: Bu retrospektif çalışma laringofaringeal reflüsü olan 32 hasta ve vokal kord nodülü olan 27 olgu dahil edilerek yapıldı. Laringofaringeal reflü hastaları Grup 1, vokal kord nodülü olan olgular Grup 2 olarak değerlendirildi. Hasta dosyaları tarandı. Nötrofil/lenfosit oranı, trombosit/ lenfosit oranı ve sistemik inflamasyon indeksi değerleri hesaplandı. Ayrıca daha önce doldurulmuş olan Reflü semptom indeksi ve videoendoskopik muayene ile yapılan Reflü belirti skorları not edildi.
Bulgular: Grup 1'de yaş ortalaması 43.21±13.26 iken, Grup 2'de 38.04±10.39 bulundu. Grup 1'de 12 erkek ve 20 kadın hasta bulunurken, Grup 2'de ise 12 erkek ve 15 kadın hasta mevcuttu. Nötrofil lenfosit oranı, platelet/ lenfosit oranı ve sistemik inflamasyon indeksi değerleri incelendiğinde Grup 1 ve Grup 2 arasında istatistiksel olarak anlamlı fark saptanmadı ($p>0.05$). Reflü semptom indeksi ve Reflü bulgu skorları Grup-1'de anlamlı olarak daha yüksek bulundu ($p<0.05$). Reflü semptom indeksi ve Reflü bulgu skorları arasında önemli ölçüde pozitif korelasyon mevcuttu
Sonuç: Bizim çalışmamızda Laringofaringeal reflü hastalarında, birçok hastalığın takibinde kullanılan nötrofil/lenfosit oranı, platelet/lenfosit oranı ve sistemik inflamasyon indeksi değerlerinde kontrol grubuna göre anlamlı fark saptanmadı ve tanısal değeri yoktu. Reflü semptom indeksi ve Reflü bulgu skorları, laringofaringeal reflü hastalarında kontrol grubuna göre anlamlı yüksek bulunurken, birbirleri ile önemli ölçüde pozitif korele bulundular.

Anahtar Kelimeler: Laryngopharyngeal Reflux, Lymphocyte, Neutrophil, Reflux Symptom Index, Reflux Finding Scor

Introduction

The inflammatory state caused by the reflux of gastric contents into laryngeal and pharyngeal tissue is known as laryngopharyngeal reflux (LPR). Although the prevalence of LPR is still unclear, it is a frequently encountered entity in ear, nose, and throat (ENT) clinical practice. It causes symptoms of a tickling sensation in the throat, voice disorders, difficulty in swallowing, chronic cough, and globus pharyngeus. These symptoms result from laryngeal epithelial damage caused by the reflux content or vagal nerve-mediated stimulation of laryngeal reflexes (1). The laryngopharynx has been reported to be potentially more sensitive to reflux content than the esophagus (2).

The diagnosis of LPR was difficult. The methods employed in diagnosis included the Reflux Finding Score (RFS) (Table 1) and were evaluated using the video laryngoscopic examination and the Reflux Symptom

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Index (RSI) (Table 2) (3,4). The RSI scores over 13 are regarded as pathological, and the RFS scores over 7 were interpreted in favor of LPR.

Table 1. Reflux Finding Score

Reflux Finding Scores	
Subglottic edema	0 Absent
	2 Present
Ventricular Obliteration	0 Absent
	2 Partial
	4 Complete
Erythema/hyperemia	0 Absent
	2 Arytenoids
	4 Diffuse
Vocal fold edema	0 Absent
	1 Mild
	2 Moderate
	3 Severe
	4 Polypoid
Diffuse laryngeal edema	0 Absent
	1 Mild
	2 Moderate
	3 Severe
	4 Obstructing
Posterior commissure hypertrophy	0 Absent
	1 Mild
	2 Moderate
	3 Severe
	4 Obstructing
Granuloma/granulation tissue	0 Absent
	2 Present
Thick endolaryngeal mucus	0 Absent
	2 Present

RSF >7 = Laryngopharyngeal Reflu

Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), and systemic inflammation index (SII) can be easily calculated by peripheral complete blood count. NLR and PLR have been identified as potential markers of systemic inflammation (5-7). It is known that NLR, PLR, and SII, which are widely studied especially in cardiovascular diseases, can be used as classical inflammatory markers (8,9). The prognostic value of the systemic inflammation index (SII), neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) have been demonstrated in many inflammatory diseases, particularly cancer (10,11).

Based on the literature, we encountered no studies investigating the relationship between LPR and SII in the literature search. This study aimed to examine the relationship between LPR, a disease frequently encountered in ENT medicine, and systemic inflammatory markers.

Table 2. Reflux Symptom Index

Within the last Month, how did the following problems affect you?	**(0=No problem-5=Severe problem)**					
Hoarseness or a problem with your voice	0	1	2	3	4	5
Clearing your throat	0	1	2	3	4	5
Excess throat mucus or postnasal drip	0	1	2	3	4	5
Difficulty swallowing food, liquids, or pills	0	1	2	3	4	5
Coughing after you ate or after lying down	0	1	2	3	4	5
Breathing difficulties or choking episodes	0	1	2	3	4	5
Troublesome or annoying cough	0	1	2	3	4	5
Sensation of something sticking in your throat, or a lump in your throat	0	1	2	3	4	5
Heartburn, chest pain, indigestion, or stomach acid coming up	0	1	2	3	4	5

RSI>13=Abnormal

Material And Method

The study was carried out under the Declaration of Helsinki and with the approval of the Non-Interventional Ethical Committee of xxx University (Date:19.03.2021, Decision 2021-KAEK-6934). Since the data in the research was obtained from electronic records of the patients, consent from the patients was not obtained.

The study was planned retrospectively. Thirty-two patients presenting to the ENT clinic between 1st October 2020 and 1st March 2021, diagnosed with LPR, and with no additional systemic disease were included in the study. These were assigned to Group 1, while 27 subjects with vocal cord nodules constituted Group 2.

Once the patient's age and sex distributions had been determined, RFS and RSI forms routinely applied in ENT clinics to assist in the diagnosis of LPR were scanned from the files. The Turkish language versions of both forms had previously been validated (12,13).

Hemoglobin values and neutrophil, platelet, and lymphocyte counts were retrieved from complete blood counts (CBC) performed for other reasons during the previous three months. CBC parameters were calculated with an automated hematologic analyzer (XN-1000-Hematology-analyzer-Sysmex Corporation,

Japan). NLR, PLR, and SII values were calculated by formula. SII (platelet×neutrophil/lymphocyte), NLR, and PLR analyses were also performed. The groups were then compared based on these values.

The study assessed patients aged 18 to 60 diagnosed with gastroesophageal reflu who followed a reflux diet for at least one month without taking medication. An ENT physician then examined these patients. A single otolaryngologist with ten years of experience obtained a thorough medical history from the study participants, and a flexible endoscopic examination of the larynx revealed laryngopharyngeal reflux. The control group consisted of subjects with vocal cord nodules with similar age and gender characteristics as the study group. This study group presented to the ENT outpatient clinic with a complaint of dysphonia but no complaints or symptoms of reflux.

Patients at the age of <18 years or >60 years, those consistently taking medications for any reason, those with blocked nasal air passages such as septum deviation, allergic rhinitis, and turbinate hypertrophy, those with postnasal purulent discharge, those smoking and consuming alcohol, those with such disorders as coronary artery disease, hypertension, diabetes mellitus, hyperlipidemia, chronic obstructive pulmonary disease, chronic liver disease, acute and chronic renal diseases, and those with previous interventional procedures or surgery in the laryngopharyngeal area, and those choosing not to participate in the study were excluded from the study.

Statistical Analysis

Statistical analyses were performed on the Statistical Package for Social Sciences (SPSS) for Windows, version 21.0 software (IBM SPSS Inc., Chicago, IL, USA). Mean±standard deviation and descriptive statistics were employed. The normality of distribution was evaluated using the Kolmogorov–Smirnov test. NLR and PLR values were not normally distributed in Group 1, and NLR, PLR, RSI, and RFS values were not normally distributed in Group 2. Normally distributed data were compared between the groups using the independent samples t-test. The Mann–Whitney U test was applied in the comparison of non-normally distributed variables between the groups. The correlation between RSI and RFS was investigated using Spearman's correlation test. A p-value of <0.05 was considered statistically significant. The Cronbach's alpha test was used to assess the intra-rater reliability. The value is 0.731.

Results

Group 1 consisted of 20 (62.5%) women and 12 (37.5%) men, and Group 2 of 15 (55.6%) women and 12 (44.4%) men. Mean ages were 43.21±13.26 years in Group 1 and 38.04±10.39 in Group 2. No significant differences were observed between the groups in terms of age (p=0.178) or sex (p=0.783).

Platelet counts, hemoglobin values, lymphocyte counts, neutrophil counts, and NLR, PLR, and SII values in groups 1 and 2 are shown in Table 3. No significant differences were observed between the groups in terms of the values shown in Table 3 (p>0.05).

Table 3. Age, platelet count, hemoglobin, lymphocyte count, neutrophil count and NLR, PLR and SII values of the groups

	Group 1	Group 2	P value
Age (years) (mean±SD)	43.21±13.26	38.92±10.39	0.178*
Platelet Count (x1000 uL) (mean±SD)	244.78±51.40	265.29±48.07	0.121*
Hemoglobin (mean±SD)	14.59±1.59	15.15±1.77	0.205*
Lymphocyte Count (mean±SD)	2.30±0.73	2.54±0.81	0.236*
Neutrophil Count (mean±SD)	5.06±1.95	4.83±1.73	0.627*
NLR [median (IQR)]	1.94 (1.38-2.32)	2.10 (1.40-3.07)	0.338¥
PLR [median (IQR)]	105.93 (80.00-139.52)	109.19 (86.33-138.91)	0.831¥
SII (mean±SD)	579.83±293.15	549.17±263.76	0.677*

*: Independent Sample t test was used. ¥: Mann-Whitney U test was used. NLR: Neutrophil/Lymphocyte ratio,

PLR: Platelet/ Lymphocyte ratio, SII: Systemic Inflammation Index, IQR: Interquartile Range

RSI and RFS values in groups 1 and 2 are shown in Table 4. RSI and RFS values were significantly higher in the LPR group than in the control group (Table 4) (p<0.05). A significant positive correlation was observed between RSI and RFS (p=0.000).

Table 4. RSI and RFS values of groups.

	Group 1 [median (IQR)]	Group 2 [median (IQR)]	***p*-value**
RSI	1.00 (0.00-6.00)	15.50 (12.25-19.50)	0.000¥
RFS	0.00 (0.00-2.00)	7.00 (4.00-9.00)	0.000¥

¥: Mann-Whitney U test was used. RSI: Reflux Symptom Index, RFS: Reflux Finding Scores

IQR: Interquartile Range

Discussion

LPR is an inflammatory disease caused by the reflux of gastroduodenal contents. It causes non-specific symptoms such as a tickling sensation in the throat and voice disorders. Its association with chronic pharyngitis,

premalignant lesions of the larynx, and squamous cell carcinoma has also been reported (14,15). Gastroesophageal reflux disease is observed in 57-80% of patients with clinical symptoms of LPR (16). However, LPR patients may not have gastroesophageal reflux findings

Although the main diagnostic test for LPR is 24-hour pH monitoring, more rapid tests have begun entering into use. Belafsky et al. defined the RSI and RFS forms (3,4). RSI exceeding 13 is compatible with LFR, while RFS above seven indicates LPR with a likelihood of 95% (3,4). RFS in the LPR group in the present study was 15.65±5.82, while RSI was 7.03±3.37.

The RSI and RFS forms are practical for the diagnosis of LPR and observing the response to treatment (3). Karakaya et al. showed that RSI and individual variables in RFI were correlated in LPR, except for posterior commissure hypertrophy (12). In agreement with the previous literature, a significant correlation was observed between RSI and RFS in the present study, and both were significantly higher in the LPR group than in the control group.

Increasing platelet and decreasing lymphocyte counts during inflammation allows the PLR to be employed as an inflammatory marker. The NLR and PLR can be used to predict prognosis in several cancers and in the evaluation of inflammation in diseases such as diabetes, hypertension, rheumatoid arthritis, and acute coronary syndrome (17,18). Ateş et al. showed that NLR values may rise in gastroesophageal reflux-related erosive esophagitis and non-erosive esophagitis (19). Arslan et al. found that PLR was significantly higher in patients with LPR than in the control group, but NLR did not differ significantly. They also suggested that the mean platelet volume value has prognostic significance in treating LPR (8). No significant difference in PLR and NLR values was observed between the LPR and control groups in the present study.

The systemic inflammation index (SII), consisting of three cell types (neutrophils, platelets, and lymphocytes), was developed by Hu et al. in 2014 (20). The SII can provide a clearer picture of immune and inflammatory conditions (21,22). It has also been shown to be a useful marker in predicting clinical outcomes in tumors and several inflammatory diseases (21-23). Our search of the literature revealed no studies investigating the relationship between LPR and the SII. In the present study, SII values were lower in the control group than in the LPR group, although no significant difference was found between the two groups.

The principal limitations of this study are its retrospective nature and the low case number. The fact that more objective tests for LPR were not used is another limitation.

LPR is a common condition frequently encountered in otolaryngology practice. Regarding the prevalence of LPR, it is clear that it is impractical to perform objective diagnostic tests on every patient. The RSI and RFS forms are practical and valuable for the initial assessment and subsequent evaluation of treatment. SII, NLR, and PLR are biomarkers that can be used to assess inflammation.

Conclusion

Our study indicated that patients with LPR exhibited significantly elevated levels of RSI and RBS, diagnostic markers for LPR. The analysis found no significant correlation between the markers SII, NLR, and PLR, extensively studied in recent years, and LFR. Prospective studies can be designed to include more patients and assess these markers before and after treatment.

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ORIGINAL ARTICLE

Examination of Vitamin D Levels in Patients with Schizophrenia and Schizoaffective Disorder: A Retrospective Study

Şizofreni ve Şizoaffektif Bozukluğu Olan Hastalarda D Vitamini Düzeylerinin İncelenmesi: Retrospektif Bir Çalışma

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ABSTRACT

Background/Aims: The relationship between vitamin D and schizophrenia has been the focus of studies in the last 20 years. Studies have shown that approximately 65% of schizophrenia patients have vitamin D deficiency. This study aimed to retrospectively investigate the vitamin D levels of schizophrenia and schizoaffective disorder (SAD) patients receiving inpatient treatment at a tertiary care hospital.
Material and Methods: Patients diagnosed with Schizophrenia and SAD who received inpatient treatment at the psychosis service of a tertiary care hospital in the last two years (2021-2023) were included in this study. The data of 230 patients were examined retrospectively from hospital and file records.
Results: Among the patients in the study, 47.8% were female with a mean age of 42.3±15.8 years, and 52.2% were male with a mean age of 37.2±14.1 years. Among women, 24.5% had SAD and 75.5% had schizophrenia, among men, 30.8% had SAD and 69.2% had schizophrenia. Vitamin D deficiency was found in 73% of the group, vitamin D insufficiency was found in 17.4%, and normal vitamin D levels were found in 9.6%. No statistically significant relationship was found when vitamin D levels were compared between male and female patient groups (p = 0.068). When vitamin D levels were compared between patient groups diagnosed with schizophrenia and SAD, no statistically significant relationship was found. (p>0.05
Conclusion: Despite advances in the treatment of schizophrenia, these advances are insufficient to reduce the morbidity and mortality of the disease, so prophylactic measures should be explored. Adequate D vitamin supplementation during critical stages of life, including pregnancy, might be a meaningful, simple, safe, and cost-effective intervention.

Keywords: Retrospective study, schizophrenia, schizoaffective disorder, vitamin D deficiency, vitamin D insufficienc

ÖZ

Amaç: D vitamini ve şizofreni arasındaki ilişki son 20 yılda yapılan çalışmaların odak noktası olmuştur. Çalışmalar şizofreni hastalarının yaklaşık %65'inde D vitamini eksikliği olduğunu göstermiştir. Bu çalışmanın amacı, üçüncü basamak bir hastanede yatarak tedavi gören şizofreni ve şizoaffektif bozukluk (ŞAB) hastalarının D vitamini düzeylerini retrospektif olarak araştırmaktır.
Gereç ve Yöntem: Bu çalışmaya son iki yıl içinde (2021-2023) üçüncü basamak bir hastanenin psikoz servisinde yatarak tedavi gören şizofreni ve ŞAB tanılı hastalar dahil edilmiştir. 230 hastanın verileri hastane ve dosya kayıtlarından retrospektif olarak incelenmiştir.
Bulgular: Çalışmaya alınan hastaların %47,8'i (n=110) kadın olup yaş ortalamaları 42,3±15,8 iken %52,2'si (n=120) erkekti ve yaş ortalamaları 37,2±14,1'di. Kadınların %24,5'i (n=27) ŞAB, %75,5'i (n=83) şizofreni; erkeklerin ise %30,8'inde (n=37) ŞAB ve %69,2'sinde (n=83) şizofreni hastasıydı. Grubun %73'ünde (n=168) D vitamini eksikliği, %17,4'ünde (n=40) D vitamini yetersizliği ve %9,6'sında (n=22) normal D vitamini düzeyleri saptandı. Kadın ve erkek hasta grupları arasında D vitamini düzeyleri karşılaştırıldığında istatistiksel olarak anlamlı bir ilişki bulunmadı (p=0,068). Şizofreni ve ŞAB tanılı hasta grupları arasında D vitamini düzeyleri karşılaştırıldığında istatistiksel olarak anlamlı bir ilişki bulunmadı (p>0.05).
Sonuç: Şizofreni tedavisindeki ilerlemelere rağmen, bu gelişmeler hastalığın morbidite ve mortalitesini düşürmekte yetersiz kalmaktadır, bu nedenle profilaktik önlemler araştırılmalıdır. Hamilelik de dahil olmak üzere yaşamın kritik aşamalarında yeterli D vitamini takviyesi anlamlı, basit, güvenli ve uygun maliyetli bir müdahale olabilir.

Anahtar Kelimeler: şizoaffektif bozukluk, şizofreni, D vitamini eksikliği, D vitamini yetersizliği, retrospektif çalışma

Introduction

Schizophrenia is among the serious mental disorders and is one of the 25 most common causes of disability worldwide (1). It is characterized by psychotic symptoms that usually begin in early adulthood and a large global burden of disease and has a high heritability rate. However, the underlying disease mechanisms are not yet fully understood (2).

Vitamin D is a steroid hormone that can be taken exogenously in the form of foods and supplements or produced endogenously through sunlight exposure. Most of it (85%) is synthesized in the skin with the effect of ultraviolet B rays in case of sun exposure, and a small amount is taken in certain foods containing vitamin D such as salmon, tuna, and fish oil (1)

The prevalence of vitamin D deficiency is increasing

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worldwide and is estimated to affect almost one in five people. The highest prevalences are found in North Asia and the Middle East. Vitamin D deficiency is also widespread in our country. Although it is not possible to screen the whole population for vitamin D deficiency, it is recommended that serum levels should be measured at least in high-risk groups and replacement should be provided if deficient because vitamin D is important for human metabolism and its deficiency is associated with serious health problems. Therefore, it is of great importance that this easily preventable and treatable vitamin Deficiency is detected and necessary interventions are performed (3).

In addition to its most well-known role in calcium, phosphate, and bone metabolism, vitamin D also plays a role in neurodevelopment, synaptic plasticity, neuroprotection and neurotransmission, dopamine system, and immune response (4).

It is obvious that vitamin D, which regulates the release of neurotrophic agents essential for neuronal differentiation and shows neuroprotective effects by supporting the production of calcium-binding proteins, is closely related to psychiatric diseases(5).

The role of vitamin D in the pathophysiology of schizophrenia is supported by many studies conducted with increasing interest, especially in the last 20 years. Several hypotheses suggesting that low vitamin D levels are a risk factor for the development of schizophrenia are based on some epidemiologic evidence linking schizophrenia with births in winter (low maternal vitamin D), urban upbringing, and migration to places with less sunlight exposure (2). Adequate cut-off values for vitamin D levels vary depending on the specific functions of the vitamin in body metabolism. In most cases, levels lower than 20 ng/mL are defined as inadequate, while blood levels of 30 ng/mL or higher are considered optimal (6). Factors such as not being able to benefit from enough sunlight, living in northern latitudes, having dark-pigmented skin, and being born in winter are common causal factors in both vitamin D deficiency and schizophrenia (3)

According to studies, vitamin D deficiency is very common in patients with schizophrenia and may be associated with negative symptoms, suicide risk, agoraphobia, and antidepressant consumption (7,8). Studies have shown that approximately 65% of schizophrenia patients have vitamin D deficiency (9). Additionally, it has been reported that the risk of schizophrenia in people with vitamin D deficiency is 2,16 times higher (10). Therefore, the present study aimed to retrospectively investigate the vitamin D levels of schizophrenia and SAD patients receiving inpatient treatment at a tertiary care hospital.

Material and Methods

Study Design and Data Collection

Patients diagnosed with Schizophrenia and SAD who received inpatient treatment at the psychosis service of a tertiary care hospital in the last two years (2021-2023) were included in this study. The data of 230 patients were examined retrospectively from hospital and file records. In the study, 0-20 ug/L (microgram/liter) deficiency, 21-29 ug/L insufficiency, and 30-70 ug/L normal range were taken as reference for the 25-hydroxy vitamin D levels of the patients (Table 1).

Table 1. Vitamin D Levels

The Reference Range	Unit	Clinical Situation
0-20	Microgram/Liter	Deficienc
21-29	Microgram/Liter	Insufficienc
30-70	Microgram/Liter	Normal Range

Measurement of Vitamin D Levels

After overnight fasting for 12 hours, 2 ml venous blood samples obtained from the participants were placed in anticoagulated tubes and centrifuged at room temperature (NF 1200R, NuveR).

After centrifugation, vitamin D levels were measured by HPLC (Chromsystems, Germany).

Ethical Approval

This research was approved by The XX University Non-Interventional Clinical Research Ethics Committee with decision number 05 dated 05.03.2023. The research complies with the provisions of the Declaration of Helsinki (as revised in Brazil 2013).

Statistical Analysis

Data were analyzed with the SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)) package program. Continuous variables were presented as mean ± standard deviation, median (25th and 75th percentiles), and minimum-maximum values; categorical variables were presented as numbers and percentages. Differences between categorical variables were analyzed using chi-square analysis. $p<0.05$ was considered statistically significant

Results

Among the patients included in the study, 47.8%

(n=110) were female with a mean age of 42.3±15.8 years, and 52.2% (n=120) were male with a mean age of 37.2±14.1 years. Among women, 24.5% (n=27) had SAD and 75.5% (n=83) had schizophrenia; among men, 30.8% (n=37) had SAD and 69.2% (n=83) had schizophrenia. Vitamin D deficiency was found in 73% (n=168) of the group, vitamin D insufficiency was found in 17.4% (n=40), and normal vitamin D levels were found in 9.6% (n=22).

In female patients, the rate of vitamin D deficiency was 80% (n = 80), the rate of vitamin D insufficiency was 13.6% (n = 15), and the normal vitamin D level was 6.4% (n = 7). In male patients, the rate of vitamin D deficiency was 66.7% (n=80), the rate of vitamin D insufficiency was 20.8% (n=25), and the normal vitamin D level was 12.5% (n=15). As shown in Table 2, no statistically significant relationship was found when comparing vitamin D levels between male and female patient groups (p = 0.068).

Table 2. Vitamin D Levels by Gender

	Deficient n (%)	Insufficient n (%)	Optimal n (%)	*p*-value
Female (n=110)	88 (80.0)	15 (13.6)	7 (6.4)	(0.068)
Male (n=120)	80 (66.7)	25 (20.8)	15 (12.5)	

The rates of vitamin D deficiency in patients with schizophrenia and SAD are shown in Table 3. When vitamin D levels were compared between patient groups diagnosed with schizophrenia and SAD, no statistically significant relationship was found as shown in Table 3 (p>0.05).

Table 3. Vitamin D Levels by Psychiatric Disorders

	Deficient n (%)	Insufficient n (%)	Optimal n (%)	*p*-value
Schizophrenia (n=166)	123 (75.3)	28 (16.9)	13 (7.8)	(0.303)
Schizoaffective Disorder (n=64)	43 (67.2)	12 (18.8)	9 (14.0)	

Discussion

Vitamin D deficiency is a global health problem for all ages, even in countries with year-round sunlight exposure. Increasing physical activity and spending more time outdoors for sunlight exposure can stimulate endogenous vitamin D production and improve vitamin D levels. In this study, 73% of patients with schizophrenia and SAD had vitamin D deficiency, 17.4% had vitamin D insufficiency and 9.6% had normal vitamin D levels. In many studies conducted in patients with schizophrenia in the literature, high vitamin D deficiency results were found at a similar rate to our results (4,11,12). Similarly, in a large-scale study including 36 articles with a total of 12528 participants, vitamin D levels of schizophrenia patients were significantly lower than controls (13)

Unhealthy eating habits decreased physical activity and less exposure to sunlight have been observed in inpatient psychiatry wards (4). Vitamin D deficiency found in patients with schizophrenia may be related to the sedentary lifestyles of these patients and their inability to utilize sunlight sufficiently due to less exposure to the outdoor environment.

Although studies in patients with SAD are much fewer in the literature, deficiency in vitamin D levels was found in 34.7% of patients in one study (6). In this study, no statistically significant relationship was found when vitamin D levels were compared between the groups of patients diagnosed with schizophrenia and SAD. This may be thought to be since the two diseases have similar neurodevelopmental backgrounds and the patients have similar characteristics in terms of symptoms and living conditions.

In our study, no statistically significant relationship was found between male and female patient groups in terms of vitamin D levels, similar to some studies in the literature (14,15). In many studies conducted in healthy populations, vitamin D levels are lower in women than in men and this has been attributed to hormonal differences (16-17). This contradictory finding is remarkable. This may be explained by the fact that many factors including race, geography, health status, cultural, genetic, and personal characteristics affect vitamin D levels (16-17).

Studies have shown that the use of antipsychotics in combination with vitamin D supplementation may improve total attention span and positive and negative symptoms of schizophrenia. Vitamin D levels should be measured regularly, replacement should be made when necessary and patients should be encouraged to be exposed to sunlight to maintain optimum vitamin D levels (18-20).

Our study has some limitations such as being a cross-sectional study, having a relatively small sample group, and not considering the factors that may affect vitamin D deficiency. Although there are many studies investigating vitamin D deficiency in psychotic disorders, we thought that our research could contribute to the literature since studies in patients with SAD are rare. Future studies are needed to investigate the causes of vitamin D deficiency and the prophylactic vitamin D administration results.

Despite the new developments in the treatment of schizophrenia and SAD, these disorders are still disorders that do not have adequate recovery rates and affect

the quality of life and functionality of patients severely. Vitamin D deficiency may be an under-recognized health risk for inpatients with schizophrenia or SAD. Supplementing with sufficient vitamin D is an efficient, simple, safe, and cost-effective approach in psychotic disorders like schizophrenia and SAD.

Declarations

Conflict of Interest

The Authors declare that they have no conflict of interest.

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Authors' Contribution

Study design: ANIK, ATG Data collection: SBT, ATG Data analysis and interpretation: ANIK, ATG, Writing-Reviewing and Editing: ANIK, SBT, ATG, Drafting of the article: SBT, ANIK Critical review: ANIK, SBT, ATG.

Ethics Approval

This research was approved by The XX University Non-Interventional Clinical Research Ethics Committee with decision number 05 dated 05.03.2023.

Presentation

This study was presented as an oral presentation at the 15th International Congress of Psychopharmacology.

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ORIGINAL ARTICLE

Efficacy of Different Surgical Methods in the Treatment of Pediatric Urolithiasis: Retrograde Intrarenal Surgery, Extracorporeal Shock Wave Lithotripsy, and Open/Laparoscopic Surgery Approaches

Pediatrik Ürolitiyazis Tedavisinde Farklı Cerrahi Yöntemlerin Etkinliği: Retrograd İntrarenal Cerrahi, Ekstrakorporeal Şok Dalga Litotripsi ve Açık/Laparoskopik Cerrahi Yaklaşımları

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ABSTRACT

Background/Aims: To evaluate in which cases Retrograde Intrarenal Surgery (RIRS) should be combined with other techniques in pediatric patients undergoing retrograde intraluminal endoscopic surgery, RIRS combined with extracorporeal shock wave lithotripsy, and RIRS combined with open/laparoscopic surgery for urolithiasis in our clinic.
Materials and Methods: This study conducted a retrospective analysis of data from 302 pediatric patients undergoing RIRS, this technique in conjunction with extracorporeal shock wave lithotripsy (ESWL), open stone surgery, and laparoscopic stone surgery for urolithiasis at our clinic from January 2013 to October 2020. The patient's demographic data, the position, and size of the stones discovered using imaging techniques, surgical interventions for stone extraction, stone-free results, and the condition of postoperative hydronephrosis were evaluated.
Results: A total of 302 pediatric patients were included in this study. The mean age was 89.719 months (SD 51.447, range 6–216). 160 patients (53%) were male, whereas 142 patients (47%) were female. The mean size of the treated stones was 7.964 mm (SD 3.516, range 2.2-25 mm). Stone-free rate was achieved in 262 (86.75%) of the patients during surgical follow-up. Imaging indicated the absence of stones in 235 participants (77.81%). In the follow-up, it was shown that hydronephrosis completely resolved in 278 (92.05%) patients.
Conclusion: Choosing minimally invasive surgical procedures is advisable, particularly for pediatric patients. It is essential to acknowledge that open or laparoscopic surgery, particularly laparoscopy, is significant in certain instances, depending upon the surgeon's expertise

Keywords: Endoscopic shock wave lithotripsy, Laparoscopy, Pediatric urinary tract calculi, Retrograde intrarenal surgery

ÖZ

Amaç: Kliniğimizde ürolitiazis nedeniyle retrograd intraluminal endoskopik cerrahi, ekstrakorporeal şok dalga litotripsi ile kombine RIRS ve açık/laparoskopik cerrahi ile kombine RIRS uygulanan pediatrik hastalarda RIRS'in hangi durumlarda diğer tekniklerle kombine edilmesi gerektiğini değerlendirmeyi amaçladık.
Gereç ve Yöntemler: Bu çalışmada kliniğimizde Ocak 2013-Ekim 2020 tarihleri arasında ürolitiyazis nedeniyle RIRS ve RIRS ile kombine ESWL, açık taş cerrahisi, laparoskopik taş cerrahisi uygulanan 302 çocuk hastanın verileri retrospektif olarak analiz edildi. Hastaların demografik verileri, görüntüleme yöntemleri ile tespit edilen taşların tarafı ve boyutu, cerrahi taş girişimleri, taşsızlık sonuçları ve ameliyat sonrası hidronefroz durumu değerlendirildi.
Bulgular: Çalışmaya 302 çocuk olgu dahil edildi. Ortalama yaş 89.719 ay (SD 51.447, dağılım 6-216) idi. Dahil edilen hastaların 160'ı (%53) erkek, 142'si (%47) kızdı. Tedavi edilen taşların ortalama boyutu 7.964 mm (SD 3.516, dağılım 2.2-25) idi. Ameliyat sonrası takiplerde hastaların 262'sinde (%86,75) taşsızlık sağlandı. Bu hastaların 235'inde (%77,81) görüntülemede taşa rastlanmadı. Takiplerde 278 (%92.05) hastada hidronefrozun tamamen düzeldiği gözlendi.
Sonuç: Sonuç olarak, özellikle pediatrik olgularda minimal invaziv cerrahi yöntemlerin tercih edilmesi uygundur. Açık veya laparoskopik cerrahinin, özellikle laparoskopinin, seçilmiş olgularda, cerrahın deneyimine göre yeri olduğu unutulmamalıdır.

Anahtar kelimeler: Endoskopik şok dalga litotripsi, Laparoskopi, Pediatrik üriner sistem taşı, Retrograd intrarenal cerrahi

Introduction

The incidence of urinary system stone illness in pediatric patients has risen in recent years (1). The incidence of urinary tract stones in children in low- and middle-income countries, including Turkey, ranges from 5% to 15% (2).

Advancements in technology have led to improvements in stone treatment for pediatric patients. Extracorporeal shockwave lithotripsy (ESWL) and retrograde intrarenal surgery (RIRS) utilizing rigid or flexible ureterorenoscopy (URS) are favored over open or laparoscopic surgical techniques due to superior outcomes and patient advantages. Nonetheless, open or laparoscopic stone therapy is warranted in some anatomical situations, during procedures like pyeloplasty, or when endourological therapies have proven unsuccessful (3).

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This study aims to evaluate in which cases RIRS should be combined with other techniques in pediatric patients undergoing retrograde intraluminal endoscopic surgery, RIRS combined with extracorporeal shock wave lithotripsy, and RIRS combined with open/ laparoscopic surgery for urolithiasis in our clinic.

Material and Methods

This study retrospectively examined the data of 302 pediatric patients who underwent RIRS, RIRS combined with ESWL, open stone surgery, and laparoscopic stone surgery for urolithiasis at our clinic from January 2013 to October 2020.

Before the procedure, patients had preoperative urinalysis, urine culture, serum biochemistry, coagulation assessments, plain abdomen X-ray, and urinary system ultrasound (USG) to determine the existence, size, and position of the stones. In necessary cases, abdominal non-contrast computed tomography (CT) was requested due to suspected stones, and the findings of patients referred from an external facility with prior CT results were also incorporated into the study. The stone length was determined using USG measurements or the longest stone measurement obtained from plain abdominal X-ray or CT scans. Patients with urinary tract infections, coagulation issues, and those who failed to attend regular follow-up were excluded from the study.

Patients were categorized into four groups: those who underwent RIRS with a JJ stent, RIRS without a JJ stent, RIRS in combination with ESWL, and open/laparoscopic stone surgery combined with RIRS. The decision to use a JJ stent in patients who underwent URS was based on the stone's location, size, the dimensions and quantity of stone fragments retrieved through lithotripsy, and the condition of mucosal edema. The decision was made to combine URS and ESWL; if initial treatment commenced with ESWL and subsequent follow-up revealed stone migration to the ureter resulting in obstruction, or if stone-free rates were not attained after three sessions of ESWL, URS treatment was initiated. However, there were renal stones that were inaccessible via URS. Individuals who underwent URS in conjunction with open or laparoscopic surgery, those from whom stones were excised during pyeloplasty, those with substantial staghorn-like stones obstructing the URS that was attempted but unsuccessful, or those who developed a significant obstructive stone tract in various locations within the ureter.

The Extracorporeal shockwave lithotripsy (ESWL) Technique

According to the patient's age, size, and location of the stones, a JJ stent was inserted in chosen patients scheduled for combination treatment with ESWL during URS. During the ESWL session, general anesthesia was delivered to the pediatric patients involved in the study who underwent URS in conjunction with ESWL. The Electromagnetic Shock Wave Lithotripter (ELMED Multimed Classic) was employed for lithotripsy. Fluoroscopy was employed to ascertain the position and breakup of the stone during lithotripsy. The supplied shock wave commenced at 13-14 kV and was elevated to a maximum power level of 20 kV. The highest number of shocks administered per session ranged from 5000 to 5500 beats. The ESWL session concluded when the stone shattered to an acceptable size, no visible stone persisted, or sufficient shocks were administered. The patients underwent follow-up with a plain abdomen X-ray and ultrasound. The JJ stent was extracted one-month post-ESWL session. Postoperative data included age, gender, stone-free rates, and the presence of hydronephrosis.

The Retrograde Intrarenal Surgery (RIRS) Technique

A semirigid 4.5 Fr ureterorenoscope (URS) (Richard Wolf, Germany) was introduced into the pelvicalyceal system under general anesthesia while the patient was in the lithotomy posture. A 0.038 hydrophilic guidewire was first placed. A JJ stent was inserted when access to the upper urinary tract via URS was unachievable, when a stone in the proximal ureter was inaccessible when a stone in the proximal ureter or the reachable pelvicalyceal tract was displaced to the lower pole during laser lithotripsy, when the procedure duration overtook one hour without complete fragmentation of the stone, and when edema likely to induce ureteral obstruction had been expected. Following three weeks, the patients had re-evaluation via ultrasound, the JJ stent was removed, and a second session of retrograde intrarenal surgery (RIRC) was scheduled. In every instance, the pelvicaliceal system was accessed using semirigid or flexible ureteroscopes under general anesthesia. Lithotripsy was conducted utilizing Holmium laser lithotripsy (30 W, Sphinx) with a 365 nm laser probe (Accu Max, Boston, USA), applying suitable power and frequency until the stone was entirely fragmented or diminished to a size amenable to drainage. A JJ stent was reinserted post-procedure due to edema, suspected injury from an enclaved stone, and potential obstruction from a fragmented stone. The stent was extracted within one month.

The Open Surgery Technique

Pediatric patients scheduled for open surgery owing to urinary system stones were selected based on the presence of renal structural defects, significant stone burden, and prior unsuccessful minimally invasive procedures. The case was sterilely stained and draped suitably under general anesthesia. A flank incision was

performed using blunt dissection to access the right/left external oblique muscle, internal oblique muscle, transverse abdominal muscle, and fascia, according to the stone's position. The retroperitoneal space was accessed. The renal pelvis and ureter were identified and elevated. Subsequently, pyelolithotomy, nephrolithotomy, or ureterolithotomy was executed. A JJ stent was inserted following the removal of the stone(s). The JJ stent was extracted after one month. The patients underwent follow-up with simple abdominal X-ray and ultrasound imaging. The postoperative data reported were age, gender, stone clearance rate, and the occurrence of hydronephrosis.

The Laparoscopic Surgery Technique

Laparoscopic surgery may be favored in expert clinics for its minimally invasive nature in a specific patient group initially designated for open surgery. Pediatric cases were subjected to sterile staining and managed under general anesthesia. Laparoscopic pyelolithotomy (LPL) was conducted under general anesthesia in the right or left lateral decubitus posture, contingent upon the side of the kidney stone. A 5-mm port was introduced into the umbilicus via the open-access technique. Subsequently, two 5-mm working ports were introduced under direct visualization along the midclavicular line, parallel to the umbilicus, and 5 cm inferior to the umbilicus in the para-rectal area. Following the establishment of the pneumoperitoneum, the colon was medially mobilized by locating and incising the line of Toldt. Upon identification of the ureter and renal pelvis, the pelvis and ureteropelvic junction were revealed. Following the ureterostomy or pyelotomy incision, the calculi were removed utilizing a laparoscopic grasper. A double-J stent was subsequently inserted antegradely into the bladder. The pelvis was sutured closed using running stitches with 5/0 or 6/0 polyglactin. A drain was not inserted, and the Foley catheter was extracted three days later. The Double J stent was extracted four weeks post-operation.

Patients in the groups underwent plain abdominal radiography and ultrasonography at regular intervals for a minimum duration of one year. Children without stones or with stones measuring less than 4 mm on simple abdominal radiography or ultrasound were considered stone-free. Follow-up intervals were established based on the imaging conducted during the initial month. Patients clear of calculi on simple abdominal radiography or ultrasound were monitored at six-month or year intervals. Patients with stones measuring less than 5 mm were monitored at three-month intervals. In patients with stones above 5 mm, the follow-up or suitable treatment technique was determined based on the location and dimensions of the stone(s).

Statistical analysis

Continuous data are given as mean ± standard deviation. Categorical data is given as a percentage (%). Shapiro Wilk's test was used to investigate the suitability of data for normal distribution. In the comparison of groups with normal distribution, one-way variance analysis (one-way ANOVA) was used for cases with three or more groups. Pearson Chi-Square and Pearson exact Chi-Square analyses were used in the analysis of the created cross-tables. IBM SPSS Statistics 21.0 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.). A value of $p<0.05$ was accepted as a criterion for statistical significance

Results

A total of 302 pediatric patients were included in this study. This study categorized patients into four groups: Group 1, the URS group without JJ stent; Group 2, the URS group with JJ stent; Group 3, patients who underwent ESWL combined with URS; and Group 4, patients who underwent open or laparoscopic surgery combined with URS. Demographic characteristics, stone size, side, position, stone-free rates, and postoperative hydronephrosis status of the patients according to the groups are reported in Table 1.

For all the patients in the study, the average age of the patients was 89.719 months (Standard deviation: 51.447, range 6–216). Statistical analysis showed a significant correlation between group age and outcome variables ($p=0.010$). This was attributed to the inherent challenges associated with the use of RIRS and ESWL procedures, particularly in cases of obstructive stone formation, and was observed to be more pronounced with decreasing patient age. Our results demonstrate the efficacy of open surgical and laparoscopic techniques, which offer a minimally invasive alternative, as adjunctive approaches in the management of patients with multiple obstructive stones and hard stones such as cystine stones.

Of the patients included in the study, 160 (53%) were male and 142 (47%) were female. Although there was no difference between the groups in terms of gender, it was found that male patients constituted a significantly larger proportion of those who underwent open or laparoscopic surgery. However, the number of patients in the group was small, which limits the reliability of this finding. In consideration of the anatomical challenges specific to the male gender, it may be necessary to supplement the RIRS technique with auxiliary techniques. It was hypothesized that male patients were more prevalent in laparoscopic and open surgical techniques for this reason.

Table 1. Demographic data, stone dimensions, stone characteristics, stone-free rates, and postoperative hydronephrosis status of patients categorized by groups (n=Number of patients, n*=Number of stones)Table 1. Demographic data, stone dimensions, stone characteristics, stone free rates, and postoperative hydronephrosis status of patients categorized by groups (n: number of patients, n*: number of stones)

URS			URS&ESWL	URS & Open/ Laparoscopic Surgery	p	
		JJ stentfree n=49 (16.23 %)	JJ stent n=185 (61.25%)	n=57 (18.87 %)	n=11 (3.65 %)	
Age (month)	**Mean±SD**	90.351±52.234	95.898±54.004	92.263±45.045	39.909±37.176	0.010
Gender	**Female n (%)**	27 (55.10)	83 (44.87)	31 (54.39)	2 (18.18)	0.089
	Male n (%)	22 (44.90)	102 (55.13)	26 (45.61)	9 (81.82)	
Stone size		7.92±3.17	7.50±2.70	11.24±3.27	11.75±3.86	<0.001
Stone side	**Right n* (%)**	36 (8.80)	116 (28.36)	32 (7.83)	10 (2.45)	0.993
	Left n* (%)	27 (6.60)	131 (32.03)	46 (11.24)	11 (2.69)	
Stone-free rate	**n (%)**	44 (89.80)	167 (90.27)	43 (75.44)	7(63.64)	<0.001
Hydronephrosis	**None n (%)**	46 (15.23)	168 (55.62)	54 (17.88)	9 (2.98)	0.457
	Continued n (%)	3 (0.99)	17 (5.62)	3 (0.99)	2 (0.66)	

Table 2. Stone-free rates based on stone localization in groups (n: number of stones)

	URS		URS & ESWL	URS & Open/ Laparoscopic Surgery
	JJ stent-free n=63	JJ stent n=247	n=78	n=21
Lower pole	2	19	9	
Pelvis renalis	3	26	38	6
Ureteropelvic junction	5	52	6	5
Distal ureter	29	80	6	1
Ureterovesical junction	16	40	1	
Stone-free rates n (%)	55 (87.30)	217 (87.85)	60 (76.92)	12 (57.14)

A standard abdomen X-ray was conducted in 299 instances involving urinary system calculi. Stones were identified as non-opaque in 95 (30.46%) instances and opaque in 202 (66.89%) instances (p<0.01). Urinary system stones were identified in 25 instances (8.25%) with non-contrast abdomen CT (p<0.001). Diagnostic ultrasound of the urinary system was conducted in 284 patients (94.03%) (p<0.001). Given that the patients were children, efforts were made to minimize the dose of ionizing radiation. However, in selected cases, a non-contrast abdominal CT was performed to visualize the location, size, and even the presence of the stone.

The average size of the treated stones was 7.964 mm (SD 3.516, range 2.2-25 mm). Patients who underwent open or laparoscopic surgery had significantly larger stone sizes compared to the other groups (p<0.001). In our opinion, these techniques should not be forgotten as an additional treatment modality for difficult and big stones when age and gender are taken into account.

Radiological scans revealed the presence of stones in 409 renal units. The lateral distribution of stones was 194 (47.43%) on the right and 215 (52.57%) on the left. There was no difference between the groups in terms of the side of the stone. We have shown that the techniques can be applied regardless of the side. The three sites with the highest incidence of stones were the distal ureter, ureteropelvic junction, and lower pole of the kidney, respectively.

Stone-free rates were attained in 262 (86.75%) of the patients throughout surgical follow-up. Stone-free rates based on stone localization in the groups are shown in Table 2. The RIRS method, whether used alone or in conjunction with ESWL, represents a viable option for the treatment of urolithiasis in children. While open and laparoscopic surgeries are not the preferred approaches in the majority of cases, they may be considered in patients who have not responded

to these stone-directed techniques, particularly in younger patients with large, tissue-inclusive, and multiple stones. In instances where the desired stone-free rates cannot be achieved with these surgical techniques, surgical intervention can be continued with RIRS.

Imaging revealed no stones in 235 patients (77.81%). During the follow-up, it was noted that hydronephrosis fully resolved in 278 (92.05%) individuals. The result of no difference between the groups in terms of regression of hydronephrosis indicates that rapid intervention in stone-related obstruction is a crucial factor in maintaining renal health.

Discussion

The advantages of minimally invasive techniques for the treatment of urolithiasis in children have been widely reviewed in the literature, especially with new technological developments (8-10). However, while age is an important advantage in some techniques, it is a disadvantage in others. Notably, several significant disadvantages are identified in the studies. Access to RIRS is challenging due to the narrow caliber of ureters, particularly in young children. In instances where access is unavailable, the ureter remains narrow at the ureteral orifice iliac vessels, or ureteropelvic junction. The dilatation of a narrow ureteric orifice may result in ureteral ischemia, perforation, vesicoureteric reflux, and stricture formation. (11-12). A study reported that ESWL was more successful in young children. The author also found that age was the only independent predictor of surgical success when multivariate analysis was performed (13). It can be used as a combined treatment modality for stones that cannot be reached by RIRS. Open surgery has been used for many years to treat urinary system stones, but its indications are limited even in guidelines. Experience with laparoscopy has also increased among surgeons and it has become the preferred alternative to open surgery (14). The smaller instruments of modern laparoscopy have made this procedure a good alternative for the treatment of urolithiasis in children. Endoscopic and laparoscopic techniques can be combined under guidance to ensure successful treatment. Laparoscopy enables the surgeon to examine the entire collecting system and to fragment and remove all stones in a single surgical procedure (15). By the findings of previous studies, our investigation revealed that age may be a determining factor in the selection of surgical techniques. It is important to note that laparoscopic surgery can be employed as an alternative approach in cases where RIRS, either as a standalone procedure or in conjunction with other techniques, has proven ineffective in the management of urolithiasis, particularly in younger patients.

The findings revealed that male patients were significantly more prevalent in the group that underwent open or laparoscopic surgery. However, the limited sample size of the patient group limits the reliability of this finding. Given the anatomical difficulties specific to the male gender, it can be hypothesized that the RIRS technique can be supported by auxiliary techniques, particularly in younger and more complex cases. However, there is insufficient data in the literature to support this hypothesis.

The size and location of the stone are crucial factors in determining the optimal surgical technique. In the literature, RIRS is recommended as a treatment option for upper ureter and renal stones measuring ≤2 cm (16). ESWL is the recommended initial treatment for pediatric renal stones with a diameter of 1.0 cm, irrespective of the Hounsfield unit (HU) value. Furthermore, ESWL is also indicated for renal stones other than those situated in the lower calyx with a HU value of 750 and a diameter between 1.0 and 2.0 cm. ESWL may also be the preferred initial treatment for renal stones with a diameter of 1.5 cm located in the upper ureter (17, 18). The EAU guidelines strongly advise that the indications for open surgery should be limited to the cases where the child is very young, large stones are present, congenital problems require surgical correction, and/or the presence of severe orthopedic deformities that cannot be positioned for endoscopic procedures (19). Furthermore, the EAU guidelines published in 2021 indicated that laparoscopic or robot-assisted surgery may be a potential option for children with complex renal anatomy (retrorenal or ectopic colon), UPJO or calice diverticulum, megaureter, or a history of endoscopic surgical failure. As previously documented, laparoscopic pyelolithotomy has been demonstrated to achieve a 100% stone-free rate in the treatment of a single stone measuring ≥1 cm in the extrarenal pelvis or ureteric stones refractory to ESWL or RIRS (20). The present study revealed that surgical techniques varied according to the size and location of the stone, a finding that is consistent with the literature. While RIRS and ESWL are two effective stone treatment modalities, it is important to note that laparoscopy also has a role in complex cases and challenging stones.

The literature provides numerous examples of studies evaluating the stone-free success of various methods applied in the treatment of urinary system stones. In a study conducted by Resorlu et al., 84% of children who underwent RIRS achieved a stone-free rate (21). In a study by Demirkesen et al., a stone-free rate of up to 90% was demonstrated in both localisations with ESWL in stones located in the renal pelvis and upper ureter (22). Gupta et al. evaluated the laparoscopic technique and reported a stone-free

rate of 79% with the laparoscopic approach alone (23). Zargooshi reported that 310 children underwent open surgery for the treatment of kidney stones, with a total postoperative stone-free rate of 95.4% (24). The results of our study align with those of previous research, indicating that RIRS and ESWL techniques result in a higher stone-free rate compared to open and laparoscopic techniques. This demonstrates the efficacy of minimally invasive techniques in achieving a stone-free rate. Consequently, these techniques should be the preferred approach for the management of urinary tract stones in children.

The retrospective nature of the study, the unavailability of all requested data from the patients, and the limited number of patients in the open and laparoscopic surgery group represent the limitations of this study. The results of open and laparoscopic surgery performed within limited indications can be obtained with multicentre studies, which provide a more comprehensive overview of the subject matter.

Conclusion

In conclusion, the study was conducted to evaluate the most appropriate techniques for the management of urinary tract stones in children, taking into account the specific clinical circumstances. It is important to note that open and laparoscopic surgical techniques, which have become less prevalent in recent years, should not be overlooked as potential adjunctive procedures in complex cases and challenging stones when indicated. The findings of this study suggest that these techniques, particularly when combined with RIRS, may offer a viable solution in challenging cases.

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ORIGINAL ARTICLE

Is Serum Troponin-I Evaluation Necessary in Pediatric Emergency Departments? A Single-Center Experience

Çocuk Acil Servislerinde Serum Troponin-I Değerlendirilmesi Gerekli mi? Tek Merkez Deneyimi

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ABSTRACT

Aim: Troponin, a structural protein of myocardial cells, is frequently used as an indicator of adult cardiac injury, but there are no established guidelines for its routine use in pediatric clinical practice. In this study, we aimed to retrospectively evaluate the demographic characteristics, symptoms, and follow-up results of patients who applied to the pediatric emergency service with various clinical complaints and requested troponin levels, and the role of serum troponin levels in diagnosis.
Materials and Methods: We retrospectively analyzed the demographic characteristics, symptoms, and follow-ups of patients aged one month to 18 years, admitted to our pediatric emergency department, and requiring troponin levels over two years.
Results: Out of the 1890 patients included in the study, 50.9% were female, and their mean age was 12.36±4.32 years. The most common reasons for requesting cardiac troponin were chest pain (59.1%), poisoning (10%), palpitations (8.3%), and syncope (7%). Only 55 (2.9%) of the cardiac troponin tests were found to be elevated based on the normal reference range. Among the patients with elevated troponin levels, chest pain was the most frequently observed complaint (n=29, 52.7%). On further examination, five patients were diagnosed with myocarditis and two patients with multisystem inflammatory syndrome (MIS-C), while the most common noncardiac cause of troponin elevation was carbon monoxide poisoning.
Conclusions: Performing troponin tests in patients with suspected cardiac pathology based on their medical history, physical examination, and electrocardiography is necessary to reduce unnecessary testing and costs. Additionally, interpreting troponin levels should take into account the patient's overall clinical evaluation.

Keywords: Cardiac, Child, Pediatric emergency medicine, Troponin

ÖZ

Amaç: Miyokardiyal hücrelerin yapısal bir proteini olan troponin, erişkin kardiyak hasarın bir göstergesi olarak sıklıkla kullanılmasına rağmen, pediatrik hasta klinik uygulamalarında rutin kullanımı için belirlenmiş bir kılavuz yoktur. Bu çalışmada çocuk acil servisine çeşitli klinik şikayetlerle başvuran ve troponin düzeyi istenen hastaların demografik özellikleri, semptomları ve takip sonuçları ile serum troponin düzeylerinin tanıdaki rolünü retrospektif olarak değerlendirmeyi amaçladık.
Yöntemler: İki yıllık sürede çocuk acil servisimize başvuran ve troponin düzeyi istenen 1 ay-18 yaş arası hastaların demografik özellikleri, semptomları, tetkikleri ve takipleri retrospektif olarak incelendi.
Bulgular: Çalışmaya alınan 1890 hastanın %50,9'u kız ve yaş ortalamaları 12,36±4,32 yıl idi. En sık kardiyak troponin isteme nedenleri göğüs ağrısı (%59,1), zehirlenme (%10), çarpıntı (%8,3) ve senkop (%7) idi. Kardiyak troponin testi sadece 55'inde (%2,9) normal referans aralığına göre yüksek bulunmuştur. Troponin düzeyi yüksek olan hastalarda en sık görülen yakınma göğüs ağrısıydı (n=29, %52,7). İleri incelemede beş hastaya miyokardit ve iki hastaya multisistem inflamatuar sendromu (MIS) tanısı konulurken, troponin yüksekliğinin en yaygın kardiyak olmayan nedeni karbon monoksit zehirlenmesiydi.
Sonuçlar: Tıbbi öykü, fizik muayene ve elektrokardiyografi ile kardiyak patoloji şüphesi olan hastalarda troponin testi yapılması gereksiz tetkik ve maliyetleri azaltmak için gereklidir. Ek olarak, troponin düzeylerinin yorumlanmasında hastanın genel klinik değerlendirmesi dikkate alınmalıdır.

Anahtar kelimeler: Çocuk, çocuk acil, kardiyak, troponin

Introduction

Troponin is found in the structure of myofibrils in the myocardial cell and is a biomarker with high specificity and sensitivity for determining myocardial damage (1). If myocardial cells are damaged by acute ischemia or another mechanism, these proteins are released into the bloodstream. In adults, myocardial damage typically develops due to ischemia due to coronary artery disease, while in children, myocardial damage can occur due to a variety of etiologies, both cardiac and non-cardiac. As a result, myocardial damage occurs due to ischemic or non-ischemic causes (myocarditis, arrhythmia, trauma, poisoning, hypoxia, hypotension, sepsis, etc.), and troponin levels increase (2,3). However, in some cases, the causes of high (positive) troponin levels may not be explained even after careful clinical evaluation and exclusion of all possible pathologies that could cause myocardial cell damage (4). Although chest pain is a common reason for hospital visits during childhood, cardiac causes play a minor role in its etiology. It has been shown that cardiac causes such as congenital and acquired heart diseases (including arrhythmias, cardiomyopathies, rheumatic

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heart diseases, and coronary artery abnormalities) account for only 0-15% of all causes of chest pain (5,6).

Non-cardiac chest pain can often be attributed to musculoskeletal, gastrointestinal, respiratory, psychogenic, and idiopathic reasons. Due to these differences in etiology, the approach to chest pain with elevated troponin levels should differ between children and adults. However, it has been shown that pediatricians tend to unnecessarily request troponin tests and/or recommend referral to pediatric cardiology due to insufficient knowledge on this subject or parental concerns (6). Therefore, it is essential to be aware of the reasons for elevated cardiac troponin levels in children and to plan follow-up and treatment accordingly.

This study aimed to determine the reasons for requesting troponin in the pediatric emergency clinic of our hospital and the frequency of patients with high troponin levels, to determine the diagnoses and to evaluate the diagnostic efficiency of troponin examination.

Material and Method

Study design

In our study, we retrospectively reviewed the files of patients aged 1 month to 18 years who presented to the Pediatric Emergency Department of Gülhane Training and Research Hospital at Health Sciences University and had cardiac troponin tests requested between January 2019 and December 2020.

Patients under the age of one month and over the age of 18 years, those with missing information in their files, and trauma patients evaluated by the adult emergency department were excluded from the study.

Data collection

A list of patients who had cardiac troponin tests requested was obtained from the laboratory records, and the patients' files were retrieved from the Hospital Registration System. The patient's age, gender, month of presentation, symptoms, cardiac troponin level, electrocardiogram (ECG) results, cardiology consultation results, diagnosis, and follow-up status were recorded. Those with repeated test requests in the same presentation were included in the study.

Cardiac troponin-I tests were performed in our hospital using the Beckman Coulter DXI 800 hormone auto-analyzer (electrochemiluminescence immunoassay method-ELISA). The normal reference range for troponin-I, according to the kits used, was 0-19 pg/mL. The findings of ECG were evaluated for rate, rhythm, presence of pathological waves, and ST-segment elevation/depression.

Statistical evaluation

The Statistical Package for Social Sciences for Windows, version 23.0 (SPSS Inc., Chicago, IL, USA) software was used for the data analysis. Descriptive analyses were used to determine the mean and standard deviations of the demographic and clinical data of the patients. The frequency data were presented as numbers and percentages. The normal distribution of the data was checked using the Kolmogorov-Smirnov test.

Ethical considerations

Approval was obtained from the University of Health Sciences Gülhane Training and Research Hospital Clinical Research Ethics Committee (2021-343) and the Medical Specialization Training Board for the collection of data.

Results

In the study, a total of 2040 cardiac troponin tests were requested for 1890 patients. Of these patients, 50.9% were female, and the mean age was 12.36±4.32 years. The most frequent time of presentation was during the winter season (37.2%), with December being the most common month for hospital visits (13.5%).

The reasons for requesting cardiac troponin tests were ranked as follows: chest pain (59.1%), poisoning (10%), palpitations (8.3%), syncope (7%), shortness of breath (6.3%), and gastrointestinal complaints (4.8%).

Among the poisoning cases, 81 patients had taken medication, 70 patients experienced carbon monoxide poisoning, and 27 patients had other poisonings (e.g., thinner, disinfectant, acetone, lighter fluid, bleach, detergent, lime solvent, grease remover, polish, and gasoline ingestion; tear gas and pepper spray inhalation; substance abuse), and 11 patients had alcohol poisoning. The characteristics of the patients evaluated for cardiac troponin are presented in Table 1.

The mean of troponin levels were 33.32±455.12 pg/mL in patients with chest pain, 7.35±49.61 pg/mL in non-carbon monoxide poisoning, 26.88±83.55 pg/mL in carbon monoxide poisoning, 5.34±22.10 pg/mL in patients with palpitations, 14.39±73.35 pg/mL in patients with syncope, 3.44±10.59 pg/mL in patients

with shortness of breath, and 2.30±3.82 pg/mL in patients with gastrointestinal complaints.

Table 1. Characteristics of pediatric patients evaluated for cardiac troponin

Age (years), mean±SD	**12.36±4.32 (One month-17 years)**
Gender Female	962 (50.9%)
Male	928 (49.1%)
Admission season Winter	705 (37.3%)
Spring	307 (16.2%)
Summer	344 (18.2%)
Autumn	534 (28.3%)
Signs and symptoms on admission Chest pain	1117 (59.1%)
Poisonings	189 (10%)
Palpitation	156 (8.3%)
Syncope	133 (7%)
Shortness of breath	119 (6.3%)
Gastrointestinal complaints	90 (4.8%)
Other reasons*	85 (4.5%)
Fever	82 (4.3%)
Change of consciousness	31 (1.6%)
Electrical shock	6 (0.3%)
Follow-up Outpatient treatment	1190
Emergency monitoring	688
Children's polyclinic service	10
Intensive care	2

*Other reasons: Arm pain, arm numbness, back pain, joint pain, scorpion sting, tick bite, weakness, myalgia, general condition disorder, SD: Standard deviation

According to the kits used in our hospital, the normal reference range for troponin-I was 0-19 pg/mL. Based on these values, serum cardiac troponin levels were high in 55 patients (2.9%). Of these patients, 29 (52.7%) had chest pain, 13 (23.6%) had carbon monoxide poisoning, five (9.1%) had syncope, four (7.3%) had palpitations, and two (3.6%) had multisystem inflammatory syndrome (MIS-C) due to SARS-CoV-2 (COVID-19) infection. Patients with high troponin levels are shown in Table 2.

Table 2. Patients with elevated cardiac troponin

Complaints	**n=55 (%)**
Chest pain	29 (52.7%)
Carbon monoxide poisoning	13 (23.6%)
Syncope	5 (9.1%)
Palpitation	4 (7.3%)
Multisystem inflammatory syndrome due to COVID-19	2 (3.6%)
Alcohol poisoning	1 (1.8%)
Electrical shock	1 (1.8%)

COVID-19: Sars CoV-2 virus

Cardiac troponin tests were repeated in 115 patients during the same presentation for control purposes. The most common reasons for repeating the troponin test were chest pain (52 patients), carbon monoxide poisoning (22 patients), and drug and other poisonings (18 patients).

Out of the patients with elevated troponin levels, 40 (72.7%) had a normal sinus rhythm reported in their ECGs. Pathological findings were detected in the ECGs of 15 patients, including sinus tachycardia, ST elevation, ST depression, and supraventricular tachycardia.

Among the patients with evaluated troponin levels, 110 were referred for consultation with pediatric cardiology. Echocardiography results were normal in 105 patients, and 5 patients were diagnosed with myocarditis.

The characteristics of patients with heart pathology are presented in Table 3. Of the patients, 688 were kept under observation in the emergency department, 10 were followed in the pediatric ward (Myopericarditis in five patients, poisoning in three patients, fever due to upper respiratory tract infection in one patient, and supraventricular tachycardia in one patient) and two were transferred to the intensive care unit (ICU).

Discussion

The study found that various non-cardiac and cardiac diseases can lead to elevated troponin levels in children. Therefore, these patients must be evaluated through medical history in the first step and examined with electrocardiography and echocardiography in the second step. However, the progression and degree

Table 3. Characteristics of patients with elevated troponin and cardiac pathology

Age/Gender	Complaint	Troponin level (pg/mL)	Echocardiography	Diagnosis	Setting of Follow-up
16-year-old Males	Chest pain	1035	Compatible with myopericarditis	Myopericarditis	Service
15-year-old Males	Chest pain	2604	Compatible with myocarditis	Myocarditis	Service
14-year-old Females	Syncope, Chest pain	296	Compatible with myopericarditis	Myopericarditis	Service
17-year-old Females	Chest pain, shortness of breath	1229	Compatible with myocarditis	Myocarditis	Service
12-year-old Males	Fever, general condition disorder	321	Pleural Pericardial Effusion	MIS-C	ICU Referral
10-year-old Males	Fever, abdominal pain	33.9	None	MIS-C	ICU Referral
11-year-old Males	Chest pain	376	Compatible with myocarditis	Myocarditis	Service
5-year-old Males	Palpitation	29.7	Normal	Supraventricular tachycardia	Service

ICU: Intensive care unit, MIS-C: Multisystem inflammatory syndrom

of troponin elevation may not always help determine the underlying cause of myocardial damage in children, and even in the presence of heart disease in children, the clinical significance of this test is still controversial (7).

In our study, elevated troponin levels were found in 55 patients (2.9%). A multicenter study has shown that 12% of patients who underwent troponin level evaluation had elevated levels, and Dionne et al. reported this figure as 9.1% (7,8). Another study conducted in Turkey found the cardiac troponin elevation rate as 1.2% (9). In this study, the most common reason for requesting cardiac troponin tests was chest pain (59.1%). Similarly, in the study conducted by Akça et al., 40.7% of patients whose cardiac troponin levels were evaluated had complaints of chest pain (8). Chest pain is a concerning symptom for both the patient and their family in children, but its etiology is often non-cardiac (10-12). Cardiac causes of chest pain may include myocarditis, pericarditis, arrhythmia, rheumatic valve disease, cardiomyopathy, abnormal coronary artery, mitral valve prolapse, and Kawasaki disease. Cardiac-related chest pain is usually described as a feeling of pressure in the precordial region and may radiate to the arm and shoulder. Sweating, nausea, dizziness, palpitations, dyspnea, or syncope may also accompany chest pain (13). In cases of chest pain, cardiac troponin levels are often evaluated; however, the benefit of troponin testing in children is debatable. Troponin testing may be useful in children with chest pain, but it may also lead to over-testing due to its limited usefulness (14-16). Studies have found elevated troponin in less than 5% of children with chest pain (8,17,18). Akça et al. reported that elevated troponin levels were present in 1.5% of 1028 children with chest pain (9). In the study in which 212 pediatric patients with chest pain were evaluated, it was found that troponin levels were elevated in 17% of the patients, and cardiac cause was found in 18 patients (14). In a study conducted in our country, it was observed that the majority of patients with elevated troponin levels due to cardiac reasons presented with chest pain (19). In our study, similar to the literature, troponin elevation was detected in 29 (2.59%) of the patients who applied with complaints of chest pain, and 5 of these patients (17.2%) were diagnosed with cardiac pathology. There are no clear clinical recommendations regarding the use of troponin assessment in patients presenting with chest pain. Prospective studies are needed to demonstrate the benefits of troponin assessment

Hospital admissions due to poisoning are most commonly observed in emergency services. Cardiac effects such as arrhythmia, hypotension, and myocardial damage can result from drug or toxic agent-related poisoning, leading to elevated troponin levels. In our study, patients who presented with

poisoning were the second most frequent group to have been requested for cardiac troponin evaluation. Among these patients, the majority were those who presented with carbon monoxide poisoning (CO). Carbon monoxide is a cardiotoxic gas that affects oxygen delivery, particularly in tissues sensitive to hypoxia like the heart, leading to myocardial injury. Studies have shown that Troponin I levels increase in CO poisoning cases (20,21). In the study by Terlemez et al., CO poisoning was detected in 34.5% of children with troponin elevation (22). In our study, 13 patients (18.6%) with troponin elevation had CO poisoning. One of these patients had ST elevation on the ECG but had a normal echocardiogram. No pathological findings were observed on the ECG of other patients. Among the 11 patients who presented with alcohol poisoning, one had troponin elevation, and a regression in troponin levels was observed during their follow-ups. Cardiac troponin and ECG evaluation are necessary for children who present to the pediatric emergency department with carbon monoxide and alcohol poisoning. Cardiac effects and troponin levels may vary depending on the amount and duration of exposure.

There can be several causes for palpitations, and patients with these symptoms often seek care in the pediatric emergency department. In a study conducted in our country, it was found that 4% of patients having troponin levels checked applied to the pediatric emergency department with complaints of palpitations (9). In our study, 8.3% of patients with troponin evaluation had palpitations. Myocardial ischemia occurs due to decreased coronary perfusion and oxygen delivery due to tachycardia. Among these patients, troponin elevation was observed in 4 cases, and one of these patients was diagnosed with supraventricular tachycardia. Troponin evaluation was found to have a low predictive value in patients presenting to the pediatric emergency department with supraventricular tachycardia (23). This suggests that elevated troponin may not be detected in every patient with tachycardia.

Syncope is characterized by a sudden and brief loss of consciousness and postural tone. The causes of syncope are generally non-cardiac, but cardiac-related causes can be life-threatening. Syncope can occur in several medical conditions such as arrhythmias, myocarditis, myopericarditis, and cardiomyopathy, which lead to decreased cardiac output and cerebral perfusion (24,25). Among the patients who presented with syncope and underwent troponin evaluation, 5 of them had elevated troponin levels, and two patients were diagnosed with myocarditis. It has been determined that 5-7% of children diagnosed with myocarditis present with syncope. Patients presenting with syncope should be carefully evaluated from a cardiac perspective (26). A detailed history, physical examination, and ECG can help establish a diagnosis for many patients presenting with syncope in the pediatric emergency department. Patients suspected of having cardiac pathology should undergo troponin and cardiology evaluation.

Medical conditions like systemic inflammatory response syndrome, sepsis, septic shock, hypotension, and hypovolemia can lead to troponin elevation due to circulatory disturbances. The shortened diastolic time of the heart due to tachycardia, an early sign of shock, results in reduced coronary perfusion and myocardial ischemia. MIS-C associated with COVID-19 infection is associated with myocarditis, valve insufficiency, and reduced cardiac function in previously healthy children. Troponin elevation in children diagnosed with MIS-C is linked to myocarditis and shock syndromes (27,28). In our study, two patients with COVID-19-associated MIS-C had elevated troponin levels and were referred to an ICU.

Electrical injuries can cause arrhythmias, direct myocardial damage, or coronary artery spasms. In our study, one out of six children presenting to the pediatric emergency department with electrical injuries had troponin elevation. The ECG of these patients was found to be normal. In a multicenter study evaluating adults and children, elevated troponin levels were determined to be predictive of cardiac injury risk in patients presenting with electric injuries (29). Cardiac evaluation is necessary in children presenting to the pediatric emergency department due to electrical injuries.

Although our study had a large patient sample, it has some limitations. First, we identified the patients retrospectively from the hospital records system. Second, there was no comparison group in our study. Furthermore, we could not evaluate the follow-up results of the patients.

Conclusion

In conclusion, cardiac troponin levels can elevate due to both cardiac and non-cardiac causes. However, even a mild increase in troponin levels in healthy children can lead to unnecessary invasive

and advanced investigations and cause concern for them and their families. If there is suspicion of a cardiac cause based on the patient's symptoms, it would be appropriate to have a detailed medical history, conduct a proper medical examination, and perform an ECG evaluation, followed by consultation with a pediatric cardiology team and planning further investigations if necessary. Elevated levels of cardiac troponin should be evaluated based on the patient's clinical condition.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study

Authors' Contribution Statement

All authors have made substantive contributions to the study, and all authors endorse the data and conclusions.

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ORIGINAL ARTICLE

Do Peripheral Blood Inflammation Indices Differ Among Schizophrenia Patients with Clozapine Treatment? A Cross-sectional Investigation

Klozapin Tedavisi Gören Şizofreni Hastalarında Periferik Kan İnflamasyon İndeksleri Farklılaşır mı? Kesitsel bir Çalışma.

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ABSTRACT

Background/Aims: There remains a need to investigate alternative pathophysiological processes in schizophrenia such as neuroinflam atory processes. We aimed to compare blood count levels, with a particular focus on peripheral blood inflammatory cell levels, among three distinct groups of participants: schizophrenia patients taking clozapine, schizophrenia patients taking antipsychotics other than clozapine, and healthy controls. We also evaluated the relationship between these findings and clinical characteristics
Methods: The SC group included 47, the SA group included 61 patients and the HC group included 65 healthy controls. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and monocyte-lymphocyte ratio (MLR) were calculated by dividing the respective cell counts from white blood cell count (WBC). The relationship between these measures and clinical characteristics are done with the Positive and Negative Syndrome Scale (PANSS).
Results: WBC counts were significantly higher in the SC group than in the SA and HC groups. The log transformed NLR (LnNLR) was significantly higher in the SC group than the HC group and SA group, but there were no difference between the the SA and HC groups. LnNLR was significantly correlated with PANSS positive, general and total scores, but not significantly correlated with PANNS negative score. LnNLR was significantly different between groups after adjusting for age and gender using ANCOVA.
Conclusions: The current study sheds light on the potential immunological alterations associated with schizophrenia and its treatment with clozapine. The elevated NLR in individuals receiving clozapine treatment underscores the need for further research to elucidate the underlying mechanisms and clinical implications of this observation.

Keywords: Schizophrenia, Clozapine, Inflammation, Neutrophil-lymphocyte rati

ÖZ

Amaç: Şizofrenide nöroinflamatuar süreçler gibi alternatif patofizyolojik süreçlerin araştırılması önemlidir. Ayrıca antipsikotik ilaçların inflamatuar etkilerine dair yayınlar mevcuttur. Bu çalışmada, klozapin kullanan (SC) ve kullanmayan (SA) şizofreni hastalarını ve sağlıklı kişileri (HC), periferik kan inflamatuar indeksleri açısından karşılaştırmayı ve klinik özellikler ile ilişkilerini araştırmayı amaçladık
Gereç ve Yöntem: SC grubunda 47, SA grubunda 61 hasta ve HC grubunda 65 sağlıklı kontrol yer aldı. Nötrofil-lenfosit oranı (NLR), trombosit-lenfosit oranı (PLR) ve monosit-lenfosit oranı (MLR), son 6 aydaki tam kan sayımlarından retrospektif olarak taranarak hesaplandı. Bu ölçümler ile klinik özellikler arasındaki ilişki Pozitif ve Negatif Sendrom Ölçeği (PVNSÖ) ile araştırıldı.
Bulgular: Beyaz küre (BK) sayıları SC grubunda, SA ve HC gruplarına göre anlamlı derecede yüksekti. Log dönüştürülmüş NLR (LnNLR), SC grubunda HC grubu ve SA grubuna göre anlamlı derecede yüksekti ancak SA ve HC grupları arasında fark yoktu. LnNLR, PANSS pozitif, genel ve toplam puanlarıyla anlamlı düzeyde korelasyon gösterirken PVNSÖ negatif puanıyla ilişkili bulunmadı. ANCOVA kullanılarak yaş ve cinsiyet etkisi arındırıldıktan sonra LnNLR halen SC grubunda anlamlı olarak yüksek tespit edildi.
Sonuç: Bu çalışmanın sonuçları şizofreni etyolojisinde immünolojik süreçlerin rolüne ve klozapinin periferik kan inflamatuar indeksleri üzerine etkisine ışık tutmaktadır. Retrospektif ve kesitsel dizaynı nedeniyle nedensellik bağı kurulamamıştır, ancak prospektif çalışmalara olan ihtiyacı göstermektedir.

Anahtar kelimeler: Şizofreni, Klozapin, İnflamasyon, Nötrofil-lenfosit ora

Introduction

Schizophrenia is a pervasive mental disorder affecting approximately 1% of the global population. It manifests through a spectrum of symptoms, including positive symptoms (e.g., hallucinations, delusions), negative symptoms (e.g., social withdrawal, apathy), and cognitive impairments. Existing antipsychotic medications that modulate dopamine and serotonin pathways have been effective in managing psychotic symptoms and reducing relapse risk for some individuals with schizophrenia (1). However, there remains a need to investigate alternative treatment approaches that target other neurobiological mechanisms, such as those involving glutamate receptors or neuroinflammatory processes.

Schizophrenia's causes involve a mix of genetic and environmental factors. There is no single theory explaining its neuropathology, but multiple hypotheses have been proposed (2). Many studies have found that

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people with schizophrenia have imbalances in their immune systems compared to healthy people (3). The role of the immune system in the pathogenesis of schizophrenia and related psychotic disorders may have important therapeutic implications. Both the innate and adaptive immune responses may be involved in the pathogenesis of schizophrenia. The innate response involves neutrophils and macrophages, while the adaptive response includes T and B lymphocytes. Inflammation may increase the permeability of the blood-brain barrier, facilitating the entry of immune components into the brain, which, along with genetic studies, suggests an immune-mediated cause of schizophrenia (4, 5). Meta-analyses have shown that schizophrenia is associated with changes in the levels and production of cytokines, proteins that regulate the immune system (6), and patients with schizophrenia show signs of low-grade peripheral inflammation (7)

The neutrophil-lymphocyte ratio (NLR) is a simple, inexpensive, and emerging marker of systemic inflammation that can be used as an indicator in various diseases (8). NLR has been studied concerning schizophrenia in several studies. These studies have found that NLR levels are higher in patients with schizophrenia than in healthy controls (9). One meta-analysis found that an inflammatory activation occurs in psychosis and inflammatory ratios, especially NLR and monocyte-lymphocyte ratio (MLR), but not platelet-lymphocyte ratio (PLR) (10). The association between NLR and schizophrenia suggests that inflammation may play a role in the development or progression of the disorder.

Antipsychotic drugs have been shown to affect the NLR in schizophrenia patients, but the results are conflicting, with some studies reporting an increase and others reporting a decrease (11). Particularly clozapine, has known immunomodulatory effects, including the ability to suppress granulopoiesis and lead to neutropenia or agranulocytosis, though the exact mechanism remains unclear (12). Clozapine can also induce various transient hematologic dysfunctions, including neutropenia, eosinophilia, leukocytosis, and minor changes in the numbers of lymphocytes, monocytes, and basophilic granulocytes (13).

Although the profound effect of clozapine on inflammatory cells, we have found no study assessing differences in peripheral inflammatory markers among schizophrenia patients according to their treatment status with clozapine. Based on this information and the hypothesis that schizophrenia patients whose treatment included clozapine could differ in terms of peripheral blood inflammatory cell levels, we aimed to compare blood count levels among three distinct groups of participants: schizophrenia patients who receive clozapine alone and in combination with other antipsychotics, schizophrenia patients taking antipsychotics other than clozapine, and healthy controls. We also evaluated the relationship between these findings and clinical characteristics.

Methods

Participants

Schizophrenia patients (n:108) who met the following inclusion criteria were consecutively included in the study: They were between the ages of 18 and 65, they were being followed at an outpatient clinic of a community mental health center, they had a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5), and they had been receiving treatment with clozapine or other antipsychotics for at least 6 months. Patients were excluded from the study if they had experienced an exacerbation of psychotic symptoms within the last 6 months, needed hospitalization, or had a well-established affective component or substance use disorder history. These exclusions were made to ensure that the blood count levels were not influenced by recent acute changes in symptom severity.

The healthy control group consisted of people (n:65) between the ages of 18 and 65 who applied to the health board for reasons other than illness, such as obtaining a gun license or a pre-employment health clearance. Persons with a history of medical or psychiatric illness and complaints were excluded from the study. Also, no disease was detected in these individuals during their medical examination and psychiatric evaluation according to the DSM-5 at the same hospital.

We reviewed the medical records of all participants to screen out those with chronic diseases, such as chronic obstructive pulmonary disease, heart disease, blood disorders, neurological conditions, and immune system disorders. These diseases and their medications could have affected the participants' inflammation markers or white blood cell (WBC) count. Therefore, all participants with a history of chronic disease

irrespective of their WBC counts were excluded. We also excluded participants with WBC counts outside the normal range (4-10 x 103/µL).

Data collection

This study used a descriptive, cross-sectional, and retrospective design. A clinician recorded sociodemographic information, including age and gender, for each participant. The severity of schizophrenia was assessed by a senior psychiatrist using the Positive and Negative Syndrome Scale (PANSS), which was developed by Kay, Fiszbein, and Opfer (14). The PANSS is composed of 3 subscales: Positive Scale, Negative Scale, and General Psychopathology Scale. Each subscale is rated with 1 to 7 points ranging from absent to extreme. The validity and reliability of the Turkish version of the PANSS were established by Kostakoglu et al. (15).

The values of WBC, neutrophils (NE), lymphocytes (LY), platelets (PL), and monocytes (MO) were retrospectively collected from digital medical records of participants who had a complete blood count (CBC) available within the last 6 months from the same hospital and biochemistry laboratory. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and monocyte-lymphocyte ratio (MLR) were calculated by dividing the respective cell counts.

Statistical analysis

Data analysis was conducted using SPSS (version 24.0) to describe the demographic and other selected characteristics of the participants. The Kolmogorov–Smirnov test was used to assess the compatibility of data from the groups with normal distribution. The chi-square test was used to compare grouped data, and the Kruskal–Wallis or the one-way analysis of variance (ANOVA) was used to compare three groups. Analysis of covariance (ANCOVA) was used to control for age and gender when looking at group differences. A two-tailed p-value less than 0.05 was considered statistically significant. Significance was set at p=0.05/3 (0.017) for the post-hoc Bonferroni corrected comparisons.

Results

The participants in this study included 47 (27.2%) people with schizophrenia who were treated with only clozapine and/or clozapine with other antipsychotics (SC), 61 (35.3%) people with schizophrenia who were treated with antipsychotics other than clozapine (SA), and 65 (37.5%) healthy controls (HC).

The SC group had a higher percentage of males (74.5%) than the SA group (54.1%) or the HC group (64.6%), but the gender difference was not statistically significant (p=0.09). The average age of the participants in the SC group was 42.44 years, in the SA group was 47.39 years, and in the HC group was 36.81 years. The age difference was statistically significant across all groups (p=0.01). Demographic characteristics and the PANNS) values of the participants are given in Table 1.

Table 1. Characteristics of patients with schizophrenia and healthy comparison subjects.

	SC (n=47)	SA (n=61)	HC (n=65)	Test Statistics	p
Gender					
Male n (%)	35 (74.5)	33 (54.1)	42 (64.6)	4.805	0.09[a]
Female n (%)	12 (25.5)	28 (45.9)	23 (35.4)		
Age (mean ± SD)	42.44 ± 9.97	47.39 ± 11.36	36.81 ± 13.62	12.393	**0.01**[b]
PANNS					
Positive (mean ± SD)	14.42 ± 4.12	9.47 ± 1.59	-	8.589	**0.001**[c]
Negative (mean ± SD)	23.63 ± 4.51	16.70 ± 3.65	-	8.818	**0.001**[c]
General (mean ± SD)	44.55 ± 10.27	33.18 ± 6.88	-	6.878	**0.001**[c]
Total (mean ± SD)	82.62 ± 16.43	59.36 ± 10.64	-	8.897	**0.001**[c]

[a]Chi-Square Test, [b]One-way ANOVA, [c]Student t-test, PANSS: Positive and negative syndrome scale, SC: Schizophrenia patients on clozapine and/or clozapine with other antipsychotics, SA: Schizophrenia patients on non-clozapine antipsychotics, HC: Healthy controls

WBC counts were significantly higher in the SC group than in the SA and HC groups (p=0.001). However, there was no significant difference in WBC counts between the SA and HC groups. Neutrophil counts were also significantly higher in the SC group than in the SA and HC groups (p=0.001). However, there was no significant difference in neutrophil counts between the SA and HC groups. Lymphocyte, monocyte, and platelet levels were not significantly different across all

groups.

To obtain a normal distribution, the NLR, PLR, and MLR values were log-transformed. The log-transformed NLR (LnNLR), log-transformed PLR (LnPLR), and log-transformed MLR (LnMLR) showed no correlation with age (r = 0.076, p = 0.321; r = 0.080, p = 0.293; r = 0.053, p = 0.485, respectively). Gender was weakly correlated with LnPLR (r = -0.158, p = 0.038) and age (r = -0.239, p = 0.002), with women tending to be older and have higher LnPLR values. Gender was not correlated with LnNLR and LnMLR. Additionally, LnNLR was strongly correlated with LnPLR (r = 0.687, p = 0.001) and LnMLR (r = 0.704, p = 0.001).

The LnNLR was significantly higher in the SC group than the HC group (p = 0.001) and SA group (p = 0.007), but there was no difference between the SA and HC groups (p = 0.262) in post-hoc analysis, as the p-value was set to 0.017 after multiple comparison correction. There were no statistically significant differences between the groups in terms of the LnPLR or the LnMLR (Table 2).

In the correlation of inflammatory indices with clinical characteristics: LnNLR was significantly correlated with PANSS positive score (r = 0.290, p = 0.002), PANSS general score (r = 0.338, p = 0.001), and PANNS total score (r = 0.308, p = 0.001) but not significantly correlated with PANNS negative score (r = 0.168, p = 0.083). There was no correlation between PANSS scores and LnMLR and LnPLR values.

Table 2. Comparison of peripheral blood count parameters between groups.

	SC	SA	HC	Statistic	p	SC-SA [1]	SC-HC [1]	SA-HC [1]
WBC								
(mean±SD)	8.24 ± 1.35	7.54 ± 1.52	7.14 ± 1.45	7.810*	**0.001**	**0.014**	**0.001**	0.125
Mean rank	108.54	85.71	72.63					
Neutrophil (10^3/ µL)								
(mean±SD)	5.39 ± 1.20	4.42 ± 1.35	4.01 ± 1.04	18518*	**0.001**	**0.001**	**0.001**	0.054
Mean rank	119.66	82.93	67.20					
Lymphocyte (10^3/ µL)								
(mean±SD)	2.26 ± 0.74	2.42± 0.92	2.43 ± 0.58	0.828*	0.439	0.267	0.245	0.969
Mean rank	77.82	89.21	91.56					
Platelet (10^3/ µL)								
(mean±SD)	255.17 ± 59.31	271.88 ± 62.72	262.75 ± 58.88	1.300**	0.522	0.407	0.878	0.786
Mean rank	81.22	92.21	86.28					
Monocyte (10^3/ µL)								
(mean±SD)	0.47 ± 0.14	0.48 ± 0.12	0.46 ± 0.14	2.375**	0.305	0.947	0.942	0.609
Mean rank	87.01	94.09	80.34					
NLR								
LnNLR	0.39 ± 0.20	0.27 ± 0.24	0.21 ± 0.13	11.291*	0.001	0.007	0.001	0.262
Mean rank	114.24	84.26	69.87					
PLR								
LnPLR	2.06 ± 0.18	2.07 ± 0.18	2.03 ± 0.13	0.878*	0.417	0.838	0.340	0.213
Mean rank	87.39	91.20	82.77					
MLR								
LnMLR	0.19 ± 0.02	0.19 ± 0.02	0.13 ± 0.01	1.963*	0.144	0.858	0.087	0.100
Mean rank	92.44	91.59	78.76					

*One-way ANOVA; **Kruskal–Wallis; Bold values are statistically significant findings. (p<0.017), NLR: Neutrophil-lymphocyte ratio; PLR: platelet-lymphocyte ratio; MLR: monocyte-lymphocyte ratio. SC: Schizophrenia patients on clozapine and/or clozapine with other antipsychotics, SA: Schizophrenia patients on non-clozapine antipsychotics, HC: Healthy controls

[1]Two-way comparisons of groups

Finally, levels of LnNLR were significantly different between the three groups after adjusting for age and gender using ANCOVA (F=10.529, p=0.001). The difference between the SA and HC groups was not significant (p=0.438), but the difference between the SC and SA groups (p=0.002) and the SC and HC groups (p=0.007) remained significant after post-hoc analysis

Discussion

The present study has yielded intriguing insights into the potential immunological alterations associated with schizophrenia and its treatment with clozapine. Our main finding was elevated LnNLR levels in the SC group more than SA and HC groups. NLR has been proposed as an indicator of systemic inflammation and immune response, with higher values often associated with poorer clinical outcomes in various medical conditions (16). Our finding aligns with previous studies that have reported increased NLR levels in individuals with schizophrenia more than in healthy controls (17, 18). These studies collectively underscore the disruption of the neutrophil-lymphocyte ratio (NLR) in the context of the disorder, highlighting its potential significance as an immune marker. While the exact mechanisms underlying these alterations remain unclear, they may reflect systemic inflammation or immune dysregulation associated with the disorder and its treatment. Also in first-episode psychosis, there was a tendency toward a higher total WBC count, with significantly increased levels of neutrophils and monocytes compared to controls. These findings suggest that schizophrenia is associated with alterations in blood inflammatory markers, including cytokines in treatment naive individuals (19). Interestingly, the lack of significant differences in LnPLR and LnMLR across the groups suggests that platelet and monocyte counts might not be as prominently influenced by the schizophrenia diagnosis or its treatment.

Although we have found an elevation in the LnNLR in the SC group, the SA group was no different from the HC group. Onder et al. reported increased NLR levels in both chronic schizophrenia and first-episode psychosis (20). Moreover, Sandberg et al., reported that there was a correlation between neutrophil count and NLR with positive symptoms of schizophrenia (11). Additionally, NLR is positively associated with disease severity in drug-free patients (21). The reason for the lack of difference in LnNLR between the SA group and the HC group may be that the patients in the SA group responded better to treatment and were not resistant, and they did not need clozapine treatment before. It is plausible that more treatment-resistant patients under clozapine therapy may exhibit sustained elevated LnNLR levels despite the intervention. In a review, it was concluded that WBC counts could be a feasible biomarker and used to track treatment-resistant schizophrenia patients (22).

Another finding of our study supporting this assumption is that LnNLR was significantly correlated with PANSS scores except for the PANNS negative score. Similarly, Eric et al. have found that higher levels of granulocytosis and lymphopenia in individuals with schizophrenia predicted poorer recovery of positive symptoms after six months of antipsychotic treatment, a relationship that specifically applies to patients with initially significant positive symptoms, while those with primarily negative symptoms have normal leukocyte proportions (23). It is worth noting that, some studies are not in alignment with our findings. In the study by Shen et al., it was found that the correlation between NLR and psychiatric symptoms varied with antipsychotic therapy status, showing a negative correlation between NLR and severe negative symptoms in the drug-therapy subgroup after adjusting for potential confounding factors (24).

Divergent findings are evident in the existing literature regarding the impact of antipsychotic medications on the NLR. For instance, Sandberg et al. suggested that antipsychotic therapy might lead to a reduction in neutrophil count and NLR (11). However, contrasting results emerged from the investigation by Bustan et al., wherein a significant effect of antipsychotic medication on the NLR was not observed (25). No prior research has investigated the NLR specifically among patients undergoing clozapine treatment, despite the robust influence of clozapine on peripheral blood parameters such as agranulocytosis, which is why WBC counts are screened for as a safety measure (12). The present study's outcomes, revealing heightened LnNLR in individuals receiving either clozapine monotherapy or clozapine combined with other antipsychotics, offer an insightful standpoint in this regard. Patients who had suppressed WBC counts such as neutropenia and agranulocytosis were not included in this study. Our finding is interesting in that regard that besides this minority of patients experiencing one of the most dangerous medication side effects of clozapine, the majority of the patients seem to have oppositely elevated neutrophil counts. The findings from the

ANCOVA analysis, which accounted for age and gender, demonstrated that the differences in LnNLR between the groups remained significant. Importantly, the significant differences between the SC and SA groups, as well as between the SC and HC groups, highlight the potential influence of clozapine on immune profiles beyond what can be explained by demographic factors alone. This suggests that clozapine treatment might play a role in shaping immune parameters in individuals with schizophrenia.

Conclusion

In conclusion, the current study sheds light on the potential immunological alterations associated with schizophrenia and its treatment with clozapine. The elevated NLR in individuals receiving clozapine treatment underscores the need for further research to elucidate the underlying mechanisms and clinical implications of this observation. Future studies could explore the longitudinal changes in immune parameters with clozapine treatment, investigate potential links between immune alterations and clinical outcomes, and delve into the molecular pathways that might contribute to the observed differences in neutrophil-lymphocyte balance.

Limitations

The sample size of each group in our study may have limitations in terms of statistical power and generalizability. Our study adopted a cross-sectional design, which inherently limits our ability to establish causal relationships. Longitudinal studies with multiple time points could offer a clearer picture of the dynamic changes in immune parameters throughout treatment and their association with symptomatology. While our findings suggest an association between clozapine treatment and elevated NLR levels, we did not directly assess the specific mechanisms underlying these effects. And, it should be noted that some patients in the SC group were taking antipsychotics other than clozapine. The potential influence of other factors, such as medication dose, treatment duration, and individual variations in drug response warrants further investigation. Although we controlled for age and gender in our analysis, other potential confounding factors, such as smoking and body mass index, were not fully accounted for and HCs were evaluated only by psychiatric and physical examination, and no scale was used.

Ethical approval

It was approved by the institutional ethics committee of an Education and Research Hospital under the Declaration of Helsinki [Protocol No: 27.12.2023-2865].

Informed consent

Since participants' data were collected anonymously, with each participant assigned a protocol number, informed consent was not required.

Conflict of Interest

The authors declare no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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None declared.

Authors' Contributions

All 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

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ORIGINAL ARTICLE

Trimethylamine N-oxide, A Gut Microbiota-dependent Metabolite in Chronic Hepatitis B

Kronik Hepatit B'de Bağırsak Mikrobiyota Bağımlı Bir Metabolit Olan Trimetilamin-N-oksit

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ABSTRACT

Background: Trimethylamine N-oxide (TMAO), a gut microbiota metabolite is produced in the liver from dietary precursors such as choline, betaine, and L-carnitine. TMAO has been linked to inflammatory processes and oxidative stress, both of which are critical factors in the progression of hepatitis. This article aims to examine the impact of TMAO on chronic hepatitis B (CHB).
Materials and Methods: The study included 41 treatment-naïve CHB patients with HBV DNA levels above 2000 IU/mL, as well as 46 age and gender-matched controls. Serum TMAO levels were measured using Liquid Chromatography-Tandem Mass Spectrometry (LC/MS/MS). All statistical analysis was performed with R version 4.2.1.
Results: Patients with CHB have a more significant increase in serum level of TMAO than healthy controls (1860 [IQR, 808 – 2720] vs. 552.5 [IQR, 252 – 876.5], p<0.001). Serum ALT and AST were higher in patients with CHB (p<0.001 and p<0.001). TMAO levels were positively correlated with ALT and AST levels (r=0.466, p<0.001; r=0.376, p<0.001) and had predictive power for CHB with an area under the curve of 0.808.
Conclusions: Our results indicate that there is a link between TMAO, a gut microbiota-dependent metabolite, and CHB disease. Since TMAO is synthesized mainly in the liver, its raised levels may be associated with liver-related diseases.

Keywords: HBV, TMAO, Microbiota, LC/MS/MS

ÖZ

Giriş: Bağırsak mikrobiyota metaboliti olan Trimetilamin-N-oksit (TMAO), kolin, betain ve L-karnitin gibi besin kaynaklarından karaciğerde üretilir. TMAO, hepatit ilerlemesinde kritik faktörler olan inflamatuar süreçler ve oksidatif stres ile ilişkilendirilmiştir. Bu çalışma, TMAO'nun Kronik Hepatit B (KHB) üzerindeki etkisini incelemeyi amaçlamaktadır.
Gereç ve Yöntemler: Çalışmaya, HBV DNA düzeyleri 2000 IU/mL'nin üzerinde olan 41 tedavi-naif KHB hastası ve yaş ve cinsiyet açısından eşleştirilmiş 46 kontrol grubu dahil edilmiştir. Serum TMAO seviyeleri, Likit Kromatografi-Tandem Kütle Spektrometrisi (LC/MS/MS) kullanılarak ölçülmüştür. Tüm istatistiksel analizler R versiyon 4.2.1 ile gerçekleştirilmiştir.
Bulgular: KHB hastalarında serum TMAO düzeyleri, sağlıklı kontrollere göre anlamlı derecede daha yüksekti (1860 [IQR, 808 – 2720] vs. 552.5 [IQR, 252 – 876.5], p<0.001). Serum ALT ve AST düzeyleri KHB hastalarında daha yüksekti (p<0.001 ve p<0.001). TMAO düzeyleri, ALT ve AST seviyeleri ile pozitif korelasyon göstermiştir (r=0.466, p<0.001; r=0.376, p<0.001) ve KHB tanısı için eğri altındaki alan 0.808'di.
Tartışma: Sonuçlarımız, bağırsak mikrobiyota bağımlı bir metabolit olan TMAO ile KHB hastalığı arasında bir bağlantı olduğunu göstermektedir. TMAO esas olarak karaciğerde sentezlendiğinden, artmış seviyeleri karaciğer hastalıklarıyla ilişkili olabilir.

Anahtar Kelimeler: TMAO, Mikrobiyota, HBV, LC/MS/MS

Introduction

Trimethylamine N-oxide (TMAO), an amine oxide compound with the chemical formula (CH3)3NO, is a dietary component that is derived from trimethylamine (TMA) through oxidation (1). TMAO, a gut microbiota metabolite produced in the liver from dietary precursors such as choline, L-carnitine, and betaine by hepatic enzyme flavin-containing monooxygenase-3 (2), has garnered significant attention in recent years for its role in various health conditions such as cardiovascular diseases (3, 4), diabetes (5, 6), chronic kidney disease (7), colorectal cancer (8), and even all-cause mortality (9).

In both in vitro and in vivo studies, TMAO has been shown to exert prooxidative, proinflammatory, and profibrotic effects through the activation of key inflammatory pathways, thereby contributing to various pathological conditions (10-12). TMAO also serves as a piezolyte, providing stability to proteins and nucleic acids (10).

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Evidence from experimental studies suggests that TMAO directly may trigger liver inflammation by interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-a) (13). Oxidative stress arises when the production of reactive oxygen species (ROS) exceeds the body's ability to counteract them with its antioxidant defenses (14). This state of heightened oxidative activity leads to cellular and molecular damage, contributing to inflammation, tissue dysfunction, and disease progression (15). Elevated levels of TMAO have been linked to increased production of ROS, exacerbating oxidative stress, and promoting inflammation (16, 17). Several studies have proven that increased TMAO concentrations can result in endothelial dysfunction in cultured endothelial cells via oxidative stress (18, 19). Thus, TMAO undeniably plays a role in the pathogenesis of chronic inflammation, acting as a pivotal mediator that triggers and sustains inflammatory pathways

Chronic hepatitis B (CHB) is an infection of the liver caused by the hepatitis B virus (HBV) for more than six months, affecting millions of people worldwide. Despite significant advances in vaccination and antiviral therapies, CHB remains a major global health concern due to its potential to lead to severe liver complications, including cirrhosis and hepatocellular carcinoma. The virus is primarily transmitted through sexual, parenteral, and vertical routes, making it highly contagious.

An increasing amount of evidence highlights the crucial role of interactions between microbiota and host in maintaining overall health, affecting not only gut homeostasis but also playing a key role in various human diseases by generating biologically active substances (20). Recently, the potential impact of the gut microbiota on disease risk has led to the hypothesis that changes in the metabolome profile, specifically TMAO, could serve as a novel biomarker for assessing human health conditions associated with intestinal microbiota (2, 21).

TMAO has been linked to inflammatory processes and oxidative stress, both of which are critical factors in the progression of hepatitis. Since TMAO is synthesized mainly in the liver, its local levels may be associated with liver-related diseases. This article aims to examine the impact of TMAO on CHB. By investigating the relationship of TMAO with CHB disease, we also aim to shed light on new research avenues and potential therapeutic interventions in the fight against Hepatitis B.

Materials and Methods

Patients and Study Design

This prospective study included 41 CHB patients with HBV DNA levels above 2000 IU/mL who presented to the Infectious Diseases Department of XXX University Hospital, along with 46 age- and gender-matched controls. Participants who had received antiviral therapy or immunosuppressive treatments were excluded from the study. Moreover, individuals co-infected with hepatitis C virus (HCV) and hepatitis delta virus (HDV) were excluded. Individuals with other chronic diseases, active infections, a history of malignancy, pregnant women, and those with incomplete data were also excluded from the study. The research received approval from the Ethics Committee at XXX University Faculty of Medicine (2024/176).

Laboratory Analysis

Venous blood samples were collected into BD Vacutainer SST II Advance serum gel separator tubes (Becton Dickinson, NJ, USA) from all participants following a minimum fasting period of 8 hours. The collected blood samples were then subjected to centrifugation at 2000xg for 10 minutes. After centrifugation, serum samples were carefully separated and transferred into Eppendorf tubes. To ensure the stability of the serum samples, they were stored at -80°C until analysis.

Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), HBsAg, HBeAg, anti-HBs, and anti-HBe were measured using the Abbott Architect ci16200 and Abbott Architect i2000sr (Abbott Laboratories Ltd, Abbott Park, Illinois, US) auto-analyzers.

TMAO levels in serum samples, which were brought to room temperature, were analyzed using a Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) system. Briefly, A 250 µL aliquot of serum was taken from each sample, to which 100 µL of d9-TMAO, the isotope of TMAO, was added as an internal standard. Following this, 100% methanol was added as a precipitating agent. The tubes were vortexed for 30 followed by centrifugation at 14,000 rpm for 10 minutes. Then, the supernatant transferred to clean tubes was evaporated under nitrogen gas at 28°C. Subsequently, after adding 250 µL of High-Performance

Liquid Chromatography (HPLC) grade water as a solvent, the samples were then vortexed. After another round of centrifugation at 4,500 rpm for 10 minutes, the supernatant was collected and transferred into vials. Analytical separation was achieved using a Shimadzu HPLC system (Kyoto, Japan) coupled with a Phenomenex C18 column (50 mm x 4.6 mm, 5 µm, 100 Å). TMAO concentration was quantified using an ABSciex API 3200 tandem mass spectrometer (Applied Biosystems/MDS Sciex).

Statistical analysis

Statistical analysis was conducted using R version 4.2.1. Software (The R Foundation for Statistical Computing, Vienna, Austria; https://www.r-project.org). The normality of the data was checked via Shapiro-Wilk's normality test and the homogeneity of the variance was assessed via Levene's test. Numerical variables were summarized as mean ± standard deviation (SD) or median with quartiles [1st quartile – 3rd quartile], as appropriate. Categorical variables were described as count (n) and percentage (%). A Mann-Whitney U test (unpaired Wilcoxon test) or student's t-test was conducted to assess whether there was a statistically significant difference in demographical and laboratory parameters between groups. In addition, the Chi-square test with Yates continuity correction was used to evaluate the relationship between sex distribution and study groups. For further analysis, the receiver operating characteristic (ROC) curve analysis to identify the diagnostics performance of serum TMAO level to predict the CHB was performed. Calculation of the area under the curve (AUC) was performed, and the optimal cut-off point was derived based on the Youden index criteria. The sensitivity, specificity, negative (NPV), and positive predictive value (PPV) were calculated for the determined optimal cut-off point. Next, Spearman's rho correlation analysis was applied to assess the relationship between serum TMAO level and age, ALT and AST levels, and HBV-DNA level both in all cohorts and each study arm. A two-tailed p-value less than 0.05 was deemed to demonstrate statistical significance

Results

A total of 87 participants, among whom 54% (n=47) were females, including 41 CHB patients and 46 healthy controls who met eligibility criteria, were enrolled in this study. Table 1 provides a summary of the demographic and laboratory characteristics of the study groups. Patients were broadly comparable in terms of age (38.89 ± 10.16 vs. 38.83 ± 12.60, p=0.980) and sex (47.8% vs. 61% for females, p=0.311) distribution between the study groups. Higher serum levels of ALT and AST were found in patients with CHB than those in healthy controls. The mean HBV viral load in log10 was 4.44 ± 1.18 U/mL. 4 (9.8%) out of 41 patients with CHB were HBeAg-positive. Mann-Whitney U test revealed that CHB patients had a more significant increase in serum level of TMAO than healthy controls (1860 [IQR, 808 – 2720] vs. 552.5 [IQR, 252 – 876.5], p<0.001, Figure 1-A).

Table 1. Demographical and clinical characteristics, and laboratory findings of the study group

Characteristics	**Controls (*n*=46)**	**CHB (*n*=41)**	***p*-value**
Age (years)	38.89 ± 10.16	38.83±12.60	0.980[1]
Sex (female/ male)	22 (47.8)/ 24 (52.2)	25 (61)/16 (39)	0.311[2]
ALT (U/L)	18 [14.25 – 26.25]	31 [24-47]	<0.001[3]
AST (U/L)	19 [14.25 – 21.75]	28 [23-37]	<0.001[3]
HBV-DNA (log_{10} U/mL)		4.44±1.18	
HBeAg-positive		4 (9.8)	
Anti-Hbe		37 (90.2)	
TMAO (ng/mL)	552.5 [252-876.5]	1860 [808-2720]	<0.001[3]

1Student's t-test; 2Chi-square test with Yates continuity correction; 3Mann-Whitney U test (unpaired Wilcoxon test). Data were presented as mean±standard deviation or median with quartiles [1st quartile-3rd quartile] for numerical variables, and data were described as number (n) and percentage (%) for categorical variables. ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, CHB: Chronic hepatitis B, HBV: Hepatitis B virus, TMAO: Trimethylamine N-oxide,

The area under the curve (AUC) of serum TMAO level to distinguish CHB from healthy controls was 0.808, and ROC analysis identified that a TMAO level of 1560 ng/mL was able to predict the CHB with a sensitivity of 58.54%, a specificity of 100%, a PPV of 100% and an NPV of 73.02% (Figure 1-B).

As shown in Figure 1, Spearman's rho correlation analysis indicated that both serum ALT (Spearman's rho=0.466, p<0.001, Figure 1-C) and AST (Spearman's

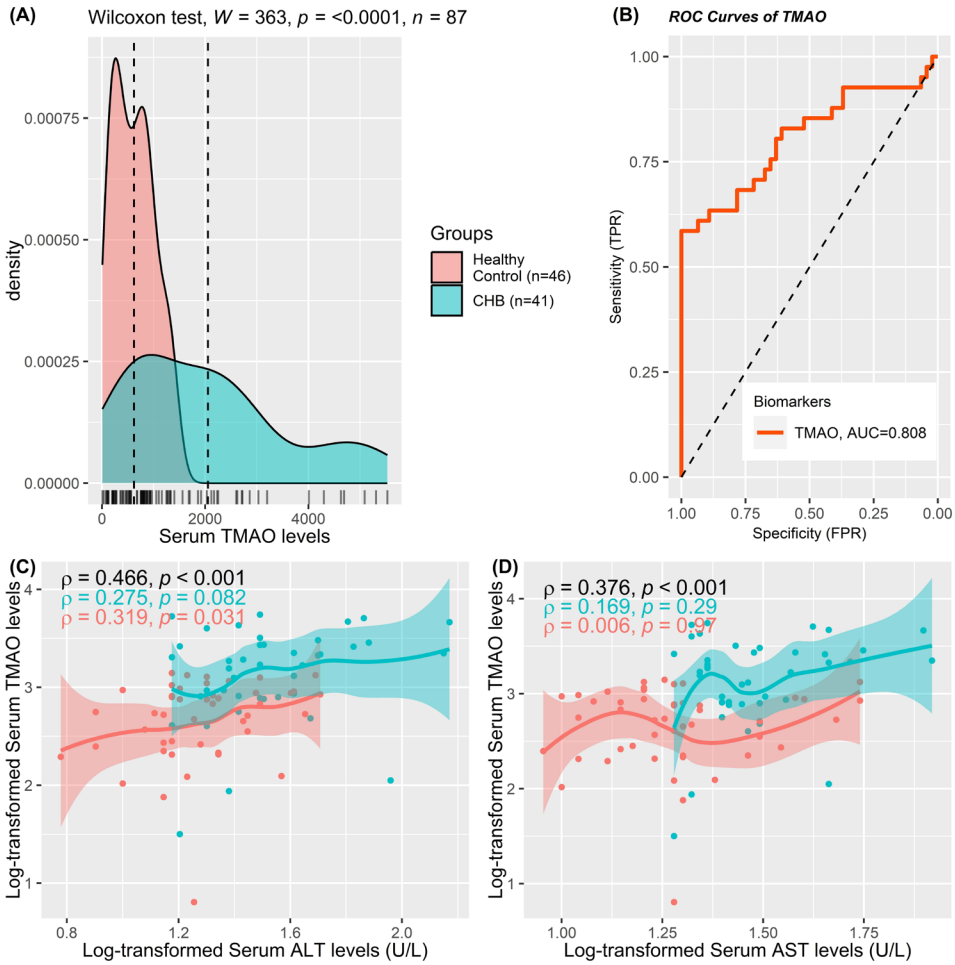

Figure 1. (A) The serum level of TMAO in patients with CHB and healthy controls. (B) ROC curve of serum TMAO level to predict the CHB. (C) The scatter plot between serum level of TMAO and serum ALT level in all cohorts (colored black) and each study arm. (D) The scatter plot between serum level of TMAO and serum AST level in all cohorts (colored black) and each study arm. TMAO: Trimethylamine N-oxide, CHB: Chronic hepatitis B, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase.

rho=0.376, p<0.001, Figure 1-D) levels positively correlated with serum TMAO level in all patients.

Discussion

In our study, we compared serum TMAO levels between patients with CHB and healthy controls and found that TMAO levels were significantly higher in CHB patients. Additionally, TMAO levels were positively correlated with ALT and AST levels and had predictive power for CHB with an AUC of 0.808.

Adequate choline intake is vital for maintaining liver health and its deficiency can exacerbate hepatic steatosis and contribute to the progression of liver inflammation and hepatic damage (22, 23). The results of a case-control study involving 297 incident cases and 631 matched controls suggest a close relationship between serum choline levels and hepatocellular carcinoma (24). The connection between TMAO and choline is crucial for comprehending their metabolic pathways. Choline, along with betaine and L-carnitine, is metabolized by gut microbiota to form TMA. This TMA is then transported to the liver, where it is oxidized to form TMAO. Recent studies have highlighted a significant connection between elevated levels of TMAO and an increased risk of colorectal cancer (8, 25, 26). Despite the limitation of direct evidence implicating TMAO in liver diseases, TMAO is linked to metabolic conditions such as diabetes mellitus (27), and dyslipidemia (28), as well as inflammation (29), all of which can potentially contribute to metabolic liver disease. Due to the close relationship between the liver and gut in TMAO formation, it has been hypothesized that TMAO could also be associated with liver diseases. Indeed, increased TMAO levels have recently been associated with non-alcoholic fatty liver disease (30, 31). A case-control study involving 671 primary liver cancer cases and 671 controls found a significant association between elevated TMAO levels and primary liver cancer (32).

The gut microbiota is essential in guiding the maturation of the immune system and modulating the functional diversity of immune cells. Changes in the gut microbiota have been observed in many liver diseases, including CHB (33). Analyzing urine samples from 42 Bangladeshi patients with Hepatocellular Carcinoma, 47 with cirrhosis, 46 with CHB, and seven healthy controls using nuclear magnetic resonance spectroscopy, they found that urine TMAO levels were statistically significantly lower in Hepatocellular Carcinoma patients and elevated, though not statistically significant, in patients with CHB compared to healthy controls (34). Shi et al. demonstrated that during a hepatotoxicity assessment with Bay41-4109, a newly recognized strong inhibitor of HBV replication, increased TMAO levels were detected in the cohort of rats with liver damage caused by Bay41-4109 (35). However, while it is evident that TMAO influences various pathways in hepatitis B through different mechanisms, the exact mechanism remains unclear.

Recent research highlights TMAO's multifaceted impact on liver inflammation through diverse molecular pathways. Beyond its association with metabolic dysregulation, TMAO is implicated in promoting inflammatory responses within hepatic tissues via distinct signaling cascades. Liu et al. suggest that TMAO induces hepatocytes to release Exos that exacerbate inflammation and impair endothelial function through miRNA-mediated mechanisms and NF-κB activation, thus stimulating the upregulation of inflammatory markers and induction of cell apoptosis and hindering cell migration (13). The intake of high carnitine, a significant precursor of TMAO, led to liver injury by increasing inflammatory hepatic cytokines, reducing the antioxidant capacity, and altering gut microbiota composition in mice (36). Sun et al. reported that TMAO has the potential to trigger oxidative stress and initiate the ROS-TXNIP-NLRP3 inflammasome signaling cascade, leading to the production of inflammatory cytokines and endothelial dysfunction in human umbilical vein endothelial cells (37). It has been found by Chen et al. that TMAO can directly bind to hepatic protein kinase R-like endoplasmic reticulum kinase, which in turn activates the unfolded protein response and promotes metabolic dysfunction (38).

The liver plays a crucial role in detoxifying endogenous and xenobiotic metabolism products, which makes it more susceptible to damage from harmful substances like ROS. Initially, hepatic inflammation induces tissue repair and the restoration of normal cellular function, however, prolonged inflammation due to persistent stressors can result in the loss of hepatocytes and the development of fibrosis (10). Oxidative stress damage has been implicated in the pathogenesis of chronic liver metabolic and inflammatory diseases through mechanisms involving alterations in lipid and glucose metabolism as well as modifications of the inflammatory response (39-41). In a three-month study by Florea et al., oral administration of TMAO in varying doses led to dose-dependent increases in liver oxidative stress and inflammation via iNOS and COX-2 activation, along with vascular alterations, but did not result in significant biochemical or histologic liver fibrosis or inflammation associated with IL-1a and TNF-a within the study period in mice (10). Their study also demonstrated that TMAO administration leads to a dose-dependent decrease in reduced glutathione levels along with a decrease in catalase and an increase in oxidized glutathione, indicating oxidative stress.

Long-term inflammation and liver toxin exposure can cause fibrog nesis by activating hepatic stellate cells to transform into myofibroblasts, leading to the production of extracellular matrix (ECM). Whereas collagen constitutes the majority of this ECM tissue, fibrosis is traditionally diagnosed through biopsy due to the lack of potential biomarkers for non-invasive diagnosis of liver fibrosis. Recently, it has been shown that TMAO induces cardiac fibrosis (42), aortic valve fibrosis (43), kidney fibrosis (44), and liver fibrosis (45). In their study, Yang et al. proved that mice supplemented with TMAO and choline demonstrated increased myocardial fibrosis, which was subsequently reversed by 3,3 Dimethyl-1-butanol, an inhibitor of microbial TMA formation (46). Florea et al., on the other hand, demonstrated in mice administered TMAO for 3 months that there was no increase in fibrosis, which could be attributed to dose or duration effects (10). It remains unclear whether TMAO contributes to fibrosis in chronic hepatitis, highlighting the need for further studies in this area.

Considering the limitations of our study, several aspects need to be addressed. Firstly, we did not simultaneously evaluate oxidative stress parameters, inflammatory markers, and liver fibrosis, which are interconnected pathways. Additionally, factors such as diet may have influenced the results. Moreover, our study was performed at a singular center, potentially limiting the generalizability of our findings to broader

patient populations. Future research should involve longitudinal follow-up of larger patient groups to evaluate whether individuals with elevated TMAO levels are more prone to developing conditions such as cirrhosis and malignancy over time.

Conclusion

This study demonstrates a significant increase in serum TMAO levels among patients with CHB compared to healthy controls. The positive correlation of TMAO with ALT and AST levels further supports its role in liver disease progression. Our study is, to the best of our knowledge, the first to investigate the relationship between CHB and TMAO. The link between TMAO and liver diseases is a relatively new area of research, and our study serves as a pioneering effort to understand this connection in the context of gut microbiota-dependent metabolite TMAO and CHB. We believe that our findings will pave the way for more comprehensive studies involving larger patient cohorts and examining other parameters of this pathway. This could ultimately lead to a deeper understanding and novel therapeutic approaches in Hepatitis B management. Whether TMAO is a causative factor or merely a consequence remains unclear, necessitating further research to elucidate its precise role in Hepatitis B.

Conflict of Interest

The authors have stated that they have no conflicts of interest.

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Author Contributions

All authors contributed equally to this study.

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ORIGINAL ARTICLE

Variation Among Evaluators of The Full Outline of Unresponsiveness Score and The Glasgow Coma Scale in Critically Ill Patients: A Prospective Study

Kritik Hastalarda Full Outline of Unresponsiveness Skoru ve Glasgow Koma Skalası Değerlendiricileri Arasındaki Varyasyon- Prospektif Bir Çalışma

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ABSTRACT

Background/Aims: This study aims to compare the reliability of the Full Outline of Unresponsiveness (FOUR) score and the Glasgow Coma Score (GCS) when used by specialists from different medical disciplines.
Methods: This prospective observational study was conducted at Selçuk University Faculty of Medicine between December 2023 and June 2024. Eighty-two patients in the Anesthesiology and Reanimation Intensive Care Unit (ICU) were assessed by three specialists—the pulmonologist, the neurologist, and the anesthesiologist—within 24 hours of ICU admission. The scores for each patient by each specialist independently were recorded within a time interval of one hour, consecutively, as possible to minimize the likelihood of any changes in the patient's condition. The variation between evaluators of both scoring systems was analyzed using the Intraclass Correlation Coefficient (ICC). If ICC was below 0.50, the agreement was interpreted as poor
Results: The study included 82 patients. There were no statistically significant differences in the FOUR and GCS scores assigned by the three specialists. The mortality rate among patients with low scores on both FOUR and GCS was higher than the hospital mortality rate.
Conclusions: Scales used in the ICU should be simple, reliable, and predictive. This study demonstrated that the FOUR is at minimum equivalent to the GCS in meeting these criteria.

Keywords: Full outline of unresponsiveness score, Glasgow coma scale, Intensive care unit

ÖZ

Amaç: Bu çalışma, farklı tıp disiplinlerinden uzmanlar tarafından kullanılan FOUR (Full Outline of Unresponsiveness) skoru ile GKS'nin (Glasgow Koma Skoru) güvenilirliğini karşılaştırmayı amaçlamaktadır.
Gereç ve Yöntem: Bu prospektif gözlemsel çalışma Aralık 2023-Haziran 2024 tarihleri arasında Selçuk Üniversitesi Tıp Fakültesi'nde gerçekleştirilmiştir. Anesteziyoloji ve Reanimasyon Yoğun Bakım Ünitesindeki (YBÜ) 82 hasta, YBÜ'ye kabul edildikten sonraki 24 saat içinde göğüs hastalıkları uzmanı, nörolog ve anesteziyolog olmak üzere üç uzman tarafından değerlendirildi. Her bir hasta için her bir uzman tarafından bağımsız olarak verilen skorlar, hastanın durumunda herhangi bir değişiklik olması ihtimalini en aza indirmek için mümkün olduğunca bir saatlik bir zaman aralığında ve ardışık olarak kaydedildi. Her iki skorlama sisteminin değerlendiricileri arasındaki varyasyon Sınıf İçi Korelasyon Katsayısı (ICC) kullanılarak analiz edildi. ICC 0,50'nin altında ise uyum zayıf olarak yorumlandı.
Bulgular: Çalışmaya 82 hasta dahil edilmiştir. Üç uzman tarafından verilen FOUR ve GKS skorları arasında istatistiksel olarak anlamlı bir fark yoktu. Hem FOUR hem de GKS skorları düşük olan hastalar arasındaki mortalite oranı hastane mortalite oranından daha yüksekti.
Sonuç: YBÜ'de kullanılan ölçekler basit, güvenilir ve öngörücü olmalıdır. Bu çalışma, FOUR skorunun bu kriterleri karşılamada en azından GKS'ye eşdeğer olduğunu göstermiştir.

Anahtar kelimeler: Glasgow koma skalası, Tepkisizlik skorunun tam taslağı, yoğun bakım ünitesi

Introduction

The scoring systems in the intensive care unit (ICU) serve as a guide in determining consciousness levels (1, 2). Scales have been developed to enable healthcare providers to communicate to each other the general clinical condition of patients, neurological and cardiopulmonary, in a concise and standardized manner (3). Among these scales, the Glasgow Coma Scale is the most widely used (4). Nevertheless, the GCS has several drawbacks. It is limited in cases where verbal responses may not be evaluated, especially in patients who are intubated and aphasic. It does not include the brainstem reflexes in the scale and fails to take into account the patient's respiration characteristics (1, 4). Quick shifts in mental state, along with changes in breathing and brainstem reflexes, can easily be overlooked.

The Glasgow Coma Scale was published 50 years ago by Teasdale and Jennet for the assessment of

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coma and impaired consciousness sources (5). Celebrating its 50th anniversary (6), this scale is still widely used today, although alternative scales have been developed. The Full Outline of Unresponsiveness (FOUR) scoring system, a recently developed coma scale from the Mayo Clinic, assesses four aspects: eye responses, motor responses, brainstem reflexes, and respiration (7). The FOUR allows for the inclusion of brainstem reflexes, respiratory patterns, and verbal responses, which provide additional information for patient assessment, aspects not covered by the GCS (8, 9). This makes it particularly useful in the ICU, where factors like intubation, sedation, or delirium can hinder an accurate assessment of verbal responses, making the FOUR a valuable alternative (8). To ensure the correct understanding and precise application of this scale in Turkey, in 2010, a reliability trial of the Turkish version of the FOUR was performed (10). Especially for unconscious patients, these scales play a crucial role in determining diagnosis and treatment, and their effectiveness can be somewhat influenced by the user.

This study aimed to evaluate the reliability of the FOUR by comparing it with the GCS assigned to the patients in the ICU by specialists from three different disciplines, the pulmonologist, the neurologist, and the anesthesiologist.

Material and Methods

This prospective observational study was conducted between 15th December 2023 and 15th June 2024 at Selcuk University, the Faculty of Medicine, the ICU of the departments of Anesthesiology and Reanimation. Three different specialists, a pulmonologist (Group A), a neurologist (Group B), and an anaesthesiologist (Group C), independently assessed the patient within the first 24 hours of admission to the ICU and applied

Table 1. GCS and FOUR scoring systems

Category	GCS	FOUR
Eye Response	4 = Spontaneous eye-opening	4 = Eyelids open, tracking, or blinking to command
	3 = Eye-opening to verbal command	3 = Eyelids open but not tracking
	2 = Eye opening to pain	2 = Eyelids closed, open to loud voice
	1 = No eye opening	1 = Eyelids closed, open to pain
		0 = Eyelids remain closed with pain stimuli
Motor Response	6 = Obeying commands	4 = Thumbs up, fist, or peace sig
	5 = Localizing pain	3 = Localizing pain
	4 = Withdrawal from pain	2 = Flexion response to pain
	3 = Abnormal flexion (decorticate posturing	1 = Extension response (decerebrate posturing)
	2 = Abnormal extension (decerebrate pos-turing)	0 = No response to pain or generalized myoclonus status
	1= No motor response	
Verbal Response	5 = Oriented	Brain Stem Reflexe
	4 = Confused	4 = Pupil and corneal reflexes presen
	3 = Inappropriate words	3 = One pupil wide and fixe
	2 = Incomprehensible sounds	2 = Pupil or corneal reflexes absen
	1 = No verbal response	1 = Pupil and corneal reflexes absen
		0 = Absent pupil, corneal, or cough refle
Respiration	N/A	Respiration
		4 = Regular breathing pattern
		3 = Cheyne-Stokes breathing pattern
		2 = Irregular breathing
		1 = Triggering ventilator or breathing above ventilator rate
		0 = Apnea or breathing only at ventilator rate

FOUR: Full Outline of Unresponsiveness score, GCS: Glasgow Coma Scale, N/A: Non-applicable

the GCS and FOUR scores (Table 1) in the neurological examination. Patients for whom all three specialists were able to rate consecutively within a one-hour time interval were included. The scoring was conducted at the earliest opportunity following admission, with each patient being evaluated only once. The raters were unaware of the other ratings or their outcomes. Demographic data of the patients, APACHE II scores, ICU length of stay, and patient's outcome as survivor or nonsurvivor were collected. Diagnosis of the patients as ischemic or hemorrhagic stroke, pulmonary and cardiac arrest, sepsis-septic shock, and others were also recorded. The study included patients between 18 and 65 years of age who were treated in the ICU for 24 hours or more and who were not sedated. The study excluded patients who were younger than 18 years or older than 65 years, those who received sedation, those who died within the first 24 hours, and those who stayed in intensive care for less than 24 hours.

Statistical Analysis

All statistical analyses were performed using R version 4.2.1 (www.r-project.org). Repeated measures analysis of variance was used to test whether there was a significant difference between the scores given by the experts for each scoring system. In addition, the agreement of the scores given by the experts both in each scoring system and between the two scoring systems was evaluated with the Intraclass correlation coefficient (ICC) and 95% confidence interval. If the ICC was below 0.50, the agreement was interpreted as poor, between 0.50 - 0.75 as moderate, between 0.75 - 0.90 as good, and above 0.90 as excellent according to the levels determined by Koo and Li(11).

Results

A total of 82 patients, 50 males (61%) and 32 females (39%), were included in the study. The mean age of the patients was 62.27 ± 19.87 years (age range: 18-91 years), the mean length of ICU stay was 24.19 (range: 2-145 days) days and the mean length of hospitalization was 34.18 (range: 4-160 days) days. The mean APACHE II score was 11.11 ± 6.79 (range: 3-39). Of the 82 patients, 47 were discharged (57.3%), 35 were died in hospital (42.7%). The mortality rate was 42.6%. Twenty-two patients (26.8%) were intubated or tracheotomized and were using mechanical ventilation, and 60 (73.1%) were breathing spontaneously. The diagnoses of the patients are indicated in Table 2.

Table 2. Diagnosis of the patients in the study

Diagnosis	*n* **(%)**
Ischemic and hemorrhagic stroke	7 (8.5)
Pulmonary and cardiac arrest	3 (3.6)
Multitraumas	18 (21.9)
Sepsis	32 (39)
Others	22 (26.8)
Total	82

Patients with low FOUR and GCS scores were found a mortality rate higher than the hospital mortality. For FOUR scores, there were found to be no statistically significant differences between groups A, B, and C (p=0.743). Nor were there any statistically significant differences in GCS scores, among groups A, B, and C (p=0.927). Reliability results for overall patients are compared in Table 3, for survivors and non-survivors in Table 4, and for female and male patients in Table 5.

Table 3. Reliability results for all patients

	FOUR	**GCS**	**ICC[1] [95% CI]**
Group A	13.04 ± 3.79	12.11 ± 3.81	0.959 [0.846 – 0.983]
Group B	13.05 ± 3.76	12.12 ± 3.75	0.959 [0.840 – 0.983]
Group C	13.06 ± 3.75	12.11 ± 3.77	0.958 [0.828 – 0.983]
p-value	0.743	0.927	
ICC[2] [95% CI]	0.999 [0.998 – 0.999]	0.981 [0.972 – 0.987]	

The data were expressed as mean±standard deviation, a p-value was obtained by Repeated Measures analysis of variance (ANOVA). ICC1 indicates overall agreement among specialists, and ICC2 indicates the agreement between scoring systems.

Abbreviations: CI: Confidence intervals, FOUR: Full Outline of Unresponsiveness score, GCS: Glasgow Coma Scale, ICC: Intraclass correlation coefficient

Discussion

The present prospective observational study compared the agreement between the evaluators of GCS and FOUR scores. The evaluators were composed of three specialists in different fields, studying as fellows in the intensive care unit, one pulmonologist, one neurologist, and one anesthesiologist. The scores for each patient were recorded as close together within a time interval of one hour as possible to minimize the likelihood of any changes in the patient's condition. In the primary outcome, agreement between evaluators, there was no significant difference between the GCS and the FOUR score, nor between the evaluations

Table 4. Reliability results for non-survivors and survivors

	FOUR	GCS	ICC[1] [95% CI]
Non-survivors (*n*=35)			
Group A	11.771 ± 4.264	11.000 ± 4.221	0.965 [0.906 – 0.985]
Group B	11.800 ± 4.234	11.000 ± 4.165	0.967 [0.900 – 0.986]
Group C	11.800 ± 4.220	11.000 ± 4.172	0.966 [0.900 – 0.985]
p-value	0.885	0.885	
ICC[2] [95% CI]	0.999 [0.999 – 0.999]	0.999 [0.998 – 0.999]	
Survivors (*n*=47)			
Group A	13.979 ± 3.138	12.936 ± 3.273	0.943 [0.671 – 0.980]
Group B	13.979 ± 3.103	12.957 ± 3.223	0.942 [0.686 – 0.979]
Group C	14.000 ± 3.071	12.936 ± 3.246	0.941 [0.638 – 0.979]
p-value	0.613	0.999	
ICC[2] [95% CI]	0.998 [0.996 – 0.998]	0.998 [0.997 – 0.998]	

The data were expressed as mean±standard deviation, a p-value was obtained by Repeated Measures analysis of variance (ANOVA). ICC1 indicates overall agreement among specialists, and ICC2 indicates the agreement between scoring systems.

Abbreviations: CI: Confidence intervals, FOUR: Full Outline of Unresponsiveness score, GCS: Glasgow Coma Scale, ICC: Intraclass correlation coefficients

Table 5. Reliability results for male and female patients

	FOUR	GCS	ICC[1] [95% CI]
Male (*n*=50)			
Group A	13.480 ± 3.632	12.560 ± 3.753	0.961 [0.820 – 0.985]
Group B	13.500 ± 3.598	12.600 ± 3.636	0.959 [0.828 – 0.984]
Group C	13.520 ± 3.558	12.540 ± 3.764	0.958 [0.784 – 0.984]
p-value	0.372	0.175	
ICC[2] [95% CI]	0.999 [0.999 – 0.999]	0.999 [0.999 – 0.999]	
Female (*n*=32)			
Group A	12.344 ± 4.004	11.406 ± 3.842	0.953 [0.844 – 0.981]
Group B	12.344 ± 3.964	11.375 ± 3.883	0.957 [0.828 – 0.984]
Group C	12.344 ± 3.972	11.438 ± 3.741	0.956 [0.848 – 0.983]
p-value	0.999	0.723	
ICC[2] [95% CI]	0.998 [0.997 – 0.999]	0.997 [0.996 – 0.998]	

The data were expressed as mean±standard deviation, a p-value was obtained by Repeated Measures analysis of variance (ANOVA). ICC1 indicates overall agreement among specialists, and ICC2 indicates the agreement between scoring systems. Abbreviations: CI: Confidence intervals, FOUR: Full Outline of Unresponsiveness score, GCS: Glasgow Coma Scale, ICC: Intraclass correlation coefficients

of the anaesthesiologist, the neurologist, and the pulmonologist.

The GCS has several disadvantages, such as the lack of ability to evaluate the verbal responses in intubated and aphasic patients, and the omission of the brain stem reflexes and the respiratory patterns from its evaluation criteria (2, 12). Thus, quick shifts in the mental status caused by alterations in the respiration patterns and the brainstem reflexes might go undetected. While assessing the patient's state of consciousness, these shortcomings of the Glasgow Coma Scale can lead to mistakes regarding the level of the coma recovery, and the brain death (10). Unlike the GCS, the FOUR has respiratory parameters. Using this parameter, healthcare professionals can determine if intubated or tracheotomized patients on mechanical ventilation are either apnoeic or breathing at the ventilator frequency. Wijdicks et al. found that the FOUR has advantages over the GCS. One key benefit is that it includes the brainstem reflexes, providing more information about the patient's progress and helping guide urgent interventions for intubated patients (13). Additionally, the FOUR scoring system predicts mortality more accurately. Patients with the low FOUR score have a higher mortality rate compared to those with

the low GCS (13). Finally, the FOUR score shows better observer compliance. However, the drawback is that it does not assess all the behavioral criteria needed to diagnose the minimally conscious state (MCS). MCS is characterized by the patients demonstrating inconsistent but noticeable minimal signs of consciousness, such as responding to noxious stimuli, eye fixation or tracking, reproducible movements to commands, or nonfunctional verbalization (14). The FOUR scale includes an assessment of eye tracking, which helps distinguish between the vegetative state and the MCS patients. However, it is important to note that both acute and chronic patients might only exhibit visual fixation, a factor that is not evaluated by the FOUR scale (15).

Temiz et al. studied 47 patients in the neurosurgical ICU, and the agreement between the practitioners in terms of FOUR and GCS evaluations was found to be high. Wijdicks et al. found that incorporating the brainstem and the respiratory parameters made the FOUR scale a more accurate predictor of mortality compared to the GCS (13). However, other studies have shown that the two scoring systems produce similar outcomes. Eken et al. concluded that the FOUR was not superior to the GCS in patients with altered consciousness arriving at the emergency department (16). Studies comparing GCS and FOUR have shown high inter-observer agreement and correlation (10, 17). In our study, both scoring systems showed similar results between the pulmonologist, the neurologist, and the anesthesiologist. We conducted a similar study in two different ICUs with two specialists from different fields in 2019 and no significant difference was found between the two evaluators. We extended our previous study to evaluate the difference in scoring between internal and surgical departments and to obtain more effective results with a larger number of evaluators. Given the advantages of the FOUR scale, the comparable results between the three specialists suggest that it may be a more beneficial tool for patient assessment. Jalali et al. studied the agreement between users in terms of scoring in a specific group of patients with traumatic brain injury and found that the FOUR score provided more neurological information than the GCS (7). The absence of a clear superiority between the two scores in our findings may be attributed to the selection of a nonspecific patient population and the relatively limited sample size.

Our study has several limitations. A key limitation is that it was conducted at a single center and within a single intensive care unit, which means its generalizability to other ICUs has not been established. Additionally, the sample size may have been relatively small. We consider that future research involving multiple centers, more ICUs, and larger sample sizes would provide a more robust evaluation.

Conclusion

While the GCS has been the standard scoring system for several decades, various scales are currently in use. These scoring systems must be simple, reliable, and predictive. This study demonstrated that the FOUR is, at minimum, equivalent to the GCS in meeting these criteria.

Informed Consent

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

Ethical Approval

The protocol of this study was approved by the Clinical Research Ethics Committee of Konya Selçuk University (No: 2023/541, 21 November 2023).

Author Contribution

Conceptualization, YŞB, and JBÇ.; Methodology, YŞB, JBÇ, FÇ.; Formal analysis, MKK.; Investigation, DCG, BP, and YC.; Resources, DCG, BP and YC.; Writing—original draft preparation, YŞB, DCG, BP and YC.; Writing— review and editing, YŞB, JBÇ and FÇ. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors have no conflicts of interest to declare

Main Points

The Glasgow Coma Scale, while widely used for assessing consciousness, has limitations such as excluding brainstem reflexes and respiratory patterns, which the recently developed FOUR scale addresses.

The FOUR score was found to be at least as reliable as the GCS when used by specialists from three different

fields—pulmonology, neurology, and anesthesiology—in a study conducted in ICU patients, with no significant differences between evaluators.

Although both the GCS and the FOUR scores showed high agreement between evaluators, the FOUR score's inclusion of brainstem reflexes and respiratory parameters makes it a potentially more informative tool, particularly in ICU settings where intubation and other factors complicate verbal assessments.

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ORIGINAL ARTICLE

Evaluation of Orthorexia Nervosa Tendency and Social Media Addiction in University Students

Üniversite Öğrencilerinde Ortoreksiya Nervoza Eğiliminin ve Sosyal Medya Bağımlılığının Değerlendirilmesi

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ABSTRACT

Background/Aim: Developments in the Internet and smartphone technology have increased the use of social media in society. Content regarding healthy nutrition attracts great attention on social media. This situation can lead to various eating disorders, especially in university students who are in an important period of their lives and can be more easily affected by environmental stimuli. Intense exposure to such content on social media can be a trigger for Orthorexia Nervosa (ON), an obsession with healthy eating. This study aimed to determine the frequency of ON tendency in university students, to examine the effects of various factors on ON tendency, and to examine the relationship between social media addiction and ON tendency.
Methods: This research, planned as a cross-sectional and descriptive study, was conducted on undergraduate students studying at Alanya Alaaddin Keykubat University. The sample of the research consisted of 1153 students reached by simple random sampling method. Data was collected between September and December 2022 by applying online data collection tools through a structured survey created in Google Forms. Data were collected using a personal information form, the Orthorexia-11 scale (ORTO-11), and the Bergen social media addiction scale (BSMAS).
Results: The average age of the students was found to be 20.4±2.0 years. ON tendency was detected as 24%. A significant difference was found between the students' ORTO-11 scores and gender and Body Mass Index(BMI) ($p<0.05$). A statistically low significant negative relationship was found between ORTO-11 scores and BSMAS scores ($r=-0.058$, $p=0.048$). According to this result, as social media addiction increases, the ON tendency also increases.
Conclusion: This study showed that social media addiction can affect ON tendency. Social media users should be made aware of choosing experts in their field who provide accurate and reliable information. More detailed research would be useful to confirm these finding

Keywords: Eating behavior, orthorexia nervosa, social media, university students

ÖZ

Amaç: İnternet ve akıllı telefon teknolojisindeki gelişmeler toplumda sosyal medya kullanımını artırmıştır. Sosyal medyada sağlıklı beslenmeye yönelik içerikler yoğun ilgi görmektedir. Bu durum özellikle hayatlarının önemli bir döneminde olan ve çevresel uyaranlardan daha kolay etkilenebilen üniversite öğrencilerinde çeşitli yeme bozukluklarına yol açabilir. Sosyal medyada bu tarz içeriklere yoğun bir şekilde maruz kalınması bir sağlıklı beslenme takıntısı olan Ortoreksiya Nervoza (ON) için tetikleyici olabilir. Bu çalışmada, üniversite öğrencilerinde, ON eğilimi görülme sıklığının belirlenmesi, çeşitli faktörlerin ON eğilimine etkisi ve sosyal medya bağımlılığı ile ON eğilimi arasındaki ilişkisinin incelenmesi amaçlanmıştır.
Yöntem: Kesitsel ve tanımlayıcı bir çalışma olarak planlanan bu araştırma Alanya Alaaddin Keykubat Üniversitesinde öğrenim gören lisans öğrencileri üzerinde yürütülmüştür. Araştırmanın örneklemini basit tesadüfi örnekleme yöntemiyle ulaşılan 1153 öğrenci oluşturmuştur. Veriler, Google Formlar'da oluşturulan yapılandırılmış bir anket aracılığıyla çevrimiçi veri toplama araçları uygulanarak Eylül ve Aralık 2022 tarihleri arasında toplanmıştır. Ankette kişisel bilgi formu, Ortoreksiya-11 ölçeği (ORTO-11) ve Bergen sosyal medya bağımlılığı ölçeği (BSMBÖ) yer almıştır.
Bulgular: Araştırmaya katılan öğrencilerin yaş ortalaması 20,4±2,0 yıl olarak bulundu. ON eğilimi %24 olarak tespit edildi. Öğrencilerin ORTO-11 puanları ile cinsiyet ve Beden Kütle İndeksi (BKİ) arasında anlamlı farklılık bulunmuştur ($p<0,05$). ORTO-11 puanları ile BSMBÖ puanları arasında istatistiksel olarak düşük düzeyde anlamlı negatif ilişki bulunmuştur ($r=-0,058$, $p=0,048$). Bu sonuca göre sosyal medya bağımlılığı arttıkça ON eğilimi de artmaktadır.
Sonuç: Bu çalışma, sosyal medya bağımlığının ON eğilimini etkileyebileceğini göstermiştir. Sosyal medya kullanıcıları doğru ve güvenilir bilgi sağlayan, alanında uzman kişileri seçme konusunda bilinçlendirilmelidir. Bu bulguları doğrulamak için daha fazla ve detaylı araştırma yapılması faydalı olacaktır.

Anahtar Kelimeler: Ortoreksiya nervoza, sosyal medya, yeme davranışı, üniversite öğrencileri

Introduction

In recent years, with the development of the Internet technology, the use of social media has become an indispensable part of life. While the correct use of social media facilitates interpersonal communication and socialization, its incorrect use causes some behavioral and psychological problems (1). Social media addiction is defined as individuals' excessive desire to use social

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media and feeling distressed when they do not use it. Social media addiction is seen in approximately 12% of social media users. Young people, who are part of the digital generation, are especially at risk for social media addiction (2). During this period, the desire for liberation and the lack of life experience make young people more easily affected by external stimuli. The university period, which covers the transition from adolescence to young adulthood, is a sensitive period in which lifestyle habits are shaped. In the meantime, it is important to be aware of the factors that lead to the acquisition of wrong habits (3).

Flawless images presented on social media increase the importance given to appearance and beauty by young people. This can increase their physical dissatisfaction and trigger their desire to be thinner and more beautiful. Individuals who are dissatisfied with their bodies have a higher risk of depression and eating disorders (1). A relationship has been found between time spent on social media networks and eating disorder symptoms (4). Interest in content related to healthy living and healthy nutrition on social media is increasing day by day (5). Dealing with these contents seems to be a beneficial action for protecting health in the first place. However, intense exposure to content related to healthy nutrition can also cause orthorexic behaviors (6). Individuals with orthorexic tendencies constantly strive to research, think, and plan the foods they will consume to be perfect and without error in healthy nutrition (7).

Orthorexia nervosa (ON) was first defined by Steven Bratman in 1997 as a term characterized by a pathological focus on healthy eating (8). Orthorexics tend not to consume processed foods containing pesticides and additives and are intensely concerned about the materials and preparation techniques used in food preparation (9). The strict attitude of individuals with ON towards eliminating impure and unhealthy foods from their diet may lead to problems in their nutrition, and social and academic functioning. (10).

When considered together with the topics of beauty and healthy nutrition being on the agenda on social media, it comes to mind that excessive social media use in young people may be a trigger for ON (11). Some studies conducted in recent years have shown a relationship between social media addiction and ON (11-15).

This study aims to determine the frequency of ON tendency in university students, to examine the effects of various factors on ON tendency, and to examine the relationship between social media addiction and ON tendency.

Material and Methods

The population of this study planned as a cross-sectional and descriptive study consisted of undergraduate students studying at Alanya Alaaddin Keykubat University Kestel campus in the 2022-2023 academic year. It was calculated that the participation of 1137 students from the study population would be sufficient for the sample of the research, with a 95% confidence interval and a 5% margin of error. The sample of the study consisted of 1153 university students reached by simple random sampling method. Those included in the study are volunteer students who are over 18 years old and do not have any health problems.

"Approval Date, No: 25.05.2022, 02/03" was received for the research from the "Alanya Alaaddin Keykubat Health Sciences Scientific Research and Publication Ethics Committee". The data was collected between September and December 2022 by applying data collection tools online through a structured survey created in Google Forms. The online survey link was shared in student "WhatsApp" groups through class representatives of the departments. Individuals participating in the research were provided with information about the purpose of the study and "voluntary participation consent" was obtained. This research was conducted under the Principles of the Declaration of Helsinki and the Research and Publication Ethics.

The data was collected using a personal information form, the Orthorexia-11 scale (ORTO-11), and the Bergen social media addiction scale (BSMAS).

The data form created by the researchers includes personal information data such as age, gender, height, body weight, faculty, economic status, and data inquiring about skipping meals, smoking status, and whether they do regular sports. When determining the economic status of students, those whose income is less than their expenses are determined as low, those whose income is equal to their expenses are determined as moderate, and those whose income is more than their expenses are determined as high. Anthropometric data were evaluated according to the classification of the WHO by calculating body

mass index (BMI) as kg/m² by using the body weight/ height (m²) formula. According to the World Health Organization (WHO), BMI classification was: BMI <18.5 kg/m2 as underweight; 18.5-24.9 kg/m2 as normal; 25-29.9 kg/m2 as preobese; ≥30 kg/m2 as obese (16).

ORTO-11, a self-rating scale consisting of 11 items developed to detect orthorexia nervosa symptoms, was used in this study. The original form of the scale is a 15-item scale developed by Donini et al. in 2005 (17). The scale was adapted to Turkish by Arusoğlu et al. in 2008, the number of items was reduced to 11 and adapted as ORTO-11. The scale has a 4-point Likert-type structure. Answers to the questions are evaluated as "always" (1 point), "often" (2 points), "sometimes" (3 points) and "never" (4 points). Only the 8th question on the scale is reverse scored. The total scores that can be obtained vary between 11 and 44, and as the scores increase, it is interpreted as a decrease in the level of orthorexic tendency. The cut-off point method was used to evaluate the scale. The cut-off point of the study was determined as 24 points in the 25% slice, and 24 points and below were considered orthorexic tendencies (18).

In this study, the Bergen social media addiction scale, a self-assessment scale consisting of 6 items developed to determine social media addiction, was used. The scale was developed by Andreassen et al. in 2016 (19). The scale was adapted to Turkish by Demirci in 2019 (20). The scale has a 5-point Likert-type structure. Answers to the questions are evaluated as "very rarely" (1 point), "rarely" (2 points), "sometimes" (3 points) "often" (4 points), and "very often" (5 points). The total scores that can be obtained vary between 6-30, and it is stated that the higher the scores, the higher the level of social media addiction. The Cronbach's Alpha value of the single-dimensional scale was found to be 0.83 (20).

For statistical analyses of the data obtained, SPSS 25.0 for Windows software (SPSS, Chicago, Il, USA) was used. Frequencies (n), percentages (%), mean, and standard deviation (±Sd) were used for the descriptive statistics. Normal distribution of the data was assessed using the Kolmogorov-Smirnov test. In determining the differences between groups, the t-test and ANOVA tests were used to evaluate continuous variables. The correlation between the scales was analyzed with the Pearson correlation test. The significance level was assessed as $p<0.05$.

Results

A total of 1153 students with an average age of 20.4±2.0 years were included in the study. Of the students, 63.7% were female and 36.3% were male. When the economic status of the students was examined, it was determined that approximately half of them (48.4%) were at a low level. It was determined that most of the students (80.0%) did not smoke. While 29.9% of the participants stated that they did not skip meals, 48.4% stated that they sometimes skipped meals, and 21.7% stated that they skipped meals. More than half (68.1%) of the participants in the study stated that they did not engage in regular physical activity. The tendency to ON was found to be 24%. The mean ORTO-11 score of the students participating in the study was 27.3±3.6, while the mean BSMAS score was 16.9±4.6 (Table 1).

Table 1. Distribution of some personal information and eating habits of the students

Variables		**n**
Age (years) (mean±SD)		(20.4±2.0)
Gender, n (%)	Female	734 (63.7)
	Male	418 (36.3)
Faculty, n (%)	Health field	449 (39.0)
	Other field	703 (61.0)
Economic status, n (%)	Low	558 (48.4)
	Moderate	468 (40.7)
	High	126 (10.9)
Smoking, n (%)	Yes	230 (20.0)
	No	922 (80.0)
Skipping meal, n (%)	Yes	250 (21.7)
	Sometimes	558 (48.4)
	No	344 (29.9)
BMI, n (%)	Underweight	128 (11.1)
	Normal	878 (76.3)
	Preobese	126 (10.9)
	Obese	20 (1.7)
Regular physical activity status, n (%)	Yes	368 (31.9)
	No	784 (68.1)
ORTO-11 score distrubition, n (%)	ON tendency	276 (24.0)
	Without ON tendency	876 (76.0)
ORTO-11 score, (mean±SD)		(27.3±3.6)
BSMAS score, (mean±SD)		(16.9±4.6)

BMI, Body mass index; BSMAS, Bergen social media addiction scale, ON: Orthorexia nervosa; ORTO-11, Orthorexia-11 scale; ON tendency, ORTO -11 ≤24; SD: Standard deviation, Without

ON tendency, ORTO -11 >24

In this study, there was no significant difference between the students' ORTO-11 scores and faculty, smoking, skipping meals, and regular physical activity status (p>0.05). However, a significant difference was found between the students' ORTO-11 scores and gender and BMI (p<0.05). In our study, ORTO-11 scores of males were found to be significantly higher than females (p<0.05). When ORTO-11 scores were evaluated according to BMI, the differences were found to be significant among all groups (p<0.05), while the highest mean score was found in the underweight and the lowest mean score in the obese (Table 2).

Table 2. Relationship between ORTO-11 score and BSMAS score of various variables

Variables		ORTO-11 score (Mean±SD)	p-value	BSMAS score (Mean±SD)	p-value
Gender	Female	26.9±3.7	**0.000***	17.1±4.9	0.063*
	Male	27.9±3.2		16.6±4.1	
Faculty	Health field	27.3±3.7	0.930*	17.0±4.1	0.569*
	Other field	27.3±3.5		16.8±4.2	
Smoking	Yes	27.6±3.7	0.140*	17.8±5.3	**0.003***
	No	27.2±3.6		16.7±4.4	
Skipping meal	Yes	27.4±3.3	0.158**	16.5±4.1	0.115**
	Sometimes	27.4±3.7		16.9±4.3	
	No	27.0±3.5		17.3±5.4	
BMI	Underweight	27.8±4.0[a]	**0.000****	16.8±5.3[a]	**0.000****
	Normal	27.3±3.6[b]		16.7±4.7[a]	
	Preobese	26.8±2.8[c]		18.3±3.4[b]	
	Obese	25.6±2.0[d]		19.6±3.6[c]	
Regular physical activity status	Yes	27.2±3.8	0.202*	16.6±4.2	0.069*
	No	27.4±3.5		17.1±4.8	

[a,b,c,d]Values shown with different letters in the same column where there are more than two groups are statistically different from each other. *Calculated with independent samples t-test. **Calculated by Anova test. BMI: Body mass index, BSMAS, Bergen social media addiction scale, ORTO-11: Orthorexia-11 scale; p<0.05, SD: Standard deviation

In this study, there was no significant difference between the students' BSMAS scores and gender, faculty, skipping meals, and regular physical activity status (p>0.05). However, a significant difference was found between the students' BSMAS scores and smoking, BMI (p<0.05). The BSMAS scores of smokers were found to be significantly higher than non-smokers (p<0.05). When BSMAS scores were evaluated according to BMI, the differences were found to be significant among all groups (p<0.05), only the difference between normal and underweight was not found to be significant (p>0.05) (Table 2)

The relationship between the participants' ORTO-11 scores and BSMAS scores is given in Table 3. A low statistically significant negative relationship was found between ORTO-11 scores and BSMAS scores (r=-0.058, p=0.048). According to this result, as social media addiction increases, the tendency toward orthorexia also increases (Table 3).

Table 3. The correlation between scores of the ORTO-11 and BSMAS

	BSMAS score	
	r	***p*-value**
ORTO-11 score	-0.058	0.048*

*p<0.05, r: Correlation coeffi ient, Pearson correlation analysis was applied. BSMAS: Bergen social media addiction scale, ORTO-11: Orthorexia-11 scale

Discussion

In this study, which was conducted to determine the frequency of ON among university students and to examine its relationship with various factors and social media addiction, the tendency to ON was found to be 24%. In a study conducted on Italian university students, the ON tendency was found to be 29% (21). Varga et al. (22) found that 56.9% of Hungarian university students tended to orthorexia. In a study conducted on Spanish and Polish university students, it was determined that the ON tendency was 10.9% in

Spanish students and 10.3% in Polish students. (23). In a study conducted on university students in France, the rate of students prone to ON was found to be 14.5% (24). According to the study conducted by Şanlıer et al. on Turkish university students, 59.8% of the students were found to be prone to ON (25). In the study conducted by Oğur et al. on Turkish university students, the rate of students with ON tendency was found to be 41.3% (26). In recent years, intense information has been shared in the media and social media around the world about food quality, naturalness, and its effects on health. The consumer's misunderstanding of the information or the publisher's misrepresentation of the information triggers the development of healthy eating obsession in people. It is thought that the high prevalence of ON in our study and many other studies may be affected by these factors. The reason why differences are observed between the ON tendency rates in different studies conducted on university students may be due to the use of different ON scales in these studies.

It has been determined that the ON rate is higher in groups such as healthcare workers and artists (27). In the study conducted by Fidan et al. (28) on medical students, it was found that 43.6% of medical students were prone to orthorexia. In a study conducted on Turkish nursing students, it was determined that 45.3% of the students were at risk for ON (29). In a study conducted on students studying in the nutrition and dietetics department in Turkey, it was determined that 72.2% of the students had an orthorexic tendency (30). In a study conducted on Turkish dietitians, the rate of individuals with a high risk of ON was found to be 41.9% (31). Alvarenga et al. (32) found that ON symptoms were observed with a frequency of 81.9% in Brazilian dietitians. The fact that students studying in health sciences departments have a higher ON tendency may be due to their sensitivity to being healthy due to the health and nutrition courses taught in these departments. The high orthorexic tendency seen especially in students studying in the field of nutrition can be attributed to the increase in anxiety about healthy nutrition as the level of nutritional knowledge increases. In this study, no significant difference was found between the ON tendency rates of students studying in the field of health and students studying in other fields. In addition to being more sensitive about healthy nutrition, students studying in the health field may not have higher ON tendencies because they are more capable of distinguishing the correct nutrition information presented in the media and social media in recent years.

In this study, the ON tendency of female students was found to be significantly higher than male students ($p<0.05$). Özkan et al. (33) similarly found that being male reduced the ON tendency. In their study in Italy, Ramacciotti et al. (34) reported that women were at twice the risk of ON compared to men. In the study conducted by Şanlıer et al. (25) on university students, the risk of ON in women was found to be 2.5 times that of men. Other studies show that female gender increases the tendency for ON (12,18,35,36). Contrary to these studies, there are also studies showing that the tendency towards ON is higher in men (28, 37). Some studies have shown that there is no significant difference between men and women in terms of ON tendency (27,38,39). In a meta-analysis study compiling 67 publications on ON, it was determined that tendencies towards orthorexic behaviors were similar between genders, but pathologies related to healthy nutrition were found to be more common in women (40). Women may be more interested in body image, healthy behaviors, and a healthy lifestyle than men, and they may be more influenced by content about healthy nutrition in the media and social media. However, as can be seen, the relationship between ON and gender is not clear in the literature.

It is stated that BMI may affect the tendency to ON through variables such as health status, diet, and eating habits (18). Gezer et al. found that the ON tendency was significantly higher in underweight individuals compared to those with normal body weight and obesity (41). In the current study, it was determined that orthorexic tendency increased significantly as BMI increased ($p<0.05$). Similar to our study, Fidan et al. (28) and Asil et al. (13) found that the risk of ON increased as the BMI value increased ($p<0.05$). The increased tendency towards ON in overweight or obese individuals can be thought to be due to the increased interest of these individuals in implementing weight loss diets and increasing the consumption of healthy foods. However, several studies do not find a relationship between ON and BMI (25, 42).

The use of social media, which has become widespread with the development of technology in recent years, has become central to life. Social media addiction is becoming increasingly common, especially among young people growing up in the digital generation (2). In this study, the BSMAS score

indicating social media addiction was found to be 16.9±4.6. In our study, social media addiction was found to be higher in female students than in males; however, the difference was not significant (p>0.05). There are other studies conducted in Turkey in which no significant difference was found between the social media addiction levels of male and female university students (43-45). This may be because men and women in this age group use social media for similar purposes and have similar free time. However, there are also studies in the literature showing that women's social media addiction levels are higher than men's (46-48). This may be due to differences in interests and work status between genders.

Time spent on social media can be a trigger for the development of eating disorders (4). It is thought that content about healthy nutrition on social media may lead to orthorexic tendencies (6). In this study, it was found that as social media addiction increases, the ON tendency increases significantly (p<0.05). In a study conducted on Turkish university students, it was determined that there was an opposite relationship between students' social media addiction and healthy eating attitudes (49). Again, in a study examining university students, it was determined that social media addiction significantly increased orthorexic tendency (p<0.05) (7). Other studies reveal that orthorexic tendency increases with the increase in social media addiction (12-15). Presenting thinness as a symbol of beauty and health on social media can trigger the development of other eating disorders in addition to the obsession with healthy eating. The fact that individuals who do not have sufficient knowledge about nutrition can easily share on social media is also a risk for the development of eating disorders.

This study contains some limitations. Because it has a cross-sectional design, causal inferences are limited. Another limitation is that the data were collected through an online survey, and measurements such as body weight and height were based on self-reports from the participants. Additionally, there are some debates in the literature about the accuracy of the ORTO-11 scale used in the study in determining orthorexic tendencies. Also, this study shows the fact that it was performed in a single center limited its generalizability to the society.

Conclusion

According to the results of our study, the tendency for ON among university students was found to be 24%. The ON tendency of female students was found to be significantly higher than that of male students. It has been determined that as BMI increases, orthorexic tendency increases significantly. Our most important result, which was our starting point in the planning of our study, was that as social media addiction increased, the ON tendency increased significantly. Suggestions and posts that trigger eating disorders should be prevented from social media content. Users should be aware of choosing experts in their fields who provide accurate and reliable information. Awareness activities should be organized about thinness imposed as the ideal body image on social media. In addition, to solve the problems of body image and perfectionism, informative activities should be carried out, especially for students. It would be beneficial to conduct future studies with more comprehensive samples and different age groups.

Ethics Committee Approval

This research complies with all the relevant national regulations, institutional policies and is under the tenets of the Helsinki Declaration, and has been approved by the Health Sciences Scientific Research and Publication Ethics Committee of Alanya Alaaddin Keykubat University (Decision dated 25/05/2022 and numbered 02/03).

Informed Consent

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

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Conflict of Interest

The authors have no conflict of interest to declare

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ORIGINAL ARTICLE

Evaluation of Knowledge, Attitudes/Behaviours, and Anxiety Levels of Academicians in the Faculty of Nursing Regarding Artificial Intelligence Applications

Hemşire Akademisyenlerin Yapay Zeka Uygulamaları Hakkında Bilgi, Tutum/Davranış ve Kaygı Düzeylerinin Değerlendirilmesi

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ABSTRACT

Aim: This study was conducted to evaluate the knowledge, attitude/behavior, and anxiety levels of nurse academics about artificial intelligence applications
Material and Methods: The research was conducted online with 202 nurse academicians in a descriptive type. The Data Collection Form and Artificial Intelligence Anxiety Scale were used to collect data. The data were also evaluated using the SPSS package program, version 21. Descriptive statistics, and the Kolmogorov-Smirnov, Shapiro-Wilk, Spearman, Mann-Whitney U, Kruskal-Wallis H tests were used to evaluate the data. A p-value of <0.05 was considered significant
Results: The study was completed with 202 nursing academicians. It was determined that the average score of the academicians on the Artificial Intelligence Anxiety Scale was 57.59±8.84. All participants stated that they had heard of the concept of artificial intelligence before. It was determined that there was a significant relationship between the academicians' receiving training on artificial intelligence, their belief that artificial intelligence will affect the nursing profession in the future, and their average score on the Artificial Intelligence Anxiety Scale
Conclusion: It has been detected that nursing academicians have high levels of anxiety about artificial intelligence. It has been determined that academicians' anxiety levels about artificial intelligence are affected by a lack of knowledge and negative attitudes. Our recommendation is to inform nursing academicians about artificial intelligence and provide the necessary support for them to take an active role in the inclusion of artificial intelligence in educational processes

Keywords: Artificial intelligence, Nurse, Academic, Anxiet

ÖZ

Amaç: Bu çalışma, hemşire akademisyenlerin yapay zeka uygulamaları hakkında bilgi, tutum/davranış ve kaygı düzeylerinin değerlendirilmesi amacıyla yapılmıştır.
Gereç ve Yöntemler: Araştırma tanımlayıcı tipte, online olarak 202 hemşire akademisyen ile yapılmıştır. Verilerin toplanmasında; Veri Toplama Formu, Yapay Zeka Kaygı Ölçeği kullanılmıştır. Verilerin değerlendirilmesinde SPSS 21 paket programı kullanılmıştır. Verilerin değerlendirilmesinde; tanımlayıcı istatistikler, Kolmogorov-Smirnov, Shapiro-Wilk, Spearman, Mann-Whitney U, Kruskal-Wallis H testi kullanılıştır. p<0.05 değeri anlamlı kabul edilmiştir.
Bulgular: Çalışma, 202 hemşire akademisyen ile tamamlanmıştır. Akademisyenlerin Yapay Zeka Kaygı Ölçeği puan ortalamalarının 57.59±8.84 olduğu belirlenmiştir. Katılımcıların hepsi yapay zeka kavramını daha önce duyduğunu belirtmiştir. Akademisyenlerin yapay zeka ile ilgili eğitim alma, yapay zekanın gelecekte hemşirelik mesleğini ekileceğini düşünme durumu ile Yapay Zeka Kaygı Ölçeği puan ortalamaları arasında anlamlı bir ilişki olduğu belirlenmiştir.
Sonuç: Hemşire akademisyenlerin yapay zeka kaygı düzeylerinin yüksek olduğu tespit edilmiştir. Akademisyenlerin yapay zekaya ilişkin kaygı düzeylerinin bilgi eksikliği ve olumsuz tutumlardan etkilendiği belirlenmiştir. Önerimiz; hemşire akademisyenlerin yapay zekaya ilişkin bilgilendirilmesi ve yapay zekanın eğitim süreçlerine dahil edilmesinde aktif rol alması için gerekli desteğin verilmesidir.

Anahtar Kelimeler: Yapay zeka, Hemşire, Akademisyen, Kaygı

Introduction

In today's world, advancements in technology have led to the widespread use of artificial intelligence applications across various fields. One of the most prominent areas is healthcare, where these applications are extensively utilized (1-4). There are many artificial intelligence applications developed for healthcare, such as telehealth, mobile applications, and smart devices (5, 6). These applications are used to expedite early diagnosis and treatment processes, reduce workload, enhance the quality of care, lower costs, and mitigate medical errors (7). Thus, healthcare professionals need to follow the advances and scientific studies regarding artificial intelligence applications (5). Artificial intelligence applications in the healthcare sector are predominantly developed through collaboration between physicians and engineers (3, 8), but the rapidly advancing artificial intelligence studies are also shaping the future of the nursing profession, and nurses must therefore actively engage in this transformative process and play a dynamic role in shaping the future of nursing (1, 8, 9).

To effectively utilize artificial intelligence applications in the nursing profession and observe their impact on nursing practices, it is essential to create awareness

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in this regard (10), and this requires the integration of content related to artificial intelligence and its applications into nursing education curricula (2, 7, 10, 11). Adding artificial intelligence applications to the nursing curriculum and using them in nursing education (12) will contribute to increasing the quality of teaching and will serve as the foundation for nurses to actively follow studies in the field of artificial intelligence and take part in applications in their professional lives (13). Nurse academicians involved in nursing education have essential roles in integrating artificial intelligence applications into the nursing profession (14). Within this context, the study aims to evaluate nurse academicians' knowledge, attitudes/behaviors, and anxiety levels about artificial intelligence applications.

Material and Methods

The Type, Location, and Time of the Research

The research was conducted in a descriptive design, utilizing an online data collection form, between April 1 and May 31, 2023.

Population and Sample

Sample calculation was not performed. The study was completed with 202 nurse academicians who met the inclusion criteria and were accessible online between April 1 and May 31, 2023. The power analysis following study completion indicated that the study's power was 85%. The inclusion criteria for the research were being an academician in the nursing field, agreeing to participate in the study, and completing and returning all surveys in full.

Data Collection Tools

'Data Collection Form' and 'Artificial Intelligence Anxiety Scale' were used to collect the data.

Data Collection Form: The data collection form was created by the researchers based on the literature (2, 8, 9, 11). The form includes questions about the sociodemographic characteristics of nurse academicians and their knowledge, attitudes/ behaviors, and anxiety levels regarding artificial intelligence applications.

Artificial Intelligence Anxiety Scale (AIAS): The Artificial Intelligence Anxiety Scale was developed by Wang and Wang (15) to measure individuals' levels of anxiety regarding developments in artificial intelligence. The Cronbach's alpha value for the entire scale is 0.964, and the alpha values for its subdimensions are as follows: learning subdimension = 0.974, job replacement subdimension = 0.917, sociotechnical blindness subdimension = 0.917, artificial intelligence configuration subdimension = 0.961 (15). The Turkish validity and reliability of the scale were established by Akkaya and colleagues (16). The Turkish version of the scale has the same four subdimensions and a Cronbach's alpha value of 0.937 for the entire scale, and 0.948, 0.895, 0.875, and 0.950 for the learning, job replacement, sociotechnical blindness, and artificial intelligence configuration subdimensions, respectively. It is a 16-item 5-point Likert-type scale, with responses ranging from 'Strongly Disagree (1)' to 'Strongly Agree (5)'. The total score that can be obtained from the scale ranges from 16 to 80. As the scale score increases, the level of anxiety towards artificial intelligence also increases (16).

Data Collection

Data was collected using an online form created with the 'Google Docs' application during the specified dates (April 1 to May 31, 2023). Nurse academicians for the sample were reached using the snowball sampling method. Information about the research was provided to participants with the text at the beginning of the survey questionnaire. It took approximately 10 minutes to complete the survey form.

Evaluation of the Data

The SPSS 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0, Armonk, NY: IBM Corp.) software package was used for data analysis. Descriptive statistics (frequency, percentage, mean, standard deviation) were employed to analyze the data. The fit of the data to normal distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. The relationship between two non-normally distributed independent variables was examined using the Spearman test, and the comparison of two non-normally distributed independent variables was conducted using the Mann-Whitney U test. The Kruskal-Wallis H test was utilized to compare three or more variables. The statistical significance level was set at $p<0.05$.

Results

The study was completed with 202 nurse academicians. Their mean AIAS score was 57.59±8.84. Their AIAS subscale score means are shown in Table 1.

Table 1. Mean Scores of AIAS and Subscales of AIAS of Academicians in the Faculties of Nursing

	Mean±SD (X±SD) (Minimum-Maximum)
AIAS Score	57.59±8.84 (34.00-79.00)
Subdimension of learning	13.70±4.12 (5.00-24.00)
Subdimension of job replacement	14.36±3.94 (4.00-20.00)
Subdimension of sociotechnical blindness	17.14±2.52 (9.00-20.00)
Subdimension of artificial intelligence configuration	12.38±2.85 (3.00-15.00)

AIAS: Artificial Intelligence Anxiety Scale, SD: Standard deviation

Nurse academicians had a mean age of 36.53±6.79 years, and the average time they worked in the profession was 12.19±7.48 years. A significant relationship was found between the length of time in the profession and the AIAS mean score (p = 0.011). No statistical difference was detected between the participants' titles and work fields and the artificial intelligence anxiety scale mean scores (p>0.05). There was no significant relationship between other sociodemographic characteristics of academicians and AIAS mean scores (p>0.05) (Table 2).

All participants stated that they had heard of the concept of artificial intelligence before: 25.2% (n=51) from school, 24.8% (n=50) from social media, 26.7% (n=54) from their circle of friends, and 23.3% (n=47) from the news. There was a significant relationship between academicians' knowledge of the concept

Table 2. Comparison of Academicians' Sociodemographic Characteristics in the Faculties of Nursing and AIAS Mean Scores

Variables (n=202)	n (%)	AIAS Mean Score		Statistical Analysis*
		Median	Min-Max	
Age (X±SD; 36.53±6.79)				
25-37	127 (62.9)	58.0	34.0-79.0	Z=-0.167 p=0.867
38-50	75 (37.1)	57.0	43.0-75.0	
Gender				
Female	178 (88.1)	58.0	34.0-79.0	Z=-1.111 p=0.266
Male	24 (11.9)	58.0	36.0-68.0	
Educational Status				
Bachelor's degree	3 (1.5)	52.0	52.0-67.0	χ^2=0.148 p=0.929
Master's degree	55 (27.2)	59.0	34.0-77.0	
Doctorate	144 (71.3)	58.0	36.0-79.0	
Marital Status				
Single	75 (37.1)	59.0	36.0-79.0	Z=-1.244 p=0.213
Married	127 (62.9)	57.0	34.0-77.0	
Having Children				
Yes	106 (52.5)	58.0	36.0-75.0	Z=-0.334 p=0.738
No	96 (47.5)	57.5	34.0-79.0	
Family Type				
Nuclear family	199 (98.5)	58.0	34.0-79.0	Z=-1.080 p=0.280
Extended family	3 (1.5)	70.0	47.0-72.0	
Income Level				
Income is less than expenses	27 (13.4)	53.0	40.0-73.0	χ^2=5.821 p=0.064
Income is equal to expenses	135 (66.8)	59.0	34.0-79.0	
Income is more than expenses	40 (19.8)	59.0	36.0-72.0	
Time spent in the profession (X±SD; 12.19±7.48)				
1-10 years	73 (36.1)	56.0	34.0-70.0	χ^2=9.070 **p=0.011**
11-20 years	60 (29.7)	58.0	40.0-79.0	
21-30 years	69 (34.2)	60.5	36.0-77.0	
Total	**202 (100)**			

Z = Mann-Whitney U test, χ^2= Kruskal-Wallis H test
AIAS: Artificial Intelligence Anxiety Scale, SD: Standard deviatio

of artificial intelligence, receiving education related to artificial intelligence, mentioning artificial intelligence applications to students in classes/practices, believing that artificial intelligence would impact the nursing profession in the future, and their mean AIAS scores (p=0.008, p=0.002, p=0.029, p=0.017, respectively) (Table 3).

Table 3. Comparison of Academicians' Mean Scores of AIAS in the Faculties of Nursing with Some Features of Artificial Intelligence

Variable (N=202)	n (%)	AIAS Mean Score		Statistical Analysis*
		Median	Min-Max	
Knowing the Meaning of Artificial Intelligence Concept				
Yes	144 (71.3)	57.0	34.0-77.0	Z=-2.646 **p=0.008**
No	58 (28.7)	60.0	46.0-79.0	
Receiving Training on Artificial Intelligence				
Yes	16 (7.9)	54.5	34.0-69.0	Z=-1.298 **p=0.002**
No	186 (92.1)	58.0	36.0-79.0	
Mentioning Artificial Intelligence Applications to Students in Classes/Practices				
Yes	45 (22.3)	57.0	36.0-77.0	χ^2=7.112 **p=0.029**
Partly	97 (48.0)	57.0	34.0-75.0	
No	60 (29.7)	61.5	40.0-79.0	
Thinking that Artificial Intelligence to affect nursing in the future				
Yes, it will affect negatively	187 (92.6)	64.0	34.0-77.0	Z=-2.396 **p=0.017**
No, it will not affect negatively	15 (7.4)	57.0	48.0-79.0	
Total	**202 (100)**			

Z = Mann-Whitney U test, χ^2= Kruskal-Wallis H test

AIAS: Artificial Intelligence Anxiety Scale, SD: Standard deviation

Table 4. Academicians' Thoughts in the Faculties of Nursing on the Use of Artificial Intelligenc

Variable	n	%
Purposes of Using Artificial Intelligence in Nursing		
Measuring vital signs	116	57.4
Facilitating medication preparation	111	55.0
Skills training	109	54.0
Reducing diagnosis and treatment errors	106	52.5
Automatic detection of patient safety issues	103	51.0
Positioning the patient	103	51.0
Ensuring nurse safety	103	51.0
Facilitating patient follow-up	102	50.5
Bathing a patient	101	50.0
Patient transport	101	50.0
Reducing nurses' workload	101	50.0
Organising patient routines or treatment plans	85	42.1
Problems That Artificial Intelligence May Cause in Nursing Care		
Legal issues	126	62.4
Ethical and patient privacy issues	110	54.5
Employment problems	109	54.0
Empathy issues	104	51.5
Security problems	104	51.5

**n and % are different because more than one option is marked

Nurse academicians expressed that artificial intelligence could be used for various purposes, such as measuring vital signs (57.4%, n=116), facilitating medication preparation (55.0%, n=111), and skills training (54.0%, n=109). They also indicated that artificial intelligence applications in nursing care could lead to different problems, including legal problems (62.4%, n=126), ethical issues and patient privacy (54.5%, n=110), employment problems (54.0%, n=109), empathy problems (51.5%, n=104) and security issues (51.5%, n=104) (Table 4).

Discussion

The study found that nurse academicians' anxiety levels towards artificial intelligence were high (57.59±8.84; minimum: 16, maximum: 80). The highest anxiety levels among academicians in the subdimensions were in the sociotechnical blindness, job replacement, learning, and artificial intelligence configuration subdimensions, respectively. In the literature, there is no detailed examination of subdimensions, and no study specifically involving nurse academicians could be found. In various studies (17-19), including nurses, moderate levels of anxiety about artificial intelligence were observed. Studies conducted with nursing students (3, 8, 20-22) showed that students were concerned about artificial intelligence. The results of the present study are consistent with the literature. This result may be due to nurse academicians not being involved in processes related to artificial intelligence starting from their educational life.

It was determined that as the duration of professional experience increased, the anxiety levels of nurse academicians about artificial intelligence also increased. Nurse academicians who did not know the meaning of artificial intelligence, had not received education related to artificial intelligence, did not mention artificial intelligence applications to students in classes/practices, and believed that artificial intelligence would negatively impact the nursing profession were found to have higher levels of anxiety about artificial intelligence. In studies involving nursing students (11, 20, 22), students reported not receiving education about artificial intelligence throughout their educational lives. In studies involving nurses working in clinical settings (11, 19, 23, 24), nurses expressed that if they received education about artificial intelligence during their training, their anxiety about artificial intelligence would be lower, and they would be more easily involved in processes related to artificial intelligence. In studies including working nurses (8, 19, 22), some participants believed that artificial intelligence would threaten their profession. A study (18) underlines that artificial intelligence should be actively used in nursing education, showing that practices were more permanent in nursing groups where artificial intelligence was used in education (25). Several studies (11, 26-30) have emphasized that educators in this field have essential responsibilities in integrating artificial intelligence into the nursing profession. Buchanan et al. (6) highlighted that nurse academicians need to receive the necessary training to actively use artificial intelligence in the education of students. Our study result is consistent with the literature. Nurse academicians' negative thoughts and attitudes toward artificial intelligence may be related to their lack of knowledge about it.

Nurse academicians stated that artificial intelligence is mainly used for measuring vital signs, facilitating medication preparation, and skill training. In the literature (3, 4, 21, 31-33), it is mentioned that artificial intelligence applications will facilitate nursing care practices. The study's results are consistent with the literature and support that using artificial intelligence in nursing will provide benefits in many areas

Participants expressed that artificial intelligence could potentially lead to legal issues, ethical problems, violation of patient privacy, employment issues, empathy problems, and security concerns. According to some studies (3, 8, 20, 21, 34, 35), artificial intelligence applications used in the field of health might cause problems such as ethics, patient privacy, and security issues. This result of the present study is consistent with the literature and may be associated with nurse academicians not actively participating in artificial intelligence processes.

Limitations of the research; data is collected online.

Conclusions

The study found that nurse academicians had high levels of anxiety about artificial intelligence. Nurse academicians who did not know the meaning of artificial intelligence, had not received education related to artificial intelligence, did not mention artificial intelligence applications to students in classes/practices, and believed that artificial intelligence would negatively impact the nursing profession were found to have higher levels of anxiety about artificial intelligence. Participants expressed that artificial intelligence could potentially lead to legal issues, ethical problems, violation of patient

privacy, employment issues, empathy problems, and security concerns. It was determined that the negative knowledge and attitudes of academicians toward artificial intelligence increased their anxiety levels. In the literature review conducted within the scope of the study, it was seen that there are very few studies on nurse academicians who play a key role in nursing education. Our recommendation is to inform nurse academics about artificial intelligence, include them in relevant processes, encourage the active use of artificial intelligence in nursing, and increase multidisciplinary studies.

Ethical Approval

Before starting the study, ethical approval (Date: 05.04.2023) and permission to use the Artificial Intelligence Anxiety Scale were obtained. Participants were provided information about the study through the text at the beginning of the survey questionnaire. Only voluntary participants were included in the study.

Author Contributions: Conceptualization, DY and AA.; Methodology, DY and AA.; Formal analysis, DY and AA.; Investigation, DY and AA.; Resources, DY and AA.; Writing-original draft preparation, DY and AA.; Writing-review and editing, DY and AA. 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.

Conflicts of Interest

There are no financial and nonfinancial 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

Automatic Segmentation of the Cerebellum in Healthy Individuals: A volBrain (CERES) Study

Sağlıklı Bireylerde Serebellumun Otomatik Segmentasyonu: Bir volBrain (CERES) Çalışması

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ABSTRACT

Aim: We aimed to investigate the total cerebellum volume and the volume of healthy individuals' right and left cerebellum lobes according to age groups and sex.
Methods: 3D T1-weighted Magnetic Resonance Images of 200 individuals (100 females, 100 males) of both sexes between the ages of 18-78 were included in our study. Total cerebellum volume and volume results of cerebellum lobules will be calculated from these images with the sub-tab CERES of the volBrain software program.
Results: The total cerebellum volume in our study was found to be 115.41±12.25 cm3 in females and 126.27±14.78 cm3 in males, and the valueswere statistically significant (p<0.001). The right side lobule I-II, lobule IV, lobule crus II, lobule VIIB, lobule VIIIA, and lobule X valuesof the cerebellum were statistically higher than the left side (p<0.05). On the left side, lobule V, VIIIB, and IX values were statistically higher than the right side (p<0.05). When evaluated according to sex, the values of males were statistically higher than females in all parameters except for the total lobule I-II, right lobule I-II, left lobule I-II, right lobule V, total lobule VI and right lobule VI values(p<0.05). According to age groups, except for total lobule I-II, right lobule I-II, and left lobule I-II values, all other parameters were statistically lower in the 50 years old and above group than in the under 50 years old group (p<0.05).
Conclusion: We believe that knowing the total cerebellum volume and volumetric analysis of its lobules in healthy adults will define the disease group and its prognosis

Keywords: Age, Cerebellum, Magnetic Resonance Imaging, Sex, volBrain, Volume

ÖZ

Amaç: Sağlıklı bireylerin toplam cerebellum hacmi ile sağ-sol cerebellum loblarının hacmini yaş grupları ve cinsiyete göre araştırmayı amaçladık.
Metod: Çalışmamıza 18-78 yaş arası her iki cinsiyete ait 200 bireyin (100 kadın, 100 erkek) 3D T1 ağırlıklı Manyetik Rezonans Görüntüleri dahil edilmiştir. Bu görüntüler üzerinden volBrain yazılım programının alt sekmesi CERES ile toplam cerebellum hacmi ve cerebellum loblarının hacim sonuçları hesaplanacaktır.
Bulgular: Çalışmamızın toplam cerebellum hacmi kadınlarda ortalama 115.41±12.25 cm3, erkeklerde ise 126.27±14.78 cm3 olarak bulundu ve değerler istatistiksel olarak anlamlıydı (p<0.001). Cerebellum'un sağ taraf lobul I-II, lobul IV, lobul crus II, lobul VIIB, lobul VIIIA ve lobul X değerleri sol tarafa göre istatistiksel olarak yüksekti (p<0.05). Sol tarafta ise lobul V, lobul VIIIB ve lobul IX değerleri sağ tarafa göre istatistiksel olarak yüksekti (p<0.05). Cinsiyete göre değerlendirildiğinde toplam lobul I-II, sağ lobul I-II, sol lobul I-II, sağ lobul V, toplam lobul VI ve sağ lobul VI değerleri dışındaki diğer tüm parametrelerde erkeklerin değerleri kadınlara göre istatistiksel olarak yüksekti (p<0.05). Yaş gruplarına göre toplam lobul I-II, sağ lobul I-II ve sol lobul I-II değerleri dışındaki diğer tüm parametrelerde 50 yaş ve üzeri grubun değerleri 50 yaş altındaki gruba göre istatistiksel olarak düşüktü (p<0.05).
Sonuç: Sağlıklı yetişkinlere ait toplam cerebellum hacmi ve loblarının hacimsel analizinin bilinmesi hastalık grubunun tanımlanması ve prognozu açısından anlamlı olacağını düşünmekteyiz.

Anahtar Kelimeler: Yaş, Cerebellum, Manyetik Rezonans Görüntüleme, Cinsiyet, volBrain, Hacim

Introduction

The cerebellum (1), the small tongue in Latin, is located in the fossa cerebellaris of the occipital bone (2). It constitutes 10% of the total brain volume and is also a part of the metencephalon, which contains approximately half as many neurons as all neurons in the brain (2, 3). It connects to the brainstem via three peduncles (4). The cerebellum consists of two hemispheres called hemispheric and is connected by the vermis. It is divided into 3 main sub-lobes: the anterior lobe (lobules I-V), posterior lobe (lobules VI-IX), and flocculonodular lobe (lobules X) by the primary fissure and posterolateral fissure (5, 6). Lobules IV, V, VI, and VIII are effective in motor tasks, while lobules VI, Crus I, Crus II, VIIB, IX, and X are effective in cognitive tasks (7). It is stated that the cerebellum plays a role in motor skills, balance, coordination functions, and higher cognitive tasks (8, 9).

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Previous studies have reported that schizophrenia (10), depression (11), multiple sclerosis (12), tinnitus (13), alcohol (14) and drug use (15, 16) affect the cerebellum. Studies have reported age-related volumetric decreases in different parts of the cerebellum (17, 18, 19). Han et al. (20) reported that the cerebellum hemispheres showed a more significan volumetric decrease with age than the vermis lobules. In addition to these studies, the cerebellum volume does not change with age (21, 22). When the cerebellum volume results were evaluated according to male and female sex, differences were reported (23-25).

Recently, it has been observed that the volBrain software program is used for automatic volume analysis and segmentation of the cerebellum in different age groups and diseases (11, 26). With volBrain's sub-segmentation tool CERES, we obtain information about the cerebellum lobes and tissues (27, 28). Therefore, the present study aimed to evaluate the interaction of the volume of the right/left hemispheres at the lobules level with age groups and sex, as well as the total cerebellum volume, using the volBrain CERES program.

Material Method

Participants

Magnetic Resonance (MR) images of 200 healthy individuals (100 females, 100 males) between the ages of 18-78 were included in the study. Healthy individuals who applied to Ankara Etlik City Hospital with headaches, who did not have a neurological diagnosis, and who did not undergo brain surgery were included in the study. Approval was received from the Ankara Etlik City Hospital Scientific Research Evaluation and Ethics Committee with the decision number AEŞH-BADEK-2024-770.

MR Protocol

MR images were examined using a standard head coil on a 3 Tesla (Philips Ingenia Elition, 2020). For more detailed imaging of the body structure, a high-resolution, sagittal plane, T1-weighted 3D TFE sequence was obtained. Repetition Time (TR): 6.8 ms, Echo Time (TE): 3.2 ms, Field of View (FOV): 256x256 mm2, matrix: 256x256, slice thickness was 1 mm. A total of 195 slices were obtained with the specified parameters in an average of 2 minutes and 35 seconds.

MR segmentation

MR images of participants of both sexes (n=200) included in the study were exported with Picture Archiving and Communication Systems (PACS) in the first stage. In the second stage, these data in Digital Imaging and Communications in Medicine (DICOM) format were anonymized with MRIcron (https://www.nitrc.org/projects/mricron). Then, they were converted to the Neuroimaging Information Technology Initiative format with the same program. The processed MR images were uploaded to volBrain's segmentation tools, the CERES pipeline system. The CERES pipeline is an online, open-access, web-based data processing system that automatically segments cerebellum tissues and lobules. Analysis results are presented as PDF and CSV files (27) (Figure 1)

Image Information

Orientation	radiological
Scale factor	0.67
SNR	14.79
Total intracranial volume (cm^3)	1225.17

Volumes[1]	Total (cm^3/%)	Right (cm^3/%)	Left (cm^3/%)	Asym.(%)[2]
Cerebellum	106.86 (8.7224) [7.9791, 10.7199][5]	53.70 (4.3833) [4.0144, 5.3808]	53.16 (4.3391) [3.9516, 5.3522]	1.0142 [-3.1662, 5.1619]
Lobule I-II	0.19 (0.0154) [0.0000, 0.0269]	0.08 (0.0068) [0.0000, 0.0127]	0.11 (0.0086) [0.0000, 0.0147]	-24.1135 [-44.3086, 37.2144]
Lobule III	1.78 (0.1450) [0.0736, 0.1604]	0.86 (0.0706) [0.0355, 0.0796]	0.91 (0.0744) [0.0361, 0.0828]	-5.2592 [-24.9907, 19.1816]
Lobule IV	3.54 (0.2892) [0.2191, 0.4142]	2.04 (0.1668) [0.0981, 0.2096]	1.50 (0.1224) [0.1110, 0.2146]	30.7026 [-33.9661, 22.2315]
Lobule V	7.55 (0.6166) [0.2191, 0.4142]	3.68 (0.3000) [0.0981, 0.2096]	3.88 (0.3166) [0.1110, 0.2146]	-5.3710 [-33.9661, 22.2315]
Lobule VI	14.73 (1.2025) [0.9752, 1.6064]	7.41 (0.6047) [0.4834, 0.8151]	7.32 (0.5977) [0.4755, 0.8075]	1.1596 [-15.0072, 17.5399]
Lobule Crus I	17.54 (1.4313) [1.4170, 2.3812]	8.87 (0.7237) [0.7127, 1.2107]	8.67 (0.7076) [0.6884, 1.1863]	2.2453 [-10.5788, 15.9092]
Lobule Crus II	13.12 (1.0710) [0.8399, 1.5195]	6.86 (0.5599) [0.4169, 0.7846]	6.26 (0.5111) [0.4054, 0.7525]	9.1140 [-15.4607, 23.0644]
Lobule VIIB	8.46 (0.6906) [0.5018, 0.8782]	3.93 (0.3204) [0.2474, 0.4548]	4.54 (0.3702) [0.2391, 0.4386]	-14.4333 [-19.2651, 26.3492]
Lobule VIIIA	10.45 (0.8528) [0.6226, 1.0599]	4.97 (0.4055) [0.2964, 0.5293]	5.48 (0.4473) [0.3047, 0.5522]	-9.8109 [-26.9777, 19.8886]
Lobule VIIIB	6.85 (0.5589) [0.4352, 0.7265]	3.47 (0.2831) [0.2089, 0.3722]	3.38 (0.2758) [0.2103, 0.3702]	2.6121 [-24.8315, 24.9395]
Lobule IX	7.01 (0.5719) [0.3760, 0.7454]	3.67 (0.2999) [0.1914, 0.3737]	3.33 (0.2721) [0.1821, 0.3743]	9.7143 [-10.9810, 14.9470]
Lobule X	1.11 (0.0903) [0.3760, 0.7454]	0.57 (0.0468) [0.1914, 0.3737]	0.53 (0.0435) [0.1821, 0.3743]	7.3627 [-10.9810, 14.9470]

Lobule segmentation

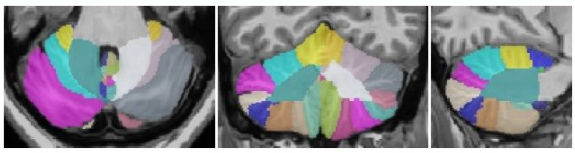

Figure 1. VolBrain CERES segmentation result of a participant

CERES data were visualized in three dimensions with ITK-Snap (https://www.itksnap.org) and 3D Slicer (https://www.slicer.org/, version 5.6.2) (Figures 2 and 3).

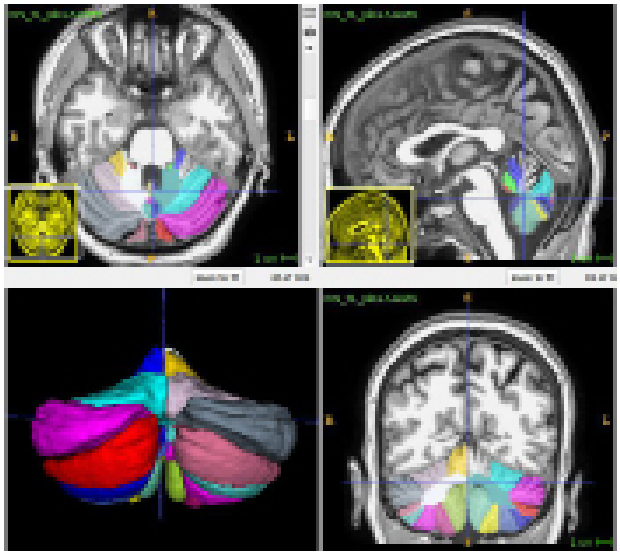

Figure 2. Visualization of volBrain CERES data with ITK-Snap

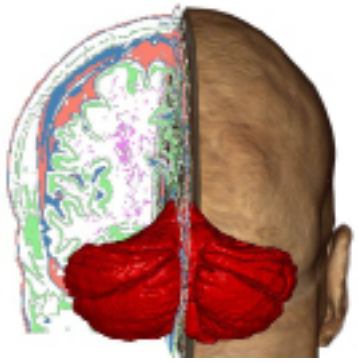

Figure 3. Visualization of volBrain CERES data with 3D Slicer

Results

A total of 200 healthy individuals, 100 males, and 100 females, were included in the study. The ages of the participants ranged from 18 to 78 years, and the mean age was 43.9±15.7 years. According to Table 1, total cerebellum and right and left cerebellum volume values were statistically higher in males than in females (p<0.05). According to Pearson correlation coefficient analysis, a statistically significant negative correlation was found between total cerebellum, right and left cerebellum volumes, and age (p<0.05; r1=-0.368, r2=-0.363, and r3=-3.68, respectively).

There was no statistically significant relationship between lobule I-II total, lobule I-II right, lobule I-II left, lobule V right, lobule VI total, and lobule VI right volume values of males and females (p>0.05). In all other lobe measurements, the measurement values of males were statistically higher than females (p<0.05). In the Pearson correlation coefficie t findings, no statistically significant relationship was found between age and lobule I-II total, lobule I-II right, lobule I-II left, and lobule III right volume values (p>0.05). A statistically significant negative correlation was found between all other lobe volumes and age (p<0.05) (Table 2).

Total cerebellum and right and left cerebellum volume values were statistically lower in the 50 and over group compared to the under 50 group (p<0.05) (Table 3).

According to Table 4, the differences between the lobule I-II total, lobule I-II right, and lobule I-II left volume values of the under 50 and 50 and over groups were not statistically significant (p>0.05). In all other parameters, the volume results of the 50 and over group were statistically lower than the under 50 group (p<0.05).

The right side lobule I-II, lobule IV, lobule crus II, lobule VIIB, lobule VIIIA, and X volume values were statistically higher than the left side (p<0.05). The lobule V, VIIIB, and IX volume values were statistically higher on the left side (p<0.001). There was no statistical difference in the volume values of lobule III, lobule VI, and lobule crus I on the right and left sides (p>0.05) (Table 5).

Statistical Method

Data were evaluated using the Statistical Package for Social Sciences for Standard Concurrent User, version 29.0 (SPSS, IBM Corp., Armonk, New York, USA). Descriptive statistics were given as mean ± standard deviation. Two-group comparisons were made using the t-test in independent samples. Differences between right and left-side volume measurements were compared using the paired t-test. Relationships

Table 1. Comparison of Cerebellum Volume by Sex and Correlation of Measurements with Age

Variables		Sex				Age (years)	
		Female	Male	t value	*p* value†	r	*p*
Cerebellum volume (cm^3)	T	115.417±12.258	126.277±14.784	5.655	**<0.001**	**-0.368**	**<0.001**
	R	57.938±6.202	63.340±7.498	5.552	**<0.001**	**-0.363**	**<0.001**
	L	57.479±6.104	62.937±7.443	5.670	**<0.001**	**-0.368**	**<0.001**

Data are summarized as mean±standard deviation. †: Independent samples t-test. *r*: Pearson correlation coefficient (T: Total, R: Right, L: Left)

Table 2. Comparison of Cerebellum Lobe Measurements Under Sex and Correlation with Age

Cerebellum lobe volume (cm^3)		Sex				Age (years)	
		Female	Male	*t* value	*p* value†	r	p
Lobule I-II	T	0.126±0.048	0.125±0.040	0.208	0.836	0.109	0.123
	R	0.064±0.021	0.063±0.021	0.077	0.939	0.083	0.245
	L	0.063±0.032	0.061±0.023	0.271	0.787	0.112	0.116
Lobule III	T	1.387±0.261	1.523±0.305	3.393	**0.001**	**-0.151**	**0.033**
	R	0.706±0.146	0.763±0.159	2.646	**0.009**	-0.134	0.059
	L	0.681±0.133	0.760±0.161	3.786	**<0.001**	**-0.152**	**0.032**
Lobule IV	T	4.142±0.615	4.690±0.737	5.716	**<0.001**	**-0.216**	**0.002**
	R	2.046±0.333	2.293±0.380	4.906	**<0.001**	**-0.260**	**<0.001**
	L	2.096±0.334	2.397±0.419	5.615	**<0.001**	**-0.147**	**0.037**
Lobule V	T	7.742±1.188	8.136±1.155	2.379	**0.018**	**-0.195**	**0.006**
	R	3.872±0.641	4.022±0.620	1.689	0.093	**-0.182**	**0.010**
	L	3.870±0.609	4.114±0.612	2.821	**0.005**	**-0.185**	**0.009**
Lobule VI	T	15.829±2.382	16.528±2.782	1.910	0.058	**-0.335**	**<0.001**
	R	7.937±1.245	8.256±1.500	1.639	0.103	**-0.331**	**<0.001**
	L	7.892±1.210	8.272±1.392	2.060	**0.041**	**-0.316**	**<0.001**
Lobule Crus I	T	22.627±3.514	24.550±4.037	3.593	**<0.001**	**-0.359**	**<0.001**
	R	11.424±1.833	12.463±1.995	3.833	**<0.001**	**-0.339**	**<0.001**
	L	11.202±1.761	12.087±2.128	3.204	**0.002**	**-0.363**	**<0.001**
Lobule Crus II	T	14.961±2.259	16.275±2.696	3.738	**<0.001**	**-0.318**	**<0.001**
	R	7.607±1.191	8.305±1.474	3.684	**<0.001**	**-0.308**	**<0.001**
	L	7.354±1.181	7.970±1.350	3.437	**0.001**	**-0.299**	**<0.001**
Lobule VIIB	T	8.360±1.199	9.346±1.547	5.039	**<0.001**	**-0.266**	**<0.001**
	R	4.222±0.627	4.770±0.921	4.920	**<0.001**	**-0.259**	**<0.001**
	L	4.138±0.658	4.576±0.762	4.354	**<0.001**	**-0.234**	**0.001**
Lobule VIIIA	T	10.296±1.488	12.202±2.007	7.630	**<0.001**	**-0.274**	**<0.001**
	R	5.086±0.829	5.951±1.046	6.480	**<0.001**	**-0.249**	**<0.001**
	L	5.209±0.798	6.251±1.110	7.620	**<0.001**	**-0.266**	**<0.001**
Lobule VIIIB	T	7.173±0.957	8.389±1.211	7.881	**<0.001**	**-0.261**	**<0.001**
	R	3.516±0.517	4.112±0.636	7.264	**<0.001**	**-0.213**	**0.003**
	L	3.656±0.504	4.277±0.678	7.349	**<0.001**	**-0.278**	**<0.001**
Lobule IX	T	6.614±1.278	7.279±1.297	3.652	**<0.001**	**-0.272**	**<0.001**
	R	3.379±0.653	3.721±0.678	3.628	**<0.001**	**-0.251**	**<0.001**
	L	3.234±0.635	3.558±0.638	3.592	**<0.001**	**-0.287**	**<0.001**
Lobule X	T	1.115±0.154	1.194±0.188	3.251	**0.001**	**-0.256**	**<0.001**
	R	0.567±0.079	0.605±0.104	2.898	**0.004**	**-0.234**	**0.001**
	L	0.548±0.080	0.590±0.091	3.402	**0.001**	**-0.263**	**<0.001**

Data are summarized as mean ± standard deviation. †: Independent samples t-test. *r*: Pearson correlation coefficient (T: Total, R: Right, L: Left)

Table 3. Comparison of Cerebellum Measurements According to Age Groups

Variables		Groups		Test Statistics	
		<50	≥50	t value	*p* value†
Cerebellum volume (cm^3)	T	125.116±15.151	114.444±11.037	5.413	**<0.001**
	R	62.747±7.657	57.478±5.652	5.270	**<0.001**
	L	62.369±7.627	56.966±5.441	5.473	**<0.001**

Data are summarized as mean±standard deviation. †: Independent samples t-test (T: Total, R: Right, L: Left)

Table 4. Comparison of Cerebellum Lobe Measurements According to Age Groups

Cerebellum Lobe Volume (cm^3)		Groups		Test Statistics	
		<50	≥50	*t* value	*p* value†
Lobule I-II	T	0.123±0.043	0.129±0.046	-0.973	0.332
	R	0.063±0.022	0.064±0.018	-0.020	0.984
	L	0.060±0.024	0.066±0.033	-1.530	0.128
Lobule III	T	1.504±0.314	1.380±0.235	3.021	**0.003**
	R	0.760±0.167	0.696±0.127	2.899	**0.004**
	L	0.744±0.163	0.684±0.129	2.809	**0.005**
Lobule IV	T	4.562±0.777	4.197±0.596	3.568	**<0.001**
	R	2.252±0.393	2.046±0.318	3.909	**<0.001**
	L	2.311±0.434	2.151±0.344	2.772	**0.006**
Lobule V	T	8.189±1.254	7.564±0.965	3.776	**<0.001**
	R	4.072±0.660	3.759±0.544	3.520	**0.001**
	L	4.117±0.663	3.804±0.500	3.587	**<0.001**
Lobule VI	T	16.890±2.649	15.110±2.149	5.009	**<0.001**
	R	8.455±1.408	7.558±1.163	4.725	**<0.001**
	L	8.435±1.337	7.552±1.090	4.915	**<0.001**
Lobule Crus I	T	24.592±4.093	22.083±3.029	4.692	**<0.001**
	R	12.420±2.084	11.229±1.574	4.349	**<0.001**
	L	12.172±2.098	10.854±1.539	4.821	**<0.001**
Lobule Crus II	T	16.259±2.712	14.656±1.988	4.533	**<0.001**
	R	8.306±1.439	7.430±1.106	4.613	**<0.001**
	L	7.953±1.383	7.227±1.035	4.005	**<0.001**
LobuleVIIB	T	9.159±1.582	8.394±1.137	3.728	**<0.001**
	R	4.666±0.889	4.241±0.668	3.644	**<0.001**
	L	4.493±0.799	4.153±0.600	3.243	**0.001**
Lobule VIIIA	T	11.671±2.041	10.615±1.781	3.769	**<0.001**
	R	5.700±1.017	5.246±1.011	3.101	**0.002**
	L	5.971±1.148	5.369±0.906	3.941	**<0.001**
Lobule VIIIB	T	8.013±1.248	7.432±1.170	3.303	**0.001**
	R	3.915±0.645	3.661±0.632	2.749	**0.007**
	L	4.097±0.678	3.771±0.617	3.457	**0.001**
Lobule IX	T	7.252±1.378	6.487±1.104	4.153	**<0.001**
	R	3.696±0.711	3.331±0.585	3.816	**<0.001**
	L	3.556±0.682	3.157±0.534	4.413	**<0.001**
Lobule X	T	1.194±0.180	1.096±0.152	3.998	**<0.001**
	R	0.605±0.098	0.557±0.078	3.617	**<0.001**
	L	0.589±0.089	0.539±0.078	4.120	**<0.001**

Data are summarized as mean±standard deviation. †: Independent samples t-test (T: Total, R: Right, L: Left)

Table 5. Comparison of the Right- and Left-sided Measurements

Cerebellum lobe volume (cm^3)	Side		Test Statistics	
	Right	Left	*t* value	*p* value‡
Lobule I-II	60.639±7.378	60.208±7.320	3.565	**<0.001**
Lobule III	0.063±0.021	0.062±0.028	0.968	0.334
Lobule IV	0.735±0.155	0.720±0.153	2.062	**0.041**
Lobule V	2.169±0.377	2.247±0.407	-3.814	**<0.001**
Lobule VI	3.947±0.634	3.992±0.621	-1.536	0.126
Lobule Crus I	8.096±1.384	8.082±1.315	0.287	0.774
Lobule Crus II	11.943±1.981	11.645±1.998	5.247	**<0.001**

Lobule VIIB	7.956±1.382	7.662±1.302	5.260	**<0.001**
Lobule VIIIA	4.496±0.832	4.357±0.743	3.378	**<0.001**
Lobule VIIIB	5.519±1.036	5.730±1.096	-4.097	**<0.001**
Lobule IX	3.814±0.650	3.967±0.672	-4.909	**<0.001**
Lobule X	3.550±0.686	3.396±0.655	11.018	**<0.001**

Data are summarized as mean±standard deviation. ‡: Paired t-test

between age and volume values were evaluated using the Pearson correlation coefficient. A $p<0.05$ value was considered statistically significant

Discussion

The cerebellum is a neuroanatomical structure providing important connections with the brainstem. In the literature, volumetric studies of the cerebellum have been analyzed according to age and sex using different techniques. Our aim in this study was to investigate the right-left cerebellum volume of healthy individuals at the lobular level by creating groups of under 50 and over 50 years of age according to age/sex using the CERES program, which is the lower toolbar of volBrain.

Previous studies reported that the cerebellum volume varied according to sex using the stereological method, but age did not have a significant effect (29). In another study using the same method, cerebellum volume was estimated in 19 healthy Caucasian males aged between 19 and 84. The total cerebellum volume was reported to decrease by 16% without any neuronal loss. The same study also emphasized that there is a decrease in frontal lobe volume with age (30).

In a study conducted on healthy volunteers, the total cerebellum volume remained constant until age 50 and decreased with age (17). Similarly, in our study, total cerebellum volume values in the group aged 50 and over were statistically lower than those under 50.

In the study of Yilmaz et al. (31), cerebellum volume was analyzed using three different software on MR images of 18 male individuals aged 22-30. With the volBrain CERES method, the total cerebellum volume was reported as 152.12±20.40 cm3 on mean, right cerebellum volume as 75.69±10.41 cm3, left cerebellum volume as 76.40±10.00 cm3. The findings were higher than our results. In the volBrain CERES study of Sahin et al. (13), which included 10 healthy groups (mean age 48 years), the total cerebellum volume was reported as 138.06 cm3 on mean lobules IV as 5.06 cm3, and lobules V as 8.62 cm3. In our study, which was conducted with the same method, lobules IV and V were partially similar, and the total cerebellum volume was lower. We think that the differences in the findings may be related to sample size and mean age.

In one part of the study by Özgen et al. (32), the total cerebellum volume of 24 healthy individuals with a mean age of 59.62±7.34 years was reported as 115.53±10.44 cm3, and the total flocconodular lobe volume as 1.29±0.71 cm3. In the literature, the flocculonodular lobe is expressed as lobules X (5, 6). Based on this, in our study, the total cerebellum volume of the 50-year-old and older group was 114.44±11.03 cm3, while the total lobules X volume was 1.09±0.15 cm3. The findings are consistent with our current study.

Romero et al. (33) reported that cerebellum volume was higher in males in the volBrain CERES study of a healthy group (1-94 years of age). It was reported that lobules IV, VIIIA, V, VI, VIIB, IX, and crus I differed according to sex. In another volBrain study, it was reported that the cerebellum volume of 20 depressed patients and 20 healthy groups did not show any statistical difference. The total cerebellum volume of the healthy group of the same study was reported as 143.70 cm3 in males and 141.26 cm3 in females. It was stated that cerebellar lobe volume was not statistically significant in the healthy group according to sex. According to the study of Özmen et al. (11), in which we used the same software program, it was seen that total cerebellum volume was higher than our results according to sex. In addition, in our current study, cerebellum volume and some lobule volume results were statistically higher in males. We think the sample size and average age will create differences in the measurements (11).

In a pediatric study of 670 individuals aged 1-18 years, it was reported by the volBrain CERES method that the absolute volumes of the total cerebellum and lobules were larger in males. In addition, when evaluated according to age groups, it was stated that there were greater sex differences in the volumes of lobules IV, VIIB, VIIIA, and VIIIB (26). Another pediatric study reported that the cerebellum volume of 100 healthy

individuals between 0-15 was positively correlated with age. In addition, it was reported that the values of lobules I-II, VI, VIIIB, IX, and X were statistically significant in the right and left cerebellum volume analysis (34).

Hutchinson et al. (35) evaluated the cerebellum volume of musician and non-musician groups according to sex. The cerebellum volume of male musicians was larger than that of non-musician males, while no difference was reported when looking at the female group.

Recently, we have seen many studies in the literature using up-to-date software on cerebellum volume. Thanks to this software, cerebellum volume results at the lobular level are presented objectively and reliably. In our current study, cerebellum volume measurements of healthy individuals were made using the CERES method, a sub-tab of the volBrain software program. As far as we know from the literature, results evaluating the cerebellum volume at the right/left lobular level and by creating age groups according to sex have not been reported so far.

Conclusion

Cerebellum volume varies according to age, sex, and disease type. Of course, in this situation, clinicians must evaluate the individual's development and follow the course of the disease.

In our study, the volumes of the cerebellum at the lobular level in healthy individuals were analyzed. In the parameters examined, except for lobule I-II total, lobule I-II right, lobule I-II left, lobule V right, lobule VI total, and lobule VI right values, the values of males were found to be statistically higher than those of females.

In all parameters except for lobule I-II total, lobule I-II right, and lobule I-II left values, participants aged 50 and over were statistically lower than those under 50. We believe that the results of our study will contribute to clinicians.

Conflict of Interest

The authors declare no conflict of interest

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Author contributions NGC Idea/Hypothesis, Conception, design, supervision, data processing, analysis-interpretation, literature review, writer, critical review, approval of the version to be published. MO: Materials, data collection, data processing, analysis, interpretation, literature review, writer, critical review, approval of the version to be published.

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REVIEW ARTICLE

Relationship Between Autism Spectrum Disorder and The Brain-Gut Axis

Otizm Spektrum Bozukluğu ile Beyin-Bağırsak Ekseni Arasındaki İlişki

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ABSTRACT

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by a rising prevalence, deficits in social communication and interaction, and repetitive behavioral patterns, the etiology of which remains elusive. The collective assembly of microorganisms inhabiting the gastrointestinal tract (GI) is termed the microbiota. Metabolites and molecules synthesized by the microbiota exert regulatory effects on the nervous system, modulating various brain functions. Acting as a pivotal communication conduit, the microbiota mediates interactions between the GI system and the brain, known as the brain-gut axis. Extensive scholarly literature indicates that perturbations in the microbiota composition can profoundly influence brain functions
Studies indicate that individuals with ASD exhibit alterations in microbiota profiles compared to the general population. Patients with ASD may harbor distinct microbial communities in their intestines, with a general decrease in microbiota diversity. However, whether these changes are a cause or a consequence of ASD remains to be fully determined.
It has been hypothesized that ASD may arise from any disturbance that affects the balance of the microbiota-brain-gut axis, and the disruption of any component of this delicate mechanism potentially triggers disturbances that could occur in the chain.
Research into the causes and treatment of ASD is ongoing, and studies in this area hold promising potential. It is believed that future research will contribute to the development of new treatment approaches for individuals with ASD.

Keywords: Autism spectrum disorder, brain-gut axis, microbiota

ÖZ

Otizm spektrum bozukluğu, prevalansı giderek artan, sosyal iletişim ve etkileşim bozuklukları, tekrarlayıcı davranışlarda bozukluklar ile karakterize, sebebi bilinmeyen gelişimsel bir farklılıktır. Bağırsaklarda yaşayan mikroorganizmaların tamamına mikrobiyota denir. Mikrobiyotanın ürettiği metabolik ürünler ve moleküller, sinir sistemi üzerinde etkili olmakta ve beyin fonksiyonlarını düzenlemektedir. Mikrobiyota, beyin-bağırsak aksı, bağırsaklar ile beyin arasındaki iletişimi sağlamaktadır. Mikrobiyotadaki değişikliklerin beyin fonksiyonları üzerinde etkili olduğuna dair literatürde pek çok çalışma bulunmaktadır.
Çalışmalar, otizm spektrum bozukluğu (OSB) olan bireylerde mikrobiyota profilinde normal popülasyona göre değişiklikler olduğunu göstermektedir. Otizm spektrum bozukluğu olan hastaların bağırsaklarında farklı mikroorganizma toplulukları bulunabilmekte ve genel olarak mikrobiyota çeşitliliği azalmaktadır. Bununla birlikte, bu değişikliklerin otizmin nedeni mi yoksa sonucu mu olduğu henüz tam olarak belirlenmemiştir.
Otizm Spektrum Bozukluğunun mikrobiyota-beyin-bağırsak ekseni dengesini etkileyebilecek herhangi bir bozukluktan kaynaklanabileceği hipotez edilmiştir ve bu hassas mekanizmanın herhangi bir halkasının bozulması potansiyel olarak zincirde meydana gelebilecek bozuklukları tetiklemektedir.
Otizm spektrum bozukluğunun nedenleri ve tedavisi konusunda araştırmalar halen devam etmekte olup bu alanda yapılan araştırmalar umut verici bir potansiyele sahiptir. Gelecekte otizm spektrum bozukluğu (OSB) olan bireylere yönelik yeni tedavi yaklaşımlarının geliştirilmesine katkıda bulunacağı düşünülmektedir.

Anahtar Kelimeler: Beyin bağırsak aksı, mikrobiyota, otizm spektrum bozukluğu

Introduction

The human body is inhabited by a multitude of microorganisms, including bacteria, fungi, viruses, and protozoa. Most of these microorganisms are localized in the intestines (1). This complex community of microorganisms residing in the intestines is referred to as the microbiota or microbiome. There exists a mutualistic and symbiotic relationship between these microorganisms and humans (1,2).

Microbiota refers to the intricate communication and interaction among millions of microorganisms residing in the brain-gut axis, central nervous system (CNS), gastrointestinal (GI) system, and intestines (1,2).

Autism spectrum disorder is a neurodevelopmental

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condition marked by clinical heterogeneity. It is characterized by communication and interaction difficulties, and repetitive and restricted behaviors, and involves developmental and connectivity abnormalities in the brain (3).

The exact etiology of autism remains unknown. Recent studies aiming to understand the condition have highlighted brain functions, and genetic, immunological, and neurochemical factors (4). Additionally, it is thought that an underlying dysbiosis (imbalance) in the intestinal microbial community may also play a role (5). This is supported by the GI disorders observed in individuals with autism, which can range from severe constipation to diarrhea. Recent studies have shown that approximately 40% of those diagnosed with autism experience GI symptoms (3). Recent clinical and preclinical studies on the microbiota-brain-gut axis indicate a significant interaction between gut microbiota and the brain (5,6). It is also known that a significant subset of autism spectrum disorder (ASD) is caused by dysfunction in the brain-gut axis. There is a high correlation between psychiatric comorbidities and GI system dysfunction in these patients (5,6). In this review, we will address the potential role of the brain-gut axis in ASD and focus on the current understanding of the gut microbiota in this population.

Maternal Microbiota

The impact of microbiota and bacterial colonization on human health has been extensively studied in recent years. Research in the field of microbiota links the pathophysiology of many diseases to changes in the microbiota and the brain-gut axis (3,6).

Birth marks the beginning of bacterial colonization in the microbiota. The formation of bacterial microbiota begins during pregnancy and continues through labor and delivery (whether by vaginal birth or cesarean section) and into infancy.

During these periods, numerous factors influence this process, including the mother's nutrition and lifestyle, smoking or alcohol consumption, breastfeeding or formula feeding, and nutrition during the transition periods to complementary and solid foods. Additionally, genetic makeup is another factor shaping the microbiota (7).

As a result of the various changes occurring in the mother's body from the onset of pregnancy, differences in microbiota emerge. Some studies suggest that bacteria in the GI microbiota of the mother during pregnancy and lactation periods reach the mammary glands through a mechanism associated with immune system cells (8). The mother's diet and lifestyle, as well as bacteria from the vagina, GI tract, and breast milk, significantly influence the baby's microbiota. Additionally, it has been suggested that harmful bacteria may pass into breast milk and impact the microbiota, influenced by factors such as the mode of delivery (vaginal birth or cesarean section), certain hormones, and exposure to physiological stress (8,9). It is also suggested that changes in the microbiota occur as a result of babies being born via cesarean section, as they do not come into contact with the beneficial vaginal bacteria that they would be exposed to during a normal birth process through the birth canal. Studies also suggest that the bacteria encountered during a cesarean section may lead to alterations in the baby's intestinal microbiota, potentially contributing to the development of ASD (10).

Microbiota colonization, especially during infancy, plays a crucial role in the development and maturation of the GI mucosa. It is also well-established that breastfeeding is particularly important during the first months of infancy. It is also recognized that breast milk contains numerous beneficial bacteria, particularly Bifidobacterium (10).

Bifidobacterium, often referred to as oriented microbiota or microbiome, plays a significant role in protecting against infections during infancy and certain chronic diseases in adulthood (8).

Intestinal Microbiota

Microbiota is a community of microorganisms, including symbiotic, commensal, mutualistic, and pathogenic microorganisms, residing in various parts of our body. This community may vary depending on factors such as diet, lifestyle, medication use, and inflammation (1).

In this symbiotic and mutual relationship, microorganisms can benefit from human substrates, while humans can benefit from microbial activities such as the digestion of carbohydrates, production of essential vitamins (such as B vitamins and K, biotin, cobalamin, folates, nicotinic acid, pantothenic acid, riboflavin, and thiamine), immune system modulation,

and production of secondary bile acids and short-chain fatty acids (11).

Intestinal bacteria such as Bifidobacteria and Lactobacillus synthesize gamma-aminobutyric acid (GABA) from monosodium glutamate. Similarly, Bacillus, Escherichia, and Saccharomyces synthesize norepinephrine, while streptococci, candida, escherichia, and enterococci synthesize serotonin. Bacillus and Serratia are associated with dopamine synthesis (11).

Microbiota is distributed throughout the body, colonizing areas such as the skin, upper and lower respiratory tract, urogenital system, eyes, and especially the intestines, which harbor the majority of the microbiota (12). The colonization of GI by the microbiota begins during the prenatal period. There is evidence of microorganism presence in the placenta, amniotic fluid, meconium, and umbilical cord blood. In the first days after birth, the infantile microbiota changes due to exposure to various physiological and non-physiological factors, such as breast milk, formula use, antibiotic administration, prolonged hospital stays, and early weaning. Our microbial components are influenced by various external factors, including genetics, medication use, dietary habits, lifestyle, and hygiene. Indeed, it is evident that we are exposed to numerous bacterial organisms from the beginning to the end of our existence. Many studies have demonstrated the role of the GI tract microbiota in symptoms of ASD. Approximately 70-80% of children with ASD experience GI system disorders, including bloating, constipation, and diarrhea (13,14). This provides evidence for a relationship between gut physiology and altered microbiota in ASD. Children with ASD generally consume fewer vegetables compared to other children in the same age group (14,15). Additionally, their diet lacks fibrous foods as they tend to consume more foods with higher energy density (14).

The microbiota of children with ASD differs from that of other children in terms of bacterial species and metabolites, such as short-chain fatty acids (SCFAs) (16). In these children, beneficial bacterial species such as Bifidobacterium were found in lower numbers, whereas potentially pathogenic bacterial species such as Desulfovibrio and Clostridium were found in higher numbers (17). A recent study detected Clostridium perfringens bacteria and its toxin genes in the intestines of children with ASD and linked this toxin to digestive system diseases (17,18). Intestinal microbiota also encompasses the array of microorganisms and genomes present in the intestinal environment. The intricate role of the gut microbiota in the brain-gut axis underscores the bidirectional communication between the enteric nervous system (ENS) and CNS (3). Research in this field provides several strategic approaches to assessing the impact of communication between the gut microbiota and the brain-gut axis on behavior. Treatment methods such as probiotic therapy, antibiotic therapy, fecal transplantation procedures, and exposure to various infections can be cited as examples (3,17).

Some studies have noted a correlation between GI symptoms and the severity of clinical symptoms in ASD (18), suggesting that autism symptomatology might be more prevalent and severe in children with GI issues compared to those without. As for the " microbiota-brain-gut axis" concept, recent scientific advancements propose that gut microbiota influences brain development and function via the endocrine, immune, and nervous systems. Consequently, alterations in the gut microbiota could potentially trigger not only some GI symptoms observed in autistic children but also certain neuropsychiatric symptoms. (18,19).

Brain Intestinal Axis Communication Pathways

The microbiota communicates through neuronal, hormonal, and immunological pathways within the brain-gut axis and plays a critical role in maintaining brain-gut homeostasis (3). Generally, the microbiota-brain-gut axis encompasses ENS, CNS, neuroendocrine and neuroimmune systems, parasympathetic and sympathetic pathways of ANS, the hypothalamic-pituitary-adrenal axis, and intestinal microbiota (20).

Neuronal Communication Pathways

Communication between the brain and intestine occurs through neurotransmitters, neurohormones, neuropeptides, cytokines, chemokines, growth factors, and other regulatory molecules (3,21). Factors facilitating brain-gut communication include serotonin, cytokines released from mucosal cells, the vagus nerve, as well as afferent and efferent nerve pathways (3,22). Bacteria within the GI microbiota possess the capability to produce a wide array of neuromodulatory and neurotransmitter substances. Several studies indicate that neurochemicals synthesized by gut bacteria play

a role in influencing behavior in both human and animal models of ASD (20). However, certain foods may contain neurochemical substances such as histamine, and excessive consumption of these foods can alter the composition of the microbiota. Symptoms such as vomiting, hypertension, and headache may manifest as a result of overconsumption of foods with high histamine concentrations (23). The GI system is regulated by a distinct nervous system known as ENS (24). Often referred to as the "second brain," ENS boasts an extensive neural network. Both intestinal physiology and microbiota are governed by both ENS and CNS. Comprising sensory neurons, interneurons, and motor neurons, ENS oversees and senses functions such as secretion, absorption, motility, and visceral sensitivity (24).

Communication between CNS and ENS occurs through the vagus nerve, pelvic nerve, and sympathetic pathways. ENS and ANS communicate with afferent and efferent neurons innervating the intestine, utilizing neurotransmitters such as noradrenaline, adrenaline, and acetylcholine (25). CNS plays a significant role in governing the GI system, overseeing acid secretion and contractile activity through vago-vagal reflexes (26). Moreover, research has demonstrated that certain probiotics establish communication with the brain and regulate behaviors associated with CNS via the vagus nerve (27). For instance, the correction of anxiety and depressive behaviors induced by Lactobacillus rhamnosus JB1 bacteria was achieved through vagotomy. The modulatory effect of Lactobacillus reuteri on behaviors linked to ASD and oxytocin signaling pathways has been demonstrated to rely on the vagus nerve (27). Notably, 80% of vagal fibers between the gut and the brain are afferent, underscoring the crucial role of the vagus nerve in the perception of gut signals (25).

Vagal afferents terminate within the intestinal muscular layer and mucosa, detecting mechanical stimuli like luminal volume and chemical stimuli such as neurotransmitters, hormones, and cytokines, which could be modulated by the intestinal microbiota (24,25). Three key regions in CNS are linked to the GI system. Vagal afferents convey chemosensitive and mechanosensitive information from the esophagus, stomach, and intestine to CNS, but they are not capable of transmitting pain. Thoracolumbar and lumbosacral afferents, however, perceive pain originating from the intestines (25).

Chemical Signalling Pathways or Endocrine Communication Pathways

Enteroendocrine cells, numbering over 20 different types in the body, secrete endocrine hormones within the GI tract. They play a role in regulating digestive activities via ENS, as well as through endocrine and paracrine signaling via vagal afferents. While enteroendocrine cells are responsible for the release of intestinal hormones, their regulation is influenced by the intestinal microbiota (28). Gut hormones such as ghrelin, gastrin, leptin, galanin, and orexin play crucial roles in regulating energy homeostasis, feeding behavior, sexual behavior, circadian rhythm, and anxiety. Additionally, hormones like calcitonin gene-related peptide (CGRP), substance P, neuropeptide Y (NPY), somatostatin, vasoactive intestinal peptide (VIP), and corticotropin-releasing factor (CRF) are believed to play significant roles in facilitating bidirectional communication within the brain-gut axis (29).

Serotonin is a pivotal neurotransmitter in the brain-gut axis. Peripheral 5-hydroxytryptamine (5-HT) contributes to intestinal motility, regulation of GI functions, and pain perception, while also influencing mood changes and the regulation of perception (29). Different subtypes of serotonergic receptors are found in enteric neurons, CNS, and the smooth muscles of the GI tract. The concentration of 5-HT in the plasma is believed to originate primarily from enterochromaffin cells. Intestinal 5-HT contributes to over 90% of the body's 5-HT, yet its peripheral levels do not directly impact its levels in the brain due to the inability of 5-HT to cross the blood-brain barrier. The role of intestinal 5-HT in regulating the physiological function of the GI tract has been well-established (29-31). Certain members of the Lactobacillus and Escherichia coli families within the GI tract lumen convert glutamic acid to Gamma-aminobutyric acid (GABA) (32). Locally produced GABA by the resident bacterial microbiota plays a significant role in signaling among intestinal bacteria (32,33).

The gut microbiota directly or indirectly regulates the homeostasis of CNS through various chemical signals, including short-chain fatty acids, serotonin, bile acids, and gamma-aminobutyric acid (GABA) (33). Many intestinal bacteria such as Lactobacillus, Bacteroides, Parabacteroides, and Bifidobacterium produce GABA, the primary inhibitory neurotransmitter (32,33). As an acidic mechanism, GABA secretion by

intestinal microorganisms influences the environmental pH in the intestine. Bacteroides exhibits a high capacity to produce GABA within the pH range of the human large intestine. GABA synthesized in the gut microbiota facilitates brain-gut communication through enteroendocrine and neuroimmune pathways (33). Certain chemical molecules produced by the intestinal microbiota directly affect the brain by crossing both the intestinal epithelial barrier and the blood-brain barrier. Additionally, some chemical molecules indirectly transmit signals by interacting with enteroendocrine cells situated among the intestinal epithelial cells (34).

SCFAs are one of the lipid clusters produced by the intestinal microbiota through the fermentation of dietary fiber in the intestinal lumen. They are believed to mediate microbiota-brain-gut interactions directly or indirectly. Additionally, SCFAs directly influence neurological processes by crossing the blood-brain barrier (34).

Brain-Gut Axis and Immune System Pathways

The immune system plays a crucial role in brain development. A significant portion of the body's immune cells are located in the GI tract. Cytokines can influence intestinal hormones and vagal afferent neurons, thereby facilitating brain-gut interaction (35). Enterocytes contribute to the release of certain cytokines and chemokines and produce innate immune receptors. Alterations in the microbiota are key factors that can trigger GI immune activation (36). The interaction between ENS and mast cells further contributes to the bidirectional communication between the gut and CNS.

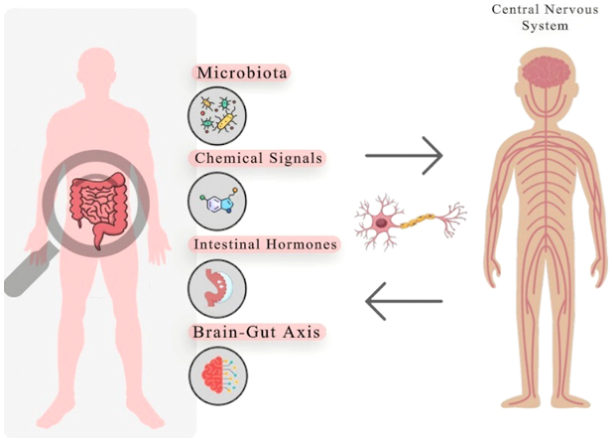

Figure 1. The communication pathways of the brain-gut axis and central nervous system

Additionally, serotonin is known to regulate immune system responses and influence inflammatory events in the intestinal system. Some 5-HT receptors have been observed to play an immunomodulatory role. Studies have found that changes in 5-HT concentration in the GI tract and alterations in enterochromaffin cells are associated with conditions such as ulcerative colitis and Crohn's disease (30,36).

Microbiota's Role in Autism Spectrum Disorder (ASD)

With the increasing understanding of the brain-gut axis, the communication pathways between the gut microbiota and CNS are gaining significant attention. The gut microbiota influences CNS activity through microbial metabolites, immune system mediators, gut hormones, and the vagus nerve (37). Dysbiosis in the gut microbiota is prevalent in individuals (38). Recent reviews have emphasized the importance of nutrition in modulating the gut microbiome to alleviate GI symptoms. The use of oral probiotics and prebiotics may reduce ASD-related symptoms via the brain-gut axis. Several clinical studies have suggested that probiotics and prebiotics could serve as promising therapeutic options for ASD (37,38).

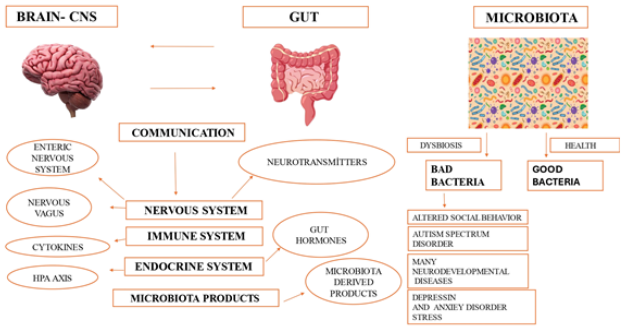

Figure 2. Relationship between brain- gut axis and microbiota

Probiotics are beneficial live microorganisms that aid human health by regulating intestinal transit, enhancing the renewal rate of enterocytes (39), and increasing the production of SCFAs (40). Well-known bacterial species such as Lactobacillus and Bifidobacterium are widely utilized as probiotic supplements. Prebiotics, in contrast, are organic compounds that selectively stimulate the growth and metabolic activity of beneficial microorganisms, thereby improving gut microbiota composition and intestinal health. Notable examples of prebiotics include oligosaccharides, galactans, and fructans. Due to their high tolerability and minimal side effects,

the application of prebiotics and probiotics presents significant therapeutic potential for ASD (41).

Clinical studies suggest that the use of prebiotics and probiotics can improve symptoms of autism and regulate the distribution and content of bacteria in the gut microbiota. In a 2018 study by Shaaban SY et al., stool samples were collected from patients aged five to nine years diagnosed with ASD after three months of probiotic supplementation. Bacterial analysis was performed using quantitative real-time PCR. To assess the severity of GI symptoms in autistic children, the Gastrointestinal Severity Index questionnaire was modified, and the Autism Treatment Evaluation Checklist was used to evaluate autism symptoms. The analysis focused on the bacterial species Lactobacillus rhamnosus, Lactobacillus acidophilus, and Bifidobacterium longum. The study reported a decrease in body weight, GI symptoms, and autism scale scores in children with ASD. Additionally, the bacterial analysis revealed an increase in the numbers of Bifidobacteria and Lactobacilli (42)

In a study where probiotics and prebiotics were administered simultaneously, researchers compared differences in gut microbiota profiles (using 16S rRNA sequencing), fecal SCFAs, and plasma neurotransmitters between 26 children with ASD and 24 neurotypical children. All 26 children with ASD participated in the intervention phase, receiving either probiotics + fructooligosaccharide (FOS) (n=16) or placebo supplementation (n=10). The gut microbiota profiles, SCFAs, and neurotransmitter levels were measured both before and after the intervention. During the intervention phase, it was observed that children with ASD had dysbiotic gut microbiota, characterized by significantly lower levels of Bifidobacteriales and Bifidobacterium longum. Following the probiotics + FOS intervention, an increase in beneficial bacteria (Bifidobacteriales and B. longum) and a suppression of pathogenic bacteria (Clostridium) were noted, along with a marked reduction in autism severity and GI symptoms. Moreover, post-intervention, the SCFAs levels in children with autism significantly increased and approximated those of the control group. The probiotics + FOS intervention was associated with improvements in ASD symptoms, including the regulation of gut microbiota, SCFAs, and serotonin levels, thus addressing the hyperserotonergic state and dopamine metabolism disorder observed in ASD (43).

In a study conducted by Billeci and colleagues (2023), potential alterations in brain activity induced by probiotic therapy were examined in 46 children diagnosed with ASD, aged between 12 and 72 months, using electroencephalography (EEG). This investigation was carried out as a randomized controlled trial. After the probiotic intervention, a reduction in gamma and beta band power in the frontopolar regions, along with modifications in frontal asymmetry, was detected among the participants. These changes suggest a shift towards typical healthy brain functioning. Furthermore, notable correlations were identified between EEG findings and various clinical and biochemical parameters (44).

In a placebo-controlled study involving individuals diagnosed with ASD, children were stratified into two groups based on the presence or absence of GI issues. These groups consisted of individuals with GI symptoms and those without such symptoms. Both cohorts underwent probiotic treatment for five months. Upon completion of the treatment regimen, the group without GI symptoms displayed amelioration in core autism symptoms, while the group experiencing GI symptoms exhibited enhancements in adaptive functions and sensory profiles compared to the placebo-administered group (45). Furthermore, researchers noted a positive correlation between the plasma levels of 25(OH)D and the response to probiotic intervention in mitigating the severity of autism (46).

Numerous clinical studies have been conducted to explore the role of gut microbiota in the onset and progression of ASD. These studies have noted that individuals with ASD exhibit dysbiosis in both the diversity and abundance of gut bacteria, unlike neurotypical individuals (47). Despite conflicting results, meta-analyses in the literature suggest a correlation between ASD and changes in microbiota composition, underscoring the need for further cohort studies to assess this relationship (47). Moreover, a thorough investigation into gut microbiota may facilitate the customization of microbiological interventions and serve as a supplementary treatment approach for ASD (37). Indeed, certain clinical trials and animal studies have indicated that restoring gut microbiota balance through antibiotics, prebiotics, probiotics, or fecal microbiota transplantation (FTT) can induce alterations in neurological functions, behaviors, and associated symptoms in children with autism (48).

Therapeutic Approaches to Target Gut Microbes in

Autism Spectrum Disorder

Probiotic Therapy

Probiotic therapy is proposed as a non-pharmacological treatment method to alleviate the severity of GI symptoms in children diagnosed with ASD (49). Due to its lack of potential side effects, it is also recommended as an adjunctive therapy for children with ASD (49, 50). The literature indicates that patients with ASD frequently suffer from GI complaints, and probiotics are hypothesized to address gut inflammation, mitigate GI symptoms in children with Inflammatory Bowel Disease (IBD), and enhance behavioral symptoms in autistic children (50). Numerous studies indicate that probiotic consumption fosters beneficial modifications in gut microflora, thereby conferring numerous health benefits (51)

Although the precise mechanisms by which probiotics exert their effects remain unclear, several hypotheses have been proposed (51). Firstly, probiotics alter the function and composition of gut-residing microbes and directly interact with the host, facilitating immune system engagement (52). Secondly, probiotics can sustain the integrity of the mucosal barrier by enhancing mucin production, mitigating bacterial overgrowth, promoting antioxidant synthesis, and modulating Immunoglobulin A (IgA) secretion to bolster mucosal immunity (52).

Dietary Intervention

Numerous environmental factors can influence the microbiota-brain-gut axis, with daily food intake being one of the most significant. Dietary components can modify the composition of gut microbiota and affect serum metabolites, thereby modulating brain activity in the host. Consequently, various dietary supplements can help restore microbial balance in the gut and exert therapeutic effects on ASD-related deficits (53). While dietary interventions are increasingly popular for children with autism, they can also lead to adverse effects, as restrictive diets may result in other nutritional deficiencies. Parents of children with autism frequently report issues with their children's selective eating habits. Currently, a range of dietary interventions is employed, including gluten- and casein-free diets, ketogenic diets, yeast-free diets, food allergen restrictions, and supplementation with vitamins A, C, B6, folic acid, B12, minerals such as magnesium, and omega-3 fatty acids (53,54).

Antibiotic Intervention

The treatment of GI infections can be managed with antibiotics, which tend to alter the composition of gut microbiota. Research indicates that early antibiotic exposure may be a potential trigger for autism; however, certain antibiotics, such as aminoglycosides, have shown efficacy in alleviating autism symptoms to some extent (55). One hypothesis proposed by researchers is that aminoglycoside antibiotics might ameliorate autism symptoms by correcting a premature stop codon mutation in a polymorphic gene potentially linked to autism. Several studies have demonstrated that antibiotics can be beneficial in alleviating ASD symptoms by selectively eliminating residual microbiota. Vancomycin and Metronidazole have been employed in the treatment of ASD symptoms (56).

However, Metronidazole is generally not preferred due to its systemic side effects. In a study involving 11 children with ASD treated with Vancomycin, significant communication, and behavioral improvements were observed following the planned 8-week treatment. Another study reported that a 10-day course of amoxicillin led to improvements in autism symptoms in a child, as reported by the parents. Contrarily, there are studies suggesting that early antibiotic exposure may indeed trigger autism (56). In a rodent model study, maternal use of oral antibiotics (non-absorbable Sulfonamide, Neomycin, Bacitracin) resulted in offspring exhibiting impaired social interactions. Fecal samples from these offspring exposed to antibiotics showed a 50% reduction in Lactobacillus abundance and an increase in Clostridium, indicating that early antibiotic exposure can cause behavioral outcomes in offspring. The association between gut microbiota and antibiotic treatment remains to be fully confirmed and continues to be a subject of ongoing research (56,57).

Fecal Microbiota Therapy (FMT) and Microbiota Transfer Therapy (MTT)

The FMT technique represents a notable approach to treating ASD. Here, the gut microbiota from a healthy individual is transferred to the patient, offering a diverse array of thousands of bacterial species naturally occurring in the gut. This stands in stark contrast to probiotic treatments, which typically involve only a limited number of bacterial species derived from milk cultures. FMT therapy holds promise in

addressing chronic inflammatory conditions like insulin sensitivity (58). Research further suggests that FMT can ameliorate symptoms of constipation and contribute to normalizing the gut microbiota in conditions such as irritable bowel syndrome. Consequently, researchers have shown a keen interest in employing FMT for the treatment of children with ASD. Recently, an advanced version of the FMT protocol, known as Microbiota Transfer Therapy (MTT), has gained traction (58,59). This approach involves a two-week course of antibiotics followed by bowel cleansing, succeeded by a seven-to-eight-week period of administering a substantial initial dose of standardized human gut microbiota. MTT has demonstrated significant improvements in GI symptoms, including constipation, indigestion, abdominal pain, and diarrhea, while also alleviating ASD-related symptoms (59, 60). Additionally, there have been instances where recipients of FMT from obese donors developed new-onset obesity (60).

Kang and colleagues conducted a clinical trial involving 18 children diagnosed with autism to investigate the effects of microbiota transplant therapy on gut microbial composition and the alteration of GI and ASD symptoms. The study observed substantial improvements in behavioral symptoms persisting for eight weeks post-treatment, coupled with an 80% reduction in gastrointestinal symptoms (61).

Conclusion

In conclusion, there are many pathways through which the gut microbiota influences neurodevelopment in ASD. The effects of these pathways can be both simultaneous and interconnected. Despite extensive research, there are still many issues to be addressed regarding how the gut microbiota regulates or influences autism. The studies conducted give rise to numerous inquiries. In this review, we discussed various treatments aimed at addressing ASD concerning its pathogenesis and the gut microbiome. These treatments may help manage problems and symptoms associated with autism. Research has shown promising results in a variety of therapies including probiotics, prebiotics, FMT, MTT, and dietary changes. However, to achieve meaningful outcomes in autism research, more rigorously conducted randomized controlled trials are needed. In the future, further elucidation of the relationship between the microbiota-brain-gut axis and ASD will be an important area where we can improve the quality of life of patients and develop potential treatment strategies.

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CASE REPORT

Unilateral Koilonychia with Rapid Response to Combined Treatment with Vitamin B12 and Folic Acid: A Case Report

B12 vitamini ve folik asit kombinasyonu tedavisine hızlı yanıt veren unilateral koilonişi: Olgu Raporu

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ABSTRACT

Introduction: Koilonychia, also called a spoon-shaped nail, is a nail deformity characterized by the concavity of the nail plate. The diagnosis of koilonychia is based on clinical findings. Koilonychia can be idiopathic, genetic, or acquired due to related causes such as anemia, malnutrition, trauma, or thyroid hormone dysregulation.
Case: A 20-year-old woman presented with deformity of the nails on her right hand for two weeks. The patient stated that her hands had been intermittently exposed to chlorine bleach (sodium hypochlorite of 5.25%) for household cleaning for about three months. Dermatologic examination revealed thinning, fragility, concavities in the distal part of the nails, and orangish discoloration in the second to fifth nails on the right hand. These findings were compatible with koilonychia. Examination of the left-hand nails was normal. A vitamin B12 level of less than 100 ng/L and a folate level of 3.59 ng/mL were detected. A clinical diagnosis of sodium hypochlorite–induced koilonychia was performed. The patient was recommended to stop contact with chlorinated bleach and stop household cleaning. The following medications were started: 1000 mcg/mL cyanocobalamin administered by intramuscular injection once a week and 5 mg/day folic acid administered orally. No topical treatment was applied to the nails. After one month, it was observed that the koilonychia regressed.
Discussion: Our case is valuable in terms of the association of vitamin B12 and folic acid deficiencies with unilateral koilonychia and the rapid improvement of koilonychia due to vitamin B12 and folic acid replacement. In conclusion, this preliminary observation suggests that it is required to check vitamin B12 and folic acid levels in patients with unilateral koilonychia and the replacement of vitamin B12 and folic acid in cases of deficiency may be part of the treatment for koilonychia

Keywords: Folic acid deficiency, Nails, Nail abnormality, Vitamin B12 deficien

ÖZ

Giriş: Koilonişi, tırnak plağının konkavitesi ile karakterize bir tırnak deformitesidir. Tanı klinik bulgulara dayanır. Koilonişi idiyopatik, genetik, veya anemi, malnütrisyon, travma, tiroid hormon düzensizliği gibi edinsel nedenlerle ortaya çıkabilir.
Olgu: Yirmi yaşında kadın hasta sağ el tırnaklarında iki haftadır olan şekil bozukluğu nedeniyle başvurdu. Hasta ev temizliği amacıyla ellerinin yaklaşık üç aydır aralıklı olarak klorlu çamaşır suyuna (sodyum hipoklorit %5.25) maruz kaldığını ifade etti. Dermatolojik muayenede sağ el 2-5.tırnaklarda incelme, frajilite, tırnakların distalinde konkavlaşma, ve turuncumsu renk değişikliği gözlendi. Mevcut bulgular koilonişi ile uyumlu değerlendirildi. Sol el tırnaklarının muayenesi normaldi. B12 vitamini seviyesi 100 ng/L'nin altında ve folat seviyesi 3.59 ng/mL olarak tespit edildi. Hastaya klinik olarak sodyum hipoklorite bağlı koilonişi tanısı konuldu. Hastaya klorlu çamaşır suyu ile teması kesmesi ve ev temizliğine ara vermesi önerildi. Haftada bir kez siyanokobalamin 1000 mcg/ml intramüsküler enjeksiyonla ve folik asit 5 mg/gün ağızdan tedavileri başlandı. Tırnaklara herhangi bir topikal tedavi uygulanmadı. Bir ay sonra koilonişinin gerilediği gözlendi.
Tartışma: Vakamız, B12 vitamini ve folik asit eksikliğinin unilateral koilonişi ile birlikteliği ve B12 vitamini ve folik asit replasmanına bağlı olarak koilonişinin hızla düzelmesi açısından değerlidir. Sonuç olarak, bu ön gözlem unilateral koilonişi hastalarında B12 vitamini ve folik asit düzeylerinin kontrol edilmesi gerektiğini ve eksiklik durumunda bu vitaminlerin replasmanının koilonişi tedavisinin bir parçası olabileceğini düşündürmektedir.

Anahtar kelimeler: Folik asit eksikliği; Tırnaklar; Tırnak anormallikleri; Vitamin B12 eksikliği

Introduction

Koilonychia, also called a spoon-shaped nail, is a nail deformity characterized by the concavity of the nail plate. Its diagnosis is based on clinical findings. Koilonychia can be idiopathic, genetic, or acquired due to related causes such as anemia, malnutrition, trauma, or thyroid hormone dysregulation (1). It may also be associated with dermatoses such as psoriasis and lichen planus, or systemic disorders such as Reynaud's disease, systemic lupus erythematosus, and diabetes mellitus. There is no specific treatment other than the removal of the underlying cause (2). In this case, we describe a dramatic response to vitamin B12 and folic acid replacement in a 20-year-old woman with unilateral koilonychia on the right hand.

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Case

A 20-year-old woman presented with deformity of the nails on her right hand for two weeks. The patient stated that her hands had been intermittently exposed to chlorine bleach (sodium hypochlorite 5.25%) for household cleaning for about three months. The patient was right-handed and had no history of mechanical trauma, familial nail disorder, chronic disease, or drug use. The patient had applied henna to the affected nails, thinking that it would improve the deformity. Dermatologic examination revealed thinning, fragility, concavities in the distal part of the nails, and orangish discoloration in the second to fifth nails on the right hand. These findings were compatible with koilonychia. There was also transverse leukonychia on the first fingernails of both hands. Examination of the left-hand nails was normal (Figures 1a and 1b).

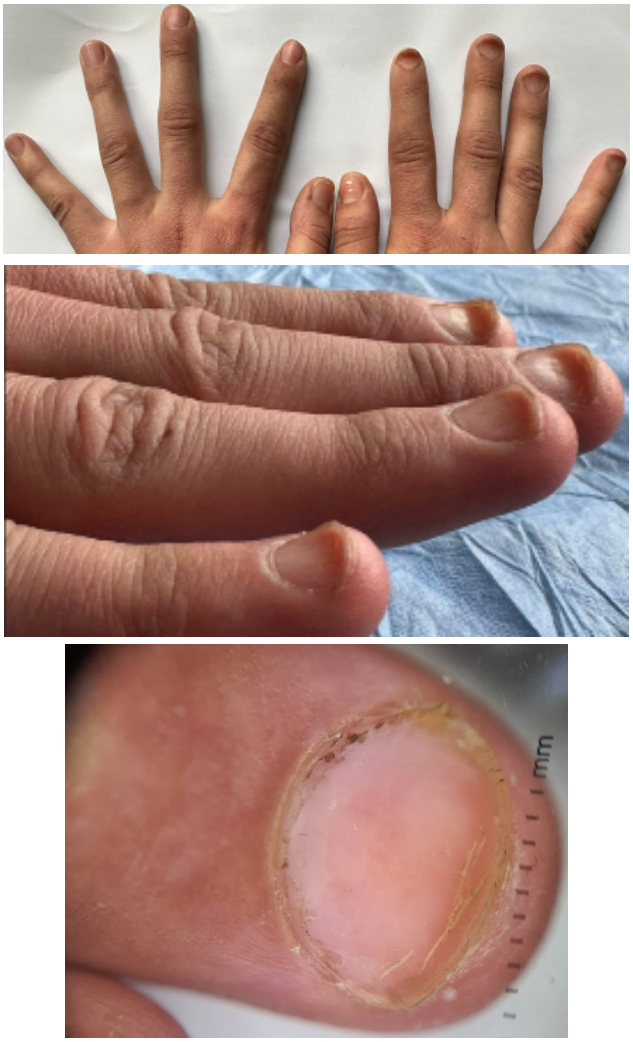

Figure 1 (a). Thinning, fragility, concavities in the distal part of the nails, and orangish discoloration in the second to fifth nails on the right hand. **Figure 1 (b).** Side view of the koilonychia. **Figure 1 (c).** Dermoscopic image of the affected nail.

Dermoscopic examination revealed horizontal splitting distal to the second to fifth nails of the right hand and punctate brown-gray discoloration (thought to be due to henna) on the cuticles and distal free edges of the second to fifth nails of the right hand (Figure 1c). The patient had no symptoms of psoriasis or lichen planus, and the oral mucosa examination was normal. Laboratory tests including hemogram, sedimentation, renal and liver function tests, ferritin and iron level tests, iron-binding capacity, and thyroid hormone level tests were within normal limits. Chest radiography and electrocardiogram were also normal. A vitamin B12 level of less than 100 ng/L and folate level of 3.59 ng/mL were detected (reference ranges of 197–771 ng/L and 3.8–16 ng/mL, respectively). A clinical diagnosis of sodium hypochlorite–induced koilonychia was made. The patient was recommended to stop contact with chlorinated bleach and to stop household cleaning. The following medications were started: 1000 mcg/ml cyanocobalamin administered by intramuscular injection once a week and 5 mg/day folic acid administered orally. No topical treatment was applied to the nails. After one month, it was observed that the koilonychia regressed (Figure 2). The patient stated that she did not stop household cleaning until the one-month follow-up visit while reducing the frequency of exposure to chlorinated bleach from twice a week to once a week. No signs of koilonychia were observed for the following six months.

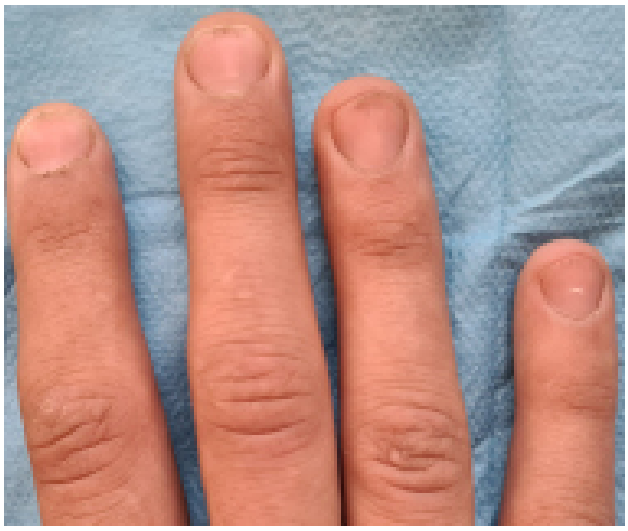

Figure 2. Improvement in nail appearance after one month.

Discussion

The patient's occupation has an important role in the etiology of koilonychia. The textile industry, industries requiring high contact with certain chemicals, and

industries requiring frequent hand washing may be particularly affected by koilonychia. Mechanical trauma such as nail biting and exposure to chemicals such as acids, alkalis, solvents, and motor oils may cause koilonychia (2). Alkaline chemicals can cause koilonychia as they disrupt the integrity of the nail plate; the attractive effect of connective tissue bundles extending from the subungual tissue to the nail plate causes the nail to become spoon-shaped (3). Sodium hypochlorite is an easily accessible alkaline chemical that is frequently used for bleaching and surface disinfection. It is known to cause urticaria, irritant dermatitis, and allergic contact dermatitis (4). The corrosive effect of sodium hypochlorite (5.25%) on nails has been previously demonstrated by Hartnett et al. (5). According to the results of this in vitro study, the free edge of the fingernails dissolved within six hours following submersion in bleach. Since our patient was right-handed, the primary exposure of the right hand to sodium hypochlorite may explain this case of unilateral koilonychia. It has also been reported that the predominant involvement of the first three fingernails may be a sign of occupational koilonychia (2, 6). In our case, although the second to fifth nails of the right hand was affected by koilonychia, the nail deformity was more severe in the second and third nails than in the last two nails, consistent with the relevant literature. Our patient did not have any symptoms associated with dermal exposure to sodium hypochlorite. This may be because the turnover time of the nail plate (months) is longer than that of the skin (days) and repetitive damage is less tolerated in the nail plate than in the skin.

Treatment of the underlying cause and avoidance of occupational or traumatic factors are recommended for the treatment of koilonychia. An effective response to topical tazarotene (0.1%) gel has been reported in an occupational case of unilateral koilonychia with subungual hyperkeratosis (6). Our case was treated with a combination of vitamin B12 and folic acid, and no topical treatment was applied. Vitamin B12 and folic acid are critical for DNA synthesis, protein synthesis, and keratinocyte proliferation (7, 8). Deficiencies in vitamin B12 and folic acid deficiencies are known to be associated with skin and nail hyperpigmentation, stomatitis, and cheilitis (9). However, none of these symptoms were present in our case. Although koilonychia secondary to vitamin B12 deficiency has been previously described (2), to our knowledge, koilonychia accompanied by folic acid deficiency has not been reported in the existing literature. One of the factors responsible for the pathogenesis of koilonychia is the deficiency of sulfur-containing amino acids (2). Vitamin B12 and folic acid play an important role in the metabolism of methionine and cysteine, the best-known sulfur-containing amino acids. Methylcobalamin, an active form of vitamin B12, and folic acid as a methyl group donor are essential for the functioning of the enzyme methionine synthase, which is involved in the synthesis of methionine from homocysteine (10). In our patient, vitamin B12 and folic acid deficiency may have triggered koilonychia by disrupting the metabolism of sulfur-containing amino acids. In our case, it is not clear which of the two supplements contributed to the improvement of the patient's condition, especially in the nails, or whether there was a synergistic effect.

Our case is valuable in terms of the association of vitamin B12 and folic acid deficiencies with unilateral koilonychia and the rapid improvement of koilonychia due to vitamin B12 and folic acid replacement. In conclusion, this preliminary observation suggests the need to check vitamin B12 and folic acid levels in patients with unilateral koilonychia and that replacement of these vitamins in cases of deficiency may be part of the treatment for koilonychia.

Teaching Points:

1. Koilonychia, also called a spoon-shaped nail, is a nail deformity characterized by the concavity of the nail plate, which may occur due to idiopathic, genetic, or acquired causes. Acquired koilonychia may be associated with anemia, avitaminosis, dermatologic and systemic disorders, mechanical trauma, or exposure of the nails to chemicals such as acids, alkalis, and solvents.

2. Treatment of the underlying cause and avoidance of occupational or traumatic factors are recommended for the treatment of koilonychia.

3. In patients with unilateral koilonychia, vitamin B12, and folic acid levels should be checked, and the replacement of vitamin B12 and folic acid in cases of deficiency may be part of the treatment for koilonychia.

Author contributions

The author confirms sole responsibility for the following: literature search, drafting the case, editing, and writing

the manuscript.

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CASE REPORT

Being Immobilized Involves A High Risk of Pulmonary Embolism

Hareketsiz Kalmak Pulmoner Emboli İçin Yüksek Risk İçerir

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ABSTRACT

Introduction: The clinical symptoms of pulmonary embolism are diverse and in some patients, pulmonary embolism can be easily overlooked and cause serious clinical consequences.
Case Report: This report describes a case of acute pulmonary embolism whose first symptom wa presyncope. A 23-year-old male patient presented with presyncope and dyspnea. Acute coronary syndrome and neurological disorders such as stroke and seizures were excluded by clinical history and dynamic changes in the electrocardiogram. After the diagnosis was completed with computed tomography pulmonary angiogram, the severity of acute pulmonary embolism was evaluated and then the fibrinolytic drug was given to the patient
Conclusion: This case is of guiding importance for the early diagnosis and treatment of these patients who had pulmonary embolism after long-term immobilization, which poses a potential risk for venous thromboembolism. Cardiopulmonary diseases should be highly suspected in patients with problems with basic vital signs. After evaluating the possibility of pulmonary embolism and performing a D-dimer scan, a computed tomography pulmonary angiogram should be performed as soon as possible. Additionally, the critical degree of pulmonary embolism should be assessed and appropriate reperfusion and anticoagulation therapy should be administered.

Keywords: Emergency department, hospitalization, immobilization, pulmonary embolism

ÖZ

Giriş: Pulmoner embolinin klinik semptomları çeşitlidir ve bazı hastalarda pulmoner emboli kolayca gözden kaçabilir ve ciddi klinik sonuçlara neden olabilir.
Vaka Raporu: Bu raporda ilk semptomu presenkop olan akut pulmoner emboli vakası anlatılmaktadır. 23 yaşında erkek hasta presenkop ve dispne ile başvurdu. Akut koroner sendrom ve inme ve nöbetler gibi nörolojik bozukluklar klinik öykü ve elektrokardiyogramdaki dinamik değişikliklerle dışlandı. Tanı bilgisayarlı tomografi pulmoner anjiyogram ile tamamlandıktan sonra akut pulmoner embolinin şiddeti değerlendirildi ve ardından hastaya fibrinolitik ilaç verildi
Sonuç: Bu vaka, uzun süreli hareketsiz kalma sonrasında pulmoner emboli geçiren ve venöz tromboembolizm için potansiyel risk oluşturan bu hastaların erken tanısı ve tedavisi için yol gösterici öneme sahiptir. Temel hayati belirtilerinde sorun olan hastalarda kardiyopulmoner hastalıklardan şüphelenilmelidir. Pulmoner emboli olasılığını değerlendirdikten ve D-dimer taraması yaptıktan sonra, mümkün olan en kısa sürede bilgisayarlı tomografi pulmoner anjiyogram yapılmalıdır. Ek olarak, pulmoner embolinin kritik derecesi değerlendirilmeli ve uygun reperfüzyon ve antikoagülasyon tedavisi uygulanmalıdır.

Anahtar kelimeler: Acil servis, hastaneye yatış, immobilizasyon, pulmoner emboli

Introduction

Venous thromboembolism (VTE) includes deep vein thrombosis (DVT), and pulmonary embolism (PE) and represents different clinical symptoms of the same disease process. VTE is one of the most common causes of death in hospitalized patients. Immobilization is a common risk factor for VTE, and prolonged inactivity reduces blood flow and leads to venous stasis. Endothelial damage along with hypercoagulation also plays a role and contributes to the pathophysiology of venous thrombosis(1). PE is a common and life-threatening disease. PE usually results from a thrombus originating from the deep venous system of the lower extremities. However, rarely, it also originates from the pelvic, renal, upper extremity veins or right heart chambers. After reaching the lung, large thrombi can settle in the bifurcation of the main pulmonary artery or lobar branches and cause hemodynamic deterioration. Pulmonary thromboembolism is not a disease in itself. Rather, it is a complication of underlying venous thrombosis (2). The

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causes of PE are multifactorial. Causes include deep vein thrombosis, hypercoagulable, immobilization, surgery and trauma, pregnancy, oral contraceptives and estrogen replacement, malignancy, and hereditary factors. The classical presentation of PE is the sudden onset of pleuritic chest pain, shortness of breath, and hypoxia. However, most patients with PE don't have any obvious symptoms at presentation. On the contrary, symptoms can range from sudden devastating hemodynamic collapse to gradually progressive dyspnea (3). The diagnosis of PE should be suspected with unexplained respiratory symptoms that may be considered with an alternative diagnosis.

Atypical symptoms such as seizures, syncope, abdominal pain, fever, cough, wheezing, decreased level of consciousness, new-onset atrial fibrillation, hemoptysis, flank pain, and delirium in elderly patients may be observed in PE patients. Syncope may be the only symptom of PE; however, syncope or loss of consciousness is the main symptom in less than 1% of PE patients (4). In this article, a case of acute PE detected in a 23-year-old male patient who presented with presyncope and dyspnea is explained.

Case Report

A 23-year-old male patient, who was previously fit and healthy and a non-smoker, was brought to the emergency department of our hospital with dyspnea and presyncope. He was a person who had no medical history, no allergies and not used medication regularly. The patient described dyspnea, pleuritic chest pain, pain, and swelling in the right leg that had been going on for 4 days. He stated that he had taken a 2-hour train ride 5 days ago and had been studying intensively for approximately 12 hours for the last 4-5 days. In the primary evaluation, the patient was awake, isochoric pupils and light reflexes were positive and his Glasgow Coma Scale (GCS) was calculated as 15/15. Breath sounds in both lungs and heart rhythm were regular, and no pathological murmur was heard in the auscultation area of both valves. However, there was painful swelling in the right extremity without any temperature increase. The physical examination results at admission were as follows: Fever, 36.5°C; pulse, 100 times/minute; breathing 24 times/minute; and blood pressure 100/60 mmHg. The hemoglobin level of the case was 16.3 g/dl, white blood cell (WBC) count was 7,22/µL, and platelet count was 205.000/µL. His prothrombin time and activated partial thromboplastin time were 1.07 (INR) and 30.5 sec, respectively. However, the D-dimer level was elevated to 4188 ng/mL. Electrocardiogram (ECG) results were the following: sinus rhythm, typical S1Q3T3 manifestation on electrocardiogram (Figure 1), and no dynamic changes in the recheck. Acute

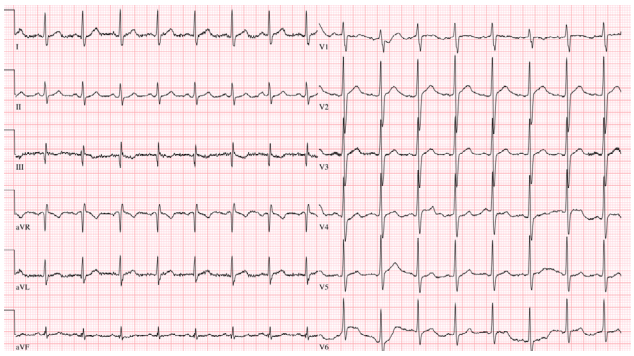

Figure 1. The patient's electrocardiogram on admission

coronary syndrome and neurological disorders such as stroke and seizures were excluded by clinical history and dynamic changes in the electrocardiogram. Deep vein thrombosis was not detected in bilateral lower extremity venous Doppler ultrasonography. Because he spent most of his time working at a desk, a computed tomography pulmonary angiogram (CTPA) was performed to diagnose PE associated with reduced mobility, although there was no evidence of deep vein thrombosis. In CTPA, a filling defect in favor of massive embolism was observed in both pulmonary arteries and all lobar branches (in Figure 2,3). In addition,

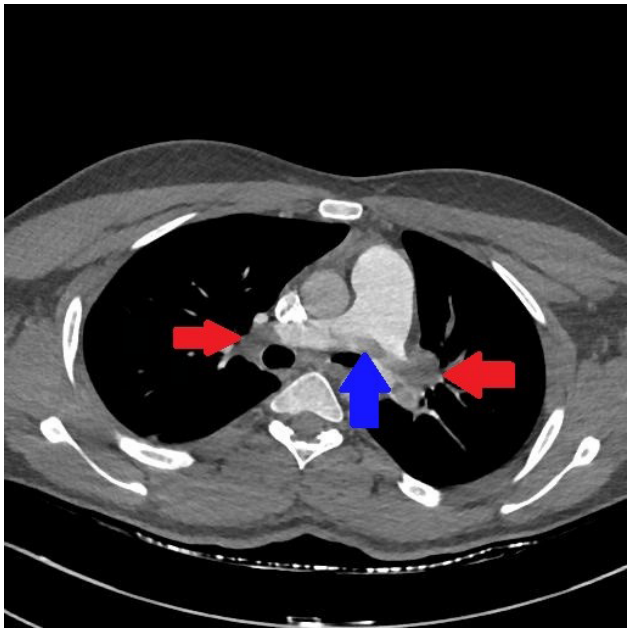

Figure 2. Axial section CTPA image shows the appearance of saddle pulmonary embolism (blue arrow) and pulmonary embolism extending to the lobar branches distal to both pulmonary arteries (red arrows).

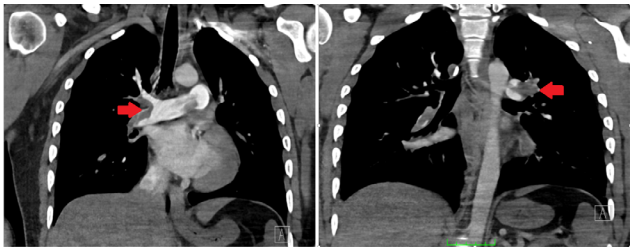

Figure 3. Coronal section CTPA images show pulmonary embolism (red arrows) extending to the lobar branches distal to both pulmonary arteries.

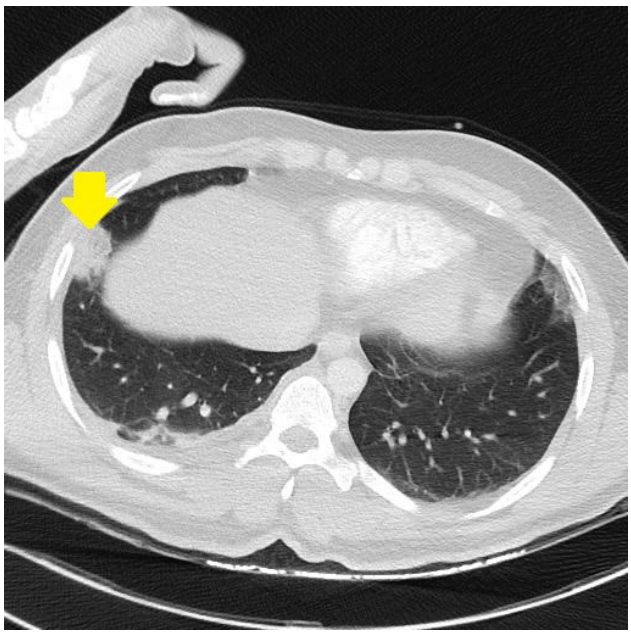

Figure 4. Axial section CTPA image shows consolidation (yellow arrow) consistent with pulmonary infarction in the anterobasal segment of the lower lobe of the right lung.

consolidation compatible with pulmonary infarction was observed in the right lung in the CTPA (Figure 4). Echocardiography (ECHO) revealed an increase in pulmonary artery systolic pressure (58 mmHg), right ventricle dilatation, and mild-moderate tricuspid valve regurgitation were observed. The severity of acute PE was assessed by vital signs, right heart strain findings on bedside ECHO, and massive pulmonary embolism on imaging, and the young patient was given a fibrinolytic drug. Following this, the patient's vital signs were stable and this patient was discharged without any complications 8 days later. Genetic tests were performed 4 months after the patient was diagnosed and were evaluated as negative. In the thrombophilia panel, homocysteine, protein C, and antithrombin III were detected within normal limits, while the level of protein S was below the normal limit.

Discussion

PE is a clinical condition characterized by obstruction of blood flow in the pulmonary artery, typically caused by a thrombus advancing from a vein in the lower extremity. PE is a recurrent cardiovascular disease frequently encountered in emergency departments. The diagnosis of PE can be difficult to determine and can be easily overlooked due to nonspecific symptoms or clinical findings such as acute dyspnea, chest pain, cough, hemoptysis, and syncope, which are also present in other cardiopulmonary diseases. However, early diagnosis and treatment of PE, especially when massive PE is present or complicated by shock and cardiopulmonary arrest, can significantly reduce morbidity and mortality. PE is a common and life-threatening condition that requires immediate evaluation and treatment to improve the results. Acute PE is the most common cause of acute right ventricular (RV) pressure overload.

The primary cause of death after acute PE is acute RV dysfunction (5,6). The incidence of PE is approximately 60 to 120 cases per 100.000 people per year. Approximately 60.000 to 100.000 patients die from PE each year in the United States. PE remains a diagnostic challenge because symptoms are nonspecific, and less than 10% of patients evaluated for PE are diagnosed with PE (4). Our patient was a young man whose first symptom of PE was presyncope, followed by shortness of breath and chest pain. ECG, ECHO, D-dimer, and other examinations made us think about the possibility of PE. After the diagnosis of PE was confirmed by CTPA, fibrinolytic therapy was applied to the patient

Immobilization is defined as being bedridden for at least three days or having spent most of the time lying or sitting. Immobilization, for VTE, is a common risk factor and prolonged inactivity reduces blood flow and leads to the development of venous stasis. Venous stasis, along with endothelial damage and hypercoagulability, also play a role and contribute to the pathophysiology of venous thrombosis. The risk of PE increases with prolonged bed rest, prolonged sedentary work at a desk, or immobilization of an extremity in a cast. In this case, venous thrombosis may have occurred after our patient had recently studied intensively for a long time and had lower extremity immobility, and this situation may have led to PE.

As an initial symptom of PE, presyncope or syncope can be difficult to diagnose. But these symptoms may be the ''forgotten sign'' of life-threatening PE disease. The need for rapid diagnosis is clear because, with

appropriate treatment, the majority of patients can survive. The possibility of PE should be kept in mind, especially in patients with presyncope or syncope accompanied by shortness of breath. The vital signs, heart rate, ECG, respiratory rate, and oxygen saturation of these patients should be determined immediately and high-risk patients should be given appropriate respiratory support and blood pressure support as soon as possible. When the clinical assessment of the probability and D-dimer screening for PE is completed, CTPA should be performed on a case-by-case basis to help clarify or exclude the diagnosis of PE. Meanwhile, the severity of PE should also be evaluated and reperfusion or anticoagulation treatment should be performed accordingly.

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CASE REPORT

A Very Rare Presentation of Tubal-Ovarian Torsion in A Patient with Endometrioma: A Case Report

Endometriomalı Bir Hastada Nadir Görülen Tubal ve Over Torsiyonu: Olgu Sunumu

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ABSTRACT

Endometriosis is increasingly diagnosed in women of reproductive age and is estimated to affect up to 10% of women. Endometrioma in rare cases occurs with an acute abdominal picture. However, adnexal torsion with endometrioma is very rare in such patients. A 38-year-old female patient was admitted to the outpatient clinic of the maternity department urgently with intermittent left groin pain lasting for four hours. The patient had intermittent pain and concomitant vomiting. Biochemical examination was evaluated within normal ranges. There were no abnormalities in the vital signs of the case. Ultrasound (US) imaging revealed endometrioma and heterogeneous images in the left adnexal space. Considering endometrioma torsion, emergency surgery was decided, and laparoscopy was planned. During the operation, endometrioma and tubal-ovarian torsion were observed in the left ovary. During the operation, it was detorsioned. Endometrioma cyst excision was performed. The patient was discharged from the hospital in good health. Torsion is very rare in cases with endometrioma. Endometriomas are often tightly adherent to neighboring structures, and therefore seem less likely to cause adnexal torsion, although there is insufficient data on the torsion rate in the cysts. With this case report, we considered contributing to the literature on torsion in endometrioma.
It should be kept in mind that patients with endometrioma have tubal-ovarian torsion, which can be seen very rarely if they present to the emergency department with an acute abdomen.

Keywords: Endometrioma, Laparoscopy, Tuba-ovarian torsion

ÖZ

Endometriozis üreme çağındaki kadınlarda giderek daha fazla teşhis edilmekte ve kadınların %10'unu etkilediği tahmin edilmektedir. Nadir vakalarda endometrioma akut karın tablosuyla birlikte görülür. Ancak bu hastalarda endometrioma ile adneksal torsiyon çok nadirdir. 38 yaşında bir kadın hasta, 4 saattir başlayan aralıklı sol kasık ağrısıyla acilen kadın doğum polikliniğine başvurdu. Hastada aralıklı ağrı ve eşlik eden kusma vardı. Biyokimyasal inceleme normal aralıklarda değerlendirildi. Yaşamsal bulgularında anormallik yoktu. Ultrason görüntülemede endometrioma ve sol adneksal boşlukta heterojen görüntüler ortaya çıktı. Endometrioma torsiyonu düşünülerek acil cerrahiye karar verildi. Laparoskopi planlandı. Operasyon sırasında sol overde endometrioma ve tuba-ovarian torsiyon görüldü. Operasyon sırasında detorsiyone edildi. Endometrioma kist eksizyonu yapıldı. Hasta iyileşmek üzere hastaneden taburcu edildi. Endometrioma vakalarında torsiyon çok nadirdir. Endometriomalar genellikle komşu yapılara sıkıca yapışıktır ve bu nedenle, bu kistlerdeki torsiyon oranı hakkında yeterli veri olmamasına rağmen, adneksal torsiyona neden olma olasılıkları daha düşük görünmektedir. Bu olgu sunumuyla, endometriomadaki torsiyon hakkındaki literatüre katkıda bulunmayı düşündük.
Endometrioma hastalarının akut karınla acil servise başvurduklarında çok nadir görülebilen tuba-ovaryan torsiyona sahip oldukları akılda tutulmalıdır.

Anahtar kelimeler: Endometrioma, Laparoskopi, Tuba-ovaryan torsiyon

Introduction

Endometriosis is the presence of endometrial glands and stroma outside the uterine cavity (1). Endometriosis affects 6–10% of women of reproductive age and may cause disturbances in the quality of life of women due to pain and infertility (2).

Endometriosis mainly occurs in pelvic organs, such as the peritoneum, ovary, and recto-vaginal septum. The pathogenesis and clinical entities are different from each specific anatomical lesion (3). Ovarian endometrioma may originate from adhesion between peritoneum and ovarian surface implants, and the pseudo cyst may be formed by incessant bleeding from endometriotic lesions (4). A variety of pain symptoms are associated with endometriosis, including dysmenorrhea, dyspareunia, dysuria, dyschezia, and chronic pelvic pain (5, 6). Adnexal torsion as a cause of pelvic pain is rare in endometrioma cases. Perhaps the reason for the absence of torsion in the cases of endometrioma may be their adhesion to the surrounding tissues. Therefore,

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we have presented this very rare case.

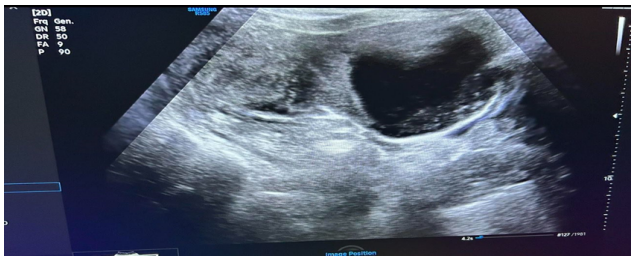
Case

Our case is a 38-year-old female patient. She had endometrioma for five years, which was previously diagnosed by healthcare professionals. There was no use of medication. She had a history of two cesarean deliveries. The patient was admitted to our emergency department with the complaint of episogenic inguinal pain starting four hours ago. The pain was intermittent and severe and considered to be associated with an episode of vomiting. There was no history of similar incidents in the past. There was no vaginal discharge, and the bowel and bladder habits were normal. The patient had undergone a cesarean section operation eight years ago. She had suffered from heavy menstruation previously.

C-reactive protein (CRP) values were within the normal range in the patient's biochemical tests. Even so, beta HCG revealed negativity. The leukocyte count gave a moderate elevation. Hemoglobin value was 9.7 gm/dL, and liver and kidney function tests were normal. Serum cancer antigen 125 was 194 IU/L, and serum cancer antigen 19-9 was 314 IU/L.

Abdominal ultrasound (US) suggests a large anechoic cystic lesion with dimensions of 6.79 cm x 5.41 cm (Figure 1), extending to the abdomen in the left adnexa, with

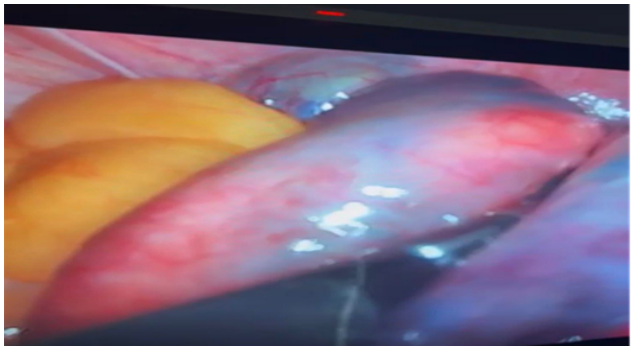
Figure 1. Preoperative ultrasound imaging: Endometrioma cyst and adjacent ovarian tissue with increased density



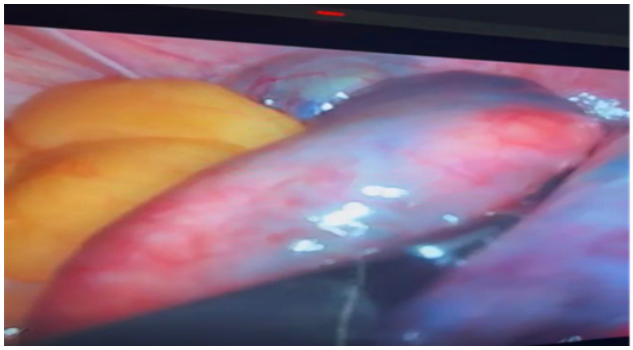
small septa with thin walls near the upper pole, without arterio-venous flow on color Doppler flow imaging. There was an increase in density in the ovarian tissue adjacent to the cyst. It was likely to be the ovarian torsion. The Doppler examination showed a decrease in ovarian flow. The other adnexal areas were normal. There was a 6-cm intramural myoma in the posterior part of the uterus. Since the patient's symptoms did not respond to the first injected analgesics, and as the US findings suggested ovarian torsion, an urgent laparoscopy decision was performed. Laparoscopy revealed that the left tube (Figure 2a) and ovary (Figure 2b) were torsioned. Interestingly, the torsion was detected in the left utero-ovarian ligament rather than the infundibulopelvic ligament, which was intact

Figure 2. Appearance within the surgery

a. The tuba is torsion and bruised

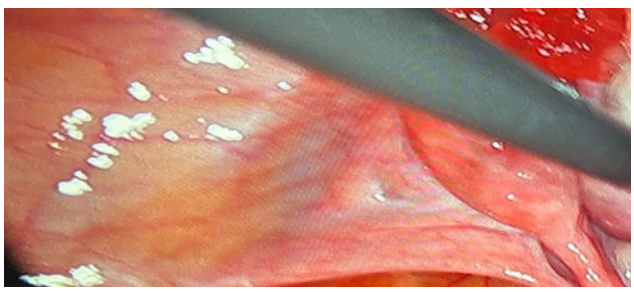


b. The ovary is edematous, enlarged, and bruised appearance



in this case. It was seen that the torsioned ligament rotated sideways parallel to its axis and was visibly blocked. After the ovarian pedicle was detorsioned, the ovary returned to its normal color and showed no signs of bleeding or necrosis (Figure 3). After the cysts were aspirated by the surgeon during the mobilization

Figure 3. View after intraoperative detorsion; The color of the ovary has come to a normal appearance



of the adnexes, the endometrioma ruptured, shedding a large amount of dark brown fluid into the peritoneal cavity. Then, a routine laparoscopic myomectomy was performed. The patient's postoperative course

was uncomplicated.

Discussion

Gynecological causes of acute abdomen in female patients can be varied. When we investigated the gynecological causes of acute pelvic pain in non-pregnant women, the gynecological causes of pelvic pain in such women include ovarian bleeding, ovarian torsion, pelvic inflammatory disease, endometriosis (especially deep infiltrating endometriosis), endometriomas, adenomyosis, and pelvic pain. Congestion syndrome may also be observed due to incorrectly positioned intrauterine contraceptive devices (7). Our patient had a 6-cm endometrioma in the left ovary. It was considered that she might have pain due to endometriosis.

Endometriosis is an important cause of chronic pelvic pain. The quality of endometriosis-related chronic pelvic pain varies widely. Affected menstruating individuals experience cyclical and non-cyclical pain, and dysmenorrhea; non-menstrual pain may sometimes be accompanied by dyschezia, dysuria, and, among those who are sexually active, dyspareunia. Pain may be felt throughout the pelvis and abdomen, and can be referred to the back and legs (8).

Our patient had menstrual pain. However, the pain starting in the last four hours was intermittent and was not a constant pain.

Acute abdominal or pelvic pain may be intermittent with or without nausea and vomiting, and fever may be the initial and main clinical manifestations of ovarian torsion both in children and female patients of reproductive age (9–11). Approximately 70% of women with ovarian torsion may have the symptoms of nausea and vomiting (12). In light of this information, the pain in our patient was intermittent, severe, and accompanied by vomiting, which led us to the preliminary diagnosis of endometrioma torsion.

İf pelvic pain persists in women with endometriosis, the clinician focuses on broadening hormonal therapy to accomplish the suppression of menses or initiates a hormonal therapy found to be effective in lessening endometriosis-associated pain (like gonadotropic-releasing agonists or antagonists rather than undertaking multiple surgeries); therefore, the clinician engages a multidisciplinary team for the management of the pain. Additional approaches to pain management may include such medications as acetaminophen, muscle relaxants, non-steroidal anti-inflammatory drugs (NSAIDs), and medications for neuropathic pain, including gabapentin, pregabalin, and duloxetine (13,1 4). If the patient's pain was persistent, we might consider medical treatment. The fact that the condition suggested the clinic of torsion pushed us to decide on surgical intervention.

Ovarian or adnexal torsion is an acute surgical emergency in which the ovary is partially or completely rotated along the axis of the pedicle, compromising blood flow. Torsion is rare, and its incidence is only 2.7%. Although it requires rapid and accurate diagnosis and treatment, it often creates diagnostic difficulties (15). While torsion may develop in a normal ovary in other respects, it also often occurs in a benign adnexal mass environment, which can act as a center of rotation around which the rest of the ovary and the extensive ligament can rotate. In the laparoscopic surgery of the patient, the tuba was torsion with the ovary. The ovary and tuba were relieved by detorsion and deposits.

Endometriosis accounts for 40-45% of pelvic pain (3). When combined with torsion, the pain becomes severe. It is difficult to detect additional torsion and make surgical decisions in a patient whose pain persists (4). It is very rare to see endometrioma with torsion. In a study, ovarian cysts were among the causes of torsion in 61.1%. In the sub-analysis of ovarian cysts, the most common cysts were detected as follows: 33.3% serous cysts, 22.2% dermoid cysts, and 5.6% mucinous cysts. In the sub-analysis, no endometrioma was observed (18). Based on the literature, the case presented here is extremely rare. We consider that endometrioma prevents torsion by creating adhesions to the tuba and surrounding tissues as a possible reason for this.

Conclusion

Endometriosis is increasingly being diagnosed among reproductive-aged women, and it is estimated to affect 10% of women (1). Endometrioma may present with acute abdominal pain. However, adnexal torsion in such patients is rare. Torsion should be considered in patients with endometrioma in case of sudden onset of intermittent pain and vomiting. In this case, the surgical option should be kept in mind. Such cases can be managed using a minimally invasive approach, assuming an optimal surgical setting.

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CASE REPORT

Munchausen Syndrome in An Adolescent Girl Mimicking Hematemesis: A Case Report

Hematemezi Taklit Eden Ergen Bir Kız Çocuğunda Munchausen Sendromu: Bir Olgu Sunumu

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ABSTRACT

Introduction: Munchausen syndrome is a psychiatric disorder characterized by the deliberate imitation of symptoms of physical or psychiatric illness by the patient to convince others and health professionals that they have a disease. The patient often exhibits a specific pattern of behavior, such as lying about their symptoms and influencing test results to prove the presence of symptoms. Munchausen Syndrome by Proxy is similar to Munchausen Syndrome; however, the clinical scenario is presented not by the child himself or herself but by the adult responsible for his/her care. This is a type of child abuse since it exposes the child to unnecessary medical procedures. The most important step in making a diagnosis for both Munchausen syndrome and Munchausen syndrome by Proxy is to suspect the condition. We aimed to raise the awareness of physicians about Munchausen syndrome, a condition that can be overlooked and rarely diagnosed in pediatric cases.
Case Report: A fifteen-year-old girl presented with hematemesis. The site and cause of the hemorrhage could not be found by endoscopy and physical examination. Munchausen syndrome was diagnosed after it was discovered that the patient was simulating hematemesis by taking venous blood from the arm with a syringe and collecting it in his mouth.
Discussion: Suspicion is a significant factor in the diagnosis of Munchausen syndrome. Therefore, medical doctors and other healthcare professionals are important to enhance their knowledge and comprehension of Munchausen syndrome.

Keywords: Factitious disorders, hematemesis, Munchausen syndrome

ÖZ

Giriş: Munchausen sendromu, başkalarını ve sağlık profesyonellerini bir hastalığa sahip olduklarına ikna etmek amacıyla hastanın fiziksel veya psikiyatrik hastalık belirtilerini kasıtlı olarak taklit etmesiyle karakterize psikiyatrik bir bozukluktur. Hasta genellikle semptomları hakkında yalan söylemek ve semptomların varlığını kanıtlamak için test sonuçlarını etkilemek gibi belirli bir davranış modeli sergiler. Munchausen Sendromu by Proxy, Munchausen Sendromuna benzer, ancak klinik senaryo çocuğun kendisi tarafından değil, bakımından sorumlu yetişkin tarafından sunulur. Bu bir tür çocuk istismarıdır çünkü çocuğu gereksiz tıbbi prosedürlere maruz bırakır. Hem Munchausen Sendromu hem de Munchasen Sendromu by Proxy için tanı koymanın en önemli adımı şüphelenmektir. Pediatrik vakalarda gözden kaçabilen ve nadiren teşhis edilebilen bir durum olan Munchausen sendromu hakkında hekimlerin farkındalığını artırmayı amaçladık.
Olgu Sunumu: On beş yaşında bir kız çocuğu hematemez ile başvurdu. Endoskopi ve fizik muayenede kanamanın yeri ve nedeni bulunamadı. Hastanın kolundan şırınga ile venöz kan alıp ağzında biriktirerek hematemezi taklit ettiği fark edildikten sonra Munchausen Sendromu tanısı kondu.
Tartışma: Şüphe, Munchausen sendromunun teşhisinde önemli bir faktördür. Tıp doktorlarının ve diğer sağlık çalışanlarının Munchausen sendromu hakkındaki bilgi ve kavrayışlarını artırmaları önemlidir.

Anahtar Kelimeler: Hematemez, Munchausen sendromu, yapay bozukluklar

Introduction

Munchausen syndrome, initially reported by Asher in 1951, is a psychological disorder named after Baron Karl Friedrich von Munchausen, a German author known for telling invented and exaggerated stories about his experiences. (1). The condition is characterized by a tendency to fabricate or exaggerate symptoms or illnesses, to receive medical attention. This can result in a prolonged and unnecessary course of treatment, as well as potential complications or even death (2). The condition is classified under the category of "factitious disorder imposed on self" in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (2, 3). Hospitalization is frequently the primary outcome and may become a chronic condition for those affected. The prevalence of this condition in the pediatric age group remains uncertain; however, it is estimated to range between 0.5 and 2% in the adult age group. The etiology of the artificial disorder remains unclear. However, several potential factors have been proposed, including genetic, social, psychodynamic, and familial influences (2, 3). The condition typically follows a chronic course, with patients experiencing multiple hospital and physician visits. Common features include a lack of organic cause, an exaggerated

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medical history, and a tendency to change physicians and hospitals when an artificial disorder is mentioned as a potential diagnosis (3).

In this report, an adolescent girl who complained of hematemesis and was diagnosed with Munchausen Syndrome is presented because it is a rare cause of pseudo-hematemesis.

Case Report

A 15-year-old girl was admitted to our pediatric gastroenterology outpatient clinic with the complaint of abundant clotted blood coming from her mouth after syncope. In her history, the patient's complaints started two years ago and were constantly recurring once or twice a month. Complete blood count, blood biochemistry (serum levels of urea, creatinine, liver enzymes, and electrolytes), and coagulation tests were normal. Digital rectal examination was unremarkable. No mucosal lesion that could cause bleeding was detected in the upper gastrointestinal endoscopic examination. The examination performed by the otorhinolaryngologist was also normal.

Approximately 6 months later, the patient was admitted to our outpatient clinic again with complaints of recurrent bloody vomiting and syncope. To investigate the etiology, the patient underwent upper gastrointestinal endoscopy again and was evaluated as normal.

After the esophagogastroduodenoscopic examination, she went into the lavatory in the pediatric endoscopy unit, saying that she needed to go to the toilet. It was noted that she stayed inside for a longer time than usual. After leaving the WC, she collapsed on the ground in front of the entrance to the pediatric endoscopy room with her eyes closed while walking, and then it was observed that clotted blood started to flow out of her mouth (Photo 1). During the detailed second evaluation, it was understood that she did not lose consciousness and that she was simulating syncope. We also detected skin areas consistent with scratch marks and ecchymosis on the antecubital region of her left arm (Photo 2). When we checked the toilet, a syringe was found there. During the detailed interview, the patient admitted that she had taken venous blood from her antecubital region with a syringe, collected her blood by mouthing, and then faked fainting and bleeding from her mouth.

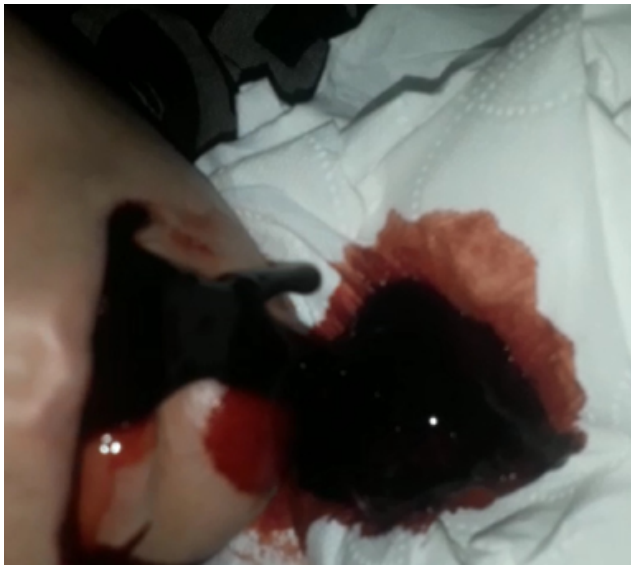

Figure 1. The figure demonstrates the blood from the mouth of the case.

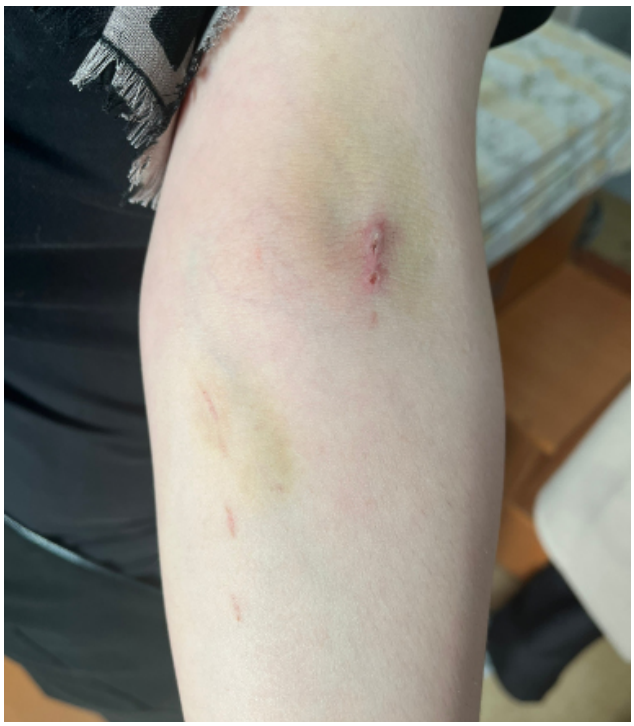

Figure 2. The figure demonstrates the injection injury on the arm.

Given the patient's past applications to health facilities registered electronically, it was revealed that she had applied to six different centers with the same complaint in total 62 times in three years. Thereupon, we referred her to our hospital's Child and Adolescent Psychiatry Outpatient Clinic for further evaluation and treatment. In the psychiatric evaluation, it was understood that she was the youngest member of a family of 11 children who had taken refuge in Turkey due to the

civil war in Syria, and it was thought that the patient's clinical picture could be related to the psychological traumas she had experienced. In the mental status examination, she had a general appearance that was appropriate for her age and was self-sufficient. When the ecchymoses on the patient's left arm were questioned, anxiety was observed. The patient's mental process and associations were natural, and no delusions were detected in her thought content.

Discussion

Upper gastrointestinal bleeding occurs proximal to the Trietz ligament and represents a rare cause of hospitalization in the pediatric age range. In a study, the rate of hospital admissions was reported as 80-90 per 100,000 (4). In the majority of cases, the quantity of bleeding is insufficient to detrimentally impact crucial bodily processes; however, severe bleeding may occasionally occur.

Munchausen syndrome is a rare condition in pediatric patients, and it is challenging to diagnose. Symptoms can manifest in various systems, and the most common causes of hospitalization are abdominal discomfort, joint pain, thoracic discomfort, low blood sugar, skin abrasions, loss of consciousness, emesis, and hemorrhaging (4). The disease can frequently be diagnosed several months or even years following the initial presentation, which results in a significant economic and workload burden on the healthcare system due to the multitude of diagnostic, imaging, and interventional procedures that are required. It is often overlooked and can result in severe harm to the patient. In one study, working in a health-related profession, being single, and being a woman were found to be risk factors. (5). In our case, the identified risk factors included a low socio-economic status, a history of migration, financial constraints, and potential domestic neglect.

By the diagnostic criteria outlined in the Diagnostic and Statistical Manual of Mental Illnesses, or DSM-5, an artificial disorder is defined as a condition in which a patient's actions can be demonstrated to be purposefully and clandestinely engaged in the production of psychiatric or bodily symptoms (2).

In the differential diagnosis, it is essential to differentiate between malingering for personal gain and conversion disorder, in which the patient displays involuntary symptoms (6). It is additionally pertinent to consider the potential for a diagnosis of haemomania or non-suicidal self-injury. Hemomania is a disorder of impulse control characterized by an attraction to the taste and smell of one's blood. Unlike other forms of blood fetishism, individuals with hemomania do not intentionally attempt to induce symptoms; rather, they derive pleasure from the taste and scent of their blood (7). In this case, it was observed that the subject simulated upper gastrointestinal bleeding by using blood from her arm. Non-suicidal self-injury is defined as direct and deliberate damage to one's body tissues without the intention to kill and for socially disapproved reasons. Common examples of acts of non-suicidal self-harm include cutting, burning, scratching, and hitting oneself (8).

Conclusion

Both Munchausen syndrome and Munchausen syndrome by Proxy are rare conditions in children. Delays in diagnosis result in unnecessary investigations, interventional procedures, and radiation exposure from imaging techniques, which can cause extensive harm and place a significant burden on the workforce and economy of the healthcare system. To make an accurate diagnosis, it is essential to gather information from multiple sources. This may include relatives, healthcare professionals, hospital roommates, past medical records, personal effects, and video recordings of symptoms. Suspicion is a key factor in diagnosing the disease and medical practitioners and allied health professionals must increase their knowledge and understanding of Munchausen syndrome.

When Munchausen syndrome, which is easily overlooked and rarely diagnosed in pediatric patients, is remembered by physicians, it can both make a significant contribution to the workforce and economy of the health system by preventing unnecessary medical examinations and intervention procedures, and treatment of the patient's psychiatric disorder can be started without delay.

Authorship Contributions

Conception: MAA, AB, Design: HHE, HAG, Supervision: HHE, HAG, MG Data Collection and/or Processing: IA, VBA, EKA, ACE, MG, Analysis and/or Interpretation: MAA, AB, HHE, HAG, MG, IA, VBA, EKA, ACE, MG, Literature Review: MAA, AB, Writing and editing: MAA, Critical Review: HHE, HAG, MG

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