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Research Article

Diabetes Mellitus Patients with Fibromyalgia have a Higher Risk of Cardiovascular Disease

Fibromyaljisi Olan Diabetes Mellitus Hastaları Yüksek Kardiovasküler Hastalık Riskine Sahipler

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Abstract

Aim: The primary aim of this study is to investigate the effect of the presence of Fibromyalgia(FM) on cardiovascular risk and cardiopulmonary capacity in diabetes mellitus (DM) patients. In addition, the prevalence of FM in DM patients was investigated according to the American College of Rheumatology (ACR) 2016 criteria.

Material and Methods: The study included 188 premenopausal female patients with Type 2 DM. The physical activity level of the study participants was assessed with the International Physical Activity Questionnaire - short form. The cardiopulmonary capacity was evaluated with the 6-minute Walk Test. The cardiovascular risks were evaluated with the Framingham risk score. Participants were examined for the presence of FM according to the ACR 2016 criteria.

Results: 63 (33.5%) participants met the ACR 2016 FM diagnostic criteria. DM patients with FM have significantly lower physical activity levels (p=0.004) and cardiopulmonary capacity (p=0.009), and they also have significantly higher cardiovascular risks (p=0.02) than DM patients without FM.

Conclusion: FM is seen in approximately one-third of DM patients, and the presence of FM reduces cardiopulmonary capacity and increases cardiovascular risk. In the management of patients diagnosed with DM, the presence of FM should be investigated, and treatment should be applied with pharmacological and non-pharmacological methods to reduce the contribution to cardiovascular risk.

Keywords: Cardiovascular risk, fibromyalgia, physical activity

Öz

Amaç: Bu çalışmanın birincil amacı, diabetes mellitus (DM) tanılı hastalarda Fibromiyalji (FM) varlığının kardiyovasküler risk ve kardiyopulmoner kapasite üzerindeki etkisini araştırmaktır. Ayrıca DM hastalarında FM prevalansını Amerikan Romatoloji Cemiyeti (ACR) 2016 kriterlerine göre araştırmaktır.

Materyal ve Metot: Çalışmaya Tip 2 DM tanılı 188 premenopozal kadın hasta dahil edildi. Katılımcıların fiziksel aktivite düzeyleri Uluslararası Fiziksel Aktivite Anketi kısa formu ile değerlendirildi. Kardiyopulmoner kapasiteleri 6 Dakika Yürüme Testi ile değerlendirildi. FM varlığı ACR 2016 FM tanı kriterlerine göre incelendi. Kardiyovasküler risk Framingham risk skoru ile hesaplandı.

Bulgular: ACR 2016 FM tanı kriterlerine göre 63 (%33.5) katılımcının FM'si vardı. FM'li DM hastalarının FM'siz DM hastalarına göre fiziksel aktivite düzeyleri ve kardiyopulmoner kapasiteleri daha düşük (sırasıyla, p=0.004, p=0.009), kardiyovasküler riskleri daha yüksekti (p=0.02).

Sonuç: FM, DM hastalarının yaklaşık üçte birinde görülür. FM varlığı kardiyopulmoner kapasiteyi azaltır ve kardiyovasküler riski artırır. DM tanılı hastaların yönetiminde FM varlığı araştırılmalı, FM'nin kardiyovasküler riske katkısını azaltmak için farmakolojik ve nonfarmakolojik tedavi yöntemleri uygulanmalıdır.

Anahtar Kelimeler: Fibromiyalji, fiziksel aktivite, kardiyovasküler risk

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INTRODUCTION

The group of diseases affecting the blood vessels and heart such as cerebrovascular disease, coronary artery disease, and peripheral vascular disease are defined as cardiovascular diseases and are a leading cause of mortality (1). Determination and modification of the risk factors of cardiovascular disease are one of the basic functions of preventative healthcare services.

The increasing incidence of Diabetes mellitus (DM), which is characterized by glucose metabolism disorder causing mortality and morbidity, presents a significant threat to societal health. DM is an independent cardiovascular disease risk factor, and the primary reason for mortality and morbidity in patients with DM is cardiovascular disease (2). There is a highly complex, multi-directional relationship between DM and cardiovascular diseases. Glyco-oxidation end-products which lead to oxidative stress, endothelial dysfunction, hypercoagulability, autonomous neuropathy, and inflammation are factors directly associated with the pathogenesis of cardiovascular disease in DM (3). Factors such as hypertension, dyslipidemia, and obesity, which often indirectly accompany DM, also increase the risk of cardiovascular disease (4).

The etiology and pathogenesis of Fibromyalgia Syndrome (FM) are not yet fully understood, but in the pathophysiology, there are known to be various neuroendocrine dysfunctions and changes in central pain mechanisms and clinical findings include chronic widespread bodily pain, fatigue, sleep disorders, and multiple somatic and cognitive disorders (5-7). Cardiovascular risk factors such as heavy smoking, low physical activity, and cardiopulmonary vitality have been reported at higher rates in FM patients than in control subjects (8,9). In a population-based cohort study by Tsai et al, the risk of coronary artery disease was shown to be 2-fold higher in FM patients compared to individuals without FM (10). Patients with FM are also known to be predisposed to atrial fibrillation, which is a rhythm disorder associated with morbidity and mortality (11). Patients with coronary pathology have also been reported to have more FM symptoms (12).

When FM is determined together with other diseases, the management of these patients is more difficult, and clinical findings are more complex. According to the American College of Rheumatology (ACR) 1990 and ACR 2010 criteria, FM is known to accompany 17-21% of DM patients (13-15). However, the clinical reflections of FM co-existing in DM patients have not yet been investigated. Therefore, the primary aim of this study was to investigate the effect of the presence of FM on cardiovascular risk and cardiopulmonary capacity in DM patients. In addition, the prevalence of FM in DM patients was investigated according to the ACR 2016 criteria, which are the current FM diagnostic criteria.

MATERIAL AND METHOD

The cross-sectional study included 188 premenopausal female patients followed up for a diagnosis of Type 2 DM in a tertiary level university hospital. The sample size of the study was calculated according to DM prevalence of 14.2% in Turkish females, d=0.05, and a 95% confidence interval (16). According to the patients' medical records or medical history, patients were excluded from the study if they had peripheral vascular disease, heart failure, coronary artery disease, cerebrovascular disease, hyperlipidemia, were using antihypertensive drugs, had any orthopedic disability, irregular menstrual cycles, myofascial pain syndrome, Vitamin D or Vitamin B12 deficiency, any metabolic disease other than DM, respiratory system disease, any psychiatric disease such as schizophrenia, inflammatory rheumatological disease, or any acute or malignant disease.

Written and verbal informed consent was obtained from all the study participants. The study was conducted with the decision of the local ethics center of Sivas Cumhuriyet University Non-Interventıonal Research Ethics Commıttee dated 10.03.2021 and decision number 2021-03/27. All procedures were applied in compliance with the Good Clinical Practice guidelines and the Helsinki Declaration.

A record was made for each participant of socio-demographic data, including age and educational level, anthropometric measurements of body mass index and abdominal circumference, DM-related microvascular complications such as retinopathy, nephropathy, and neuropathy from medical records or mediacal history, smoking status, the time since DM diagnosis, and laboratory findings of HbA1c and fasting glucose level.

The physical activity level of the study participants was assessed with the International Physical Activity Questionnaire -short form, which has been shown to have validity and reliability in Turkish (17,18). In this questionnaire formed of 7 items, the periods of sitting, walking, and physical activity in the last 7 days are evaluated and thus the level of physical activity can be calculated with the MET-minute score.

The cardiopulmonary capacity of the study participants was evaluated with the 6-minute Walk Test (6MWT). After resting, the participants were requested to walk at as fast a tempo as possible for 6 mins in a corridor 30 m in length. Before starting the test, it was explained that the patients could rest if they experienced dyspnea or excessive tiredness, but the resting time would be included in the test time. During the test, the time remaining was given at one-minute intervals. At the end of 6 minutes, the distance walked was recorded in meters (19).

The cardiovascular risks of the participants were evaluated with the Framingham risk score using a web-based calculation tool (20), by evaluating gender, age, systolic blood pressure, total and HDL cholesterol levels, antihypertensive drug use, the presence of diabetes, history of vascular disease, and smoking habits. The Framingham risk score calculates the 10-year risk of experiencing a

cardiovascular event and is a reliable method widely used for this purpose (21). The presence and level of components of the scoring system are scored on a points scale, the points are totaled, and the risk percentage equivalent to the total points is determined on a separate scale. A risk percentage of <10% indicates a low risk of cardiovascular disease, 10%-20% a moderate risk, and >20% a high risk (21).

Following these evaluations, the study participants were examined on the same day by a physiatrist for the presence of FM according to the ACR 2016 criteria. The ACR 2016 FM diagnostic criteria are the most up-to-date criteria providing a diagnosis of FM by questioning the presence, severity, and duration of symptoms such as fatigue, waking unrested and how many pains are felt from 11 common pain regions and 5 body regions defined from the extremities and axial body regions (5). According to these criteria, FM is diagnosed with symptoms of similar severity for at least 3 months, symptom severity scale score of ≥5, and general pain index score of ≥7, or symptom severity scale score of ≥9, and general pain index score of 4-6, and pain in at least 4 of the 5 common pain regions (5).

Statistical Analysis

Data were analyzed using SPSS v. 22 software (SPSS Inc., Chicago, IL, USA). Conformity of the data to normal distribution was examined using visual methods such as histogram and probability graphs, and analytical methods such as the Kolmogorov-Smirnov test and Shapiro-Wilk test. Categorical data were stated as number (n) and percentage (%) and as numerical data did not show normal distribution they were stated as median, minimum and maximum values. In the comparisons of DM patients with and without FM, the Chi-square test or the Fisher's Exact test for categorical variable, and the Mann-Whitney U-test was used for numerical variables. Type-1 error level was set as 0.05.

RESULTS

This cross-sectional study included 188 patients with Type 2 DM, of which 63 (33.5%) met the ACR 2016 FM diagnostic criteria.

The sociodemographic data, clinical findings, and laboratory test results of the DM patients with and without FM are shown in Table 1. The mean age, duration of DM, and HbA1c level were determined to be similar in both groups. The physical activity levels of the DM patients with FM were determined to be significantly lower (p=0.004).

The 6MWT results and the Framingham risk scores of the groups are shown in Table 2. The 6MWT results of the DM patients with FM were determined to be significantly lower than those of the DM patients without FM (p=0.009). The Framingham risk scores of the DM patients with FM were determined to be significantly higher than those of the DM patients without FM (p=0.02). The statistically significant difference in the Framingham risk scores was due to the difference in the groups with low and moderate Framingham risk scores (p=0.08). No statistically significant difference was determined between the groups with low and high Framingham risk scores (p=0.24) or between those with moderate and high scores (p=0.27).

Table 1. Sociodemographic data and clinical findings of the study participants

	DM patients with FM (n=63)	DM patients without FM (n=125)	p
Age (years)	51 (39-55)	51.6 (39-56)	
Duration of education (years)	9 (7-16)	9 (7-16)	0.68
Body Mass Index kg/m²	30.6 (25.8-40.3)	29.9 (24.9-39.4)	0.69
Abdominal circumference, cm	140 (129-150)	138 (125-147)	0.96
DM-related microvascular complications			0.98
Retinopathy n(%)	7 (11.1)	14 (11.2)	
Nephropathy n(%)	4 (6.3)	8 (6.4)	
Neuropathy n(%)	25 (39.7)	40 (32)	
Smoker, yes, n(%)	38 (60.3)	70 (56)	0.57
DM duration, years	8 (5-12)	9 (5-13)	0.48
HbA1c	7.6 (5.9-8.8)	7.5 (5.6-8.9)	0.81
Fasting blood glucose, mg/dl	157 (109-202)	154 (115-197)	0.11
Resting heart rate atım/dk	73 (65-78)	74 (60-77)	0.77
Physical activity level, MET-min	550 (502-2100)	749 (621-2298)	**0.04**

Table 2. Comparisons of the cardiopulmonary capacity cardiovascular risks of the groups

		DM patients with FM (n=63)	DM patients without FM (n=125)	p
6-Minute Walk Test		406 (342-490)	430 (312-584)	**0.009**
Framingham Risk Score				**0.02**
	Low	16 (25.4)	54 (43.2)	
	Moderate	34 (54)	44 (35.2)	
	High	13 (20.6)	27 (21.6)	

DISCUSSION

Previous research has shown that FM increased the cardiovascular risk compared to healthy control subjects (8,10,22). In the current study, for the first time in literature, the effect on cardiovascular risk and cardiopulmonary capacity was examined of the presence of FM in DM patients, which is a major risk for cardiovascular disease, and the results showed that cardiopulmonary capacity was lower and the cardiovascular risk was higher in DM patients with FM. The study results also showed a prevalence of 33.5% of FM in DM patients according to the ACR 2016 FM diagnostic criteria.

FM may accompany several systemic, rheumatological, infectious, and metabolic diseases (13,23,24). When determined together with other diseases, the clinical findings in particular of the patients may become more complex and patient management can be more difficult (23). For example, in cases with FM accompanying rheumatoid arthritis, which is the most common inflammatory rheumatological disease, the number of sensitive joints increases because of impaired pain perception, and the general health condition of the patient is worsened (23). Therefore, the disease activity score is affected and real difficulties are experienced in planning patient treatment. It is known that FM is present in approximately a quarter of DM patients (13-15), but how this affects DM patients has not been previously investigated. As DM is a significant risk factor for cardiovascular disease, the focus of this research was on the effect of FM on this risk.

Cardiovascular reasons are the leading cause of death in DM patients, and the results of the current study demonstrated that the risk of cardiovascular disease was higher in DM patients with FM. Many humoral, cellular, neuroendocrine, and biopsychosocial factors could be the reason for this result. One of these reasons is that inflammation plays a key factor in the development of atherosclerosis. Although FM is accepted as a non-inflammatory rheumatismal disease, recent studies have indicated that there are various cytokines, chemokines, lipid mediators, oxidative stress, and plasma-origin factors in the immunological background of FM (25). Another reason is mitochondrial dysfunction, which is a cellular factor with a common line in the pathogenesis of FM and cardiovascular diseases (26-28). Another is that mood disorders are seen in FM patients, and it has been previously shown that depression and anxiety increase the risk of myocardial infarct and adverse events related to coronary artery disease (29, 30). There is a close relationship between FM and chronic stress, and the fact that chronic stress causes impairments in the sympathetic nervous system and the hypothalamus-hypophysis-adrenal gland axis may be another reason. Changes in heart rate associated with this autonomous dysfunction have been shown to increase cardiovascular risk (9). Yet another reason is the cardiovascular side-effect profile of NSAIDs used to control the symptoms of general body pain experienced by DM patients with FM (31). Finally, it can also be considered that there are more lifestyle effects in FM patients such as smoking, sedentary lifestyle, and low levels of physical fitness, which are independent cardiovascular risk factors (8). The methodology of this research was not sufficient to assess all these factors, but of the factors focussed on, the physical activity level and cardiopulmonary fitness level were determined to be lower in the DM patients with FM.

Both the level of physical activity and the level of cardiopulmonary fitness are consociated with the risk of cardiovascular disease (32,33). Just as regular exercise is the first step in the prevention of cardiovascular diseases, it is one of the keystones in the management of DM patients and the first step in treatment (34). It is protective against cardiovascular disease through mechanisms such as reducing inflammation, improving the lipid profile, regulating blood pressure, and reducing insulin resistance (35). As in the current study, previous research has reported that females with FM have a low level of physical activity and cardiopulmonary capacity (8, 36, 37). This can cause an increase in the cardiovascular risk of DM patients with FM.

The prevalence of FM in DM patients has been investigated in a limited number of studies, and these studies have used the ACR 1990 diagnostic criteria and the ACR 2010 FM classification criteria (13-15). The ACR 1990 FM criteria only focus on the pain and sensitive points of the patient and do not question other biopsychosocial effects related to FM (38). The ACR 2010 FM criteria have the positive aspect of a holistic approach to the patient but also negative aspects of including the mistaken diagnosis of several regional pain syndromes and psychological disorders and preventing FM diagnosis in individuals

with other diseases (39). With the revision of the negative aspects of the ACR 2010 FM criteria, the ACR 2016 FM criteria were formed and are currently used. These ACR 2016 criteria have gained validity with the most important feature of the use of the concept of secondary FM when it accompanies other diseases (5). As the patient groups covered by these criteria are different, the prevalence of FM may vary according to the diagnostic criteria used (40). This could explain the higher prevalence obtained in the current study compared to previous research. In similar research of patients with rheumatoid arthritis, a higher prevalence value was also obtained using the 2016 diagnostic criteria (23).

There were some limitations to this cross-sectional study. As the duration of FM was not known in the DM patients with FM, and the FM severity was not evaluated with the FM impact scale, the findings could not be analyzed according to symptom duration and severity. In addition, the physical activity levels were evaluated according to the patients' statements, and quantitative methods to determine the actual physical activity levels were not used. Moreover, the study focussed on determining the cardiovascular risk of the presence of FM in DM patients, and all the factors which could play a role in forming this result were not investigated in detail.

CONCLUSION

In conclusion, the results of this study demonstrated that FM is seen in approximately one-third of DM patients, and the presence of FM reduces cardiopulmonary capacity and increases cardiovascular risk. In the management of patients diagnosed with DM, the presence of FM should be investigated, and treatment should be applied with pharmacological and non-pharmacological methods to reduce the contribution to cardiovascular risk. There is a need for further studies to investigate in more detail why the presence of FM increases cardiovascular risk.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *The study was conducted with the decision of the local ethics center of Sivas Cumhuriyet University Non-Interventional Research Ethics Committee dated on 10.03.2021 and decision number 2021-03/27*

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Research Article

Anti-Vaccination and COVID-19 Vaccine Hesitancy among Adolescents

Ergenlerde COVID-19 Aşı Reddi ve Aşı Tereddütü

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Abstract

Aim: The emergence of COVID-19 vaccines in the pandemic has led to discussions about vaccine hesitancy in the general population. This study, it was aimed to determine the anti-vaccination and COVID-19 vaccine hesitancy levels in a sample of adolescents.

Material and Method: This is a cross-sectional study. It was conducted with 303 individuals aged between 15-18 years who received to the pediatric outpatient clinic between October and November 2021. Study data were collected using a structured questionnaire including the 'Vaccine Hesitancy Scale' and 'Vaccine Hesitancy in Pandemics scale.' In the analysis of the relations between the variables, the t-tests in independent groups, the One-way Anova test and the Pearson correlation test were applied.

Results: 43.5% of the participants and 85.6% of the parents were vaccinated. Among unvaccinated individuals, 27.4% were not willing to get vaccinated. Even if vaccination were compulsory, 22.2% would still refuse to get vaccinated. 28.7% stated that they were affected by anti-vaccination rhetoric. The participants' mean scores were 30.2±4.8 and 48.1±17.0 on the scales. No significant difference was found between females and males. In low-income groups, vaccine hesitancy levels were higher than in those with higher income. The vaccine hesitancy level in Pandemics was significantly lower in those who suffered from Covid-19. The vaccine hesitancy levels were significantly lower in those whose parents were vaccinated. The vaccine hesitancy levels were significantly higher in those informed about vaccines from social media.

Conclusion: Knowledge of the risks and complications of diseases and information disseminated on social media platforms are factors that significantly influence attitudes towards vaccination.

Keywords: Vaccine hesitancy, COVID-19, anti-vaccination

Öz

Amaç: ACOVID-19 aşılarının pandemide gündeme gelmesi, genel popülasyonda aşı tereddütü hakkında tartışmalara yol açmıştır. Bu çalışmada, bir ergen örnekleminde aşı karşıtlığı ve COVID-19 aşı tereddüt düzeylerinin belirlenmesi amaçlanmıştır.

Materyal ve Metot: Bu, kesitsel bir çalışmadır. Ekim-Kasım 2021 tarihleri arasında çocuk polikliniğine başvuran 15-18 yaş arası 303 kişi ile gerçekleştirildi. Çalışma verileri, 'Aşı Tereddüt Ölçeği' ve 'Pandemilerde Aşı Tereddütleri skalasını' içeren yapılandırılmış bir anket kullanılarak toplandı. değişkenler arasındaki ilişkilerin analizi, bağımsız gruplarda t-testi, One-way Anova testi ve Pearson korelasyon testi uygulanmıştır.

Bulgular: Katılımcıların %43,5'i ve ebeveynlerin %85,6'sı aşılanmıştır. Aşısız bireylerin %27,4'ü aşı olmak istememiştir. Aşı zorunlu olsa bile, %22,2'si yine de aşı olmayı reddedecektir. %28,7'si aşı karşıtlığı söyleminden etkilendiğini belirtmiştir. Katılımcıların ölçek puan ortalamaları 30,2±4,8 ve 48,1±17,0 idi. Kadınlar ve erkekler arasında anlamlı bir fark bulunamadı. Düşük gelirli gruplarda aşı tereddüt düzeyleri, yüksek gelirlilere göre daha yüksekti. Pandemilerdeki aşı tereddüt düzeyi, COVID-19'dan muzdarip olanlarda önemli ölçüde daha düşüktü. Ebeveynleri aşılanmış olanlarda aşı tereddüt düzeyleri anlamlı olarak daha düşüktü. Sosyal medyadan aşı hakkında bilgi sahibi olanlarda aşı tereddüt düzeyleri anlamlı olarak daha yüksekti.

Sonuç: Hastalıkların riskleri ve komplikasyonları hakkında bilgi sahibi olunması ve sosyal medya platformlarında yayılan bilgiler aşıya yönelik tutumları önemli ölçüde etkileyen faktörlerdir.

Anahtar Kelimeler: Aşı tereddütü, COVID-19, aşı karşıtlığı

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INTRODUCTION

The vaccine is a biological preparation, developed in different ways. One of them is eliminating the pathogenic properties of microbes (e.g., viruses, bacteria) or the capacity to cause disease in humans and animals, and the other is inactivating the toxins released by some microbes (1). Vaccines contain antigens that stimulate the immune system to produce an immune response similar to that elicited by the natural infection. Many types of vaccines are named based on the classification of antigens used to prepare vaccines. Live vaccines are derived from wild viruses or bacteria that are attenuated. Inactivated vaccines are not live and cannot replicate. mRNA and DNA vaccines contain the antibody-forming antigenic structure of the mRNA or DNA of the target microorganism. Vector vaccines are produced by adding genetic information to the antibody-forming antigenic structure of the target microorganism (1).

Immunization is among the significant public health interventions to help to prevent vaccine-preventable diseases and deaths. In Turkey, the first nationwide vaccination program "The extended immunization program" was initiated in 1981, targeting five diseases. This program was expanded to include 18 doses of vaccines against seven diseases in 2005 and 13 diseases in 2013 (2). Despite the implementation of compulsory vaccination, vaccination rates have remained around 75% during the years before 2007 due to geographical and climate conditions, poor record-keeping practices, and lack of financial incentives for healthcare providers and legal measures. As of 2007, vaccination rates have exceeded 95% in Turkey (3). However, vaccine refusals have emerged worldwide in the 1990s, and Turkey since 2010.

Anti-vaccination includes indecision about vaccination, vaccine hesitancy, and vaccine rejection. But when vaccination has been started in the early 1800s, concurrently vaccine hesitancy has also started. According to the WHO and UNICEF, vaccine hesitancy refers to a delay in acceptance or refusal of vaccination for one or more vaccines despite the availability of vaccination services. On the other hand, vaccine refusal refers to deliberately refusing to get vaccinated and the rejection of vaccines altogether (4). Vaccine hesitancy is complex and context-specific, varying across time, place, and vaccines". Vaccine hesitancy is a continuum between accepting and rejecting all vaccines. The reasons for vaccine hesitancy are concerns about chemicals found in vaccines, mistrust of vaccine manufacturers and belief that the vaccines are promoted for financial gain, and beliefs such as "natural immunity register or "natural methods are more effective in preventing diseases" (5). In Turkey, the number of parents refusing vaccines has increased from 5091 in 2015 to more than 12.000 in 2016 and over 23.000 in 2017 (6).

The development of vaccines to protect from the Covid 19 disease for the emergence of the pandemic worldwide led to discussions about vaccine hesitancy in the general population. The opinions of people outside the scientific community, spread throughout mass media and social media platforms, caused the increase in the infodemic. The COVID-19 pandemic has possibly impacted public opinion about the healthcare system, leading individuals to think about vaccine refusal. However, there are limited studies on this subject in the literature. In particular, there are no studies from Turkey investigating anti-vaccination or vaccine hesitancy among adolescents. This study aimed to determine the levels of anti-vaccination and COVID-19 vaccine hesitancy in a sample of adolescents.

MATERIAL AND METHOD

This research study was conducted with 303 individuals aged between 15-18 years who received the pediatric outpatient clinic of Kahta district state hospital between October and November 2021. Study data were collected using a structured questionnaire. The questionnaire includes specific sociodemographic characteristics, reasons for vaccine refusal or hesitancy, attitudes towards COVID-19 vaccines, and responses to 'The vaccine Hesitancy Scale' and 'Vaccine Hesitancy in Pandemics scale'. The Vaccine Hesitancy scale developed by Kılınçarslan et al. has a long form with 21 items and a Cronbach alpha value of 0.905 (7). The Vaccine Hesitancy in Pandemics scale is the Turkish version of the Vaccine Hesitancy Scale developed by Larson et al. in 2015. It was modified to measure vaccine hesitancy in pandemics with 10 items. Reliability and validity of the Turkish version of the scale with ten items have been demonstrated by Çapar and Çınar. Its Cronbach alpha coefficient is 0.901 (8,9). While the vaccine hesitancy scale ranges from 21 to 105 points, the vaccine hesitancy in pandemics scale ranges from 10 to 50 points. Higher scores for both scales indicate increased mistrust towards the vaccine. At the time of the study, those who received at least two doses of vaccine were considered to be vaccinated in Turkey. For this reason, those who received two doses of vaccine in our study were accepted as vaccinated.

Approval for the study was obtained from the Ethics Committee for Non-Interventional Trials of Adıyaman University Faculty of Medicine on September 21,2021 (No. 2021/07-12). Parents of all adolescents were informed about the purpose and scope of the research in detail, and interviews were conducted with volunteer participants. Written informed consent was obtained from the parents of the participants.

Statistical analysis: Descriptive data are shown as frequency, percentage, and mean/standard deviation. Quantitative data were analyzed with the Kolmogorov-Smirnov test, and it was determined that data were distributed by the normal distribution. In the analysis of the relations between the variables in independent groups, the One-way Anova test and the Pearson correlation test were applied. Twas-value of <0.05 was considered significant for statistical significance.

RESULTS

Among 303 participants, 80.3% were boys, and 19.7% were girls. The monthly income of 21.3% of families was low, 52.5% was middle and 26.2% was high. Table 1, it was given the COVID-19 vaccine-related characteristics of the study sample.

As it was seen in Table 1, for the protection from COVID-19 disease, 72.7% of the participants considered the vaccination as the most successful method after masking, social distancing and hygiene. 1.7% considered alternative medicine (e.g., hijama (cupping therapy), hirudotherapy, acupuncture, medicinal herbs) and 25.6% considered increased intake of fruits and vegetables.

Although 85.6% of the parents were vaccinated, 43.5% of participants were vaccinated. 28.1% of unvaccinated young wanted to get vaccinated and 27.4% were not willing to get vaccinated. Even if vaccination were compulsory, 22.2% would still refuse to get vaccinated. The most motivating factors were "Announcement of scientific research findings on vaccine safety" and "Recommendation by the family physician or a doctor". The most persuasive measure of vaccination was the 'Exclusion of unvaccinated students from face-to-face education". 58.1% of the participants believed unvaccinated persons to affect all community members.

Table 1. COVID-19 vaccine-related characteristics of the study sample

Characteristics	n	%
Parental COVID-19 vaccination status		
Non vaccinated	43	14.4
Mother vaccinated	212	70.0
Father vaccinated	215	71.0
Adolescent's COVID-19 vaccination status		
Vaccinated	132	43.5
Willing to get vaccinated	85	28.1
Not willing to get vaccinated	83	27.4
Unsure	3	1.0
Think of getting vaccinated if vaccination was mandatory?		
Yes	70	41.0
No	38	22.2
Unsure	63	36.8
Motivating Factors for getting vaccinated		
Public disclosure of the findings of scientific research on vaccine safety	245	80.9
Recommendation by the family physician or a doctor	230	75.9
Famous people getting vaccinated or recommending vaccination	121	39.9
Measures imposed on unvaccinated individuals	85	28.1
Incentives of cash or gifts for vaccination	46	15.2
Measures considered to be persuasive for getting vaccinated		
Exclusion of unvaccinated students from face-to-face education	270	89.1
Greater fines for unvaccinated individuals without face masks	237	78.2
Not being able to receive outpatient services care except for emergency healthcare	232	76.6
Curfew enforcement for unvaccinated individuals at certain hours	225	74.3
Unvaccinated individuals banned from public transport	159	52.5
Unvaccinated individuals are barred from parks and holiday locations	143	47.2
Unvaccinated individuals are not allowed to enter public places	72	23.8
The impact of unvaccinated people on the community		
The entire community will be affected	175	58.1
Only that person will be affected	60	19.9
Close contacts will be affected	48	15.9
Nobody will be affected	18	6.0

Table 2, it was given the opinions of the participants on COVID-19 vaccine refusal.

As it was seen in Table 2, among the participants, 22.9% believed that vaccination was not indispensable for public health, and 36.7% did not regard vaccine refusal as a threat to public health. 28.7% of the participants stated that they were affected by anti-vaccine discourses. It was found that 52.8% of the participants thought that people could be forced to get vaccinated, and 62.3% tried to persuade vaccine-hesitant people around them to get vaccinated. 92.7% reported that they would get tetanus and rabies vaccines when necessary (e.g., in the case of an injury/accident, cat/dog bite), and 65.4% were willing to get the seasonal flu vaccine.

Table 3, it was given the means of vaccine hesitancy scores of the study sample by descriptive characteristics, COVID-19 status and COVID-19 vaccination status.

As it was seen in Table 3, the participants' mean scores were 30.2±4.8 for the "Vaccine Hesitancy in Pandemics Scale" and 48.1±17.0 for the "Vaccine Refusal Scale", respectively. When the participants were evaluated according to sex, no significant difference was found between females and males in the mean scores for Vaccine Hesitancy in Pandemics scale and Vaccine Hesitancy scale. In low-income groups, vaccine hesitancy levels were higher than in those with higher income.

The vaccine hesitancy level in Pandemics was significantly lower in those who suffered from Covid-19, while there was no significant difference in the mean scores for the general vaccine hesitancy. There was no significant difference between the participants, those parents suffered from COVID-19 in the mean scores on both scales. The vaccine hesitancy levels were significantly lower in those whose parents or close contacts were hospitalized or died from COVID-19.

The vaccine hesitancy levels on both scales were significantly lower in those who were willing to receive the COVID-19 vaccine, those who did not believe in the anti-vaccine content of videos circulating on social media, and those who were not influenced by anti-vaccination rhetoric, those who believed in all vaccines safe.

The vaccine hesitancy levels on both scales were significantly higher in those whose parents were unvaccinated or vaccine-refusing, those with the primary source of information about vaccines were neighbours, friends, relatives, religious leaders, and those informed about vaccines from social media, and those who believed in all vaccines unsafe.

72% correlation in the same direction was found between levels of vaccine hesitancy during the pandemic and vaccine refusal levels among adolescents. While vaccine hesitancy in pandemics can increase the level of rejection of all vaccines; Similarly, vaccine rejection can increase vaccine hesitancy in pandemics.

In Table 4, it was given the reasons for distrusting COVID-19 and other vaccines in the study sample.

As it was seen in Table 4, the most common reason for rejecting the COVID-19 vaccine was concerns about the adverse effects. The most common reason for considering the other vaccines as unsafe was rumours about their harmful ingredients.

Table 2. Opinions of the participants on COVID-19 vaccine refusal

Opinions	Agree n (%)	Disagree n (%)	Unsure n (%)
Vaccine refusal is a problem that poses threat to the entire community	172 (57.9)	109 (36.7)	16 (5.4)
People can be forced to get vaccinated	159 (52.8)	132 (43.9)	10 (3.3)
Anti-vaccination arguments influence me	82 (28.7)	192 (67.1)	12 (4.2)
Vaccination is necessary for public health	204 (67.8)	69 (22.9)	28 (9.3)
I try to persuade vaccine-hesitant people around me to get vaccinated	187 (62.3)	87 (29.0)	26 (8.7)
I would get tetanus and rabies shots when it becomes necessary (e.g.. in the case of an injury/accident. cat/dog bite)	278 (92.7)	19 (6.3)	3 (1.0)
I am willing to get a seasonal influenza vaccine	197 (65.4)	91 (30.2)	13 (4.3)

Table 3. Mean vaccine hesitancy scores of the study sample by descriptive characteristics, COVID-19 status and COVID-19 vaccination status

Characteristics	n	%	Vaccine hesitancy scale in Pandemics Mean Score	p	Vaccine hesitancy scale Mean score	p
Sex						
Male	216	80.3	29.9±4.7	0.543	46.9±16.6	0.346
Female	53	19.7	30.4±5.1		49.4±16.7	
Monthly Household Income						
3000 TL or less	60	21.3	30.6±5.2	0.024	51.9±17.8	0.004
3000 to 5000 TL	148	52.5	30.4±4.8		48.4±17.2	
5000 TL or more	74	26.2	28.8±3.9		42.5±13.9	
Suffered from COVID-19						
Yes	104	34.7	29.2±4.6	0.016	45±16.1	0.230
No	196	65.3	30.6±4.9		49.6±17.3	
Parents suffered from COVID-19						
Yes	140	46.4	30.0±4.3	0.547	47.0±15.8	0.294
No	162	53.6	30.3±5.2		49.1±18.0	
Hospitalization for COVID-19 among parents or close contacts						
Yes	44	14.6	30.0±4.2	0.815	42.5±13.0	0.005
No	257	85.4	30.2±4.9		49.0±17.5	
Death from COVID-19 among parents or close contacts						
Yes	35	11.7	29.5±4.1	0.419	41.5±13.7	0.007
No	263	88.3	30.2±4.9		48.6±17.2	
COVID-19 Vaccination Status in parents						
Vaccinated	256	85.6	29.8±4.6	0.001	45.7±15.7	0.001
Unvaccinated	43	14.4	32.9±5.0		62.6±18.1	
COVID-19 Vaccine Refusal among parents						
Yes	43	14.9	34.2±4.0	0.001	63.0±12.5	0.001
No	245	85.1	29.4±4.5		45.3±16.3	
Willingness to get COVID-19 vaccine						
Willing	126	59.4	29.1±4.2	0.001	43.2±10.9	0.001
Unwilling	83	39.2	34.9±3.9		68.9±11.9	
Unsure	3	1.4	30.0±2.6		68.0±4.4	
The primary source of information about vaccines						
Physicians/Healthcare professionals	40	13.3	28.6±4.2	0.001	42.4±13.1	0.001
Media/Internet	212	70.7	29.9±4.7		46.8±16.5	
Other (neighbours, friends, relatives, religious leaders)	48	16.0	32.7±4.8		58.4±18.4	
Media outlets influencing the decision about vaccination						
TV, radio, newspapers, magazines	175	60.3	29.5±4.7	0.003	45.4±16.0	0.003
Social media	115	39.7	31.2±4.7		51.6±18.4	
Believing in the anti-vaccine content of videos circulating on social media						
Yes	38	12.6	34.9±5.1	0.001	67.2±16.9	0.001
No	252	83.7	29.3±4.3		44.5±14.8	
Unsure	11	3.7	33.2±5.5		65.6±12.3	
Influenced by anti-vaccination rhetoric						
Yes	82	27.1	31.9±4.8	0.001	51.4±18.8	0.001
No	192	63.4	29.0±4.5		44.0±14.5	
Neutral	12	4.0	33.2±2.9		70.0±7.5	
Opinions on other vaccines (flu vaccine, childhood vaccines, e.g. measles and tuberculosis vaccines)						
Vaccines are safe	221	73.9	29.1±4.1	0.001	40.8±11.7	0.001
Vaccines are unsafe	63	21.1	34.1±4.7		70.0±11.1	
Neutral	15	5.0	30.5±6.8		63.7±13.9	

Table 4. Reasons why the study sample considered COVID-19 and other vaccines as unsafe

Reasons for the reluctance of the COVID-19 vaccine	n	%
Concerns about adverse effects of vaccines	78	25.7
Negative comments of others on vaccines	57	18.8
I think the COVID-19 vaccine is ineffective	55	18.2
Believing the immune system will fight off the disease	35	11.6
Negative opinions of experts regarding vaccines	29	9.6
Waiting for a Turkish COVID-19 vaccine to be available	14	4.6
I think there are no adequate studies on COVID-19 vaccines	13	4.3
Vaccines are manufactured abroad	9	3.0
Religious concerns regarding vaccine content	10	3.3
I think that there is no such disease as COVID-19	9	3.0
I am waiting for others to get vaccinated first	8	2.6
Negative opinion of a physician/healthcare provider about the COVID-19 vaccine	7	2.3
Fear of injection	6	2.0
Considering vaccination as some plot of foreign countries (e.g., secretly implanting microchips via vaccination)	2	0.7
Reasons for considering all vaccines as unsafe	**n**	**%**
I've heard that they contain harmful substances	73	24.1
I've been told that vaccines will cause diseases at later ages	64	21.1
Some people say vaccines cause infertility	19	6.3
Vaccines are manufactured by foreign countries	15	5.0
I think foreign countries or pharmaceutical companies advocate vaccination for their interests	14	4.6

DISCUSSION

The anti-vaccine movement has been increasing in recent years, leading to poor health outcomes as well as the waste of resources. By measuring the vaccine hesitancy and causative factors, the current status of vaccine hesitancy can be determined objectively, and the effectiveness of intervention strategies can be monitored. This study, it was evaluated the approach to vaccines, vaccine hesitancy and thoughts about Covid-19 vaccines in the adolescent age group.

While nearly 73% of the participants thought that vaccination was the most successful method in the fight against Covid-19 after mask, social distancing and hygiene, approximately 44% were vaccinated. It was stated that the most motivating factors in the decision for vaccination were “Public disclosure of scientific research findings on vaccine safety”, “Recommendation by the family physician/a doctor” and “Exclusion of unvaccinated students from face-to-face education”.

In our study, one-quarter of the participants thought the vaccination was necessary for public health. One study found that the total number of people who thought the vaccination was unnecessary to prevent diseases was not very high. Undecided individuals also were half of the total participants (10). Another study underscored that the high number of vaccine-hesitant parents was a potential public health threat, and this should not be underestimated to ensure the vaccination needs of children were met (11).

In our study, in terms of the mean score of both scales, the research group has a moderate level of vaccine hesitancy that was higher than expected. No significant difference was found between females and males in the mean scores for both Vaccine Hesitancy in Pandemics scale and the Vaccine Hesitancy scale when the study participants were evaluated according to sex. In a study from Turkey, it was reported that males were statistically more likely to be hesitant about vaccination (10). However, in another study, no significant difference was found between the

sex regarding vaccine refusal and vaccine hesitancy (12). In our study, vaccine hesitancy is more common in low-income families than in higher-income families. One study reported that vaccine hesitancy decreased with higher household income (13). In another study, vaccine hesitancy was more common among parents with lower socioeconomic status (14). In a survey-based, a North American study involving pediatricians, better educated, wealthier families were found to experience more vaccine refusals (15). A study on mothers revealed increasing rates of vaccine refusal among parents with high socioeconomic status (16). In previous studies, investigating the sociodemographic and sociocultural determinants of childhood vaccine refusal and hesitancy, several factors were involved in decision-making, including younger age, religious faith, alternative medicine, and parental lifestyle. Other factors were perceptions of the child's body and immune system, perceived risk of diseases, vaccine effectiveness and side effects, concerns about vaccine safety, perceived advantages, previous negative experience with vaccination, and social environment (17-19).

In our study, suffering from COVID-19 affect the levels of vaccine hesitancy in pandemics, but did not affect the levels of other vaccines' hesitancy. The participants whose parents were hospitalized or died from COVID-19 had lower levels of vaccine hesitancy. This suggests that diseases and potential complications influence attitudes towards vaccination. Similarly, 93% of the participants reported getting tetanus or rabies vaccine in the case of an injury, accident, or cat/dog bites. Two-thirds of the participants were willing to get the seasonal flu vaccine. This suggests that perceived health risk associated with the disease, especially in emergencies, is an important determinant of vaccination decision-making.

In our study, the correlation between participants' hesitancy to both all and pandemic vaccines was 72%. A moderately strong positive correlation was found between vaccine hesitancy in pandemics and vaccine hesitancy levels in the current study. The levels of vaccine hesitancy in pandemics were higher among the participants who did not want to get other vaccines, and vaccine hesitancy levels were higher among the participants who were not willing to receive the Covid-19 vaccine. One-third of the participants reported that anti-vaccine discourse influenced getting vaccinated. An Australian study by Atwell et al. in 2017 discussed the impact of "The Unhealthy Other" propaganda on society. It was constructed by vaccine-rejecting parents employing a discourse that called the vaccinated children "unhealthy other" (20). Many studies have reported that information about various health-related issues and vaccines was obtained from the internet and social media, and parents' vaccination decisions were influenced by this information (21-24). A systematic literature review of 145 published studies on European populations showed that the primary concern of the individuals about vaccination was related to the safety of vaccines. The majority of them believed that the risks of vaccination outweigh the benefits (25).

The most common reason for the reluctance of the COVID-19 vaccine was the concern about its adverse effects and the rumours about the harmful content of the non-COVID-19 vaccines. As the reason for believing, vaccines were most commonly considered unsafe. In a 2017 study, conducted with healthcare workers in Denizli province of Turkey to investigate their attitudes towards the influenza vaccine, the most crucial reason for the reluctance to influenza vaccine was the disbelief in the necessity of the vaccine (64.5%) (26). In a study among parents who refused vaccination in Venezuela, the most critical barriers to vaccination were fear of side effects and the disbelief in the necessity of the vaccine for children in more than one dose (27).

CONCLUSION

The vaccine hesitancy level in the study group was higher than expected. Socioeconomic level, knowledge of the risks and complications of diseases, illness experience, families' approach to vaccination, opinions on the safety of vaccines, and information disseminated on social media platforms are factors that significantly influence attitudes towards vaccination. The spread of unreliable and false information on social media should be avoided, and accurate information on health-related topics and the risks and complications associated with diseases should be delivered to the community using all kinds of mass media. Since getting information from sources other than non-healthcare professionals is the main driver of vaccine misinformation, measures should be implemented to ensure that health-related information is delivered solely by health authorities.

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MEDICAL RECORDS-International Medical Journal

Research Article

Frequency of Home Accidents of Children Between 0-6 Years and Levels of Diagnosis of Mothers' Safety Measures

0-6 Yaş Arası Çocukların Ev Kazalarının Sıklığı ve Anne Güvenlik Önlemlerinin Tanı Düzeyleri

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Abstract

Aim: Children are vulnerable to home accidents and injuries due to their inability to protect themselves developmentally, and they need the protection of their parents. In the study, it was aimed to investigate the frequency of home accidents of children aged 0-6, the most common types of accidents, and the knowledge levels of mothers on Diagnosing Safety Precautions for Home Accidents.

Material and Method: The study is a cross-sectional and descriptive study and was conducted with 380 parents who applied to the pediatric outpatient clinic in December 2021. The "Scale of Diagnosing the Safety Precautions for Home Accidents of Mothers with 0-6 Age Group Children" was used in the questionnaire form. In the analysis of the relations between the variables, independent groups t-test, the One-way Anova test, the Pearson correlation test, Chi-Square test and Logistic Regression Analyze were applied.

Results: The frequency of children who had home accidents was 11.3%. The most common type of accident is falling. The mean score of the Mothers' Scale for Diagnosing Safety Measures for Home Accidents was 155.9±15.2. Identification of Safety Precautions scores are higher in mothers who graduated from college, those whose children had a home accident, and those who received first aid knowledge. The most important factors affecting the accident at home are the number of children and the caregiver.

Conclusion: Home accidents, one of the preventable risk factors, are critical health problems. Providing information about all home accidents, especially falls, should be among the priority health targets.

Keywords: Home accidents, safety measures, unwanted injuries

Öz

Amaç: Çocuklar, gelişimsel olarak kendilerini koruyamadıkları için ev kazalarına ve yaralanmalara karşı savunmasızdır ve ebeveynlerinin korumasına ihtiyaç duyarlar. Araştırmada 0-6 yaş arası çocukların ev kazalarının sıklığı, en sık görülen kaza türleri ve annelerin Ev Kazalarında Güvenlik Önlemlerini Tanılama konusundaki bilgi düzeylerinin araştırılması amaçlanmıştır.

Materyal ve Metot: Araştırma kesitsel ve tanımlayıcı tipte bir çalışma olup, Aralık 2021 tarihinde çocuk polikliniğine başvuran 380 ebebeyn ile yapılmıştır. Anket formunda Çocuklar" kullanılmıştır. Değişkenler arasındaki ilişkilerin analizinde bağımsız gruplar t-testi, One-way Anova testi, Pearson korelasyon testi, Ki-Kare testi ve Lojistik Regresyon Analizi uygulanmıştır.

Bulgular: Ev kazası geçiren çocukların sıklığı %11.3 idi. En sık görülen kaza türü düşmedir. Annelerin Ev Kazalarına Yönelik Güvenlik Önlemlerini Tanılama Ölçeği puan ortalaması 155.9±15.2'dir. Üniversite mezunu, çocuğu ev kazası geçiren ve ilkyardım bilgisi alan annelerde Güvenlik Önlemlerini Belirleme puanları daha yüksektir. Evde kazayı etkileyen en önemli faktörler çocuk sayısı ve bakıcıdır.

Sonuç: Önlenebilir risk faktörlerinden biri olan ev kazaları kritik sağlık sorunlarıdır. Düşmeler başta olmak üzere tüm ev kazaları hakkında bilgi vermek öncelikli sağlık hedefleri arasında yer almalıdır.

Anahtar Kelimeler: Ev kazaları, güvenlik önlemleri, istenmeyen yaralanmalar

INTRODUCTION

According to the World Health Organization; Situations that cause physical and mental harm that occur suddenly and outside a person in an unplanned manner are defined as 'accidents'. Injury is defined as "physical damage resulting from the sudden exposure of the human body to amounts of energy exceeding the physiological tolerance threshold or the deficiency of one or more vital elements" (1). Injuries are among the leading causes of death and disability. All types of injuries have common root causes, socioeconomic and environmental determinants. The leading types of unintentional injuries are traffic accidents, drowning, poisoning, burns and falls (2).

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Unwanted injuries experienced by children is also an important global health problem (3,4). Home injuries, which have an important place in accidents, can be defined as events that occur in a house (children's room, living room, kitchen, bathroom, etc.) or in an environment that belongs to it (garden, garage, etc.) (5).

Home accidents can occur in all age groups, but children and the elderly are more susceptible to these accidents. Children are not at the mental and physical level to protect themselves from accidents. Children aged 0-6 have a sense of curiosity because of their desire to explore their world. They cannot evaluate actions that may lead to injury due to their inability to protect themselves developmentally (6). Children are particularly vulnerable to injury and need special attention to avoid injury. Therefore, it is the responsibility of adults to take protective measures to prevent injuries and to provide a safe living space (7). Injuries and violence are a major cause of death and burden of disease in all countries; however, it is not evenly distributed among or within countries. Some people are more vulnerable than others, depending on the circumstances in which they were born, raised, worked, lived and aged. Broad societal determinants of health, such as inadequate adult supervision of children, poverty; Unsafe housing, easy access to alcohol, drugs, firearms, knives and pesticides are factors that increase the risk of accidents for children (8).

Home accidents are preventable events. Among the causes of home accidents, the situation in the home is as important as individual mistakes. The impact of accidents on children's health is greater than is thought. A child who has a home accident loses his/her balance in terms of psychological, physical and social aspects. More can result in accidents, illness, disability and even death. Exposure to any trauma, especially in childhood, can increase the risk of mental illness and suicide; smoking, alcohol and substance abuse; chronic diseases such as heart disease, diabetes, cancer and enfections (9). Health problems such as respiratory tract diseases and otitis media may develop due to mechanical obstruction as a result of home accidents (10). For these reasons, preventing injury and violence, including breaking intergenerational cycles of violence, contributes to significant health, social and economic gains. Analysis of the costs and benefits of a variety of selected injury and violence prevention measures shows that investments are made in measures that deliver great societal benefit. For example, regarding child injury prevention, it was found that every $1 invested in smoke detectors saves $65, and an investment in child seats and bicycle helmets saves $29. The social benefits of injuries prevented by home modifications to prevent falls are estimated to be at least six times the cost of the intervention (9).

In the WHO European Region, approximately 42,000 children and young people under the age of 20 die each year as a result of unintentional injuries (1). According to statistics, 72 children die every day in Europe due to home accidents. In the UK alone, 30% of deaths occur as a result of unwanted injuries at home (7). It has been reported that home accidents constitute approximately 18-25% of all accidents in childhood in Turkey, and it is the second most common reason for referral to emergency services after traffic accidents (11).

Inadequate knowledge, attitudes and behaviors of parents about children's safety, problems under the supervision of children, and lack of regulations to ensure child safety in the home are among the factors of in-home accidents (12). Home injuries, easy arrangements that can be made at home, and regular training for mothers who spend a lot of time with their children can be prevented by raising their awareness (13).

Adults are responsible for taking protective measures and providing safe living spaces, as children are particularly vulnerable to injury and need special attention to avoid injury. It should be especially taken into consideration when providing education to mothers about protection from home accidents, and the developmental characteristics of their children in this period should be explained. Knowing, predicting, and perceiving the accident risks of individuals responsible for child care, primarily mothers, and their awareness of being protected from accidents are important in terms of the accident risks that children may encounter (6). In the study, it was aimed to investigate the frequency of home accidents of children aged 0-6, the most common types of accidents, and the knowledge levels of mothers on Diagnosing Safety Precautions for Home Accidents.

MATERIAL AND METHOD

The research is a cross-sectional and descriptive study. The research was carried out in Kahta district of Adıyaman province in November-December 2021. The universe of the study consisted of parents with children aged 0-6 years who applied to the outpatient clinic of Kahta State Hospital. 380 parents were included in the study with a 95% confidence level and 0.05 margin of error. A questionnaire form, which is a data collection tool, was used, and the data were collected through face-to-face interviews. Consent form was obtained from the participants.

Survey form; sociodemographic information and "Scale for Diagnosing Safety Measures for Home Accidents of Mothers with 0-6 Age Group Children". The sociodemographic information form created by the researchers consists of 21 questions. "Scale for Diagnosing Safety Measures for Home Accidents of Mothers with 0-6 Age Group Children" is a five-point Likert-type scale consisting of 40 items. The Cronbach Alpha coefficient of the scale, which was developed by Çınar et al. (2003) and whose validity-reliability studies were conducted, was reported as 0.82. With this scale, the safety measures taken by the mothers to protect the child from falling, burning, poisoning and suffocation, which are the most common home accidents in the home environment, were evaluated. While the answer always gets 5 points, mostly 4 points, sometimes 3

points, rarely 2 points, never 1 point in items with positive statements, the scoring is reversed in 6, 9, 23, 26, 30 and 40 items with negative statements. The minimum score of the scale is 40, and the maximum score is 200. High scores indicate that the mother takes precautions to protect her child from home accidents at a higher level (14).

Statistical analysis

Descriptive data are shown as Descriptive data are shown as frequency, percentage, mean/standard deviation. Quantitative data were analyzed with the Kolmogorov-Smirnov test, and it was determined data were distributed by the normal distribution. In the analysis of the relations between the variables, t-test in independent groups, the One-way Anova test, the Pearson correlation test and Logistic Regression Analyze were applied. The Chi-Square test was used to compare qualitative data. A p-value of <0.05 was considered significant for statistical significance.

Permission for the study, dated 16/11/2021 and numbered 2021/09-29, was obtained from the Non-Invasive Ethics Committee of Adıyaman University Faculty of Medicine.

RESULTS

380 parents participated in the study, 32.6% of them were mothers, 66.1% were fathers and 1.3% were caregivers. The mean age of mothers was 32.2±4.4, and fathers were 35.6±6.0. The descriptive features of the research group are shown in Table 1.

According to Table 1, 28.4% of the mothers are college/university graduates and 41.1% of the fathers are high school graduates. 28.2% of mothers are working. While 32.1% of the families have 2 children, 55.8% of the children are between 2-5 years old. 45.8% of the families participating in the research live in an apartment. The primary caregivers of children are 65.5% mothers, 18.4% relatives and 12.9% caregivers. Table 2 presents the descriptive features of home accidents experienced by children.

According to Table 2, the frequency of children who had a home accident is 11.3%. The average number of accidents for those who had a home accident is 2.0. It was most frequently spent at home (43.8%) in the living room and next to non-mother caregivers (62.8%). The most common type of accident (37.4%) is falling by slipping or tripping over household items. As a result of these accidents, 13 children received inpatient treatment and received treatment for an average of 5 days. Table 3 shows the distribution of home accidents by age of children.

According to Table 3, the most common home accident in the 1-year-old group is falling from a height, the most common home accident in the 2-3 and 5-year-olds is falling by slipping or tripping, the most common home accident in the 4-year-old group is falling by tripping or slipping, and hitting things. The most common home accident in the 6-year-old group cuts. While the average age of incidence in falling from a height, tripping and falling, hitting objects, electric shock, and burning with hot water varies between 2 and 3 years, it is between 4 and 6 years old for the danger of drowning, falling of large objects and incisions. Table 4 shows the child's home accident status according to some characteristics of the family.

Table 1. Descriptive characteristics of the research group

n=380	Number	%
The people interviewed		
Mother	125	32.9
Father	250	65.8
Caregiver	5	1.3
Mother's educational status		
Illiterate	3	0.8
Literate	8	2.1
Primary school graduate	102	26.8
secondary school graduate	54	14.2
High school graduate	105	27.6
College/University	108	28.4
Father's educational status		
Illiterate	1	0.3
Primary school graduate	16	4.2
Secondary school graduate	57	15
High school graduate	156	41.1
College/University	150	39.5
Number of working mothers	107	28.2
Number of working fathers	353	92.9
Perception of income status		
Good	123	32.4
Middle	227	59.7
Bad	28	7.4
Number of children		
1	112	29.5
2	122	32.1
3	91	23.9
4	46	12.1
5 and above	9	2.4
Age range of children		
0-1.9	45	7.7
2-4.9	328	55.8
5-6	215	36.6
Family type		
Nuclear family	219	57.6
Large family	161	42.4
Number of individuals living in the house		
≤5	215	56.6
6-9	155	40.8
≥10	10	2.8
Type of house you live in		
Apartment	174	45.8
Detached house with garden	205	53.9
Child caregiver		
Mother	249	65.5
Caregiver	49	12.9
Relative	70	18.4
Nursery	10	2.6

The number of those who received any information about first aid before was 49 (12.9%). Those who received information from the health personnel were 22.5%, and those who received information from the school were 77.5%. The number of people who stated that there were times when they left their child alone at home was 11 (2.9%).

Table 2. Descriptive characteristics of children's home accidents

Feature	Sayı	%
Children who had a home accident	**43**	**11.3**
Number of home accidents (n=43)		
1 time	9	21.0
Two times	10	23.3
Three times	17	39.5
4 times	5	11.6
5 times	1	2.3
6 times	1	2.3
Places of Home Accidents (n=43)		
Living room	35	43.8
Children's room / Bedroom	21	26.2
Stairs, Garden	12	15.0
Kitchen	8	10.0
Bath	4	5.0
Person next to the child at the time of the accident (n=43)		
Mother	16	37.2
Other (Father, Grandfather, Grandmother etc.)	27	62.8
Hospitalized Due to Home Accident (n=43)	13	30.2
Type of accident		
Falling by slipping or tripping on household items	34	37.4
Falling from height	20	22.0
Bumping into household items	20	22.0
Burning with hot water or hot food	7	7.6
Electric shock	3	3.3
Danger of drowning	3	3.3
Items such as irons/TVs falling on it	2	2.2
Cutting tool injury	2	2.2
Poisoning	0	0.0
Iron burn	0	0.0

The number of mothers participating in the study is 125. The scores of 125 mothers in the study group from the "Scale for Diagnosing Safety Precautions for Home Accidents of Mothers with 0-6 Age Group Children" ranged between 128-196. The mean score of the scale is 155.9 ± 15.2. The difference between the scores the mothers got from the scale in terms of different variables is shown in Table 4.

According to Table 4, the scale scores of the mothers who graduated from college or university compared to those from primary school graduate mothers, mothers whose children had a home accident compared to those who did not, and the mothers who received information about first aid were significantly higher than those who did not, the scale scores of diagnosing safety measures for home accidents were significantly higher.

When the correlation between some features and the scale score is examined with the Pearson correlation test; there is a significant inverse correlation between the scale score and the number of children in the family and the number of people living at home (-0.21 and -0.24, respectively). Mothers with many children have lower scores on the scale for diagnosing safety measures for home accidents. Mothers with many people living in their homes have lower scores for diagnosing safety measures for home accidents.

When the child's home accident status according to some characteristics of the family is examined by Chi-square analysis, the incidence of accidents is significantly higher in mothers over 30 years old, in mothers who do not work, and in cases where the primary caregivers are close relatives. No significant relationship was found in terms of accident incidence according to the education level of the mother or father, family type, housing type and economic status. Regression analysis was performed to determine the factors affecting the occurrence of home accidents among these factors, and the results are shown in Table 5.

In the logistic regression analysis, the factors affecting the accident at home are the number of children and the caregiver. As the number of children increases, the risk of having an accident increases 1.64 times. Children cared for by relatives have a 2.99-fold increased risk compared to those cared for by their mother.

Table 3. Types of home accidents by age of children

Age	Falling from height	Sliding and falling	Striking objects	Electric shock	Drowning	Danger Burning with hot water food	Falling of large objects	Incision	Total
1	6	1	4	-	-	1	-	-	12
2	9	14	4	1	1	3	-	-	32
3	4	11	5	2	1	2	-	-	25
4	1	4	4	-	-	-	-	-	9
5	-	3	2	-	1	1	1	-	8
6	-	1	1	-	-	-	1	2	5
Total	20	34	20	3	3	7	2	2	91*
Mean Age	2.5	3.0	3.1	2.7	4.0	2.6	6.0	6.0	3.4

* 79% of 43 children had more than one accident

Table 4. The difference between the scores of the mothers in terms of different variables

	n	Mean.± SD	t / F	p*
Age group				
<30	45	155.8±14.1	0.05	0.959
≥30	80	155.9±15.8		
Mother's Education				
Primary / secondary education*	49	151.6±13.3*	4.54	0.013
High school	26	155.1±15.8		
College/University*	50	160.5±15.5*		
Mother's working status				
Working	48	160.2±15.7	2.55	0.120
Not working	77	153.2±14.3		
Income status				
Good	44	157.8±15.9	0.54	0.582
Middle	68	155.1±14.9		
Bad	12	153.7±15.4		
Number of children				
1	44	158.1±13.8	1.67	0.178
2	49	156.9±15.5		
3	22	152.6±17.5		
4	10	148.0±11.3		
Family type				
Nuclear family	71	158.1±14.6	1.91	0.058
Large	54	152.9±15.5		
Housing type				
Apartment	65	158.4±15.7	1.96	0.053
Garden-detached house	59	153.1±14.3		
Children's home accidents				
Had a home accident	19	163.4±17.7	2.38	0.019
No home accident	106	154.5±14.4		
Getting information about first aid				
Informed	19	166.2±13.7	3.55	0.001
Not informed	105	153.6±14.2		

t-test in independent groups. the One-way Anova test *Logistic Regression Analyze
* the scale scores of the graduated from university significantly higher than the primary school

Table 5. Factors affecting the situation of having a home accident

	B	S.E.	p*	O.R	95% C.I.for O.R
Constant	-3.10	1.330	0.020	0.05	
Maternal age	0.03	0.038	0.481	1.03	0.93-1.10
Mother's working status	-0.95	0.556	0.089	0.39	0.19-2.00
Number of children	0.50	0.200	0.013	1.64	1.19-2.98
Child caregiver (Mother is reference)			0.046		
Caregiver	-0.15	0.772	0.842	0.86	0.10-2.53
Close relative	1.10	0.501	0.029	2.99	1.31-10.32
Nursery	0.65	0.979	0.504	1.92	0.37-29.51

*Logistic Regression Analyze

DISCUSSION

The first six years of human life are considered as a period that children are very active. This period is important for occurring home accidents and related injuries. In our study, the frequency of children who had home accidents was 11.3%. In studies conducted in Turkey, the rates of home accidents reported by mothers vary between 15.5% and 70.0%, respectively (12,13,15-20).

In our study, home accidents occurred most frequently (43.8%) in the living room. Similarly, in other studies, the highest number of accidents occurred in the living room and the kitchen (17,21). The reason why home accidents are most common in the living room, living room or kitchen may be because families spend most of their time there. The living room is a resting place for parents and at the same time a play and leisure area for children. As used for various activities, it becomes an accident area for children (22).

The most common type of accident (37.4%) is falling by slipping or tripping over household items. Similarly, in other studies, the most common type of accident was found to be falling (13,16-19,23-25). When the distribution of home accidents according to the age of the children is examined, the most frequent falls are falling from a height in the 1 age group, falling by tripping or slipping in the 2, 3 and 5 age groups, falling and hitting objects in the 4 age group, and cuts in the 6 age group. The average age of incidence for fall, shock, electric shock and burn accidents is between 2 and 3 years, while the average age for drowning hazard, the large object falls and cuts is between 4 and 6 years old.

When the factors affecting the child's accident at home according to some characteristics of the family were examined, it was determined that the number of children and the caregiver were factors. This finding is supported by correlation analysis; there is a significant inverse correlation between the scale score and the number of children in the family and the number of people living at home (-0.21 and -0.24, respectively). Mothers with many children have lower scores on the scale for diagnosing safety measures for home accidents. Mothers with many people living in their homes have lower scores for diagnosing safety measures for home accidents. Similarly, in another study, the frequency of home accidents was lower in children living in a nuclear family than in those living in an extended family and the scale scores of those with only one child were found to be higher (22). No significant relationship was found in terms of accident incidence according to mother's age, employment status, education level of mother or father, family type, housing type and economic status. Similarly, studies are showing that accident frequency is not affected despite the increase in maternal education (6,19,26). In some studies, the accident frequency of those whose mothers' education level was "university" was found to be higher than those whose mothers were in "primary school and below" (19,27). This situation may make us think that the training programs are not sufficient in terms of accidents and the importance of home accidents.

In our study, the mean score of 125 mothers in the study group from the "Scale for Diagnosing Safety Precautions for Home Accidents of Mothers with 0-6 Age Group Children" was at a moderate level (155.9 ± 15.2). While this score is higher (163.4 ± 17.7) in those who have had a home accident, it is lower (154.5 ± 14.4) in those who have not. Similarly, in the study of Özmen et al., mothers whose children had an accident in the last year were found to have higher scores on the scale, and it was reported that they might have scored higher on the scale due to their experiences as a result of these accidents (5). Erdem et al. In the study of Karatepe and Akis, the mean score was both higher and, unlike our study, the mean score was found to be higher in those who did not have a home accident (6,19). Similar to our study, Nadeeya and her friends (2016) state that mothers have moderate knowledge and perception scores regarding home injuries and safety precautions (31).

In our study, when the difference between the scores of the mothers in terms of different variables was examined, the scale score of the mothers who graduated from college or university, compared to the mothers who graduated from primary school, the scale scores of the mothers whose children had a home accident were higher than those who did not, and the scale scores of the mothers who received information about first aid were significantly higher than those who did not. In the study of Erdem et al., Rezapur-Shahkolai et al. (2017) found a statistically significant relationship between mothers' knowledge of safety precautions and the severity of children's injuries in their cross-sectional study (32). Alrimawi et al. (2019) state that many environmental factors such as low economic status, the physical environment of the home, social environment (for example, fatalism) and political environment affect mothers' home accident prevention practices (33). In other studies, when the total score values of the mother's education levels are examined, it is stated that the probability of an accident decreases as the mother's education level increases (13,17,25,34). In some studies, it has been determined that the frequency of children having home accidents does not change according to the education level of the mothers (21,35).

There was no significant difference in scale scores according to mother's age, employment status, income status, number of children, family and housing type. In our study, while the frequency of accidents was higher in mothers over the age of 30, no significant difference was found in terms of scale scores according to age. In other studies, the mean score of the scale was found to be higher in mothers under the age of 30 (19,28). On the other hand, in some studies, the scale scores of middle-aged mothers were found to be higher than others (5,29,30). In our study, the scale score also decreases as the number of children increases. This shows that the awareness of the mothers as a result of the experiences they have with their children is more important than the age and number of children. In other studies, no statistically significant difference was found between family type, income status, type of house, number of children living in the house, number of individuals living in the house, number of rooms in the house, child age groups, and mothers' total mean scores (17,25).

CONCLUSION

In our study, the frequency of children having home accidents is 11.3% and the most common is falling. Mothers' knowledge of Diagnosing Safety Precautions for Home Accidents is moderate. The most important factors affecting the accident at home are the number of children and the caregiver. Considering these factors, home accidents should be included in the agenda of health issues as a critical public health problem. Home accidents are preventable situations. Considering that children spend a large portion of their time in the living room, it is also necessary to identify the risk factors involved in this area and to take measures against them to reduce home accident based injuries. Mothers and all other caregivers

are open to any information that may be given. This is an opportunity to raise awareness about home accidents, which are preventable health concerns. Informing mothers about all home accidents, especially falls, through health, educational institutions and communication channels should be among the priority health targets.

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MEDICAL RECORDS-International Medical Journal

Research Article

Comparison of the Reliability of the "GÖK Atlas" and the "Gilsanz-Ratib Atlas" in the Determination of Bone Age in Turkish Children

Türk Çocuklarında Kemik Yaşı Tespitinde "GÖK Atlas" ile "Gilsanz-Ratib Atlas"ın Güvenilirliğinin Karşılaştırılması

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Abstract

Aim: In this study we aimed to evaluate which of the GÖK and GR atlases is more compatible with chronological age in Turkish children aged 5-10 years.

Material and Method: In this study, the wrist radiographs of patients aged 5-10 years who applied to İzmir Bakırçay University Çiğli Training and Research Hospital due to trauma were retrospectively analyzed. A total of 360 wrist radiographs were evaluated. Bone age estimates in both groups were compared with chronological ages.

Results: In the correlation analysis, the prediction rate with 1-difference tolerance is 88.9% in the GR atlas and 76.7% in the GÖK atlas, while both atlases predict 99% correctly with two-difference tolerance. GR Atlas 168 (46.2%) and GÖK Atlas 147 (40.8%) predicted correctly regardless of gender and age. Of the correct estimations, 53.5% in the GR atlas and 57.8% in the GÖK atlas were male cases. İn male age group at the age of 6 and 10, the GR atlas is more successful, at the age of 7, the GÖK Atlas is more successful, and at the age of 5, 8, and 9 the success of both atlases is the same. İn female age group at the age of 5,7, 8, and 10 the GR atlas is more successful, at the age of 6 and 9 the GÖK Atlas is more successful

Conclusion: The GR Atlas was more accurate than the GÖK Atlas. Both the GR Atlas and the GÖK Atlas predicted more accurately in males. Since reference values for bone age can change with environmental and genetic factors all over the world, it is beneficial for all races to create atlas models with multicenter studies in order to establish their own standards.

Keywords: GR atlas, GÖK atlas, Bone age

Öz

Amaç: Bu çalışmada amacımız, 5-10 yaş arası Türk çocuklarında GÖK ve GR atlaslarından hangisinin kronolojik yaş daha uyumlu olduğunu araştırmaktı.

Materyal ve Metot: Çalışmada Bakırçay Üniversitesi Çiğli Eğitim ve Araştırma Hastanesi'ne travma nedeniyle başvuran 5-10 yaş arası hastaların sol el bilek grafileri retrospektif olarak incelendi. Toplamda 180 kız ve 180 erkek çocuğun el bilek grafileri uzman bir radyolog tarafından değerlendirilerek GR ve GÖK atlasları üzerinden kemik yaşı tayini yapıldı.Her iki gruptaki kemik yaşı tahminleri ile kronolojik yaşlar karşılaştırıldı.

Bulgular: Korelasyon analizinde 1 fark tolerans ile tahminleme oranı GR atlasında %88.9 GÖK atlasında %76.7 oranına ulaşmakta iken her iki atlas 2 fark tolerans ile %99 oranında doğru tahminlemede bulunmaktadır. Uyum analizinde cinsiyet ve yaştan bağımsız olarak GR Atlası 168 (%46.2) ve GÖK Atlası 147 (%40,8) doğru tahminde bulunmuştur. Doğru tahminlemelerin GR atlasında %53,5'i GÖK atlasında %57,8'i erkek olgulardır. Erkek olgularda 6 ve 10 yaşında GR atlası daha başarılı, 7 yaşında GÖK atlası daha başarılı, 5, 8 ve 9 yaşında ise her iki atlasın başarısı aynı idi. Kadın olgularda 5, 7, 8 ve 10 yaşında GR atlası daha başarılı, 6 ve 9 yaşında GÖK atlası daha başarılıydı.

Sonuç: GR Atlası, GÖK atlasından daha yüksek oranda doğru tahminlemede bulunmuştur. Hem GR Atlası hem de GÖK Atlası erkeklerde daha doğru tahminlemede bulunmuştur.Kemik yaşı referans değerleri tüm dünyada çevresel ve genetik faktörlerle değişebildiğinden, tüm ırkların kendi standartlarını oluşturabilmeleri için çok merkezli çalışmalarla atlas modelleri oluşturmalarında fayda vardır.

Anahtar Kelimeler: GR atlası, GÖK atlası, Kemik yaşı

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INTRODUCTION

Identification of human parts found in disasters and unknown skeletal remains such as in mass graves is a very important part of forensic studies and is one of the first steps of forensic analysis in these cases. The basic features of identity are generally the age, sex, height, and ethnic origin of the individual (1-4). Bone age determination is a frequently used data for identification, especially in forensic cases, and to support the diagnosis in endocrine disorders. In studies on age estimation, it has been reported that determining bone age can be useful in solving personal, social, and legal problems. If appropriate criteria and methods are not used in age determination, a wrong judgment may be made and a significant loss of rights may could occur as a result (5,6).

Bone age has been shown to be as important as chronological age in the evaluation of an adolescent's physical development (7). Evaluation of skeletal maturity is an important method in the diagnosis, treatment, and follow-up of response to treatment in endocrine disorders (8,9).

It is seen that radiological, morphological, and histological methods are used in age determination in the past, and in recent years, radiological methods are used most frequently. Radiography is one of the most widely used radiological methods in children to evaluate bone age, which is the main indicator of skeletal development (10-17).

Bone age is an indicator of an individual's skeletal and biological maturity. This is different from the chronological age calculated using an individual's date of birth. Bone age estimation is made by radiologists, forensic medicine specialists and pediatricians based on radiological imaging (11,18).

In our country, bone age determination in the pediatric age group is evaluated by forensic medicine physicians with the GÖK Atlas standards, which are often adapted from the Greulich-Pyle Atlas on wrist radiography. In radiology clinics, Giltsanz Ratib (GR), and unmodified Greulich-Pyle (GP) atlases are both available for bone age determination, and preferences vary by institution (5,6,8).

In this study, we aimed to investigate whether the atlases published by GÖK and GR, which are widely used in Turkey, are reliable for use in children aged 5-10 years, and which results are more correlated with their chronological age.

MATERIAL AND METHOD

Population data and grouping

In this study, the wrist radiographs of patients aged 5-10 years who applied to İzmir Bakırçay University Çiğli Training and Research Hospital Emergency Department due to trauma were retrospectively analyzed. Measurements were made on the wrist radiographs of 180 female and 180 male patients aged 5-10 years. Thirty subjects were used for each age of male and female.

Ethics committee approval was obtained for the study numbered 201 dated 4.3.2021 and the decision numbered 219.

Children with endocrinological and metabolic diseases, and with growth and development disorders were excluded from the study, as they may affect the measurement standards and analysis results. The children who were not between 3rd and 97th percentiles according to height and weight standards, determined by Neyzi et al were excluded (19). Cases who were not citizens of the Republic of Turkey were excluded from the study.

Sample landmarks and hand – wrist measurements

The left hand and wrist and for standardization elbow were placed on the extraction table and the third metacarpal bone was centered at a distance of approximately 70-80 cm and exposed in the posteroanterior (P-A) position.

While determining the bone age, the determination was made by deciding the bone age closest to the image over reference points such as the maturation of the bones and the epiphyseal plate on the wrist x-ray (Figure 1).

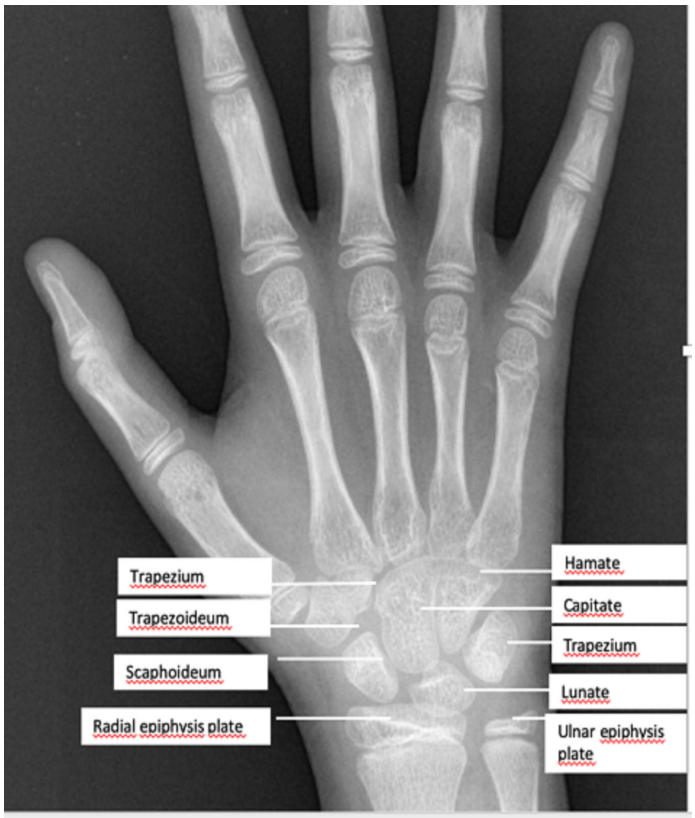

Figure 1. The maturation of the carpal bones, epiphyseal lines and the status of the styloid process used in the determination of bone age in the wrist radiography

Evaluation procedures

First, the chronological ages of the subjects were compared for each gender according to the GR and GÖK Atlas, and in the second step, the differences between chronological and skeletal ages were determined for each age group.

Wrist roentgenograms were compared with the GR Atlas and GÖK Atlas, and the age of the closest picture was taken as the bone age of the film. If the bone age of the film was between two picture ages, but not suitable for both pictures, the age in the completed picture was accepted as the bone age.

All evaluations on X-ray images were performed by the radiologist (ZAO, with at least 5 years of experience evaluating musculoskeletal X-Ray images). For intra-observer reliability, measurements were re-examined under blinded conditions by the same radiologist on the randomly chosen 10% (n= 36) of the images after four weeks.

Statistical analyses

Data collection and statistical analysis were performed with R and SSPS for Windows (version 22; SPSS, Chicago, IL, USA). Agreement correlation (0 tolerance, 1 tolerance and 2 tolerance) were performed to reveal which atlas predicted bone age more accurately for both sexes and for each age range. A randomized review of 36 subjects was performed using KAPPA analysis for within-observer variations.

RESULTS

A total of 360 wrist radiographs of 30 male and female children from every age group between 5-10 years of age were evaluated (Table 1). The intra-observer agreement rate was 94% for both atlases. KAPPA analysis showed that there was a high consistency in age assessment by the same observer in different times.

In the correlation analysis, the GR atlas made 168 (46.2%) correct estimations in general, regardless of sex and age, and made lower estimations in 103 (28.6%) cases and higher estimations in 89 (24.7%) cases according to chronological age (Table 2). The GÖK Atlas made 147 (40.8%) correct estimations in general, regardless of sex and age, and made lower estimations in 69 (19.1%) cases and higher estimates in 144 (40%) cases according to chronological age (Table 2).

Table 1. Distrubition of subjects in each age group

Age (years)	Female	Male	Total samples
5	30	30	60
6	30	30	60
7	30	30	60
8	30	30	60
9	30	30	60
10	30	30	60
Total	**180**	**180**	**360**

When we examined the group in which the GR atlas was correlated with chronological age, 53.5% of the correct predictions were males and 46.5% were females. When we examined the group in which the GÖK atlas was correlated with chronological age, 57.8% of the correct predictions were males and 42.1% were females. Both GR atlas and GÖK atlases made more accurate predictions in males (Table 2).

Estimation rates of correlation with chronological age by age groups GR atlas at 5 years old (38.3%) - GÖK atlas (33.3%), at 6 years old GR atlas (31.6%) - GÖK atlas (35%), at 7 years old GR atlas (48.3%) - GÖK atlas (35%), at 8 years old GR atlas (63.3%) - GÖK atlas (48.3%), at 9 years old (55%) - GÖK atlas (63.3%), at 10 years old GR atlas (43.3%) - GÖK atlas (30%) ; GR atlas is more successful at the age of 5, 7, 8, and 10 years, while GÖK atlas is more successful at 6 and 9 years of age (Table 2).

In male age groups, at 6 years old GR atlas (43.3%) - GÖK atlas (36.6%), at 7 years old GR atlas (40%) - GÖK atlas (53.3%), at 10 years old GR atlas (43.3%) - GÖK atlas (20%) and at 5, 8, and 9 years old, with 56.6%, estimated with same ratio in both atlases correctly. At the age of 6 and 10, the GR atlas is more successful, at the age of 7, the GÖK atlas is more successful, and at the age of 5, 8, and 9 the success of both atlases is the same (Table 2).

Table 2. Agreement correlation analysis (0 tolerans) of GR and GÖK atlases for all ages and genders

	5		6		7		8		9		10	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
CA=GR	17(56.6%)	6(20%)	13(43.3%)	6(20%)	12(40%)	17(56.6%)	23(76.6%)	15(50%)	12(40%)	21(70%)	13(43.3%)	13(43.3%)
CA>GR	10(33.3%)	5(16.6%)	14(46.6%)	10(33.3%)	15(50%)	7(23.3%)	6(20%)	7(23.3%)	12840%)	0	7(23.3%)	10(33.3%)
CA<GR	3(10%)	19(63.3%)	3(10%)	14(46.6%)	3(10%)	6(20%)	1(3.3%)	8(26.6%)	6(20%)	9(30%)	10(33.3%)	7(23.3%)
CA=GÖK	17(56.6%)	3(10%)	11(36.6%)	10(33.3%)	16(53.3%)	5(16.6%)	23(76.6%)	6(20%)	12(40%)	26(86.6%)	6(20%)	12(40%)
CA>GÖK	10(33.3%)	2(6.6%)	14(46.6%)	1(3.3%)	10(33.3%)	3(10%)	6(20%)	0	12(40%)	0	1(3.3%)	10(33.3%)
CA<GÖK	3(10%)	25(83.3%)	5(16.6%)	19(63.3%)	4(13.3%)	22(73.3%)	1(3.3%)	24(80%)	6(20%)	4(13.3%)	23(76.6%)	8(26.6%)
Total	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**	**30**

CA: Chronological Age, GÖK: Gök Atlas, GR: Gilsanz- Ratib Atlas

In female age groups, at 5 years old GR atlas (20%) - GÖK atlas (10%), at 6 years old GR atlas (20%) - GÖK atlas (33.3%), at 7 years old GR atlas (56.6%) - GÖK atlas (16.6%), at 8 years old GR atlas (50%) - GÖK atlas (20%), at 9 years old GR atlas (70%) - GÖK atlas (86.6%), and at 10 years old GR atlas (43.3%) - GÖK atlas (40%) estimated correctly. At the age of 5, 7, 8, and 10 the GR atlas is more successful, at the age of 6 and 9 the GÖK atlas is more successful (Table 2).

In the correlation analysis, with 0 tolerance, the GR atlas estimated the bone age 46.2%, 88.9% with 1 difference tolerance and 99.5% with 2 difference tolerance. In the correlation analysis, with 0 tolerance, the GÖK atlas estimated the bone age 40.8%, 76.7% with 1 difference tolerance, and 99.8% with 2 difference tolerance (Table 3).

Table 3. Agreement correlation analysis (0 tolerans) of GR and GÖK atlases for all ages and genders

	0 tolerance	1 tolerance	2 tolerance
CA -GR	46.2 %	88.9 %	99.5 %
CA-GÖK	40.8 %	76.7 %	96.8 %

CA: Chronological Age, GÖK: Gök Atlas, GR: Gilsanz- Ratib Atlas

DISCUSSION

The GR Atlas made 46.2% correct estimations in general, regardless of sex and age, and made lower estimations in 28.6% cases and higher estimations in 24.7% cases according to chronological age. The GÖK Atlas made 40.8% correct estimations in general, regardless of sex and age, and made lower estimations in 19.1% cases and higher estimates in 40% cases according to chronological age. In general, although the GR atlas gave modestly better results than the GÖK atlas, there was roughly similar agreement between both atlases in some age groups.

The GR atlas estimated the bone age 88.9% with 1 difference tolerance and 99.5% with 2 difference tolerance while the GÖK atlas estimated the bone age 76.7% with 1 difference tolerance, and 99.8% with 2 difference tolerance. In the correlation analysis, the percentages of correct estimation of bone age increase approximately two times with "1 tolerance", and again, the GR atlas is more successful, as is the case with zero tolerance. In 2 tolerances, both atlases make similar and fairly accurate estimations.

We see that in the GÖK atlas, no sex discrimination was made between the ages of 5-10, and the same ossification criteria were accepted for male and female children. However, there are separate criteria according to sex in GR Atlas. It has been observed that GR atlas makes more descriptive definitions in this age range.

In our study for males, GR and GÖK atlases are equally accurate in the 5, 8, and 9 age groups, while GR is more successful in the 6 and 10 age groups, GÖK is more successful at the age of 7. The predictions for females are more accurate in the 5, 7, 8, and 10 age groups in the GR atlas, while GÖK was more accurate at 6 and 9 years old. Both the GR atlas and the GÖK atlas made more accurate predictions in males. Opposite of this in the study of Baransel Isır et al., it was reported that chronological age and bone age did not correlate in males and there was a significant discrepancy (20). While the GR atlas is more compatible with the chronological age in the 5, 7, 8, and 10 age groups, the GÖK Atlas is compatible in the 6 and 9 age groups. In the age estimation study by Büken et al. using the GÖK Atlas, it is reported that the difference between chronological age and bone age in both male and female is more than one year and it is reported that the reliability index of the GÖK Atlas, which is generally used in Turkey, is not sufficient (11).

The fact that both atlases are based on populations of European origin and do not include the Turkish population may explain the trend of similar results. It has been reported that there are many studies indicating that these atlases are not suitable for use in Turkish children (6). Although there are some anthropometric studies on individuals living in our country, there is no widely accepted atlas of age estimation conducted on Turkish people.

Forensic age determination is one of the important topics of forensic science. For unidentified and suspicious deaths and child deaths, and for those living in a situation who cannot express themselves, age determination may be requested by the judicial authorities (10). GÖK Atlas, which Şemsi Gök et al. prepared in 1985, adapted from the GP Atlas, is widely used in Forensic Medicine practices for age estimation. The Greulich-Pyle (GP) Atlas has been prepared in white children from a high socioeconomic level, who were born between 1917 and 1947 in the USA (20-22). Racial, socioeconomic, and environmental differences between Turkish children and the group of children which the GP Atlas was derived may result in differences in sexual development and skeletal maturation.

In order to avoid legal consequences, we tried to reveal which of the existing atlases is more suitable for the Turkish population. The digital era, it is easier to produce a new atlas than before. Because bone development varies with ethnicity, geography and time, radiologists around the world could make their own atlases in the same way.

One of our limitations in the study was that the entire patient population consisted of patients in the province of İzmir, and although İzmir is one of the largest provinces,

it was not an optimal sample group to reflect the Turkish population due to its western location. Therefore, a multicenter evaluation is needed.

While it was possible to make a more detailed comparison of 3-4 images in the anterior-posterior and lateral projections for both genders in the GR atlas, another limitation of the GÖK atlas was the age determination based on only one image and a written text, regardless of gender.

CONCLUSION

The aim of our study is to evaluate how compatible the standards of GR and GÖK Atlases are with chronological age in Turkish children. In general, both the GR Atlas and the GÖK Atlas made more accurate predictions in men. While GR Atlas was more accurate than GÖK Atlas in the estimations made with 0 and 1 tolerance, the estimations made with 2 tolerances were almost completely correct and similar in both atlas. It may be practical to use GR or GÖK Atlases according to the age and gender of the children.

Since reference values for bone age can change with environmental and genetic factors all over the world, it is beneficial for all races to create atlas models with multicenter studies in order to establish their own standards.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *Izmir Bakircay University ethics committee for non-interventional clinical trials it has been approved by decision. Decision no: 219, Date: 04.03.2021*

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MEDICAL RECORDS-International Medical Journal

Research Article

Evaluation of Satisfaction Level in Family-Centered Intensive Care Concept; A Single-Center Survey Study

Aile Merkezli Yoğun Bakım Konseptinde Memnuniyet Düzeyinin Değerlendirilmesi; Tek Merkezli Bir Anket Çalışması

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Abstract

Aim: In our study,it was aimed to determine and improve the quality of the intensive care unit(ICU) of our hospital by evaluating the satisfaction perception of patient relatives through a questionnaire.

Materials and Methods: The revised version of the questionnaire named FS-ICU-24 was applied to the patients relatives whose patients had been treated for at least 48 hours in Eskişehir Osmangazi University Anesthesia ICU.

Results: According to evaluation results of 79 questionnaires that fit the criteria of the study, it was seen that the satisfaction with the decision-making process of the patients with high satisfaction with care was also significantly higher ($p<0.01$). The lowest satisfaction was related to being involved in the decision-making process and being able to see their patients whenever they wanted. The highest satisfaction rate was in meeting the requests of relatives of patients by ICU staff.

Conclusion: The only thing that the relatives of patients who experience anxiety due to the fear of losing a family member want to see their patient impulsively.In our study,similar to the literature, the subject with the lowest satisfaction rate wasn't being able to see their patients when they wanted.We showed the importance of being able to respond to the expectations of patient relatives in accordance with the family-centered intensive care concept. We found that it is important for the relatives of the patients to feel that they participate in the decision-making process and that this seriously affects the satisfaction rates. We think that research should be done on how family members can be more involved in the decision-making process when planning quality improvement interventions for ICU.

Keywords: Intensive care unit, family satisfaction, questionnaire

Öz

Amaç: Çalışmamızda anket aracılığı ile hasta yakınlarının memnuniyet algısı değerlendirilerek hastanemiz yoğun bakım ünitesi(YBÜ) kalitesinin belirlenmesi ve geliştirilmesi amaçlanmıştır.

Materyal ve Metot: Eskişehir Osmangazi Üniversitesi Anestezi YBÜ'de hastası en az 48 saattir tedavi gören hasta yakınlarına FS-ICU-24 isimli anketin revize edilmiş hali uygulanmıştır.

Bulgular: Çalışmanın kriterlerine uyan 79 anketin değerlendirme sonuçlarına göre bakımla ilgili memnuniyeti yüksek olan hastaların karar alma sürecine dair memnuniyetleri de anlamlı olarak yüksek olduğu görülmüştür ($p<0.01$). En düşük memnuniyet karar alma sürecine dahil olma ve hastalarını istedikleri zaman görebilme ile ilgiliydi. En yüksek memnuniyet oranı YBÜ çalışanlarının hasta yakınları isteklerini karşılamasındaydı.

Sonuç: Bir aile bireyini kaybetme korkusu nedeniyle kaygı yaşayan hasta yakınlarının tek isteği hastasını dürtüsel olarak görmektir. Bizim çalışmamızda da literatür ile benzer olarak memnuniyet oranının düşük olduğu konulardan biri, hastalarını istedikleri zaman görememek olmuştur. Çalışmamızda aile merkezli yoğun bakım anlayışına uygun olarak hasta yakınlarının beklentilerine cevap verilebilmesinin önemini gösterdik. Hasta yakınlarının karar verme sürecine katıldıklarını hissetmelerinin önemli olduğunu ve bunun memnuniyet oranlarını ciddi şekilde etkilediğini bulduk. Yoğun bakım ünitelerinde kalite iyileştirme müdahaleleri planlanırken aile bireylerinin karar verme sürecine nasıl daha fazla dahil olabileceği konusunda araştırma yapılması gerektiğini düşünüyoruz.

Anahtar Kelimeler: Yoğun bakım ünitesi, hasta yakını memnuniyeti, anket

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INTRODUCTION

Evaluation of the quality of the health service has gained importance in this period when the health sector has become privatized and private health insurances have become widespread, as in every field in the world. Evaluating the quality and safety of health care and improving the service provided has been an important goal all over the world (1). The increase in the elderly population around the world and the increase in the socio-education level of the society have paralleled the increase in the number of patients in need of intensive care, and this has brought high costs (2,3).

In the beginning mortality, length of stay and functional status of patients were considered as quality determinants in intensive care units, and later on, the satisfaction of patients and their relatives in intensive care units began to be evaluated (4,5). As a result of the studies, it has been seen that the measurement of satisfaction plays a key role in the evaluation of quality (5-7).

Intensive care patients are high-risk patients and if their conscious abilities are considered, the information given and the decisions taken are generally made together with the relatives of the patients. For this reason, the patient and the patient's relatives should always be considered as a whole in the intensive care unit. Meeting the needs of patients' relatives is a necessity of the family-centered intensive care concept, and it is our duty to inform them, to see their patients, to relieve their stress and anxiety (8-10).

The aim of our study is to measure the satisfaction level of the relatives of the patients treated in the anesthesia intensive care unit, to evaluate the intensive care perception of the relatives of the patients in the light of the results obtained, and to find answers to the changes that will increase the satisfaction of the relatives of the patients in the intensive care unit. It is aimed to determine the issues that the relatives of the patients care about the most, to develop the concept of family-centered intensive care and to increase the level of satisfaction.

MATERIAL AND METHOD

Study design and settings

The study was carried out with the permission of Eskişehir Osmangazi University Faculty of Medicine Non-Interventional Clinical Researchs Ethics Committee (Date: 18.09.2018 Decision No: 14). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Relatives of patients whose patients were hospitalized for at least 48 hours between September 2018 and September 2019 were included in the study after the approval of the ethics committee in our hospital Anesthesia ICU.

There are many questionnaires that evaluate the satisfaction of patient relatives, and the questionnaire that we will use was selected by literature research. The power of the "Family Satisfaction in Intensive Care Unit (FS-ICU 34/24) questionnaire" developed by Heyland et al. has been demonstrated in many multicenter studies (3,9,11). While creating the questionnaire for our study, this questionnaire named FS-ICU 34/24 was used and the Turkish version of the questionnaire was revised for the purposes of our study.

Data collection

The prepared questionnaires were administered to one or more relatives of each patient, after obtaining the consent of the relatives, on the third or later days of the patients' hospitalization in the intensive care unit.

The questions were reviewed together and any points they did not understand were clarified. After completing the questionnaire, it was requested to be delivered to us on the same day or in the following days. From the relatives of the patients hospitalized; Those who did not want to fill out the questionnaire, whose native language was not Turkish, whose patient was in the intensive care unit for ≤48 hours, who did not submit the questionnaire and who answered less than half of the questions, were excluded from the study.

Between September 2018 and September 2019, the number of patients hospitalized in our anesthesia intensive care unit was 412, and the number of patient relatives who did not want to participate in the survey was 182. The relatives of patients whose native language was not Turkish (n:13), the patient was in the intensive care unit for ≤48 hours (n:163), and 27 questionnaires in which less than half of the questions were answered were excluded from the study. The number of patient relatives who took the questionnaire but did not submit was 32. As a result, 79 patient relatives questionnaires were analyzed. The flowchart is shown in Figure 1.

The questionnaire was analyzed in two main parts: satisfaction with care (1st part-14 questions) and family satisfaction with decision-making process (2nd part-10 questions). In our study, it was requested to evaluate the questionnaire questions in the scale section according to a 5-point evaluation scale. (1;poor, 2;partially good, 3;good, 4;very good, 5;excellent.) The satisfaction averages of the answers given to the questions were grouped as the 1st part, the 2nd part and the general satisfaction average in the intensive care unit.

Data analyses

Descriptive values of the scales were given as mean±standard deviation and median (Q1 – Q3), and frequency distributions were given as frequency tables. In the descriptive presentation of the answers of the scale, each subsection (satisfaction with care, family satisfaction with decision-making process) was evaluated between 1 and 5, and the degrees of satisfaction were analyzed by

converting the Likert scale to scores between 0 and 100.

In the evaluation of the differences between the groups, t-test for 2-group variables with normal distribution, one-way analysis of variance test for 3 and more groups; Mann Whitney U test was used for the 2-group variables that did not conform to the normal distribution, and the Kruskal Wallis H test was used for the 3 or more groups. Shaphiro Wilk's test was used as normality test. Analyzes were made in IBM SPSS Statistics 21.0 package program. The criterion value of $p<0.05$ was accepted as the statistical significance level.

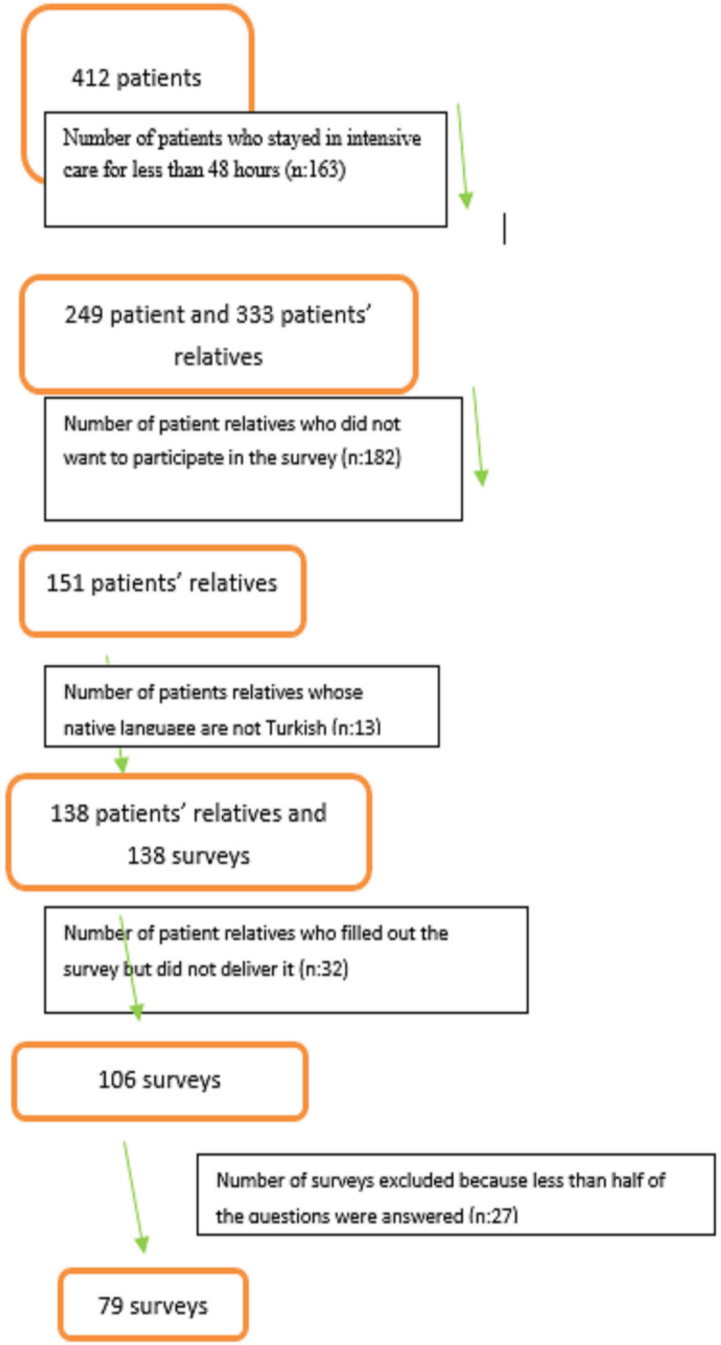

Figure 1. The flowchart of inclusion and exclusion criteria

RESULTS

A total of 79 questionnaires were included in the study. Since patients relatives did not answer all the questions completely, there are questions where the total number of answers to the questions is below 79. 57.3% of the patients' relatives who filled out the questionnaire were male. (p=0.248). 53.8% of the patients' relatives had previously been treated in another intensive care unit.(p=0.572). Demographic data and characteristics of patient relatives are shown in Table 1 (Table 1).

Considering the satisfaction rates, the mean satisfaction with patient care was 74.1±16.3 (very good), the mean satisfaction with the decision-making process was 64.3±12.7 (very good), and the mean overall satisfaction was 69.2 (very good) in the intensive care unit. (p=0.387) (Table 2)

The highest satisfaction rate was in meeting the requests of the relatives of the patients by the intensive care workers. (81.4±18.8). The lowest satisfaction rate was related to 'involvement' in the decision-making process (41.7±22.4). Relatives of patients with high satisfaction with care were also significantly more satisfied with the decision-making process regarding their patients' care (p<0.001). Satisfaction scores according to the questions of the departments are given in Tables 3 and 4.

When the questionnaires included in the study are evaluated; It was seen that the satisfaction level of the relatives of the patients was not significantly related to the education level of the patient's relative, the age of the patient, or whether he had a patient followed in the intensive care unit before.

Table 1. Distribution of demographic characteristics of patient relatives

		N	%	p
Gender	Female	32	42.7	0.248
	Male	43	57.3	
The degree of proximity	Parents	8	10.3	<0.001
	Wife/husband	8	10.3	
	Brother/sister	5	6.4	
	Child	43	55.1	
	Others	14	17.9	
Presence of relatives previously hospitalized in intensive care	Yes	36	46.2	0.572
	No	42	53.8	
Cohabitation with the patient	Yes	41	51.9	0.822
	No	38	48.1	
Frequency of meeting with the patient by the relative who does not live with the patient	More than once a week	20	52.6	<0.001
	Once a week	6	15.8	
	Once a month	8	21.1	
	Once a year	4	10.5	
Living place	In the city where the hospital is located	50	63.3	0.024
	Out of city	29	36.7	
Level of education	No read and write	1	1.3	0.500
	Primary education	21	26.6	
	High school	21	26.6	
	University	36	45.6	
Number of patient visits	None	1	1.3	0.002
	1-3	24	32.0	
	4-6	14	18.7	
	7-10	9	12.0	
	>10	27	36.0	
Time of patient visit	1-3 min	2	2.7	<0.001
	4-6 min	26	35.1	
	7-10 min	15	20.3	
	10-15	18	24.3	
	>15 min	13	17.6	

Table 2. Distribution of scores calculated from sections

	Mean±SD	p
Satisfaction with patient care	74.1±16.3	
Family satisfaction with the decision-making process	64.3±12.7	0.387
Overall satisfaction rate	69.2	
Mann-Whitney U		

Table 3. Satisfaction with patient care

Questions	Mean±SD
Evaluation of behavior towards the patient	79.7±17.4
Symptom management- pain	78.8±18.8
Symptom management-dyspnea	76.7±20.4
Symptom management-agitation	78.7±21.1
Evaluation of behavior towards the patient relatives	81.4±18.8
Emotional support to the patient	70.7±24.0
Coordination of care	76.2±17.7
Interest of intensive care unit staff to patient relatives	80.0±20.4
Skills and competence of intensive care unit nurses	77.2±18.0
Frequency of informing intensive care nurses	68.4±24.6
Skills and competence of intensive care unit doctors	80.0±20.0
Physical conditions of the intensive care unit	68.1±23.9
Physical conditions of patient relatives waiting area	57.2±24.5
Level and adequacy of health care	74.9±19.0

Table 4. Family satisfaction in the decision-making process regarding the care of critically ill patients

Questions	Mean±SD
Frequency of communication with intensive care unit doctors	65.6±25.2
Ease of obtaining information	68.7±24.3
Understanding of knowledge	74.7±21.0
Accuracy of information	74.9±19.5
Completeness of information	72.9±21.5
Consistency of information	72.5±21.3
Sense of involvement in the decision-making process	41.7±22.4
Sense of support in the decision-making process	46.4±17.6
Feeling of control over patient care	52.7±20.7
Time adequacy in the decision-making process	85.8±9.15

DISCUSSION

In our study, we showed the importance of being able to respond to the expectations of patient relatives in accordance with the family-centered intensive care concept in parallel with the literature. We found that it is important for the relatives of the patients to feel that they participate in the decision-making process and that this seriously affects the satisfaction rates.

In our study, the number of questionnaires filled in according to the number of patients was found to be quite low. In our study, we attributed this situation to the fact that the patients' relatives did not want to fill in because their patients were still receiving treatment, as in other studies (12,13).

It is known that the satisfaction of the relatives in the intensive care unit can be affected by many parameters such as the expectation level of the relatives, information sharing and communication, intensive care infrastructure and physical conditions (4,14). In many survey studies measuring the level of satisfaction in intensive care, the results show similar characteristics. While there are studies like our study that found the evaluation of the care and treatment of patients to be more satisfied, there are also studies where satisfaction is higher in the decision-making process (15).

The satisfaction rate obtained from the care and treatment department of the patients was found to be successful by us. (Satisfaction with patient care: 74.1±16.3). From the answers given, it can be concluded that the relatives of the patients think that their patients are cared for, that their treatment is complete, that the knowledge and skills of the doctors and other personnel are good. Erdal et al. also attributed the high results to the same reasons (4).

In our study, it was seen that the mean satisfaction score of the decision-making process regarding the patient was 64.3±12.7. In their study, Heyland et al. observed that the satisfaction rate of the relatives of the patients was high in questions about the decision-making process (11). They attributed this to the fact that the relationship between the doctor and the patient's relatives is strong, that the concerns of the relatives of the patients are resolved and their questions are answered in sufficient time, and that sufficient time is provided for the relatives of the patients to reach a decision. In our study, the feeling of being involved in the decision-making process, the feeling of support in the decision-making process, and the feeling of control over patient care were the sections with the lowest scores in our questionnaire, and their satisfaction scores were 41.7±22.4, 46.4±17.6, 52.7±20.7, respectively. This showed us that we should be more careful about including the relatives of the patients in the process.

In the studies, the subject with the lowest satisfaction rate was that they could not see their patients when they wanted. The only thing that the relatives of patients who experience anxiety due to the fear of losing a family member want to see their patient impulsively (16,17). Jensen et al. investigated the factors affecting family satisfaction in intensive care, and examined two countries, Denmark and the Netherlands. The satisfaction rate was found to be significantly lower in the Netherlands than Denmark, where the intensive care treatment protocol is almost exactly the same, and they attributed this to the strict visitation policies of the Netherlands (18). Family and kinship relations especially in Turkish culture are pretty close and important. In Turkish society, individuals try to keep their morale high by seeing the patient frequently, and they believe in the healing effect of keeping the patient's morale high (19). In our study, this situation was similar to the literature, and the fact that they could not see their patients when they wanted was one of the issues with the lowest satisfaction rate.

Considering the studies conducted, it has been determined that the relatives of patients all over the world are weak or moderately satisfied with the waiting rooms of the intensive care units. (5,20). The satisfaction rate of the physical conditions of the waiting area is 57.2±24.5 and it has a low rate. It is thought that the low satisfaction with the waiting room is due to the fact that our waiting room is close to our intensive care unit and does not have sufficient physical conditions. In addition, this result was interpreted as the necessity of improving the waiting room conditions.

Limitations of the study

The most important limitation of our study is the low number of patient relatives surveys. A comprehensive survey with a larger number of patients is planned in our new intensive care building, whose construction has been completed.

CONCLUSION

In our study, we found that it is important for patients' relatives to feel that they participate in the decision-making process, and how seriously this affects their satisfaction rates. We think that research should be done on how family members can be more involved in the decision-making process when planning quality improvement interventions for intensive care units.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *The study was carried out with the permission of Eskişehir Osmangazi University Faculty of Medicine Non-Interventional Clinical Researchs Ethics Committee (Date: 18.09.2018 Decision No: 14).*

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Research Article

Assessment of Association Rule Mining Using Interest Measures on the Gene Data

Gen Verileri Üzerinde İlginçlik Ölçütleri Kullanılarak Birliktelik Kuralları Madenciliğinin Uygulanması

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Abstract

Aim: Data mining is the discovery process of beneficial information, not revealed from large-scale data beforehand. One of the fields in which data mining is widely used is health. With data mining, the diagnosis and treatment of the disease and the risk factors affecting the disease can be determined quickly. Association rules are one of the data mining techniques. The aim of this study is to determine patient profiles by obtaining strong association rules with the apriori algorithm, which is one of the association rule algorithms.

Material and Method: The data set used in the study consists of 205 acute myocardial infarction (AMI) patients. The patients have also carried the genotype of the FNDC5 (rs3480, rs726344, rs16835198) polymorphisms. Support and confidence measures are used to evaluate the rules obtained in the Apriori algorithm. The rules obtained by these measures are correct but not strong. Therefore, interest measures are used, besides two basic measures, with the aim of obtaining stronger rules. In this study For reaching stronger rules, interest measures lift, conviction, certainty factor, cosine, phi and mutual information are applied.

Results: In this study, 108 rules were obtained. The proposed interest measures were implemented to reach stronger rules and as a result 29 of the rules were qualified as strong.

Conclusion: As a result, stronger rules have been obtained with the use of interest measures in the clinical decision making process. Thanks to the strong rules obtained, it will facilitate the patient profile determination and clinical decision-making process of AMI patients.

Keywords: Data mining, association rules, apriori algorithm, interest measures, gene expression data

Öz

Amaç: Veri madenciliği, önceden büyük ölçekli verilerden ortaya çıkarılmayan faydalı bilgilerin keşfedilme sürecidir. Veri madenciliğinin yaygın olarak kullanıldığı alanlardan biri de sağlıktır. Veri madenciliği ile hastalığın tanı ve tedavisi ile hastalığı etkileyen risk faktörleri hızlı bir şekilde belirlenebilmektedir. Birliktelik kuralları, veri madenciliği tekniklerinden biridir. Bu çalışmanın amacı, birliktelik kuralı algoritmalarından biri olan apriori algoritması ile güçlü birliktelik kuralları elde ederek hasta profillerini belirlemektir.

Materyal ve Metot: Çalışmada kullanılan veri seti 205 akut miyokard enfarktüsü (AMI) hastasından oluşmaktadır. Hastalar ayrıca FNDC5 polimorfizmlerinin rs3480, rs726344, rs16835198 genotipini de taşımaktadır. Apriori algoritması ile elde edilen kuralları değerlendirmek için destek ve güven ölçüleri kullanılır. Ancak bu ölçütler ile elde edilen kurallar doğrudur ancak güçlü değildir. Bu nedenle, daha güçlü kurallar elde etmek amacıyla iki temel ölçütün yanı sıra ilginçlik ölçütleri kullanılmaktadır. Bu çalışmada daha güçlü kurallara ulaşmak için ilginçlik ölçütlerinden kaldıraç, kanaat, kesinlik faktörü, cosine, korelasyon katsayısı (phi) ve karşılıklı bilgi ölçütleri uygulanmıştır.

Bulgular: Çalışmada 108 kural elde edilmiştir. Bu kurallara ilginçlik ölçütlerinin de uygulanması ile elde edilen kural sayısı 29 olmuştur ve bu kurallar güçlü kural olarak nitelendirilmiştir.

Sonuç: Sonuç olarak, klinik karar verme sürecinde ilginçlik ölçütlerinin kullanılmasıyla daha güçlü kurallar elde edilmiştir. Elde edilen güçlü kurallar sayesinde AMİ hastalarının hasta profili belirleme ve klinik karar verme sürecini kolaylaştıracaktır.

Anahtar Kelimeler: Veri madenciliği, birliktelik kuralları, apriori algoritması, ilginçlik ölçütleri, gen ifadesi verisi

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INTRODUCTION

Acute myocardial infarction (AMI) is the formation of necrosis in the heart tissue as a result of insufficient blood supply to the heart muscle due to the blockage of the coronary arteries feeding the heart. The heart muscle cannot be fed and damaged in terms of blood and oxygen due to the narrowing or blockage of the coronary arteries. The non-feeding heart muscle is damaged, and the area of the heart muscle cells loses its ability to contract. AMI is an important public health problem because it is a disease that can result in death, it is generally seen in all age groups and then serious complications occur (1).

Data mining, which is also called discovery of data in the systems including data bases, is a process of beneficial information from the large data sets. This new-found information can be used in areas, consisting of information management, inquiry work, and decision-making process control in this aspect (2). Researchers working in the fields of database systems, knowledge base systems, artificial intelligence, machine learning, data collection, statistics, spatial databases and data visualization show great interest in data mining. (3,4). The use of data mining is very important, especially in the field of health. (5,6). For instance, the data mining is used for evaluating the efficiency of medical treatment carried out. Also, the data mining techniques such as classification, association, clustering make a major contribution to detecting epidemics and to preventing various diseases from appearing (6).

Association rules mining is the most important technique of data mining to produce strong association rules in data base (6). The aim of this technique is to reveal relationships between sets of items in transactional databases or other data warehouses (7). By spreading area of usage, the association rules can be applied in field of medical. Thanks to these rules, connection of various variables can be identified in medical information and that situation helps to reach diagnosis (8). Algorithms such as apriori, eclat and FP-growth algorithms are used in association rules mining and apriori algorithm is the most commonly used among these algorithms (6,9). For generating stronger rules by interest measures such as lift, conviction, certainty factor, cosine, coefficient of correlation (phi) and mutual information, this study intends to constitute strong association rules by using the studied data of the patients suffering from acute myocardial infarction. In this study, apriori algorithm is applied in order to constitute association rules from a gene dataset.

MATERIAL AND METHOD

Dataset

The dataset includes 225 patients, suffering from AMI disease in coroner intensive care unit of Firat University Medical Faculty Cardiology Department, Elazig, Turkey. The patients have also carrying the genotype of the FNDC5 (rs3480, rs726344, rs16835198) polymorphisms. In order to generalize the results obtained, the suggested number of observations should be 5 per independent variable, but this number is expected to be above 10, especially between 15 and 20. When these numbers are reached, it is said that the results can be generalized, provided that the sample represents the population. Since the number of independent variables is 15, the minimum sample size was determined as 150 based on the assumption of a multiple of 10 (10). Patients who did not suit the inclusion criteria were excluded from the study, and the study was conducted on 205 patients. The patients included in the study were determined by simple random sampling method. The study received ethics approval from Firat University's Faculty of Medicine Local Ethics Committee (14.10.2014, Decision No: 17/07). AMI is the death of a part of myocardium after coroner arterials supplying to heart are blockaded by blood clot. Criteria for taking part in the experiment are set by assessing AMI diagnosis, clinic symptom and superficial Electrocardiogram (ECG), which was accepted as critic for intensive care unit admission and/or cardiac biomarkers (11). All the association rules analyses were carried out by "arules" package in R programming language (12). Rstudio Version 1.1.463 program language was used for attaining analysis of the data (13). Detailed explanations about the variables used in the current study are given in Table 1.

Table 1. The detailed explanation of the variables in the dataset

Abbreviation	Explanation
Age	Birth year (year)
Height	Height (cm)
Weight	Weight (kg)
BMI	Body Mass Index (kg/m^2)
Troponin	Troponin (ng/ml)
CK-MB	Creatine Kinase Myocardial Band (ng/ml)
Irisin	Irisin (ng/mL)
LDH	Laktat Dehidrogenaz (mg/dL)
Gender	Gender(1=male, 2=female)
Hypertension	Hypertension (1= presence, 2= absence)
Smoke	Current Smoker (1= presence, 2= absence)
Diabetic	Diabetic (1= presence, 2= absence)
Family history	Family History (1= presence, 2= absence)
Mtype	Myocardial Infarction Type (1=acute inferior, 2=acute anterior, 3= non-ST segment elevation MI)
Rs3480in FNDC5gene	Rs3480 (1=AA wild, 2=AG: heterozygote genotype, 3= GG: polymorphism genotype)
Rs726344in FNDC5 gene	Rs726344 (1=GG wild, 2=GA: heterozygote genotype, 3= AA: polymorphism genotype
Rs16835198in FNDC5 gene	Rs16835198 (1=GG wild, 2=GT: heterozygote genotype 3= TT: polymorphism genotype)

Association Rules Mining

Association rules is one of the data mining methods, which focuses on interesting association among large-scale information. The first studies carried out in the field of data mining aimed to detect similarities between different products in data bases consisting of customer operations and customer purchasing profile. Association rules area of usage is expanded by later studies. One of them is the field of medicine. The use of association rules in the field of medicine has discovered the association of features in the medical data, which has been very useful in the diagnosis of medical conditions (8).

The form of association rules is formulated as X⇒Y. In that formula, X is antecedent of rule and Y is known as consequence (14,15).

Apriori Algorithm

Apriori Algorithm is the most classic and significant algorithm that used for finding frequent data sets in a specific data base (14,16). The apriori algorithm enables multi-transaction on database. During these transactions, an iterative approach is used throughout the research space. In other words, k item set is used for defining (k+1) item set. First, frequent 1- item set is obtained. This set includes an item which provides support threshold and indicated with L1. In every next transition, it begins with the biggest item set of former seed set. This seed set is used to create potentially large item sets, called candidate item sets, and the real support value is taken into account during the process of transferring data to the candidate item set. At the end of the transaction, it is determined which candidate items value is bigger (in frequency) actually and it naturally becomes source for next transaction. By this way, L1 is applied for calculating L2, which is also had to be found for discovering L3 value. The transaction continues until not finding k-item set (14).

Basic Measures

Even if numerous interest measures are developed for assessing association in data mining, two basic measures used for forming strong association rules with frequent item sets are support and confidence (17).

1. Support: Support shows percentage of processes in database. This is calculated as the probability of P(XUY). XUY means, the operation includes X and Y together, in short it means association of X and Y.

It can be defined by support (X⇒Y) = P(XUY) formula (18).

2. Confidence: Other basic measure used for association rules is confidence. Confidence gives certainty degree of association discovered. P(Y|X) means, possibility of including Y in an operation with X together and it is defined as below,

confidence (X⇒Y) = P (Y|X) (18).

Interest Measures

Sometimes conventional confidence measures fall short to explain real interesting associations patterns fully, so various interest measures discussed for association rules. These interest measures are categorized in two groups as subjective and objective. Subjective measures take both data and users into consideration. In this respect, if a pattern discloses unexpected information about data, it is classified as subjective. On the other hand information, which attracts interest of a user, may not get attention of another one. Because of that, objective measures are needed. Objective measures are mostly dependent on contingency, statistic and information theory. Objective measures don't require any information about users and impact area beforehand. It measures interest of an association rule in the way of structure and basic information on the discovery process. Objective measures are generally calculated with frequency counts on contingency table. Some objective measures are mentioned below (19).

1. Lift: Lift is a measure of how many times X and Y are together more than expected if they are statistically independent. It is defined below.

$$Lift(X \Rightarrow Y) = \frac{\text{confidence } (X \Rightarrow Y)}{\text{support } (Y)}$$

Indicates that if the lift value is greater than 1, X and Y appear more often together. If this value is less than 1, it indicates that X and Y appear together less than expected (17).

2. Conviction: That measure is an alternative of confidence measure. If there is a relationship between the actual occurrences of X without Y, conviction compares the probability that X will do so. In this respect, it is similar to lift, but unlike lift, it also uses knowledge of the absence of the consequence (17,20). It is defined in the form of;

$$Conviction\ (X \Rightarrow Y) = \frac{1 - support\ (Y)}{1 - confidence\ (X \Rightarrow Y)}$$

3. Certainty Factor: Certainty factor is interpreted as a measure of the probability that Y is involved in a transaction when only X is considered and it is described below (15).

$$CF(X \Rightarrow Y) = \begin{cases} \frac{confidence\ (X \Rightarrow Y) - support\ (Y)}{1 - support(Y)} & \text{confidence } (X \Rightarrow Y) > support(Y) \\ \frac{confidence\ (X \Rightarrow Y) - support\ (Y)}{support\ (Y)} & \text{confidence } (X \Rightarrow Y) < support(Y) \\ 0 & \text{in other conditions} \end{cases}$$

4. Cosine: It is similarity measure used widespread for vector space model and it is described below (21).

$$Cosine = \frac{P(X,Y)}{\sqrt{(P(X)P(Y)}}$$

5. Correlation Coefficient (Phi): It is a measure assessing association between X and Y by calculating coefficient of correlation for continuous variables and it can be stated as below (18,21).

$$\varphi(X \Rightarrow Y) = \frac{P(X,Y) - P(X)P(Y)}{\sqrt{P(X)P(Y)(1-P(X))(1-P(Y))}}$$

6. Mutual Information: Mutual information is an entropy-based measure that used to assess dependence between variables. When the value of a second variable is known, it represents the amount of decrease of a variable's entropy (21). Mutual information is employed to boost performance of data mining process (22).

$$\varphi(X \Rightarrow Y) = \frac{P(X,Y) - P(X)P(Y)}{\sqrt{P(X)P(Y)(1-P(X))(1-P(Y))}}$$

RESULTS

Descriptive statistics according to the demographic information and diagnostic test results of the patients are given in Table 2. For continuous variables, mean, standard deviation was given as descriptive stastistic, whereas numbers and percentages was given for categorical variables.

Age, height, weight, BMI, troponin, irisin, LDH and CK-MB continuous variables, they were transformed into categorical variables in order to the generation of association rules. For experimental results, minimum support value was set as 12 % and confidence value was set as 94 %. At the result of analysis, there were 108 rules, including triple and quadruple association rules, which were the most-observed with confidence and support values. It is possible to conclude that the rules, constituted by taking support and confidence measures into consideration, are right; but not so strong. Many interest measures, used in literature, are recommended to obtain stronger rules. In this study, lift, conviction, certainty factor, cosine, coefficient of correlation (phi) and mutual information measures are used in addition to support and confidence. Lift value is referred to how many times X and Y are seen together (23). Lift value, which is over 1, indicates that X and Y are seen more frequently (17). The present study included lift values over 1. Cosine is geometric mean among interest factor and support values. As cosine (X=>Y) approaches to 1, operations with the X item includes Y item, too (17). So values close to 1 are taken into consideration. The correlation coefficient (phi) close to 0 when X and Y are independent (24). Conviction value (X=>Y) gives X's conditional possibility if Y is absentee. It can be commented similarly with lift. As a distinguishing difference, conviction value measures Y' presence possibility when X is present, but the lift take how often X and Y are seen together into consideration. As a result of that, conviction values are used over 1 (17). Certainty factor value approaching to 1 is reckoned that rules, which are obtained during the study, are indicators of fairly high accuracy (15).

Considering support and confidence measures, 108 rules were constituted in the analyses. Those association rules were right; but not strong so that new rules are obtained by using six interest measures. In this respect, 29 of 108 rules are qualified as strong. The rules obtained are given in Table 3.

Generally, in associative classification methods, the rule with the highest confidence is used for classification (25). In this context three examples of interpretation of the rules given in table 3 are given below.

Rule 20: Patients, who with a weight of 80 to 105, a troponin value between 0.01 and 0.48 and male are 100% of the rs726344 polymorphism genotype type is GG wild.

Rule 24: Patients, who height between 170 and 185 with myocardial infarction type acute inferior and rs726344 polymorphism genotype type GG wild are 100% of male.

Rule 25: Patients, who height between 170 and 185, smoke, rs726344 polymorphism genotype type GG wild, and don't have hypertension are 100% of male.

The other rules given in Table 3 will be interpreted similarly.

Table 2. Descriptive statistics of patients according to demographic information and diagnostic test results

Variables		AMI (n=225) (Mean±SD)
(Mean ± SD)		
Age (years)		64.95±12.45
Height		164.94±17.95
Weight		73.87±13.79
BMI (kg/m^2)		26.37±4.52
Troponin (ng/mL)		13.08±18.29
CK-MB (ng/mL)		70.49±66.8
Irisin (ng/ml)		3.12±2.06
LDH (mg/dL)		347.13±154.22
Gender (%)	Male	148 (72.2)
	Female	57 (27.8)
Hypertension (%)		107 (52.2)
Smoking (%)		89 (43.4)
Diabetes (%)		85 (41.5)
Family history (%)		135 (65.9)
Mtype (%)	A. inferior	109 (53.2)
	A. anterior	62 (30.2)
	NSTEMI	34 (16.6)
Rs3480 in FNDC5 gene	AA	59 (28.8)
	AG	111 (54.1)
	GG	35 (17.1)
Rs726344 in FNDC5 gene	GG	180 (87.8)
	GA	15 (7.3)
	AA	10 (4.9)
Rs16835198in FNDC5 gene	GG	108 (52.6)
	GT	86 (42.0)
	TT	11 (5.4)

Table 3. The generated association rules

ID	Rule No	Association Rules (X =>Y)	Confidence	Count	Lift	Support	Certainty Factor	Conviction	Cosine	Mutual Information	Phi
1	1	familyhistory=1. rs3480=3=>rs16835198=1	1	26	1.898	0.127	1	NA	0.491	NA	0.361
2	2	rs3480=3, rs726344=1=>rs16835198=1	1	25	1.898	0.122	1	NA	0.481	NA	0.353
3	3	diabetic=1, rs3480=1=> rs726344=1	1	28	1.139	0.137	1	NA	0.394	NA	0.148
4	4	rs3480=1, rs16835198=2=>rs726344=1	1	31	1.139	0.151	1	NA	0.415	NA	0.157
5	5	hypertension=1, rs3480=1=>rs726344=1	1	36	1.139	0.176	1	NA	0.447	NA	0.172
6	6	mtype=1, rs3480=1=>rs726344=1	1	27	1.139	0.132	1	NA	0.387	NA	0.145
7	7	smoke=2, rs3480=1=>rs726344=1	1	35	1.139	0.171	1	NA	0.441	NA	0.169
8	8	diabetic=2, rs3480=1=>rs726344=1	1	31	1.139	0.151	1	NA	0.415	NA	0.157
9	9	familyhistory=1, rs3480=1=>rs726344=1	1	42	1.139	0.205	1	NA	0.483	NA	0.189
10	10	gender=1, rs3480=1=> rs726344=1	1	43	1.139	0.210	1	NA	0.489	NA	0.192
11	11	age=[27,59), troponin=[0.01,0.48)=>rs726344=1	1	25	1.139	0.122	1	NA	0.373	NA	0.139
12	12	weight=[80,105], troponin=[0.01,0.48)=>rs726344=1	1	29	1.139	0.141	1	NA	0.401	NA	0.151
13	13	age=[27,59), familyhistory=2=>rs726344=1	1	26	1.139	0.127	1	NA	0.380	NA	0.142
14	14	ldh=[389,919], familyhistory=2=>rs726344=1	1	26	1.139	0.127	1	NA	0.380	NA	0.142
15	15	familyhistory=2, rs16835198=2=>rs726344=1	1	27	1.139	0.132	1	NA	0.387	NA	0.145
16	16	height=[170,185], mtype=1=>gender=1	1	34	1.385	0.166	1	NA	0.479	NA	0.277
17	17	hypertension=1, smoke=2, rs3480=1=>rs726344=1	1	27	1.139	0.132	1	NA	0.387	NA	0.145
18	18	hypertension=1, familyhistory=1, rs3480=1=>rs726344=1	1	26	1.139	0.127	1	NA	0.380	NA	0.142
19	19	gender=1, familyhistory=1, rs3480=1=>rs726344=1	1	28	1.139	0.137	1	NA	0.394	NA	0.148
20	20	weight=[80,105], troponin=[0.01,0.48), gender=1=>rs726344=1	1	25	1.139	0.122	1	NA	0.373	NA	0.139
21	21	weight=[80,105], gender=1, rs16835198=2=>rs726344=1	1	25	1.139	0.122	1	NA	0.373	NA	0.139
22	22	height=[170,185], hypertension=2, smoke=1=>gender=1	1	28	1.385	0.137	1	NA	0.435	NA	0.247
23	23	height=[170,185], smoke=1, familyhistory=1=>gender=1	1	28	1.385	0.137	1	NA	0.435	NA	0.247
24	24	height=[170,185], mtype=1, rs726344=1=>gender=1	1	30	1.385	0.146	1	NA	0.450	NA	0.257
25	25	height=[170,185],hypertension=2,smoke=1,rs726344=1=>gender=1	1	26	1.385	0.127	1	NA	0.419	NA	0.237
26	26	height=[170,185], hypertension=2 => gender=1	0.974	38	1.350	0.185	0.908	10.844	0.500	0.104	0.273
27	27	height=[170,185], smoke=1, rs726344=1=>gender=1	0.974	37	1.349	0.180	0.905	10.566	0.493	0.102	0.268
28	30	height=[170,185], hypertension=2, rs726344=1=>gender=1	0.973	36	1.348	0.176	0.903	10.288	0.486	0.100	0.263
29	98	weight=[0,70), gender=1=> bmi=[0,25.1)	0.944	34	2.847	0.166	0.917	12.029	0.687	0.396	0.601

NA*: Not available

DISCUSSION

In conventional association rules mining, rules are constituted if rules meet the measures of support and confidence and their threshold values. However, these rules may be sometimes misleading. So, confidence and support values are not enough while constituting association rules. There are many alternative interest measures for attaining stronger rules in association rules mining. In association rules mining, if it does not take interest measures into consideration it can cause misleading assessments (15). Assessing association rules by using only confidence and support measures might create a lot of disadvantages; so it will be more accurate to assess it with certainty factor, asserted by Shortliffe and Buchanan (26). It demonstrates similar characteristics with the result of study carried out by Berzal and his friends (15). Ilayaraja and Meyyappan in their study aimed at identify frequency of diseases in particular geographical area at given time period with the aid of association rule based Apriori data mining

technique (27). Nahar et al. presented a rule inference on heart disease data using three different association rule mining algorithms: Apriori, Predictive Apriori and Tertius. In their study, they made rule mining analysis by classifying data based on gender. They also found significant risk factors for heart disease for both men and women (28). Sathyavani and Sharmila show that in addition to support and confidence measures, using mutual information measure we can obtain more effective rules (22). Besides, Marimaran et al. suggested that in addition to support and confidence measures, and can discover more interesting rules by applying eight interest measures as lift, chi-square, hyper-lift, hyper-confidence, conviction, coverage, leverage, and cosine (17).

Rules are created when the threshold support and confidence value is provided in the apriori algorithm used in association rules mining. However, these rules are not strong enough. There are many interest measures proposed in the literature to obtain stronger rules. In the experiment of the current study, 108 rules were constituted in order to eliminate misleading rules and obtain stronger rules. It was determined that if lift, conviction, certainty factor, cosine, coefficient of correlation (phi), mutual information measure values were added to those rules 29 strong association rules were generated as a result of more comprehensive analysis.

Similar to this study, Karolis et al. used the different algorithms of rule extraction and evaluation like the C4.5 decision trees and the apriori algorithms for coronary heart events. They found that there were extracted rules with risk factor like sex (male), smoking, high density lipoprotein, glucose, family history, and history of hypertension (29). Safdari et al. employed the data mining techniques for predicting the risk of myocardial infarction. The seven predictive algorithms and one association rule algorithm were applied on the database. The result of the study indicated that variables such as gender, age, family history of coronary artery disease, history of smoking, history of hypertension history of diabetes, history of high blood fat, and body mass index were the most important variables that can be used for predicting the risk of myocardial infarction (30). Licastro et al. assessed a new risk approach for AMI by an innovative algorithm, the predictive capacity of Artificial Neural Networks (ANNs) in consistently distinguishing the two different conditions (AMI or control) and the identification of variables with the maximal relevance for AMI. Their findings showed that ANNs were useful in distinguishing risk factors selectively associated with the disease (31). Known risk factors such as hypertension, smoking, gender, BMI and family history in terms of AMI were found to be among the most important risk factors similar to the literature in terms of 100 % association rules in the present study. In addition, the 20th, 24th and 25th rule associations of polymorphisms of the FNDC5 gene with other physical properties have been shown to have a 100 % risk for the disease. In particular, these data indicated that the association of rs726344 polymorphism wild types in the FNDC5 gene might be a risk factor.

The rs726344 polymorphism does not affect the amino acid sequence of the protein formed because it is located in the intron 5 region of the FNDC5 gene. As with the rs726344 polymorphism, intronic genomic variants can affect gene expression and thus phenotype by altering mRNA stability, alternative mRNA splicing, or binding of transcription factors (32). The minor A-allele of rs726344 is characterized by higher luciferase activity compared to the wild-type G-allele and has recently been associated with decreased insulin sensitivity in vivo (33). The A poliymorphic allele of rs726344 has also been associated with cardiometabolic risk factors (34). However, Staiger et al. (2013) found that there was no relationship between the A allele of the rs726344 SNP and FNDC5 mRNA expression in human myotubes (35). All of the studies summarized above are data obtained from control group comparisons and are case control studies. However, as in the current study, there are no studies in which polymorphisms are associated with other risk factors only within the patient group. In the current study, generally significant rules were found between wild genotypes and other parameters, since the wild allele was found in high density in the patient group. The relationships generally show the inheritance patterns of polymorphic variants or how familial transmission occurs. Rules 1,2,4 and 9 are typical examples of this transmission. As in the 1st rule, rs3480 polymorphic variant and rs16835198 wild variant are transmitted together in our society in individuals with positive family history. In rules 12 and 20, the rs726344 wild genotype was associated with high weight [80,105] and low troponin [0.01,0.48] levels. In rule 11, low age [27,59] and low troponin [0.01,0.48] resulted in rs726344 wild genotype. These data indicate that this genotype poses a risk for AMI at an early age. Similarly, rs726344 wild genotype was associated with hypertension positivity in rule 5. In general, both diabetes and hypertension are known important risk factors for AMI (36). In terms of hypertension, hypertension and non-smoking in rule 17 and hypertension and family history positivity in rule 18 support rule 5.

The dataset used in this article includes AMI patients with FNDC5 polymorphism and their risk factors. To obtain association rules, the apriori algorithm, which is one of the data mining methods, was applied to this data set. With these obtained rules, the interest measures such as lift, conviction, certainty factor, cosine, coefficient of correlation (phi) and mutual information were used, and stronger rules were obtained.. Thanks to the strong rules obtained, the patient profiles of AMI patients were revealed. By using these profiles, it has become easier to determine the clinical profiles of AMI patients in clinical implications.

CONCLUSION

In conclusion, the use of interest measures in the clinical decision making process is very important in terms of eliminating misleading rules and avoiding wrong decisions.

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MEDICAL RECORDS-International Medical Journal

Research Article

Prognostic Significance of Tumor Budding in Urothelial Carcinomas of the Bladder: Comparison of Two Different Tumor Budding Evaluation Methods

Mesanenin Ürotelyal Karsinomlarında Tümör Tomurcuklanmasının Prognostik Önemi: İki Farklı Tümör Tomurcuklanma Değerlendirme Yönteminin Karşılaştırılması

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Abstract

Aim: In our study, we aimed to reveal the effect of tumor budding(TB) on prognosis in urothelial carcinomas and to compare the most commonly used alternative method (AM) and the International Tumor Budding Consensus Conference (ITBCC) system. TB can be easily assessed on routine hematoxylin and eosin-stained slides. In studies, TB was found to be associated with prognostic parameters in many organs. TB assessment in many organ cancers is based on ITBCC or alternatively different values used by different authors.
Material and Method: Forty-eight urothelial cancers were obtained from 2010 to 2016 that was comprised of those having undergone surgical staging with a cystectomy or cystoprostatectomy and at least 5 years followed up. All hematoxylin and eosin-stained slides were re-evaluated for the status of TB according to ITBCC and AM.
Results: According to ITBCC TB was not correlated with pT, lymphovascular invasion, lymph node involvement (LNI), tumor stage and 5-year mortality (p=0.102, p=0.722, p=0.165, p=0.431, p=0.524). According to AM, TB was more frequent as pT advanced, and was marginally associated with LNI (p=0.027, p=0.058). There was no relationship between TB and overall survival (p=0.130).
Conclusion: We found the cut-off value in AM more useful than ITBCC recommendations. Although the association of TB with some of the prognostic parameters suggests that it may also be associated with prognosis, no relationship was found with overall survival. This may be related to the number of our cases.

Keywords: Tumor budding, bladder, urothelial carcinoma

Öz

Giriş: Çalışmamızda ürotelyal karsinomlarda tümör tomurcuklanmasının (TT) prognoza etkisini ortaya koymayı ve en sık kullanılan alternatif metod (AM) ile Uluslararası Tümör Tomurcuklanması Konsensus Konferans (ITBCC) sistemini karşılaştırmayı amaçladık.TT, rutin Hematoksilen&Eozin boyalı preparatlarda kolayca değerlendirilebilmektedir. Yapılan çalışmalarda TT'nin birçok organ kanserinde prognostik parametrelerle ilişkili olduğu bulunmuştur. TT değerlendirmesi, birçok organ kanserinde ITBCC'ye veya alternatif olarak farklı yazarlar tarafından kullanılan farklı değerlere dayanmaktadır.
Materyal ve Methot: Çalışmaya 2010'dan 2016'ya kadar, sistektomi veya sistoprostatektomi ile cerrahi evreleme yapılan ve en az 5 yıl takip edilen vakalardan oluşan kırk sekiz ürotelyal kanser dahil edildi. Tüm hematoksilen ve eozin boyalı preparatlar, ITBCC ve AM'ye göre TT durumu açısından yeniden değerlendirildi.
Bulgular: ITBCC'ye göre TT, pT, lenfovasküler invazyon, lenf nodu tutulumu(LNT), tümör evresi ve 5 yıllık mortalite ile korele değildi (p=0.102, p=0.722, p = 0.165, p=0.431, p=0.524). AM'ye göre, TT, pT ilerledikçe daha sıktı ve LNT ile marjinal olarak ilişkiliydi (p=0.027, p=0.058). TT ile genel sağkalım arasında ilişki yoktu (p=0.130).
Sonuç: Çalışmamızda AM'deki eşik değeri ITBCC önerisinden daha faydalı bulduk. TT'nin bazı prognostik parametrelerle ilişkisi prognozla da ilişkili olabileceğini düşündürse de, genel sağkalım ile bir ilişki bulunamadı. Bu durum vaka sayımızla ilgili olabilir.

Anahtar Kelimeler: Tümör tomurcuklanması, mesane, ürotelyal kanser

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INTRODUCTION

Bladder cancer is the most common urinary tract cancer and the thirteenth most mortal of malignant neoplasms (1). Urothelial carcinoma is the most frequent cancer type of bladder and is characterized by a propensity of divergent differentiation. Stage, grade, angiolymphatic invasion, and presence of some histological variants such as poorly differentiated and small cell differentiation are important prognostic parameters (2). According to the International Tumor Budding Consensus Conference (ITBCC) tumor budding (TB) is an isolated single tumor cell or non-glandular small cancer cell cluster with less than 5 cells in front of the invasive margin (3). TB can be easily assessed on routine Hematoxylin&Eosin-stained slides. In studies, TB was found to be associated with prognostic parameters in colorectal, endometrial, laryngeal, and esophageal carcinomas (4-9). TB assessment in many organ cancers is based on ITBCC or alternatively different values used by different authors (3-9). ITBCC recommends the triple assessment system with 1-4 buds as Bd1, 5-9 buds as Bd2, 10 and above buds as Bd3. In the alternative method (AM) used in most of the studies that are not based on ITBCC, the presence of 5 buds or more is assessed as TB, and the presence of fewer than 5 buds as no TB (8-10). There is a limited number of studies that have been conducted on TB in bladder cancer (10-15). Therefore, there is no consensus on how to evaluate TB in urothelial carcinomas of the bladder, and the ITBCC system has never been studied in bladder cancer. In our study, we aimed to reveal the effect of TB on prognosis in urothelial carcinomas and to compare the most commonly used AM and ITBCC system.

MATERIAL AND METHOD

A retrospective review of all cases of bladder urothelial carcinoma diagnosed at the Izmir Kâtip Celebi University Ataturk Training and Research Hospital from January 2010 through January 2016 was carried out. The patients included in the study were comprised of those having undergone surgical staging with a cystectomy or cystoprostatectomy and at least 5 years followed up.

Parameters such as patient demographics, tumor grade, histological type, lymph node status, and follow-up data were gathered from our medical records. Tumors were classified according to histological typing and surgical staging described in the WHO 2016 classification system (2).

Overall survival data were gathered from The Death Notification Service. All patients were followed up, and the median follow-up period was 14 months. The study approval was obtained from the institutional review board at Izmir Kâtip Celebi University medical faculty (2021-GOKAE-0116).

Histopathological Analysis

All available hematoxylin and eosin (H&E) stained sections of tumoral tissue (median 14 slides) were collected from the archive. All slides were re-examined by an expert pathologist (I.O.) and a pathology resident (I. G.), who were blind to the clinical outcomes, in an attempt to evaluate tumor budding. Cases called TB by two observers were considered TB positive.

Tumor budding was defined as an isolated single cancer cell or small cell clusters composed of <5 tumor cells found in the invasive margin. To assess TB in surgical resection specimens, 10 fields in the invasive margins had been scanned and tumor buds had been counted in the selected hotspot area (20xobjective, Olympus BX-50) (Figure 1). According to ITBCC, TB positive cases were grouped as 0-4 buds low budding (Bd 1), 5-9 buds medium budding (Bd 2), and 10 or more buds high budding (Bd 3) (3). According to AM, the presence of 5 buds or more was evaluated as TB, while the presence of fewer than 5 buds was evaluated as as no TB.

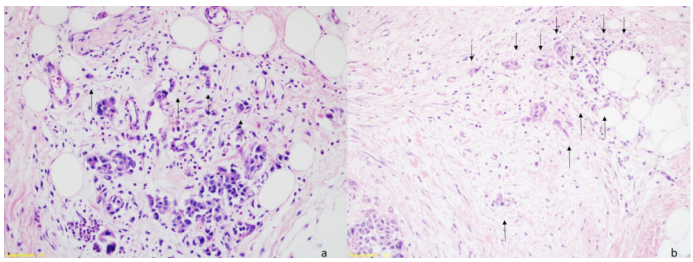

Figure 1. Example of tumor budding that is defined as single tumor cells or tumor cell clusters at up to four cells (a-b, on 20x magnification)

Statistical analysis

Statistical analysis was conducted by Jamovi (version 1.2). The comparison of the groups and the relationship between tumor budding and the other parameters were investigated using non-parametric tests, such as the Kruskal-Wallis test, Pearson's Chi-square test, and Mann–Whitney U test. Survival analyses were calculated using the Kaplan–Meier method. The Log-rank test was used for univariate analysis, while Cox proportional hazard regression (HR) models were performed for multivariate analysis. The probability level of 0.05 or less was chosen to represent statistical significance.

RESULTS

Patients features

A total of 48 patients with invasive urothelial carcinoma were included in the study. The clinicopathological characteristics of the patients are shown in table 1. The median age was found to be 61. Five cases with nested pattern, two cases with squamous differentiation, and one case with sarcomatoid differentiation were seen.

Based on WHO 2016 grading system, all tumors were histologically graded as high grade. Seven patients (15%) were present with pT1, 12 (25%) with pT2, 22 (46%) with pT3, and 7 (15%) with pT4 according to WHO TNM classification of carcinomas of the urinary bladder. Lymph

node involvement (LNI) was present in 13 patients (27%), while 5 cases with N1, 5 cases with N2, and 3 cases with N3. Five patients were stage I (10%), 11 patients were stage II (23%), 30 patients were stage III (62%), and 2 patients were stage IV (4.2%).

pT stage and TNM staging was associated with overall survival (OS) (p=0.00027, p<0.001). LVI was not associated with OS (p=0.24). A total of 40 patients (83.33%) died during follow-up, 39 of them within the first 5 years after surgery. LNI was found to worsen overall survival (OS) (p=0.026).

Table 1. Clinicopathologic caracteristics of the patients

Feature (N=48)	Frequency N(%) or mean (SD)
Operation Age (mean (SD)	63(8.01)
Sex	
Male	47(97.9%)
Female	1(2.1%)
pT	
1	7(14.6 %)
2	12(25%)
3	22(45.8%)
4	7(14.6 %)
Lymph node involvement	
Absent	35(72.9%)
Present	13(27.1%)
pN	
0	35(72.9 %)
1	5(10.4%)
2	5(10.4%)
3	3(6.3%)
Stage	
I	5(10.4%)
II	11(22.9%)
III	30(62.5%)
IV	2(4.2%)
TB according to ITBCC	
Low	29(60.4%)
Mild	5(10.4%)
High	14(29.2%)
TB according to AM	
Absent	29(60.4%)
Present	19(39.6%)
Lymphovascular invasion	
Absent	35(72.9%)
Present	13(27.1%)
N is the number of non-missing value	

Tumor Budding based on the International Tumor Budding Consensus Conference

The relationship between TB and clinicopathological features is shown in table 2.

TB was not correlated with pT, LVI, LNI, tumor stage and 5-year mortality (p=0.102, p=0.722, p=0.165, p=0.431, p=0.524).

Table 2. Clinicopathological features associated with Tumor Budding Based on the International Tumor Budding Consensus Conference

	N	Bd1	Bd2	Bd3	Test Statistic
	48	**29**	**5**	**14**	
pT	**48**				**P=0.102**
1		24.1%	0.0%	0.0%	
2		31.0%	20.0%	14.2%	
3		31.0%	80.0%	64.2%	
4		13.7%	0.0%	21.4%	
Lymphovascular invasion	**48**	**27.5%**	**40%**	**21.5%**	**P=0.722**
Lymph node involvement	**48**	**17.3%**	**42.9%**	**40.0%**	**P=0.165**
pN	48				P=0.132
N0		82.7%	57.1%	60.0%	
N1		6.8%	14.2%	20.0%	
N2		10.3%	7.3%	20.0%	
N3		0.0%	21.4%	0.0%	
Stage	**48**				**P=0.431**
I		17.2%	0.0%	0.0%	
II		27.5%	20.0%	14.2%	
III		51.7%	80.0%	78.5%	
IV		3.4%	0.0%	7.1%	
5-year mortality	48	79.3%	80.0%	92.8%	P=0.524
N is the number of non-missing value. TB=Tumor Budding					

Tumor Budding Based on the Alternative Method

The relationship between TB and clinicopathological features is shown in table 3.

Table 3. Clinicopathological features associated with Tumor Budding Based on the Alternative Method

	N	No TB	TB	Test Statistic
		29	**19**	
ptgroups	**48**			**P=0.027**
1		24.1%	0.0%	
2		31.0%	15.7%	
3		31.0%	68.4%	
4		13.7%	15.7%	
Lymphovascular invasion	**48**	**27.6%**	**26.4%**	**P=0.923**
Lymph node involvement	**48**	**17.3%**	**42.2%**	**P=0.058**
pN	48			P=0.093
N0		82.7%	57.8%	
N1		6.8%	15.7%	
N2		10.3%	10.5%	
N3		0.0%	15.7%	
Stage	**48**			**P=0.143**
I		17.2%	0.0%	
II		27.5%	15.7%	
III		51.7%	78.9%	
IV		3.4%	5.2%	
5-year mortality	48	79.3%	89.4%	P=0.356
N is the number of non-missing value. TB=Tumor Budding				

TB was not associated with LVI, stage, and the clinical outcome (p=0.722, p=431, p=0.248). TB was more frequent as pT advanced (p=0.027). It was revealed that TB was marginally associated with LNI (p=0.058). According to the absence or presence of TB, the median survival was 16 months and 10 months, respectively. Statistically, there was no relationship found between TB and overall survival (p=0.130).

DISCUSSION

Bladder cancer is the most common urinary tract cancer and the thirteenth most mortal of malignant neoplasms (1). Urothelial carcinoma is the most frequent cancer type of bladder and is characterized by a propensity of divergent differentiation. Stage, grade, angiolymphatic invasion, and presence of some histological variants such as poorly differentiated and small cell differentiation are important prognostic parameters (2).

There have been limited studies on TB in bladder cancer and there is no consensus to evaluate TB (10-15). TB cut-off values in bladder urothelial carcinoma change according to the studies. In Brieu et al. each tumor bud, in Kucuk et al. 5 tumor buds, in Seker et al. and Raventós Busquets et al. 6 tumor buds, in Fukumoto et al. 10 tumor buds and in Lorenzo Soriano et al. 14 tumor buds cut-offs were used (10-15). In this study, ITBCC recommendations and most used AM were followed (3,8-10). TB was significantly associated with pT as Seker et al. and Brieu et al. (11-12). While TB was found to be associated with LVI in the study of Seker et al., Raventós Busquets et al., and Fukumato et al., it was unrelated in our study and Kucuk's study (10, 12-14). While TB was statistically significant with LNI in Lorenzo Soriano et al., in this study as Seker et al., was found to be marginally significant (12,15).

The evaluation of TB in many organ cancers is based on ITBCC and different cut-off values used by different authors (3-9). In our study, we evaluated TB in urothelial carcinomas according to ITBCC and the cut-off value most commonly used in alternative methods (3,8-10).

CONCLUSION

While according to ITBCC recomendations, TB was insignificant with prognostic parameters, in AM TB was found to be associated with pT and marginally significant with lymph node involvement suggesting that TB may also be associated with a worse prognosis in urothelial carcinomas. Therefore, we found the cut-off value in AM more useful than ITBCC recomendations.

In our study, although overall survival decreased in the presence of TB, no relationship was found between TB and overall survival. This may be due to the relatively small number of cases in our study. Therefore, studies with larger case series are needed on this subject.

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Conflict of Interest: *The authors declare that they have no competing interest.*

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MEDICAL RECORDS-International Medical Journal

Research Article

Investigation of Usability of Artificial Intelligence Semantic Video Processing Methods in Medicine

Yapay Zekâya Dayalı Anlamsal Video İşleme Yöntemlerinin Tıpta Kullanılabilirliğinin Araştırılması

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Abstract

Aim: The goal of this study is to produce user-friendly software for healthcare professionals with various approaches such as detection, identification, classification, and tracking of polyps contained in endoscopic images utilizing appropriate video/image processing techniques and CNN architecture.

Material and Method: There were 345 photos in total in the study. These photographs are images depicting anatomical milestones, clinical findings, or gastrointestinal procedures in the digestive tract that have been documented and validated by medical specialists (skilled endoscopists). Each class has hundreds of images. The photos were downloaded from https://datasets.simula.no/kvasir, which is a free source for educational and research purposes. In the modeling phase, CNN and the Max-Margin object detection technique (MMOD), one of the deep neural network designs in the Dlib package, were employed. The data set was separated as 80% training and 20% test dataset using the simple cross-validation method (hold-out). Precision, recall, F1-score, average precision (AP), mean average precision (mAP), ideal localization recall precision (oLRP), mean optimal LRP (moLRP), and intersection over union (IoU) were used to evaluate model performance.

Results: When the previously described steps were performed on the open-access video image dataset of endoscopic polyps in the current study, all performance metrics examined in the training dataset received a value of 1, whereas, in the test dataset precision, sensitivity, F1-score, AP, mAP, oLRP, and moLRP were 98%, 90%, 94%, 89%, 89%, 48%, and 48% respectively.

Conclusion: The proposed approach was found to make accurate predictions in the diagnosis of gastrointestinal polyps based on the values of the calculated performance criteria.

Keywords: Object recognition, deep learning, decision support system, gastrointestinal polyps, convolutional neural networks

Öz

Giriş: Bu çalışmada endoskopik görüntülerde yer alan poliplerin tespiti, tanımlanması, sınıflandırılması ve takibi için uygun video/görüntü işleme teknikleri ve CNN mimarisi kullanılarak sağlık profesyonelleri için kullanıcı dostu bir yazılımın geliştirilerek sunulması amaçlanmıştır.

Material ve Methot: Çalışmada yer alan veri seti 345 görüntü içermekte olup görüntüler anatomik olarak bilinen dönüm noktaları, patolojik bulgular veya sindirim sistemindeki gastrointestinal prosedürler gibi her sınıf için yüzlerce görüntüden oluşmakta ve çeşitli tıp doktorları (deneyimli endoskopistler) tarafından açıklanmış ve doğrulanmıştır. Görseller araştırmalarda ve eğitimlerde kullanılmak amacıyla açık kaynak olan https://datasets.simula.no/kvasir adresinden alınmıştır. Modelleme esnasında Dlib kütüphanesinde yer alan derin sinir ağı mimarilerinden olan CNN ve Max-Margin nesne algılama yöntemi (MMOD) kullanılarak modellemeler yapılmıştır. Veri seti basit çapraz geçerlilik yöntemi (hold-out) kullanılarak %80'i eğitim, %20'si test veri seti olacak şekilde ayrıştırılmıştır. Model performansının değerlendirilmesinde ise kesinlik, duyarlılık, F1-skor, ortalama kesinlik (average precision, AP), ortalama kesinlik değerlerinin ortalaması (mean average precision, mAP), kesiştirilmiş bölgeler ölçütleri (intersection over union, IoU), en uygun konumlandırma kesinliği ve duyarlılığı (optimal localization recall precision, oLRP), ortalama en uygun LRP (Mean Optimal LRP, moLRP) kullanılmıştır.

Bulgular: Mevcut çalışmada endoskopik poliplerin açık erişimli video görüntü veri kümesi üzerinde daha önce açıklanan adımlar gerçekleştirildiğinde, eğitim veri kümesinde incelenen tüm performans metrikleri 1 değerini alırken, test veri kümesinde kesinlik, duyarlılık, F1-skoru , AP, mAP, oLRP ve moLRP sırasıyla %98, %90, %94, %89, %89, %48 ve %48 idi.

Sonuç: Çalışmada sonucunda elde edilen performans metriklerine ait değerler dikkate alındığında, önerilen sistemin gastrointestinal poliplerin tanısında başarılı tahmin sonuçları verdiği belirlenmiştir.

Anahtar Kelimeler: Nesne tanıma, derin öğrenme, karar destek sistemi, gastrointestinal polipler, evrişimsel sinir ağları

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INTRODUCTION

Clinical decision support systems provide support to physicians in diagnosing diseases and providing appropriate treatments with computer software, using the patient's health-related data such as text, audio, video, and images. Thus, while the data of the patient is evaluated clinically, the relevant decision support software helps the physician by trying to predict the best possible among the appropriate options. In this way, it affects the change in the result between death and life with early diagnosis and appropriate treatment (1-4).

Machine learning and deep learning networks that make up artificial intelligence are used in clinical decision support systems. Machine learning is a system that can make predictions on data and reveal inferential results by applying various algorithms (5-9). This system is used in the solution of many problems and has also enabled the use of deep learning networks with the development of new algorithmic approaches. Deep Learning is the technique of obtaining a learning representation from the data by using computational methods in each layer of the architecture consisting of successive layers and discovering the hidden features in data sets. With the advancement of this technique in recent years, deep learning algorithms have started to be used in areas such as video processing, image processing, voice recognition, and robotics. Among these areas, video/image processing is one of the most important research topics in the development of clinical decision support systems (10-12).

Polyps are lesions that can be detected as mucosal growths within the intestine. Polyps are flat, raised, or peduncled and can be distinguished from normal mucosa by color and surface patterns. Most bowel polyps are harmless, but some have the potential to turn into cancer. Therefore, detecting and removing polyps is important to prevent the development of colorectal cancer (13).

Convolutional Neural Networks (CNN) are one of the most important neural networks in deep learning. These networks can perform complex tasks such as images, sounds, text, videos, and are most commonly applied for analyzing visual images. CNN uses an adaptation of multi-layer sensors designed to require minimal preprocessing. In computer vision, CNNs are known to be powerful visual models that provide feature hierarchies that enable accurate segmentation. It is also reported that CNNs perform classification estimates relatively faster than other algorithms (11,14).

In this study, it is aimed to develop a user-friendly software for healthcare professionals with various methods such as detection, identification, classification and tracking of polyps in endoscopic video images using appropriate video/image processing techniques and CNN architecture. In addition, this study aims to help healthcare professionals make clinical decisions about the disease, as well as provide support for disease diagnosis, follow-up, and development.

MATERIAL AND METHOD

Data Set of the Study

The Kvasir data set was collected by the Bærum Hospital of the Vestre Viken Health Foundation in Norway and checked by the experts at the Norwegian Cancer Registry Center. The data set consists of a total of 4000 images and 8 classes, and there are 500 images in each class. These images are described and verified by medical practitioners (experienced endoscopists).

In our study, a total of 345 images in JPG image compression format belonging to the polyp class in the Kvasir data set were used. The data were obtained by decomposing the video images in the gastrointestinal tract into pictures. Images were obtained from https://datasets.simula.no/kvasir , which is open access for research and education purposes.

Deep Learning

Deep learning, which is a sub-field of machine learning (ML), has increased in popularity in recent years due to the fact that its computing power has greatly increased and large new data sets are increasing day by day. The field of deep learning has shown and demonstrated groundbreaking performances in a variety of complex tasks, including image classification, object detection, speech recognition, language translation, natural language processing, and gameplay. The ability of deep learning models to work on the graphics processing unit has enabled them to outperform many classical machine learning approaches in terms of modeling large data sets. Deep learning systems can accept multiple types of data as input, which is particularly important for the same type of health data (15). It uses many layers of nonlinear processing units for deep learning, feature extraction, and conversion. Each successive layer uses the output from the previous layer as input (16).

CNN deep learning architecture is frequently used in the processing of medical image and video data. Recently, deep learning algorithms such as CNN, detection of breast cancer on mammograms, segmentation of liver metastases with computed tomography (CT), brain tumor segmentation with resonance (MR) imaging, classification of high-resolution chest CT images of interstitial lung patients as a decision support system started to be used (17). The units in the layers in the CNN are locally connected, meaning each unit receives weighted inputs from a narrow range known as the receiving area in the previous layer. Stacks layers to create multi-resolution pyramids. The higher-level layers learn from the increasingly wider receptive fields. The main computational advantage of CNNs is that all receiver fields in a layer share weights, resulting in far fewer parameters than fully connected neural networks. Some of the best-known CNN architectures are AlexNet, VGGNet, ResNet, GoogLeNet, MobileNet, and DenseNet (18).

Image Processing

Image processing is the process of digitizing the image by applying different methods and techniques to extract useful information from images and obtain advanced images. In other words, image processing can be defined as computer studies aimed at changing the digital image data with the help of a computer or software in accordance with the targeted situation. Image analysis, on the other hand, can be summarized as the process of obtaining the numerical data needed for the targeted purpose from the available data (19). The most widely used open-source image processing libraries are OpenCV, Scikit-image, Dlib and BoofCV.

Modeling Stage

The methods used in this study can be examined in 5 stages. These;

1. Image pre-processing,
2. Drawing bounding boxes and labeling the images,
3. Establishing a deep learning model,
4. Training of the model,
5. Development of desktop video processing software,

Image Pre-Processing

Images in the data set contain green or black boxes that help determine the current position of the endoscope tip within the length of the bowel. Since these boxes do not make any sense for the whole image, they have been cropped out of the image. In addition, the process of converting images with different resolutions from 720x576 to 1920x1072 pixels into 350x350 pixels has been applied. Standardized images were obtained with this process.

It is important that the images in the data set have the same dimensions. Because the CNN input layer creates a pyramid for each image. This pyramid enables the detection of an object of any size, so the CNN model learns to detect larger or smaller objects in the image data set.

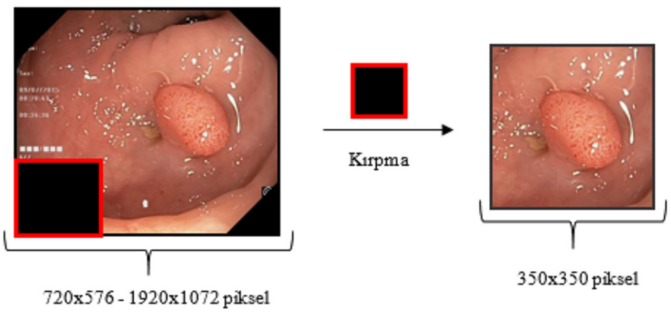

Figure 1. Illustration of polyp preprocessing

Drawing Bounding Boxes and Labeling the Images

An XML data set was created with the Imglab tool to draw bounding boxes on pre-processed images and start the labeling process. The Imglab graphical interface has been accessed to draw bounding boxes and label the images in the XML data set created. A window containing a list of images in the Imglab tool folder was opened and a bounding box was drawn and labeled for the boxes for each image.

Deep Learning Model Used in the Study

In our study, Convolutional Neural Networks (CNN) and Max-Margin object detection method (MMOD), which are among the deep neural networks architectures in Dlib Library, were used. In this thesis, Lenet architecture, which has a special multi-layered neural network, was used (20) .

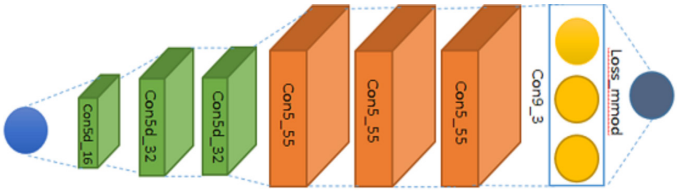

Figure 2. CNN architecture used in the study

MMOD is a method used to learn to detect objects in images. In this method, the detector takes every window in the image during the training phase and is scored with an appropriate objective function that aims to balance false perceptions and overlooked perceptions. It does not perform any subsampling with the MMOD method, instead, it optimizes all sub-windows.

Training of the Model

Images in the data set were taken and an image pyramid was created for each image. With the created pyramid image, it has been provided to find objects at the scale expected by the detectors. Thus, the image pyramid, which is several times larger than the normal image, has a rectangular structure, making it easy to work and process at high speeds on the graphics processing unit(GPU) using CNN.

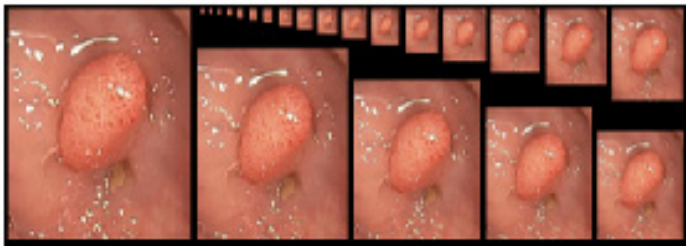

Figure 3. Image pyramid of the model

CNN took the image pyramid as its input and created a new image set using the convolution layers. A heat map was created in all parts of the image set that may contain polyp. The bright red areas in the heat map are the places that CNN thinks contain polyps, while the dark blue regions are the places that they think do not contain polyps. It was observed that the heat map detected the polyp correctly when placed on the image pyramid.

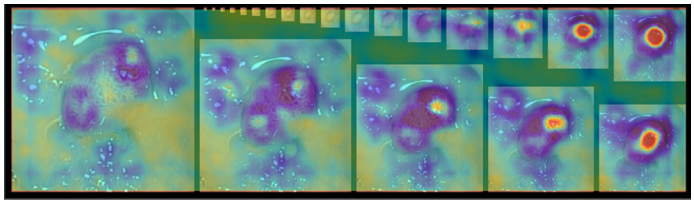

Figure 4. The heatmap image pyramid of the model

After finding all hot spots in the CNN outlet, non-maximum suppression method was applied and the sections corresponding to the determined hot spots were removed. Thus, a model that recognizes polyps was created using CNN+MMOD.

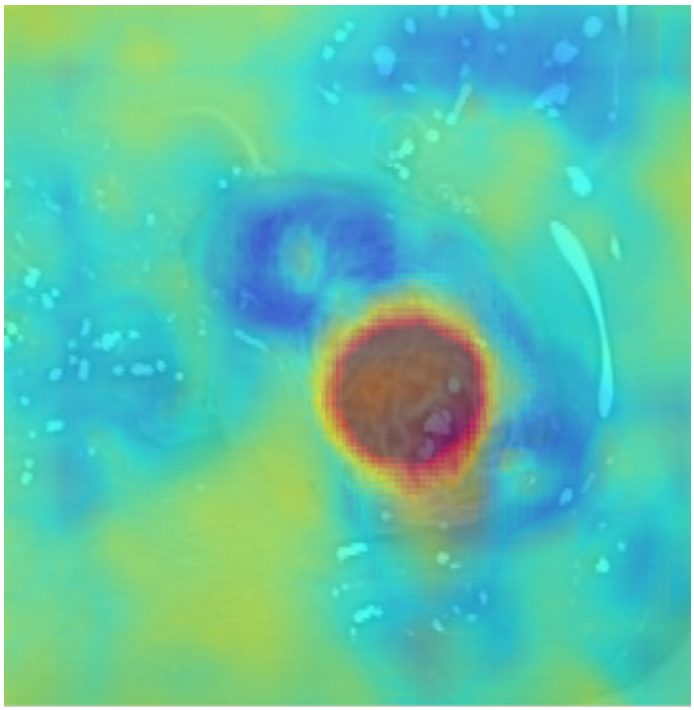

Figure 5. CNN + MMOD heat map

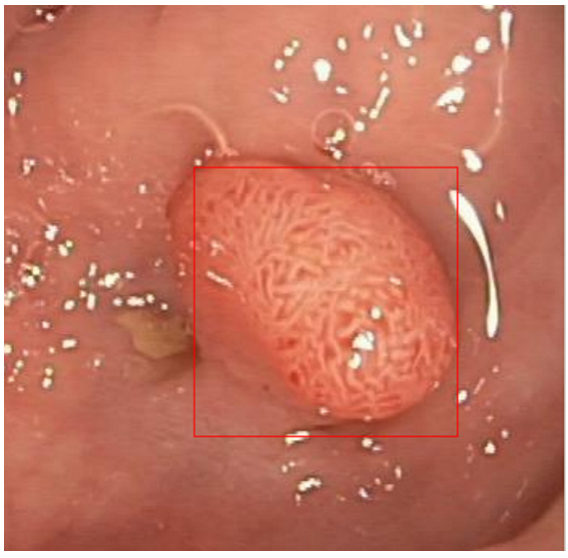

Figure 6. Determination of the polyp

Development of Desktop Video Processing Software

Video processing software was developed in Python language using Dlib and OpenCV libraries. In the software, the model trained by CNN+MMOD created in the C++ programming language was used.

Video processing software divided the images taken from the uploaded video or camera into frames and reduced in size. The images divided into frames were scanned by CNN detectors belonging to our model. Thus, the polyps in the video images were found and their positions were determined. Locations are enclosed in a red frame and visibility is provided. The working principle of the software is given in figure 7.

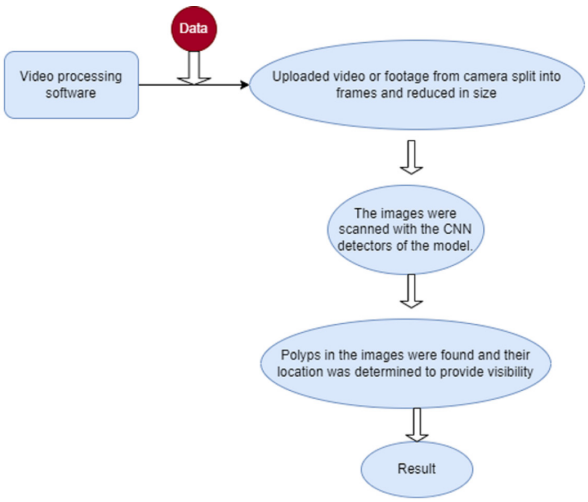

Figure 7. The working principle of the software

The procedures performed are given in Figure 8.

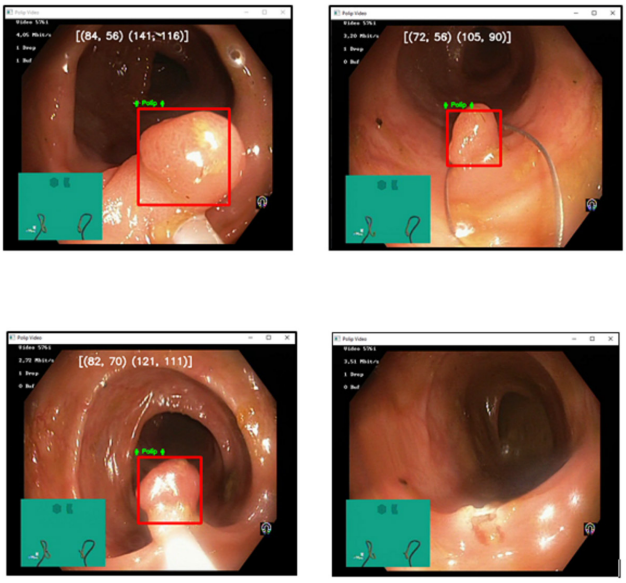

Figure 8. Finding polyps with video processing software

Video processing software also includes video recording feature. Thus, it is ensured that the processed videos are archived at the same time.

Performance Evaluation Metrics

In this study, Precision, Recall, F1-Score, Average Precision (AP), Mean Average Precision (mAP), IoU (Intersection over Union), LRP (Localization Recall) Precision - Positioning Precision and Precision) performance metrics were used. Of these metrics, mAP is a metric that combines recall and sensitivity for sequential retrieval results. The average precision criterion is used to evaluate detection algorithms. mAP metric is the sensitive and recall product of detected bounding boxes. The mAP value ranges from 0 to 1. The higher the better. It is an evaluation metric used to measure the accuracy of the object detector in the IoU dataset. The IoU is calculated by dividing the area where the predicted bounding box and the real bounding box intersect the area where these two limiters meet. It can be said to be a good estimate if the IoU has a value above 0.5. LRP moves along the recall sensitivity (RP) curve by specifying a performance score for each point consisting of positioning, precision, and sensitivity errors, and finally finds the best configuration the detector can achieve.

RESULTS

The images used in our study were divided into 276 for training and 69 for testing. Separated images were reduced to a resolution of 350x350 pixels, standardization was achieved and made suitable for the CNN model. Initial parameter values of the CNN model are given in Table 1.

Table 1. Beginning parameter values of the CNN model

Parameter	Value
Net Layer	21
Net size	0.955304 MB
Overlaps_nms	(0.1, 0.1)
Overlaps_ignore	(0.5, 0.95)
İterations without progress threshold	
	50000
Test iterations without progress threshold	
	1000
Optimization algorithm	SGD (Stochastic gradient descent)
Learning rate	0.0001
Min learning rate	0.0001
Learning rate shrink factor	
	0.1
Weight decay	0.0001
Momentum	0.9
Truth match IOU thresh	0.5
Loss per miss	1
Loss per FA	1

In the testing of the model created with CNN+MMOD, 69 polyp images and 71 bounding boxes were created as test data. Training and testing of the model were carried out on an Intel® Xeon® E5-1630 v3 (8 Core, 3.70 GHz) processor, 32GB memory, and NVIDIA GeForce GTX1080 Ti 11GB video card. The training lasted approximately 21 hours and was completed in 140581 iterations.

The CNN network is trained by convolutions of 21 layers and 5x5 filter sizes. The learning rate shrink factor was chosen as 0.1 as the initial value and continued until 127915 iterations. The training is completed when the minimum learning speed reaches 0.0001.

When the training of the model is completed, the test loss value is 0.46462 and the training loss value is 0.01058.

An example of the specified reference border boxes and the limit boxes estimated by the model are given in Figures 8 and 9, and the results of 69 polyp images belonging to the test data and the estimation results of 71 border boxes are given in Table 2.

Table 2. Estimated values

Prediction	Border Box
True Positive	64
False Positive	1
False Negative	7

While calculating the estimation values, the images of the test data were checked. In Figures 8, red boxes show reference boundary boxes, and blue boxes show the boxes predicted by the model. Box number 1 is false positive, box number 2 is true positive, and box number 3 is false negative.

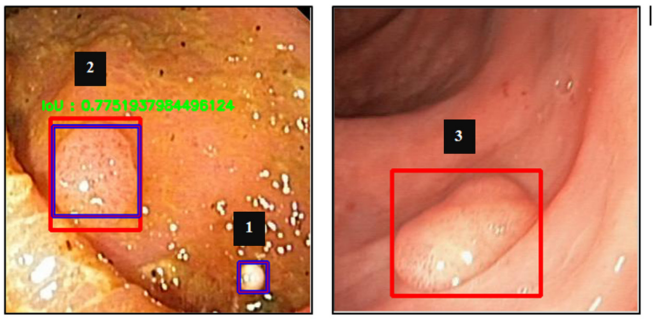

Figure 9. Diagnostic Values

The diagnostic performance of the model was calculated according to the specified evaluation criteria. Localization Recall Precision (LRP), a new performance criterion, was used for object detection in the calculation. The IoU value obtained from the training and test data was used to calculate the LRP. Performance Evaluation Metrics values of the training and test image data set are given in Table 3.

Table 3. Performance evaluation metric values of training and test image dataset

Metric	Training	Test
Precision	1	0.9846
Recall	1	0.9014
F1-Score	1	0.9412
AP	1	0.8942
mAP	1	0.8942
oLRP (τ=0.5)	0.4064	0.4862
moLRP (τ=0.5)	0.4064	0.4862

Since it is a single object class, the AP value gave the same results as the mAP value and the oLRP value gave the same results as the moLRP value at the end of the calculation.

DISCUSSION

Medical image processing is one of the most important components of artificial intelligence applications in medicine, and the development of deep learning has made great contributions to this field. There are three main types of objectives in medical image processing, namely classification, perception and segmentation, and they are closely related to each other. Object detection, in particular, forms the basis of many medical image processing tasks. Developments in deep learning in recent years have contributed greatly to the object detection performance of models. (21). In this study, a user-friendly software was developed for healthcare professionals by providing the detection, definition, classification, and tracking of polyps using open-access video image data set video/image processing techniques and deep learning architectures for polyps contained in endoscopic video images. The aim of this study is to help healthcare professionals make clinical decisions about the disease, as well as provide support for disease diagnosis, follow-up, and development.

In this study, all performance metrics examined in the training data set took the value 1. In the test data set, precision, recall, F1 score, AP, mAP, oLRP, and moLRP obtained from the model were 98%, 90%, 94%, 89%, 89%, 48% and 48% respectively.

In a study, a computer-based system based on color wavelet and convolutional neural network properties of endoscopic video frames has been proposed to support gastrointestinal polyp detection. In this context, it was determined that the proposed system detects and classifies gastrointestinal polyps from endoscopic video outperforms existing methods in datasets from different open databases (22).

In a study, a computer-based system based on color wavelet and convolutional neural network properties of endoscopic video frames was proposed to support gastrointestinal polyp detection. In this context, it has been determined that the proposed system for detecting and classifying gastrointestinal polyps from endoscopic video performs better than existing methods in data sets from different open databases (23).

CONCLUSION

As a result, very successful results were obtained in the prediction of endoscopic polyps with the model used according to the performance evaluation metrics. The proposed computer-aided system will be able to provide clinical support to clinicians during the diagnosis, treatment, and follow-up process.

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Ethical approval: *Ethics committee approval is not required.*

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MEDICAL RECORDS-International Medical Journal

Research Article

Adjuvant Radiotherapy for the Multimodal Treatment of Pediatric Ewing Sarcoma

Pediatrik Ewing Sarkoma Hastalarının Multimodal Tedavisinde Adjuvan Radyoterapi

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Abstract

Aim: This study aimed to report the adjuvant radiotherapy results of pediatric patients with Ewing sarcoma who received multimodal treatment for this rare disease using modern radiotherapy (RT) techniques.
Material and Methods: Pediatric patients with Ewing Sarcoma (ES) who received adjuvant radiotherapy were evaluated retrospectively. The study's primary endpoint was overall survival (OS) and disease-free survival (DFS). The secondary endpoint was local relapse-free survival after RT (LRFS- RT) and overall survival after RT (OS-RT).
Results: The results of 18 pediatric patients diagnosed with Ewing Sarcoma in our clinic between 09.12.2013-04.04.2021 and underwent RT for adjuvant were evaluated retrospectively. The three patients were excluded since they did not meet the inclusion criteria. The median age of the patients at the time of diagnosis was 10.5 (range 3-17). The time from diagnosis to the onset of RT was 8.6 (range 2-20) months. The median fraction dose was 180 cGy, and the median total RT dose was 50.4 (range 45-55.80) Gy. The median follow-up period of the study was 27 (range 11-86) months. The 12 (80%) patients survived, and 3 (20%) died. The median OS diagnosis of the patients was 27.3 (range 11 to 86.5) months. The overall survival of the patients after RT was median 17.3 (range 4.4-83.9) months. Recurrence (local+distant) was observed in 7 patients (46.7%); 2 (13.3%) local, 3 (20%) distant and 2 (13.3%) both. The median DFS was 24 months (range 1-86.5). Median LRFS-RT is 14.2 (range 1-83.9) months. The relationship between LRFS-RT and age (<10 vs. ≥10 years old) (p=0.050; HR:2.30; %95 CI 0.70-3.17) was significant. Significantly higher LRFS-RT was observed in the older age.
Conclusion: In patients with Ewing's sarcoma who are at high risk of local failure after surgery, adjuvant radiotherapy could be applied to increase local control rate, with reasonable side effects.

Keywords: Adjuvant radiotherapy, ewing sarcoma, pediatric oncology

Öz

Amaç: Bu çalışmada Ewing sarkomu nedeniyle multimodal tedavi uygulanan çocuk hastaların adjuvan radyoterapi sonuçlarını bildirmeyi amaçladık.
Materyal Metot: Adjuvan radyoterapi (RT) alan Ewing Sarkomlu pediatrik hastalar geriye dönük olarak değerlendirildi. Çalışmanın birincil sonlanım noktası, Genel Sağkalım (GS) ve hastalıksız sağkalım (HS) idi. İkincil sonlanım noktaları, RT den sonra lokal nükssüz sağkalım (LRFS-RT) ve RT'den sonra genel sağkalım (GS-RT)'di.
Bulgular: Kliniğimizde 09.12.2013-04.04.2021 tarihleri arasında Ewing Sarkomu tanısıyla adjuvan RT uygulanan 18 çocuk hastanın sonuçları retrospektif olarak değerlendirildi. Üç hasta dahil edilme kriterlerini karşılamadıkları için çalışma dışı bırakıldı. Hastaların tanı anındaki ortanca yaşı 10.5 (dağılım 3-17) idi. Tanıdan RT başlangıcına kadar geçen süre 8.6 (2-20) aydı. Ortanca fraksiyon dozu 180 cGy ve ortanca toplam RT dozu 50.4 (aralık 45-55.80) Gy idi. Çalışmanın ortanca takip süresi 27 (dağılım 11-86) aydı. Oniki (%80) hasta sağ ve 3 (%20) hasta ölü idi. Hastaların ortanca GS değeri 27.3 (dağılım 11 ila 86,5) aydı. Hastaların RT sonrası GS ortanca 17.3 (aralık 4.4-83.9) aydı. Yedi hastada (%46.7) nüks (lokal+uzak) vardı; 2 (%13.3) lokal, 3 (%20) uzak ve 2 (%13.3) lokal+uzak met vardı. Ortanca HS 24 aydı (aralık 1-86.5). Ortanca LRFS-RT 14.2 (aralık 1-83.9) aydı. LRFS-RT ile yaş (<10 ve ≥yaş üstü) arasındaki ilişki (p=0.050; HR:2.30; %95 GA 0.70-3.17) anlamlıydı. İleri yaşta anlamlı olarak daha yüksek LRFS-RT gözlendi.
Sonuç: Ameliyat sonrası lokal başarısızlık riski yüksek olan Ewing sarkomlu hastalarda adjuvan radyoterapi ile lokal kontrol şansı arttırılmaya çalışılmaktadır.

Anahtar Kelimeler: Adjuvan radyoterapi, ewing sarkomu, pediatrik onkoloji

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INTRODUCTION

Ewing Sarcoma is a rare type of cancer that affects bones and soft tissues. It accounts for 10-15% of all primary malignant bone tumors. It mainly occurs in children and young adults in the first and second decades of their lives. It has a high propensity to metastasize to the lung, bone, and bone marrow (1). Ewing sarcoma was first described by James Ewing, an American pathologist, as diffuse endothelioma, a highly radiosensitive tumor, in 1921 (2). Today, the standard of care is systemic treatment with surgery and/or radiotherapy. Tumors amenable to resection are treated primarily with surgery; otherwise, radiation therapy is the treatment of choice. Adjuvant Radiotherapy (RT) is generally considered if surgical margins are compromised or give poor response to chemotherapy.

In selecting the local treatment, function loss due to surgery, secondary malignancies, and other complications due to radiotherapy factors are considered. Although there is no study with a high level of evidence comparing these treatment modalities, it is reported that surgical outcomes are more favorable in retrospective series. However, it should be kept in mind that the patients who received radiotherapy in retrospective series had a worse prognosis in terms of location and size in which surgical treatment could not be performed (3-5). Radiotherapy was applied with old techniques in previous studies. The radiotherapy doses and schemes used differ; on the other hand, the development of surgical procedures makes it very difficult to compare these two local treatment modalities. Most of the studies in the literature are based on the evaluation of chemotherapy agents, and studies evaluating local treatment are generally retrospective (4,6).

This study aimed to report the adjuvant radiotherapy results of pediatric patients with Ewing Sarcoma who received multimodal treatment using modern radiotherapy techniques.

MATERIAL AND METHOD

For the study, pediatric patients with Ewing Sarcoma who received adjuvant RT in the Radiation Oncology Clinic of Ankara City Hospital were evaluated retrospectively. Patient interview information, patient files, and electronic system data were used for the study. Demographic status of the patients, tumor localization, clinical and pathological stage of the disease, chemotherapy, radiotherapy and surgery details, treatment response, and final status were noted. Ethics committee approval for the study was obtained from ethics committee no. 1 of Ankara City Hospital Hospital.

Patient Selection

Pediatric patients diagnosed with Ewing's Sarcoma, whose treatment details and follow-up information are available, were included in the study. Patients > 18 years old and those with the second malignancy were excluded. The statistical analyses were based on the following variables: gender (female vs. male), age at diagnosis <10 years vs ≥10 (7), recurrences (present vs. absent), tumor size (<8cm vs. ≥8cm) (8), RT total dose (under the 50 Gy and over the 50Gy), the margin status for patients undergoing surgery (R0 vs. R+) and tumor size (the longest axis measured on Magnetic Resonance Imaging (MRI)).

Treatment Details

The multidisciplinary tumor board evaluated patients after the pathological diagnosis. Patients were treated according to international multimodal protocols. The patients were assessed before the treatment, one and three months after the end of CT (chemotherapy), and every three months before and after the operation, and their examinations were carried out. Patients were treated using the Eclipse (Varian Oncology System Inc. CA, USA). External RT was applied to the patients five days a week.

Primary and Secondary Endpoints

The study's primary endpoints were Overall Survival (OS) and disease-free survival (DFS). The date of pathological diagnosis was accepted as the starting date for OS and DFS. The end date for OS was the last control date for surviving patients and the exitus date for ex-patients. The endpoint for DFS was the date of relapse for patients with relapse, the date of last check for patients without relapse. The secondary endpoint was local relapse-free survival after RT (LRFS-RT) and overall survival after RT (OS-RT). The last day of RT was taken as the starting date for OS-RT and LFS-RT values, which are the survival evaluation parameters after RT. The end date for OS-RT was the last check date for surviving patients and the exitus date for ex-patients. The end date for LRFS- RT was the date of relapse for patients with relapse, the date of last control for patients without relapse after RT.

Statical Analysis

Descriptive statistics for continuous (quantitative) variables were expressed as mean, standard deviation, minimum-maximum, and median values; categorical variables were expressed as number (n) and ratio (%). The categorical demographic characteristics of the patients were calculated with Chi-square with Fisher's exact test. Kaplan Meier was used in univariate survey analyses and compared with the log-rank test. Cox regression test was used in multivariate analysis. Analyses were performed with IBM SPSS Package Program version 23.0 (IBM Corporation, Armonk, NY, USA). The statistical significance level was set as $p<0.05$. The hazard ratio (HR) and 95% Confidence Interval (CI) values were noted for significant results.

RESULTS

The results of 18 pediatric patients diagnosed with Ewing Sarcoma in our clinic between 09.12.2013- 04.04.2021 and who underwent RT for adjuvant were evaluated retrospectively. The three patients were excluded since they did not meet the inclusion criteria.

The median age of the patients at the time of diagnosis

was 10.5 (range 3-17). The age of the patients was divided into two groups as under ten years old and above (7); 6 (%40) patients were younger than ten years, and 9 (60%) patients were ten years or older. In terms of gender, 8 (53.3%) patients were male, and 7 (46.7%) were female. The tumor size (long axis of the tumor) was median 106 mm (range 40-200), smaller than 8 cm in five patients (33.3%); 8 cm or larger in 10 patients (66.7%). Localization was lower extremity 3 (20%), upper extremity 3 (20%), costal 5 (33.3%), pelvic 3 (20%), head and skull base 1 (6.7%).

Patient and disease characteristics are summarized in Table 1.

Table 1. Patient and disease characteristics

Age	**Median**	**10.5 (range 3-17)**
	<10 y	6(40%)
	≥10 y	9(60%)
Gender	Male	8(53.3%)
	Female	7(46.7%)
Tumor size (Long axis of tumor)	Median	106mm(range 40-200)
	<8 cm	5 (33.3%)
	≥ 8 cm	10 (66.7%)
Localization	Lower extremity	3 (20%)
	Upper extremity	3 (20%)
	Costal	5 (33.3%)
	Pelvic	3 (20%)
	Head and skull base	1 (6.7%)
Surgical Margin Status	R0	7 (46.7 %)
	R1	4 (26.7%)
	R2	4 (26.7%)
Chemotherapy prior to RT	Median course number	6 (range 4-8)
Chemotherapy prior to RT -protocols	VIDE	10 (66.7%)
	VIDE + VAI	4 (26.7%)
	VIAE	1 (6.7%)
Concurrent CT	Yes	13 (86.7%)
	No	2 (13.3%)
Concurrent CT course	Median	2 (range 0-3)
Concurrent CT protocols	IE	4 (26.7%)
	VI	2 (13.3%)
	VIE	5 (33.3%)
	VCR	2 (13.3%)
Chemotherapy after RT	Yes	14 (93.3%)
	No	1 (6.7%)
Chemotherapy after RT course	Median	6 (range 1-14)
Post RT Local Recurrence	No	11 (73.3%)
	Yes	4 (26.7%)
Recurrence	No	8(53.3%)
	Yes	7(46,7%)
Recurrence Site	Local	2 (13.3%)
	Distance	3 (20%)
	Local+Distance	2 (13.3%)
Last Status	Alive	12 (80%)
	Ex	3 (20%)

Abbreviations: VIDE: vincristine, ifosfamide, doxorubicin and etoposide; VIE: vincristine, ifosfamide, and etoposide; VAI: vincristine, actinomycin-D and ifosfamide BVIT: bevacizumab, vincristine, irinotecan and temozolamide

Chemotherapy

All the patients received pre-RT chemotherapy. All but one patient were treated with the European Ewing tumor Working Initiative of National Groups Ewing Tumor Studies 1999 (EURO-EWING 99) Chemotherapy protocol. Only 1 (6.7%) patient was treated with the EICESS (European Intergroup Cooperative Ewing's Sarcoma Study) protocol. As induction CT, median six courses of vincristine, ifosfamide, doxorubicin, and etoposide (VIDE) (range 4 to 8 courses) were given to 14 patients treated according to the EURO-EWING 99 protocol. After induction, surgical excision was performed in all patients, except for one. All but one patient received concurrent chemotherapy (median two courses, range 1-3) during adjuvant RT. Anthracyclines or actinomycin-D were avoided as concomitant chemotherapies. After RT, patients completed 14 cycles of chemotherapy according to the protocol. After RT, CT consisted of vincristine, actinomycin-D, and ifosfamide in 11 patients median five courses (range, 4-8). One patient underwent autologous stem cell transplantation, then RT. Three patients developed progressive disease or relapse; second-line CT containing irinotecan and temozolomide was given. After RT, patients received a median of 7 (range 4-17) cycles of CT.

Surgery

All patients were operated. Of the patients, 7 (46.7 %) were R0, 4 (26.7%) patients were R1 and 4 (26.7%) patients were R2.

Radiotherapy

RT was administered to patients for adjuvant purposes. The period from diagnosis to the onset of RT was 8.6 (range 2-20) months. The median fraction dose was 180cGy. The median total fraction number was 28 (range 25-31), and the median total RT dose was 50.4 (range 45-55.8) Gy.

Radiotherapy was examined in terms of the total dose, and 3 (20%) patients received less than 50 Gy, and 12 (80%) patients received 50 Gy or more. Radiotherapy technique was applied with IMRT in 6 patients and with 3D-CRT technique in 9 patients.

Overall Survival Analyses

Two different OS analyses were performed, namely overall survival from diagnosis and overall survival after RT. The median follow-up period of the study was 27 (range 11-86) months. 12 (80%) patients survived, and 3 (20%) died. The median OS of the patients was 27.3 (range 11 to 86.5) months. The overall survival of the patients after RT was median 17.3 (range 4.4-83.9) months (Figure 1).

There was no significant relationship between overall survival and gender (female vs. male) (p=0.350), age at diagnosis (10y and under vs. older than 10y) (p=0.757), margin status (R0 vs. R+) (p=0,579), tumor size (<8cm vs. ≥8cm) (p=0.619), total RT doses (under the 50 Gy and over the 50 Gy) (p=0.411) (Figure 2).

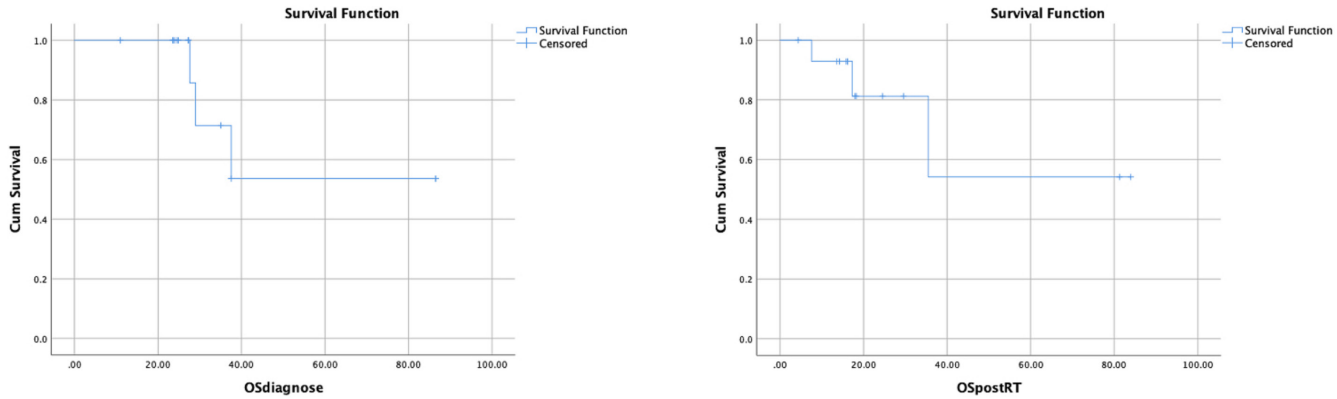


Figure 1. Kaplan Meier Analysis Results for Overall Survival

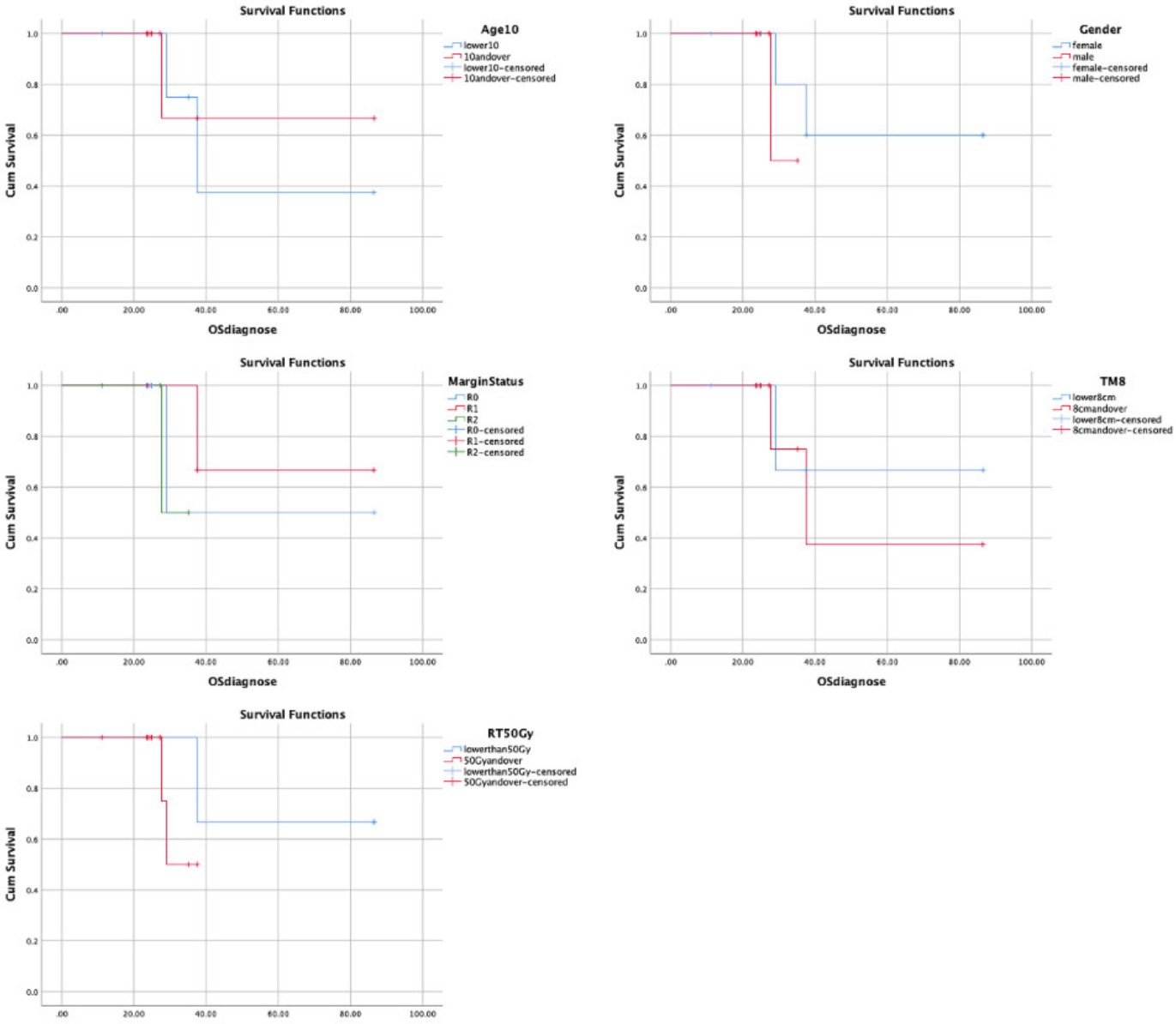


Figure 2. Kaplan Meier Analysis Results for Overall Survival from diagnosis

Similar results were also seen in the OS-RT analysis; gender (female vs. male) (p=0.938), age at diagnosis (<10 vs. over ≥ years old) (p=0.672), margin status (R0 vs. R+) (p=0.663), tumor size (<8cm vs. ≥8cm) (p=0.994), total RT doses (under the 50 Gy and over the 50 Gy) (p=0.353) (Figure 3).

Disease-Free Survival Analyses (From diagnosis)

The median DFS was 24 months (range 1-86.5). Recurrence (local+distant) was observed in 7 patients (46.7%); 2 (13.3%) local, 3 (20%) distant and 2 (13.3%) both. No significant relationship was found between DFS and the following variables: gender (female vs. male) (p=0.167), age at diagnosis <10 years vs ≥10 (p=0.813), tumor size (<8cm vs. ≥8cm) (p=0.610), margin status (p=0.945), RT total dose (under the 50 Gy and over the 50 Gy) (p=0.167) (Figure 4 and 5).

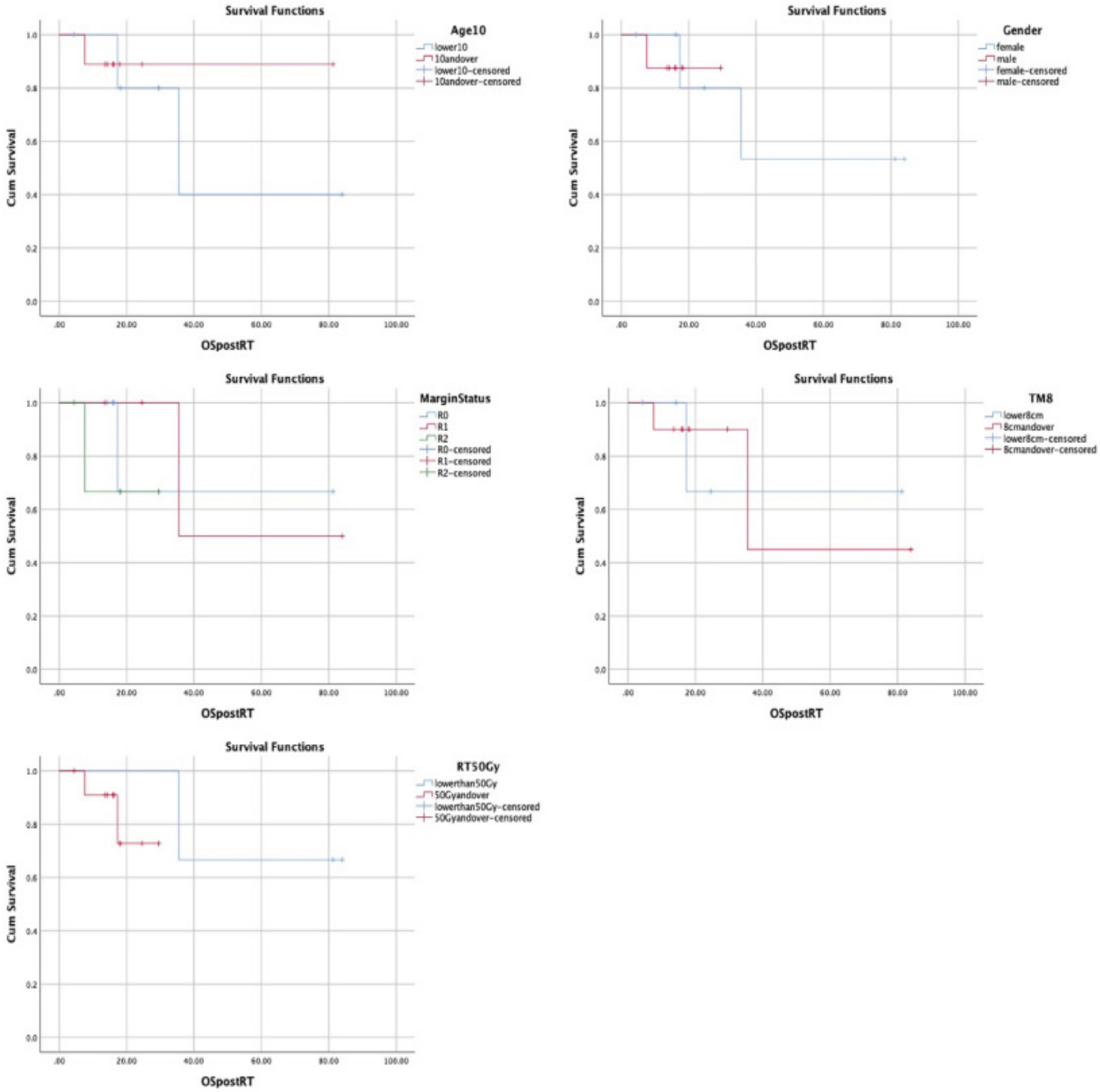


Figure 3. Kaplan Meier Analysis Results for Overall Survival from RT

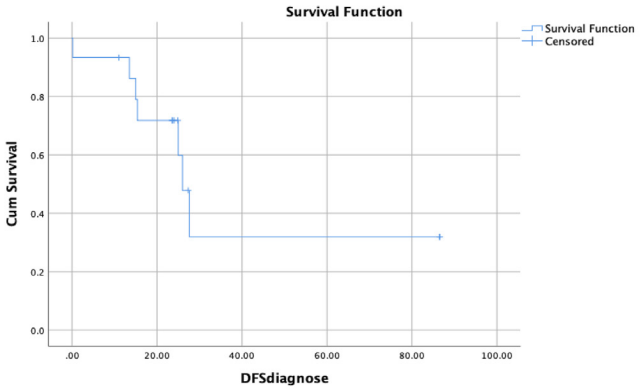


Figure 4. Kaplan Meier Analysis Results for DFS and LRFS-RT

Local Recurrence Free Survey from RT

Median LRFS-RT is 14.2 (range 1-83.9). The relationship between LRFS-RT and age (<10 vs. over ≥ years old) (p=0.050; HR:2.30; 95% CI 0.70-3.17) was significant. Significantly higher LRFS-RT was observed at the older ages (Figure 6 and 7).

There was no significant relationship between LRFS-RT and other variables; gender (male vs female) (p=0.253), tumor size (<8 cm vs. ≥8 cm) (p=0.416), RT total dose (under the 50 Gy and over the 50 Gy) (p=0.977), margin status (R0 vs. R+) (p=0.317) (Figure 8).

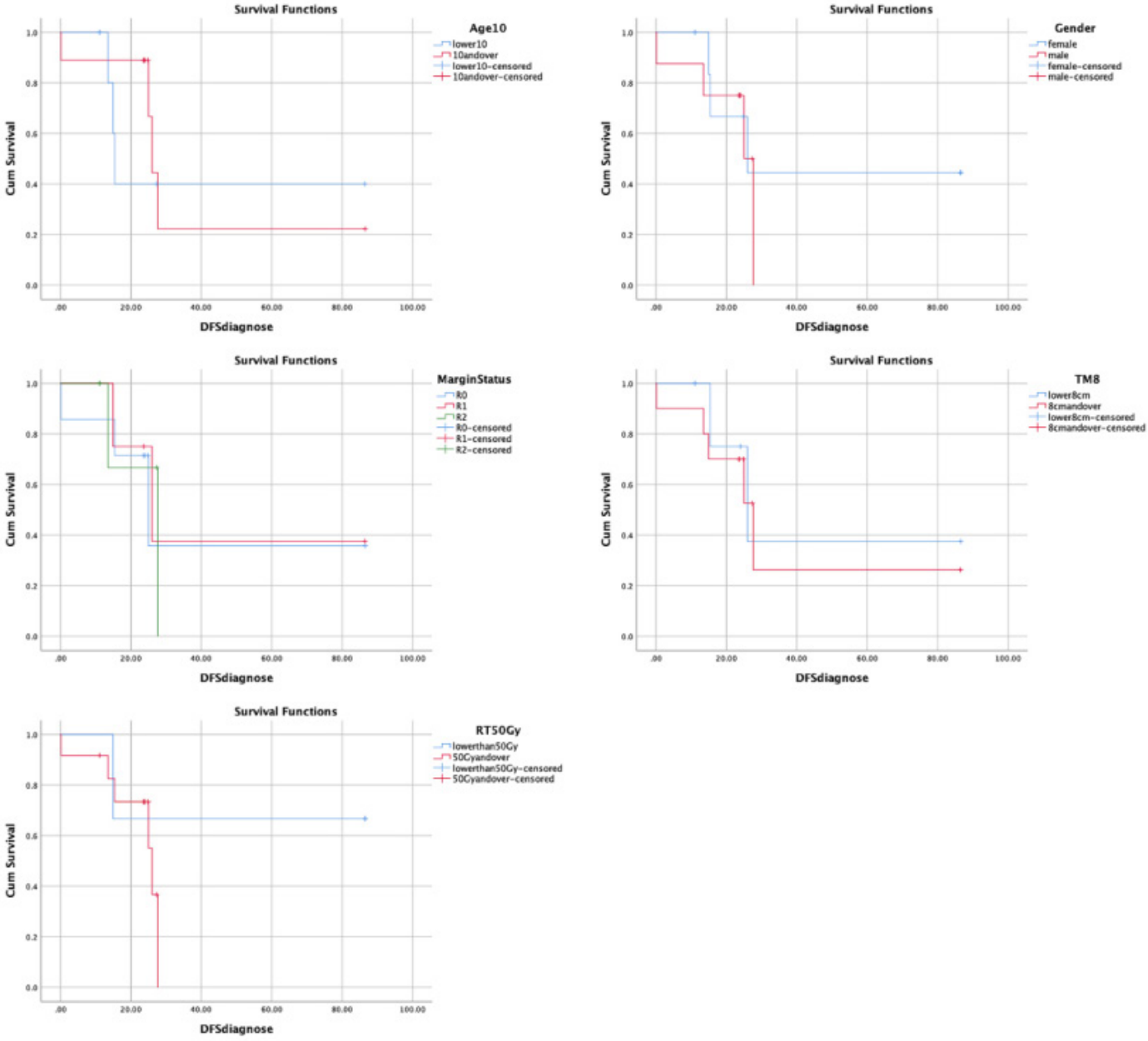


Figure 5. Detailed Kaplan Meier Analysis Results for DFS

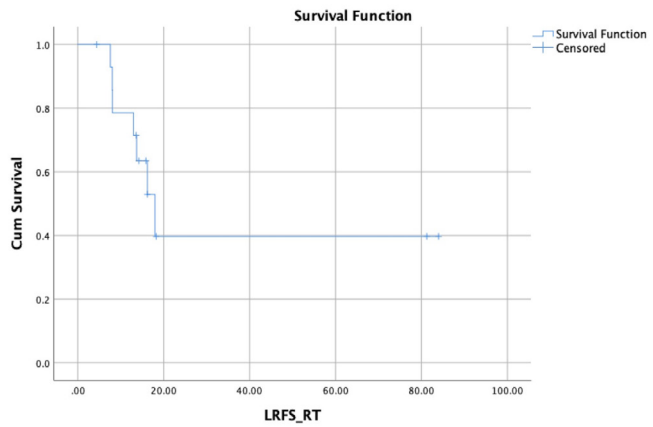


Figure 6. Kaplan Meier Analysis for LRFS-RT

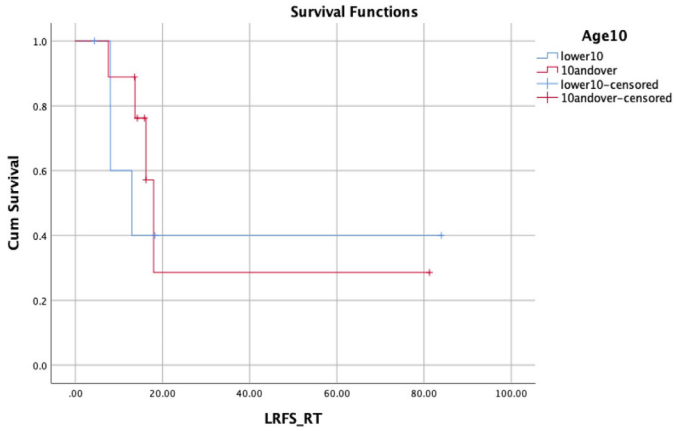
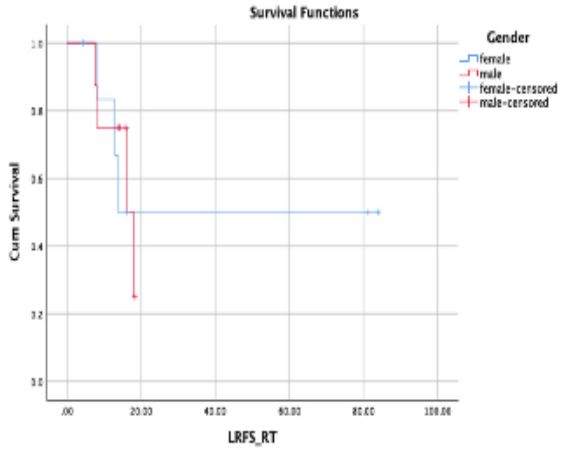
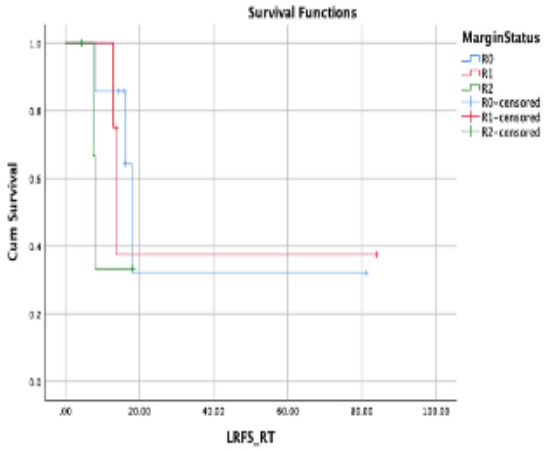
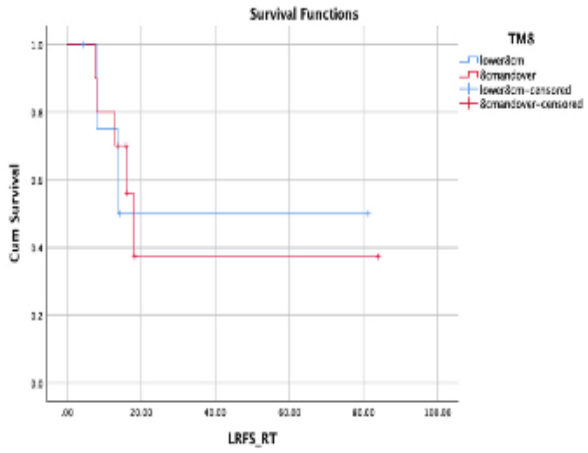


Figure 7. LRFS-RT and Age Relationship with Kaplan Meier Analysis







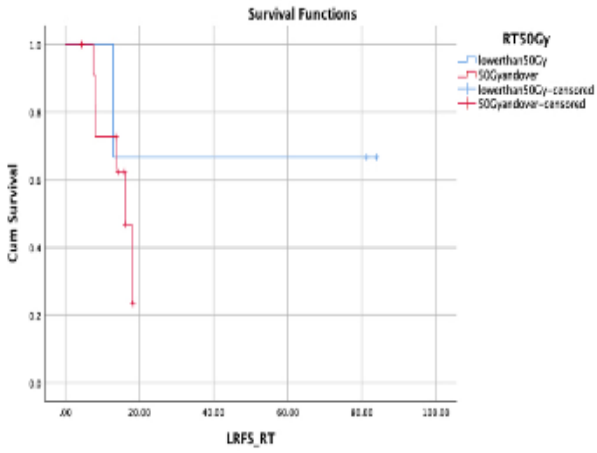


Figure 8. Detailed Kaplan Meier Analysis for LRFS-RT

	Age	Younger than 10	10 and older	p	HR
LRFS-RT	Median	10.5 (4.4-83.9)	15.8 (7-81)	0.050	0.14 (0.014-1.36)

Table 2. Patient Detail

Pt	Age, Gender	Localization	Size (mm)	Pre-RT CT	CCT	Post RT CT	MS	RT Details	Last Status	OS mo	DFS
1	11, M	UE	184	6c VIDE	VIE	Beva +8c VAI	R0	50 Gy/1.8 AE: Grade 1 RD	Alive LR:-	OSdiagnosis: 23.4 OSRT:15.8	DFSdiagnosis:23.4LRFS-RT:15.8
2	11,F	LE	200	6c VIDE+ 1cVAİ	3c VIE	Beva +4c VAI	R0	55.8 Gy/1.8 AE: NS	Alive LR:-	OSdiagnosis: 24.9 OS RT:16.2	DFSdiagnosis:24.9LRFS-RT:16.2
3	8,F	Pelvic	180	6cVIDE+ 1cVAİ	2c VI	OKIT ICE BIT	R1	45 Gy /1.8 AE: Grade 1 Diarre	Ex LR:+CT + for recurrence	OSdiagnosis: 37.5 OSRT:35	DFSdiagnosis: 14.9LRFS-RT:12.9
4	8,F	Head, Skull	40	4c VİAE	-	-	R2	54Gy/1.8Gy AE: Grade 1 RD	Alive LR:-	OSdiagnosis: 11 OSRT:4.4	DFSdiagnosis:11LRFS-RT:4.4
5	13, F	LE	35	6c VIDE+1c VAİ	3c VCR	12BVIT	R1	50.4 Gy/ 1.8 Gy AE: NS	Alive LR+ Distant Met:+	OSdiagnosis: 37.5 OSRT:24.5	DFSdiagnosis: 26LRFS-RT:13.7
6	6, F	Costa	110	5c VIDE	-	Beva 1c VIDE 1c VAI 7c VAC	R1	39 Gy71.5 Gy AE: NS	Alive LR:-	OSdiagnosis: 86.4 OSRT:83.9	DFSdiagnosis:86.4LRFS-RT:83.9
7	7, M	Pelvic	90	4c VIDE	2c IE	5cVAC12c VIT	R2	55.8 Gy /1.8Gy AE: NS	Alive LR:+	diagnosis: 35 OSRT:29.5	DFSdiagnosis:13.5LRFS-RT:8
8	17, M	Costa	101	8c VIDE	2c VIE	Beva 4c VAI	R1	50.4 Gy / 1.8 Gy AE: Grade 2 RD	Alive LR:-	OSdiagnosis: 23.6 OSRT: 13.6	DFSdiagnosis:23.6LRFS-RT:13.6
9	15, M	UE	90	6c VIDE	2c VIE	Beva 5c VAI	R2	54 Gy / 1.8 Gy AE: NS	Ex LR:-DM:+ Palliative RT for DM	OSdiagnosis: 27.6 OSRT: 7.5	DFSdiagnosis:27.6LRFS-RT:7.5
10	15, M	LE	170	6c VIDE	2c IE	Beva5VAI	R0	50.4 Gy /1.8 Gy, AE: Grade 1 RD	AliveLR:-DM:+	OSdiagnosis: 24.5 OSRT:16.2	DFSdiagnosis: 1LRFS-RT:16.2
11	14, F	Costa	40	4c VIDE	VCRCY	Beva 6c VAC	R0	45Gy /1.8 Gy AE: Grade 1 RD	Alive LR:-	OSdiagnosis: 86.5 OSRT: 81.2	DFSdiagnosis:86.5LRFS-RT:81.2
12	16, M	pelvic	65	6c VIDE	3c VIE	Beva4c VAI	R0	54 Gy /1.8 Gy AE: NS	AliveLR:-	OSdiagnosis: 24 OSRT:14.2	DFSdiagnosis: 24LRFS-RT:14.2
13	3, M	UE	98	6c VIDE	2c VIE	Beva4c VAC	R2	55.8 Gy /1.8 Gy AE: Grade 2 RD	AliveLR:-	OSdiagnosis:27.3 OSRT:18.2	DFSdiagnosis:27.3LRFS-RT:18.2
14	10,M	Costa	110	6c VIDE+1c VAİ	VIE	Beva5c VAI	R0	50.4 Gy /1.8 Gy, AE: NS	AliveLR:-DM:+	OSdiagnosis: 27.2 OSRT:17.9	DFSdiagnosis:25LRFS-RT:17.9
15	4, F	Costa	51	6c VIDE	VI	Beva6c VAI	R0	50.4 Gy /1.8 Gy, AE: NS	Ex LR:+DM:+	OSdiagnosis:29 OSRT:17	DFSdiagnosis:15LRFS-RT:8

Abr: PT= Patients; M=Male; F=Female; mm=millimeter; RT=Radiotherapy; CT=Chemotherapy; CCT=Concurrent Chemotherapy; MS=Margin Status; OS: Overall Survey; DFS=Disease Free Survey; mo=months; UE=Upper Extremity; LE=Lower Extremity; c=course; VIDE= vincristine, ifosfamide, doxorubicin, and etoposide; VIE= vincristine, ifosfamide, and etoposide; Beva=Bevacisumab; VAI=?; AE: Adverse Effect; RD=Radiodermatitis; LR=Locale Recurrence; NS=Not specified; OKIT=; ICE=; BIT=; VİAE=; VCR=; BVIT=;IE=; DM=Distant Metastasis

Table 3. Retrospective trials for Ewing Sarcoma

Study	Number of patients	Special characteristics	Chemotherapy	Radiotherapy	Follow-up	Results for radiotherapy
Choi et al. (7)	91	The localized disease of ESFT	All pts received VACA Etoposid± Ifospfamid (65 pts)	Local curative therapy for 15 pts Adjuvant therapy for 32 pts Neoadj therapy for 1 pt	Med 43.8 month	The 5-year PFS was 55.9% combined RT and surgery vs. 39.4% in those treated with RT without surgery
Esmati et (2016) (13)	75	ESFT (localized+metastatic)	ND	Definitive (46) Adjuvant (16) Palliative (10)	ND	5 y OS 24% met (+) 21±17m met (-) 75±10 m
Wan et al. (2017) (14)	397	ES of bone and joints 65% <18 y (SEER data)	ND	RT alone 102 pts RT+surgery 86 pts	ND	5 y OS Surgery only 78.4% Surgery+RT 66.9% RT only 47.8%
Sarı et al. (2009) (15)	13	Extraosseos ES (<18 y)	EVAIA (7) VAIA (3) Others (3)	10 pts received surgery	48m	5 y OS 67% (Results for RT not defined)
Kaçmaz et al. 2019 (16)	39	Neoadjuvant RT applied pts	VAIA	CT+RT 28 pts NeoCT±NeoRT 11 pts	37.95m	5 y OS surgery (+) pts 26.1% surgery (-) pts 35.4%
Goyal et al. 2019 (17)	21	Non-met EFSTarisnf from head and neck	VAC/IE St Jude's	Surgery+adj RT 5 pts Definitive RT 16 pts	26.7m	At last fu 12 pts were disease-free 6 pts were alive with disease
Sathamurthy et al. 2020 (18)	65	Extraosseous ES (met and non-met)	VAC/IE (40% of pts)	Adjuvant RT 22 pts Palliative RT 5 pts Definitive RT 2 pts	The follow-up ranged from 1 to 121 months.	36 m OS RT (+) 45% RT(-) 8% Med OS RT (+) 26m RT (-) 5m
Momin et al. 2021 (19)	49	ESFT (curative intent)	VIE+VAC	Neoadj RT+ surgery 5 pts Surgery+adj RT 9 pts Definitive RT 35 pts	18m	Local control with combined surgery and radiotherapy was better than definite radiotherapy, but the difference was statistically insignificant.

Abbreviations: ESFT; Ewing Sarcoma Family Tumors, ND; Not defined, NeoCT; neoadjuvant chemotherapy, NeoRT; neoadjuvant radiotherapy

DISCUSSION

This study evaluated a small group of patients receiving radiotherapy for Ewing sarcoma, primarily in an adjuvant setting. The results of 15 pediatric patients diagnosed with Ewing Sarcoma and who underwent adjuvant RT were evaluated retrospectively. The median follow-up period of the study was 27 (range 11-86) months and within this period, 12 (80%) patients survived. The recurrence observed five patients (33.3%) . The median OS diagnosis of the patients was 27.3 (range 11 to 86.5) months. The overall survival of the patients after RT was median 17.3 (range 4.4-83.9) months. Median LRFS-RT is 14.2 (range 1-83.9). The relationship between LRFS-RT and age (<10 vs. over 10≥ years old) was significant and significantly higher LRFS-RT was observed in the older age. However, the study was conducted in a few patients with a short follow-up period.

Ewing sarcoma is a disease group in which survival increases gradually, thanks to systemic therapy and the development of multimodal treatment schemes. Especially with the development of systemic therapy, the treatment of metastatic disease seems to be the primary factor in the increase in survival in this disease with early metastasis tendency (9,10). Five-year survival rates for patients with ES increased from 36% in 1975-1984 to 56% in 1985-1994. (11). This rate has increased up to 70% with multimodal treatment for non-metastatic cases (12).

No randomized trial evaluates the role of radiotherapy in the curative or adjuvant setting. Most of the data in the literature consist of radiotherapy results obtained from retrospective analyses (Table 1) (7,13-19). Although different chemotherapy schemes and different patient groups were evaluated in these studies, generally, local control and survival rates were reported to be higher in patients who received radiotherapy as a part of multimodal therapy. Our study calculated the median follow-up period as 19 months, and the median survival was 17.9 months.

Table 2. Retrospective Trials for Ewing Sarcoma

It has been shown in previous studies that local control is increased by adjuvant radiotherapy in the presence of microscopic tumors after surgery (20,21). Krasin et al. demonstrated that a negative margin is essential for local failure control. (21). It was shown that not only R0 resection but also the rate of necrosis after chemotherapy is critical for local tumor control (22). Although this factor is not accepted as a general indication for adjuvant radiotherapy, it is effective in different study groups. Although seven patients in this cohort were defined as R0 resection, adjuvant radiotherapy was indicated due to low necrosis rates and suspicion of possible tumor seeding during surgery.

Although the number of patients in this study is limited, it consisted of only patients who received adjuvant RT, making the study important. On the other hand, the patients must be treated with modern radiotherapy techniques.

CONCLUSION

Adjuvant radiotherapy indications and approaches to treating Ewing's sarcoma may differ between clinics. Using modern radiotherapy techniques, it should be determined which patients will benefit from adjuvant radiotherapy.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *Ethics committee approval for the study was obtained from ethics committee no. 1 of Ankara City Hospital.*

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Research Article

Fear of Cancer Recurrence in Women with Breast Cancer: A Cross-Sectional Study after Mastectomy

Meme Kanserli Kadınlarda Kanserin Nüksetme Korkusu: Mastektomi Sonrası Kesitsel Bir Çalışma

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Abstract

Aim: The aim of this study was to determine the fear of cancer recurrence in women with breast cancer after mastectomy.

Material and Methods: Data were collected between March and September 2021 with the Personal Information Form and the Fear of Cancer Recurrence Inventory via social media. The sample consisted of 127 women with breast cancer, who were registered in the general surgery service of a training and research hospital in Turkey, could be reached by phone and had a social media account. Descriptive statistics, independent groups t test, One-Way ANOVA and Mann-Whitney U test analysis were used in the analysis of the data.

Results: It was determined that the Fear of Cancer Recurrence Inventory mean score was 126.12±24.88 and the coping strategies sub-dimension mean score was 30.96±6.00. It was determined that there was a significant difference between the mean score of the Fear of Cancer Recurrence Inventory and the duration of diagnosis, the status of receiving radiotherapy and chemotherapy, the status of experiencing treatment-related side effects, and the status of doing any sports/exercise ($p<0.05$). It was also determined that the average score of Fear of Cancer Recurrence Inventory was higher in women who did not receive radiotherapy and chemotherapy, did not experience treatment-related side effects, and did not do sports/exercise, between 1-12 months of diagnosis time ($p<0.05$).

Conclusion: Health professionals should evaluate the concerns of women with breast cancer and their families about fear of cancer recurrence and help them develop strategies to support their coping.

Keywords: Breast cancer, mastectomy, woman, fear of cancer recurrence

Öz

Amaç: Bu çalışmanın amacı meme kanserli kadınlarda mastektomi sonrası kanserin nüksetme korkusunu belirlemektir.

Materyal ve Metot: Tanımlayıcı ve kesitsel tipteki bu çalışmanın verileri, Kişisel Bilgi Formu ve Kanserin Nüksetme Korkusu Envanteri ile Mart-Eylül 2021 tarihleri arasında sosyal medya aracılığıyla toplanmıştır. Araştırmanın örneklemini, Türkiye'de bir eğitim ve araştırma hastanesinin genel cerrahi servisine kayıtlı, telefonla ulaşılabilen ve sosyal medya hesabı olan 127 meme kanserli kadın oluşturmuştur. Verilerin analizinde tanımlayıcı istatistikler, bağımsız gruplarda t testi, One-Way ANOVA ve Mann-Whitney U testi analizi kullanılmıştır.

Bulgular: Araştırmada Kanserin Nüksetme Korkusu Envanteri puan ortalamasının 126.12±24.88 ve baş etme stratejileri alt boyutu puan ortalamasının 30.96±6.00 olduğu belirlendi. Kanserin Nüksetme Korkusu Envanteri puan ortalamaları ile tanı süresi, radyoterapi ve kemoterapi alma durumu, tedaviye bağlı yan etki yaşama durumu ve herhangi bir spor/egzersiz yapma durumu arasında anlamlı fark olduğu tespit edildi ($p<0.05$). Radyoterapi ve kemoterapi almayan, tedaviye bağlı yan etki yaşamayan, spor/egzersiz yapmayan ve tanı süresi 1-12 ay arasında olan kadınlarda Kanserin Nüksetme Korkusu Envanteri puan ortalamasının daha yüksek olduğu bulundu ($p<0.05$).

Sonuç: Sağlık profesyonelleri meme kanserli kadınların ve ailelerinin kanserin nüksetme korkusuyla ilgili endişelerini değerlendirmeli ve baş etmelerini destekleyecek stratejiler geliştirmelerine yardımcı olmalıdır.

Anahtar Kelimeler: Meme kanseri, mastektomi, kadın, kanserin nüksetme korkusu

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INTRODUCTION

Every year, millions of individuals are diagnosed with cancer (1) and breast cancer is the most common type of cancer in females (2,3). According to Globocan 2020 data published by the International Agency for Research on Cancer (IARC), worldwide, there were 19.3 million cancer cases in 2020, 11.7% of which were recently diagnosed breast cancer cases (4). With 43%, breast cancer ranks first among all cancer types observed in women in Turkey and is seen in 1 out of every 4 women (3). Although breast cancer is very common in women, treatment outcomes can be improved and mortality can be reduced, if it is detected early. Breast cancer can be diagnosed in a short span of time with some early detection and screening methods and treatment can be started in the early period (5,6). It is known that breast cancer survival increases with regular use of early detection and screening methods, and timely and effective treatment opportunities in developed countries (7,8). Psychological problems such as anxiety, depression, irritability, uncertainty about the future, pessimism, helplessness, fear of cancer recurrence, decrease in self-esteem, deterioration of body image and fear of death are observed during the process of diagnosis and treatment of the disease (9).

Fear of Cancer Recurrence (FCR) is defined by women who are diagnosed with breast cancer as "feelings of fear, distress or anxiety stemming from the thought that cancer will return or progress" (10-12). According to studies, FCR is related to the negative perception of the disease, low level social support, thinking of the worst-case scenario, high level of anxiety or stress (13-16), which may adversely affect patients' coping skills, future plans, ability to re-adjust to their lives before the onset of the disease and quality of life (17). The perception of cancer as a life-threatening disease is one of the biggest factors that causes FCR which is defined as the concern that cancer may return or progress in the same part of the body or in another part of the body (9). Cancer patients experiencing FCR express their thoughts in the following manner: "Am I likely to be treated again? If so, will I be able to cope with the side effects? Will I become more dependent on others this time? Will I feel lot of pain and suffer? If it repeats or progresses again, will I die?" (18). When the fear of cancer recurrence increases, it adversely affects patients' ability to seek treatment, their approaches regarding problems and way of coping, problem-solving capacity, self-perceptions, perceptions about their environment and the disease, self-worth and self-esteem, anxiety and anxiety levels, work attendance and quality of life (19). The importance of an individual approach in helping cancer patients better cope with the FCR was emphasized in literature (9,20,21). Identifying patients' FCR status and supporting patients in its management are important elements in providing health care. Many factors need to be addressed in FCR management in cancer patients such as identifying and reducing the degree of anxiety and fear, supporting patients to undertake daily activities and regulating the confusion of roles (22). It is important for nurses to provide a post-treatment FCR evaluation for women diagnosed with breast cancer, to identify associated factors, and to teach and help develop appropriate coping strategies against these fears. Limited number of studies on FCR in women with breast cancer in the international literature (9,11,14,16,20,21) and lack of studies on this subject in the national literature make this research distinctive.

Study questions

1. What is the level of FCR in women with breast cancer after mastectomy?

2. What are the associated factors affecting FCR in women with breast cancer after mastectomy?

MATERIAL AND METHOD

This descriptive and cross-sectional study aimed to determine the FCR experienced by women with breast cancer after mastectomy.

The study was conducted with women with breast cancer who were registered in the general surgery service of a training and research hospital in Turkey. After obtaining the necessary ethical committee approval and institutional permissions, women with breast cancer were contacted by phone.

The universe of the study was composed of all the women with breast cancer registered in the general surgery service of the training and research hospital in Turkey where the study was conducted. Considering that the rate of FCR in women with breast cancer is 36% (23) in the literature, 127 women with breast cancer were included in the study with a 5% margin of error and a 95% confidence level (Z=1.96), assuming the variability in the population was 0.5 (24).

The inclusion criteria were as follows: (i) older than 18 years (ii) volunteered to participate in the study (iii) had mastectomy (iv) literate (v) able to use a smartphone. The exclusion criteria were as follows: (i) had any psychological problems (ii) refused to participate in the study.

Permission was obtained from the Non-Interventional Clinical Research Ethics Committee of a university in Turkey to conduct the study (Decision No: 2021/188), and it was ensured that the study complied with the principles of Helsinki Declaration. First, women with breast cancer were contacted by phone and given preliminary information about the study. Then, they read the informed consent text included in the link that presented the online questionnaire form and were informed about the purpose and rationale of the study. After reading this information, they replied the following question: "Would you like to participate in the study voluntarily?" with a "yes" or "no". The volunteering women who answered "yes" "filled out the online questionnaire. Women with breast cancer were informed that they could withdraw from the study at any time without giving any reason.

Data were collected between March and September 2021 by sharing the online questionnaire form link created by

the researchers using the URL address "surveey.com" with women with breast cancer via WhatsApp. Personal Information Form and Fear of Cancer Recurrence Inventory were used to collect data.

Personal Information Form; The form, developed by the researchers by examining the relevant literature (20,21,23), consists of a total of 15 questions about the socio-demographic and disease characteristics of women with breast cancer.

Fear of Cancer Recurrence Inventory (FCRI); The inventory was developed by Simard and Savard in 2009 to assess cancer patients' FCR (25). The five-point Likert-type scale consists of 42 items and 7 components: Triggers (Items 1-8), Severity (Items 9-17), Psychological Distress (Items 18-21), Functioning Impairment (Items 22-27), Insight (Items 28-30), Reassurance (Items 31-33), and Coping Strategies (Items 34-42). Scale items are scored between 0-4 and there is no reversed item. The total score obtained from the scale is between 0-168. A high score indicates that increased level of fear of recurrence in patients. The Cronbach-alpha value of the study was calculated as be 0.96 by Eyrenci and Berk (2019) in regards to validity and reliability in Turkey and the Cronbach-alpha value of the present study was found to be 0.84 (26).

Statistical analysis

Descriptive statistics were used in the study for continuous variables (mean, standard deviation (SD), while frequency distributions were found for categorical variables. Shapiro-Wilk test, histogram and Q-Q graph were used for normality tests. One-way ANOVA, independent groups t-test and Mann-Whitney U test were used to evaluate the difference between socio-demographic characteristics, independent variables, and mean score of FCRI of women with breast cancer. All statistical analyzes were performed in SPSS v21 (IBM Corp., Armonk, NY, USA). $p<0.05$ was considered significant.

RESULTS

Descriptive characteristics of women with breast cancer showed that the mean age of participants was 50.25±10.69 years, 73.2% were married and had children, 38.6% had a university or higher-level degree, 63.0% were unemployed and 91.3% had social security. Of these women, 42.5% had a diagnosis period of 2-5 years, 72.4% received chemotherapy, 45.7% received radiotherapy, 68.5% experienced treatment-related side effects, 65.4% used medication, 46.5% had another chronic disease and 67.7% of them were not engaged in any sports/exercise (Table 1).

When the difference between the mean/median scores of the FCRI was examined according to the descriptive characteristics of women, a significant difference was found between the FCR and the duration of diagnosis, receiving radiotherapy and chemotherapy, treatment-related side effects, and doing sports/exercise ($p<0.05$).

The result of the post-hoc analysis showed that the difference in the diagnosis period was caused by those between 1-12 months and the mean score of the women in this group was significantly higher than the other two groups ($p<0.05$). It was determined that those who did not receive radiotherapy and chemotherapy, who did not experience treatment-related side effects, and who did not do any sports/exercise had higher FCRI scores. No statistically significant difference was found between FCRI mean/median scores and age, marital status, having children, education status, employment status, social security status, medication status, and having another chronic disease the of FCRI ($p>0.05$) (Table 2).

Table 1. Distributions of descriptive characteristics of women with breast cancer (n=127)

Descriptive characteristics	n	%
*Age (X±SD) 50.25 ±10.69		
Marital status		
Married	93	73.2
Single	34	26.8
Having child(ren)		
Yes	93	73.2
No	34	26.8
Educational level		
Literate	15	11.8
Primary school	15	11.8
Secondary school	48	37.8
University and above	49	38.6
Employment status		
Working	47	37.0
Not working	80	63.0
Social security		
Yes	116	91.3
No	11	8.7
Duration of diagnosis		
1-12 month	49	38.6
2-5 year	54	42.5
6 year and above	24	18.9
Receiving chemotherapy		
Yes	92	72.4
No	35	27.6
Receiving radiotherapy		
Yes	58	45.7
No	69	54.3
Having an experience of treatment-related side effects		
Yes	87	68.5
No	40	31.5
Medication status		
Yes	83	65.4
No	44	34.6
Having another chronic disease		
Yes	59	46.5
No	68	53.5
Any sport/exercise situation		
Yes	41	32.3
No	86	67.7
Total	**127**	**100.0**

*X: Mean; SD: Standart deviation

Table 2. Difference in FCRI mean/median scores of women with breast cancer according to their descriptive characteristics

Variables	n	FCRI		Test	p
Age		X	SD		
18-49	70	128.35	24.79	1.121	0.264*
50 and above	57	123.38	24.93		
Marital status					
Married	93	127.76	23.63	1.229	0.221*
Single	34	121.64	27.89		
Having child(ren)					
Yes	93	127.76	23.63	1.229	0.221*
No	34	121.64	27.89		
Educational level					
Literate	15	143.66	25.26	2.756	0.056**
Primary school	15	119.53	36.86		
Secondary school	48	125.64	21.17		
University and above	49	123.24	22.03		
Employment status					
Working	47	125.46	21.79	0.051	0.951*
Not working	80	126.21	26.61		
Social security					
Yes	116	125.29	24.14	-1.227	0.222*
No	11	134.90	31.72		
Duration of diagnosis					
1-12 month (a)	49	135.46	21.66	8.518	0.000**
2-5 year (b)	54	124.00	22.92		
6 year and above (c)	24	111.83	28.15	a>b.c	
Receiving radiotherapy					
Yes	58	115.65	23.55	-4.697	0.000*
No	69	134.92	22.58		
Having an experience of treatment-related side effects					
Yes	87	121.51	24.31	-3.188	0.002*
No	40	136.15	23.37		
Medication status					
Yes	83	124.48	24.50	-1.023	0.308*
No	44	129.22	25.57		
Having another chronic disease					
Yes	59	123.20	27.17	-1.235	0.219*
No	68	128.66	22.61		
Any sport/exercise situation					
Yes	41	118.34	26.88	-2.484	0.014*
No	86	129.83	23.12		
Receiving chemotherapy		**Median**	**Min Max**		
Yes	92	124.0	58-180	961.500	0.000***
No	35	144.0	75-166		

*t= Independent t test; **F=One-Way ANOVA; ***U=Mann-Whitney U

The study concluded that the FCRI mean score was 126.12±24.88 for the participating women. In the FCRI, women with breast cancer had a mean score of 24.50±6.31 in the Triggers sub-dimension, 27.84±5.55 in the Severity sub-dimension; 12.53±3.72 in Psychological Distress sub-dimension; 30.96±6.00 in the Coping Strategies sub-dimension; 15.23±5.82 in the Functioning Impairment sub-dimension, 7.85±3.16 from the Insight sub-dimension and 7.18±2.90 from the Reassurance sub-dimension (Table 3).

Table 3. FCRI total/sub-dimension mean score of women with breast cancer

Total FCRI and sub-dimensions	X ± SD	Min-Max
Triggers	24.50 ± 6.31	8.00-40.00
Severity	27.84 ± 5.55	11.00-41.00
Psychological distress	12.53 ± 3.72	4.00-20.00
Coping strategies	30.96 ± 6.00	15.00-44.00
Functioning impairment	15.23 ± 5.82	6.00-30.00
Insight	7.85 ± 3.16	3.00-15.00
Reassurance	7.18 ± 2.90	3.00-15.00
Total FCRI	**126.12 ± 24.88**	**58.00-180.00**

DISCUSSION

This study is significant for the national literature for assessing the FCR levels of women with breast cancer after mastectomy and the relevant factors that affect FCR. In addition, this study demonstrates that FCR remains a cause for concern after mastectomy in women with breast cancer.

For most cancer patients, the end of treatment means living with FCR (27). As a matter of fact, women with breast cancer consider FCR as one of the top five problems (14). Findings from this study demonstrated that women with breast cancer experienced this fear in varying degrees. It was found that the mean FCRI score of women was high after mastectomy. Previous studies conducted with cancer patients and/or breast cancer reported that after treatment, patients experienced FCR in varying degrees, from moderate to high (16,21,28,29). In addition, it was reported that receiving the hormonal therapy after primary treatment and hormonal therapy related-physical symptoms were also considered as signs of recurrence of the disease (21,30,31).

The study found that the coping strategies sub-dimension mean scores were close to high levels. The fact that having different roles such as gender, spouse, parent and employee may affect the ability to cope with FCR (12). Interacting with other breast cancer individuals around women with breast cancer and hearing about relapsing patients may affect their coping skills and cause them to experience FCR (16,32). In addition, inadequacy of the perceived social support mechanisms can lead to a decrease in coping levels and trigger FCR (33,34). The results in this study are similar to those found in the literature, and it can be argued that support by health professionals is important for women so that they can cope with physical symptoms, changing roles and daily life activities after mastectomy without anxiety.

A significant difference was found between the mean/median FCRI score of women with breast cancer and the

duration of diagnosis, the status of receiving radiotherapy and chemotherapy, the side effects of the treatment, and the status of doing any sports/exercise. It was determined that the duration of diagnosis ranging from 1-12 months had higher mean FCRI scores. Previous studies reported that patients with a recent diagnosis period had higher FCR levels (15,28). As the duration of diagnosis increases in women with breast cancer, a decrease in FCR level may be observed because anxiety about recurrence continues (11). This can be explained by the fact that the treatment options of breast cancer are quite advanced, diagnosis can be made at an early stage, the postoperative period is improved, and the life expectancy is longer. In addition, it was reported that the increase in the time elapsed after diagnosis could be related to the development of coping strategies by patients and, accordingly, feeling FCR at lower levels (21).

It was concluded that women who did not receive radiotherapy and chemotherapy, did not experience treatment-related side effects, and did not do any sports/exercise had higher mean/median FCRI scores. Although there is no data in the literature to compare with these results, early diagnosis of breast cancer, application of various treatment methods and high success levels may positively affect patients' beliefs about treatment and FCR (34). At the same time, it is reported that the expected survival rates of patients after breast cancer treatment is higher (35). For this reason, it is believed that women who did not receive radiotherapy and chemotherapy and did not experience any side effects related to treatment had higher FCR. Lifestyle change in patients with breast cancer in addition to medical treatment is accepted as an important treatment strategy (36). It is reported that regular daily physical activity reduces comorbidity in breast cancer patients (37). For instance, it was reported that exercise in patients with breast cancer reduced disease-related inflammation and biomarkers, and improved well-being and quality of life (38). In this context, the study predicts that women with breast cancer who do not do regular exercise/sports may have a high FCR because they cannot maintain a healthy lifestyle change.

Limitations

This research has some limitations. First of all, the study was carried out online on social media due to the COVID-19 pandemic. Therefore, the data collection process was interrupted. Second, the study was conducted only with women who have breast cancer registered in the general surgery service of a training and research hospital in Turkey. Third, the different disease stages and treatment modalities of women may have affected their FCR differently.

CONCLUSION

The results of this study demonstrate that FCR is a significant issue for women with breast cancer. Although the severity of FCR may vary, it can continue for a long time after mastectomy, and the coping strategies used by women with breast cancer may be inadequate. In addition, the women who were recently diagnosed, who did not receive radiotherapy and chemotherapy, who did not experience treatment-related side effects, and who did not exercise/sport had a higher level of FCR. Therefore, healthcare professionals, especially nurses, should understand and assess the concerns of women with breast cancer and their families about FCR. In addition, healthcare professionals should support these women and their families in developing strategies to cope with FCR and should inform them about services that provide psychological support.

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Research Article

Subcentimeter Solid Breast Lesions with Suspicious Ultrasonographic and Benign Histopathological Features: Sonographic Characterization

Sonografik Olarak Kuşkulu Olan ve Histopatolojik Olarak Benign Tanı Alan 1 cm'den Küçük Solid Meme Lezyonları: Sonografik Karakterizasyon

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Abstract

Aim: The aim of our study was to reveal the types and sonographic features of the margins in solid lesions less than 10 mm in dimension, considered suspicious for malignancy in breast ultrasonography, and histopathologically diagnosed as benign; and therefore, to recall the features that will facilitate the evaluation of radiology-pathology compatibility after biopsy.

Material and Methods: This study was conducted with 82 women, with BI-RADS 4-5 lesions sonographically, between 2017 and 2020. Lesion size and margins, presence of posterior shadowing and microcalcifications were scanned retrospectively. Lesions were classified according to their margins as smooth-macrolobulated, microlobulated, irregular-indistinct, angular and spiculated.

Results: Histopathologically, the most common benign lesions were fibroadenoma (n=26, 31.7%) and fibrocystic changes (n=15, 18.3%). Sonographically, the mean size of the lesions was 8.96±1.46 mm, and the most common margins were irregular-indistinct in 39%, and smooth-macrolobulated in 30%. In the statistical analysis, the incidence of fibroadenoma was found to be significantly higher in the BI-RADS 4a group compared to the patients in the other pathological diagnosis group (p:0.007).

Conclusion: In this study, it was concluded that the indistinct-irregular, microlobulated and angular margins could also be observed significantly in subcentimeter benign breast lesions, and as the size of the lesion got smaller, it becomes difficult to differentiate the features of the margins; hence they should be evaluated more carefully.

Keywords: Benign breast lesions, BI-RADS, sonographic margin, subcentimeter, ultrasonography

Öz

Amaç: Meme lezyonunun karakterini sonografik olarak değerlendirirken lezyon sınırları en önemli sonografik kriter olarak bilinir. Çalışmamızın amacı, meme ultrasonografi incelemesinde 10 mm ve daha küçük boyutlarda ölçülen ve malignite açısından kuşkulu değerlendirilen, histopatolojik olarak benign tanı alan solid lezyonların tiplerini ve sonografik kenar özelliklerini ortaya koymak; böylece biyopsi sonrası radyoloji-patoloji uyumunu değerlendirmeyi kolaylaştıracak özellikleri anımsamaktır.

Materyal ve Metot: 2017-2020 tarihleri arasında, sonografik olarak BI-RADS 4-5 olarak raporlanan 82 kadın olgu çalışmaya dahil edildi. Kitle boyutları ve kenar özellikleri, kitlede posterior gölgelenme ve mikrokalsifikasyon varlığı retrospektif olarak tarandı. Lezyonlar kenar özelliklerine göre düzgün-makrolobüle, mikrolobüle, düzensiz-belirsiz, açılı ve spiküle olarak gruplandırıldı.

Bulgular: Histopatolojik olarak en sık görülen benign lezyonlar fibroadenom (n=26, %31,7) ve fibrokistik değişiklikler (n=15, %18,3) dir. Lezyonların ortalama sonografik boyutu 8,96±1.46 mm ve sonografik kenar özellikleri %30'unda düzgün-makrolobüle, %12,2'sinde mikrolobüle, %39'unda düzensiz-belirsiz , %15,9'unda açılı ve %2,4'ünde spiküle idi. BI-RADS kategorisine göre lezyonların 48'i (%58,5) 4a, 29'u (%35,4) 4b, 3'ü (%3,7) 4c ve 2'si (%2,4) 5 olarak sınıflandırılmıştır. İstatistiksel analizde ise BI-RADS 4a grubunda fibroadenom olma oranı diğer patolojik tanı grubundaki olgulardan anlamlı düzeyde yüksek bulunmuştur (p:0.007).

Sonuç: Bu çalışma ile 10 mm ve daha küçük benign meme lezyonlarında da kaydadeğer oranda düzensiz-belirsiz, mikrolobüle ve açılı kenar özelliklerinin görülebileceği, lezyon boyutları küçüldükçe kenar özelliklerinin ayrımının zor olduğu ve daha dikkatli değerlendirilmesi gerektiği sonucuna ulaşılmıştır.

Anahtar Kelimeler: Benign meme lezyonları, BI-RADS, sonografik kenar, subsantimetre, ultrasonografi

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INTRODUCTION

Ultrasonography (US) is the most important additional modality today with high sensitivity and complementary to mammography for imaging breast lesions, since it is easily accessible, reproducible, inexpensive, and can be measured in multiple planes (1). US was previously used to distinguish between cystic and solid; however, its spectrum has expanded nowadays to make the distinction between benign and malignant, thanks to the additionally defined sonographic features as well as its internal nature (2).

With the technological advancements in screening programs and imaging, an increasingly important part of newly diagnosed cases of breast cancer consists of women with tumors of 10 mm or smaller (3,4). Small lesions are generally non-palpable, and they are more difficult to analyze with imaging methods compared to large lesions (5). Therefore, it is important to perform the characterization of these lesions accurately in order to increase detection rates of early breast cancers with a good prognosis or to reduce the number of unnecessary biopsies performed for benign lesions.

The margin of the lesion is known as the most important sonographic feature when evaluating the character of the breast lesion. Microlobulated, angular or spiculated margin, presence of microcalcification, prominent hypoechogenicity, posterior shadowing and vertical growth are signs in favor of malignancy, while the ellipsoid shape, macrolobulation, smooth margin, marked hyperechogenicity are considered as benign findings (6,7). On the other hand, it is known that the sonographic features of benign and malignant lesions may overlap.

There are many studies on the sonographic margin features of breast lesions in the literature. However, although there are few magnetic resonance imaging (MRI) studies evaluating subcentimeter breast lesions, there are very few ultrasonography studies describing lesions margin features (8-11). In this study, we aimed to identify the types and sonographic margin features of solid lesions measured as 10 mm and smaller in breast ultrasonography, considered suspicious for malignancy, and histopathologically benign; and to recall the features that will facilitate the evaluation of radiology-pathology compatibility after biopsy.

MATERIAL AND METHOD

This study was planned retrospectively, was checked for compliance with the Helsinki Declaration of Human Rights and was approved by the ethics committee of our hospital before the study (22.03.2021-107/14). The reports of the patients were analyzed, who presented to our breast department between 2017 and 2020 with various indications, who were diagnosed with solid masses of 10 mm or smaller with suspected malignancy in breast US, who underwent core biopsy and/or excision after US-guided stereotaxy. A total of 82 female patients with radiologically suspicious for malignancy but histopathologically diagnosed as benign were included in the study. The diagnosis was made by core needle biopsy in 49 patients, and by US-guided stereotaxy procedure in 19 patients. In 14 patients, surgical excision was performed after stereotaxy in addition to core biopsy due to radiological-clinical-histopathological discordance.

Breast US was performed with a 10-14 MHz linear probe (General Electric Medical Systems; Logic 6, Milwaukee, USA), and core-needle biopsy was performed using a 16 G (gauge) needle by a radiologist with minimum 10 years of experience. US scanning was performed in radial and anti-radial planes, and the longest dimensions of the lesions were measured in millimeters.

Lesions were classified according to the features of the margins specified in the Breast Imaging Reporting and Data System (BI-RADS) atlas as 1) smooth, 2) microlobulated, 3) indistinct-irregular, 4) angular, 5) spiculated (Figures 1-3). Lesions with macrolobulated margins were classified together with the smooth margin group. Findings with suspected malignancy such as microlobulated, indistinct-irregular, angular and spiculated margins were categorized as BI-RADS 4-5 (12). According to our current practice, lesions with suspicious margins in terms of malignancy, lesions with smooth /macrolobulated margins with increased size during follow-up, and lesions with heterogeneous internal structure and vascularity within the mass in doppler examination were considered suspicious, and biopsy and/or stereotaxic marking were performed for these lesions. In addition, the presence of cellular atypia and radiological-clinical-histopathological discordance after core biopsy were accepted as indications for surgical excision. When evaluating axillary lymph nodes, lymph nodes with more than 3 mm asymmetric or diffuse thickening, or obliterated fatty hilus were noted as suspicious for involvement (13).

According to histopathological diagnoses, the lesions were grouped as fibroadenoma, sclerosing adenosis, fibrocystic changes (cysts, adenosis, ductal hyperplasia without atypia, apocrine metaplasia), atypical ductal hyperplasia, intraductal papilloma, fat necrosis, inflammation-mastitis, radial scar, fibrosis and non-specific benign lesions (normal breast tissue, mature fat-connective tissue).

Male patients, patients below 18 years of age, patients whose US examination and pathological diagnosis from a remote site, lesions larger than 10 mm, lesions with intraductal localization, cystic masses and lesions reported as malignant as a result of pathology were not included in the study.

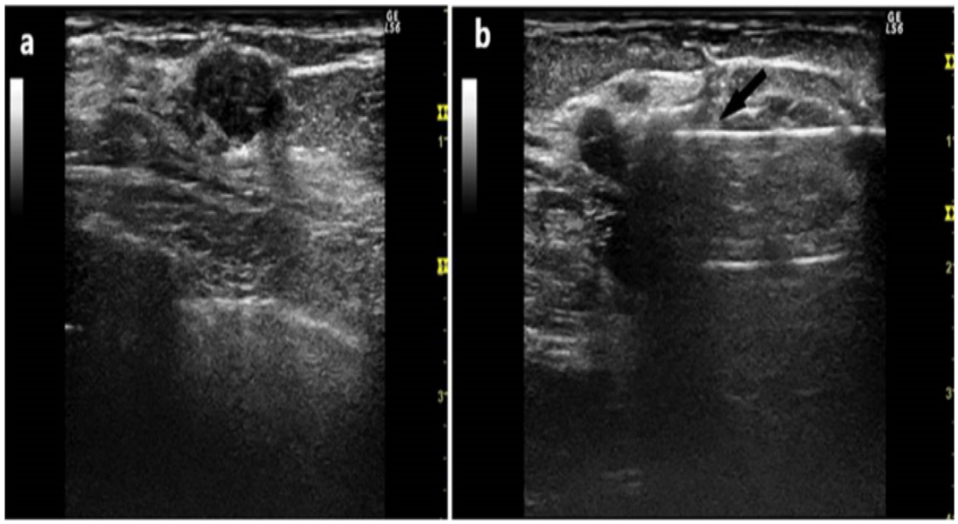

Figure 1. a) A 36-year-old woman with positive family history. US image shows a 10 mm hypoechoic mass with microlobulated margins. Histopathologic diagnosis was fibroadenoma. b) A 33-year-old woman. US image shows a 9.5 mm hypoechoic mass with microlobulated margins. Core needle biopsy image of the patient(arrow). Histopathologic diagnosis was fibrocystic changes

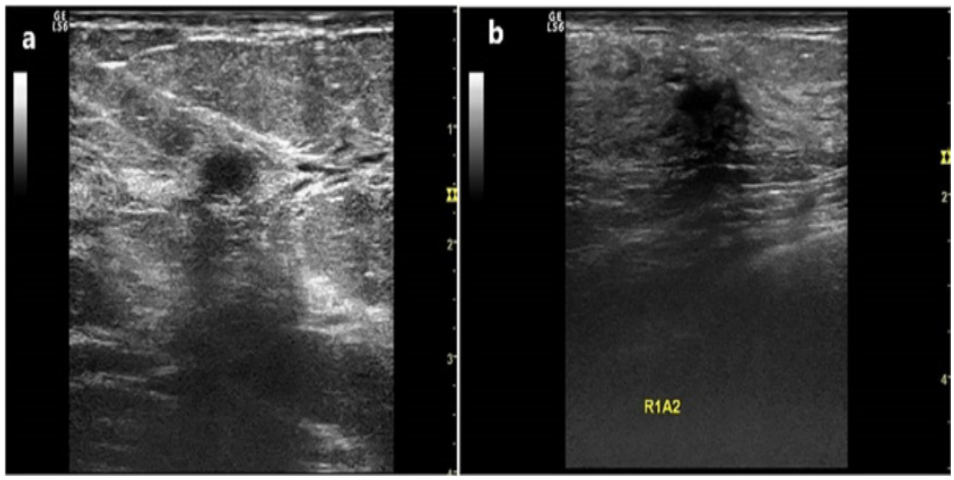

Figure 2. a) A 46-year-old woman. US image shows a 7.5 mm hypoechoic mass with indistinct-irregular margins. Histopathologic diagnosis was intraductal papilloma. b) A 68-year-old woman with positive family history. US image shows a 10 mm hypoechoic mass with indistinct-irregular margins and posterior acoustic shadowing. Histopathologic diagnosis was fibrosis

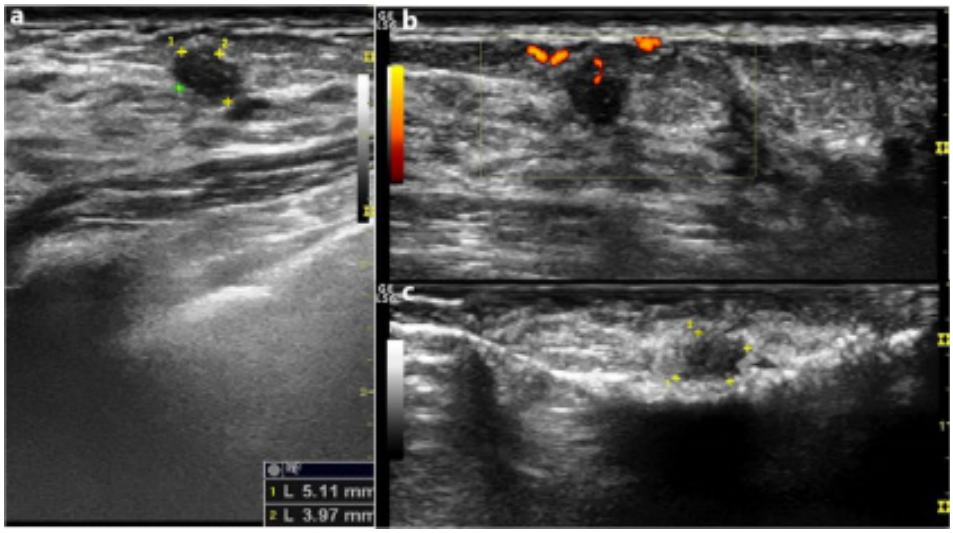

Figure 3. A 42-year-old woman with positive family history a) US image shows a 5 mm hypoechoic mass with angular margins. b) Color doppler shows vascularity within the mass. c) US image of the specimen following stereotaxis. Histopathologic diagnosis was fibrocystic changes.

Statistical analysis

In the evaluation of the findings obtained in the study, statistical analyses were performed using the IBM SPSS Statistics 22 (SPSS IBM, Turkey) software. In the study, measurements were performed as mean, standard deviation, median and frequency in the evaluation of descriptive statistics. Three and multiple groups with non-normal distribution were compared using the Kruskal-Wallis test, and the Chi-square test and Fisher Freeman Halton tests were used for the comparison of categorical data. Significance was evaluated at $p<0.05$.

RESULTS

In the study, 82 breast lesions in 82 women with range between 27 and 69 years (mean 46.87±10.13 years) were evaluated. The lesions were in the right breast in 45 of the patients, and in the left breast in 37 patients. The most common localization was the upper outer quadrant (53.7%). Demographic data of the patients were presented in detail in Table 1.

Histopathologically, the most common benign lesions were fibroadenoma (n=26, 31.7%) and fibrocystic changes (n=15, 18.3%). The proportion of the remaining pathological diagnosis groups was smaller than 10%, and 7 patients (8.5%) were classified as "non-specific" (Table 1).

Table 1. Distribution of demographic parameters

	Mean±SD	**Min-Max**
Age (years)	**46.87±10.13**	**27-69**
		n (%)
Side	Right	45 (54.9%)
	Left	37 (45.1%)
Family history	No	61 (74.4%)
	Yes	21 (25.6%)
Biopsy procedures	US-guided core needle	49 (59.8%)
	US-guided stereotaxis	19 (23.2%)
	US-guided core needle+ stereotaxis	14 (17.1%)
Histopathological diagnoses	Fibroadenoma	26 (31.7%)
	Sclerosing adenosis	7 (8.5%)
	Fibrocystic changes	15 (18. 3%)
	Inflammation-mastitis	5 (6.1%)
	Intraductal papilloma	7 (8.5%)
	Fibrosis	4 (4.9%)
	Atypical ductal hyperplasia	2 (2.4%)
	Fat necrosis	6 (7.3%)
	Radial scar	3 (3.7%)
	Non-specific	7 (8.5%)

In the ultrasonography, margins of the lesions were smooth-macrolobulated in 30%, microlobulated in 12.2%, indistinct-irregular in 39%, angular in 15.9%, and spiculated in 2.4% (Table 2). The majority of smooth-macrolobulated (13/25) and microlobulated (5/10) lesions were diagnosed with "fibroadenoma", the majority of lesions with indistinct-irregular (9/32) margins were diagnosed with "fibrocystic change". Two lesions with spiculated margins were diagnosed as "radial scar". However, no statistically significant difference was found between the pathological diagnosis groups in terms of US findings such as the margins of the lesions, the presence of microcalcifications and posterior shadowing (p1:0.088, p2:1.000 and p3:0.063, respectively) (Table 3). No significant difference was found between the pathological diagnosis groups in terms of patient age, lesion size and presence of suspicious axillary lymph nodes (p1:0.239, p2:0.369 and p3:0.073, respectively).

According to the BI-RADS category, 48 (58.5%) lesions were classified as 4a, 29 (35.4%) lesions were classified as 4b, 3 (3.7%) were classified as 4c, and 2 (2.4%) were classified as 5. The pathological diagnosis of the lesions according to BI-RADS classification was presented in Table 4. In the statistical analysis, the incidence of fibroadenoma was found to be significantly higher in the BI-RADS 4a group compared to the patients in the other pathological diagnosis group (p:0.007).

Table 2. Distribution of sonographic findings

	Min-Max	Mean±SD(medyan)
Sonographic tumor size (mm)	**5-10**	**8.96±1.46 (10)**
		n (%)
Sonographic margin	Smooth-macrolobulated	25 (30.5%)
	Microlobulated	10 (12.2%)
	Indistinct-irregular	32 (39%)
	Angular	13 (15.9%)
	Spiculated	2 (2.4%)
Microcalcification	No	77 (93.9%)
	Yes	5(6.1%)
Acoustic shadowing	No	76 (92.7%)
	Yes	6(7.3%)
Suspicious axillary	No	76 (92.7%)
lymph node	Yes	6 (7.3%)
BI-RADS score	4[a]	48 (58.5%)
	4[b]	29(35.4%)
	4[c]	3 (3.7%)
	5	2 (2.4%)

Table 3. Sonographic findings of lesions according to pathological diagnosis groups

Histopathological diagnoses	Sonographic margin					Microcalcification	Acoustic shadowing
	Circumscribed macrolobulated	Microlobulated	Indistinct irregular	Angular	Spiculated		
Fibroadenoma	13 (50%)	5 (19.2%)	6 (23.1%)	2 (7.7%)	0 (0%)	3 (11.5%)	0 (0%)
Sclerosing adenosis	2 (28.6%)	0 (0%)	3 (42.9%)	2 (28.6%)	0 (0%)	1 (14.3%)	1 (14.3%)
Fibrocystic changes	2 (13.3%)	1 (6.7%)	9 (60%)	3 (20%)	0 (0%)	1 (6.7%)	2 (13.3%)
Inflammation-mastitis	2 (40%)	1 (20%)	2 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Intraductal papilloma	1 (14.3%)	1 (14.3%)	3 (42.9%)	2 (28.6%)	0 (0%)	0 (0%)	1 (14.3%)
Fibrosis	2 (50%)	0 (0%)	2 (50%)	0 (0%)	0 (0%)	0 (0%)	2 (50%)
Atypical ductal hyperplasia	0 (0%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)
Fat necrosis	0 (0%)	1 (16.7%)	4 (66.7%)	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)
Radial scar	0 (0%)	0 (0%)	1 (33.3%)	0 (0%)	2 (66.7%)	0 (0%)	0 (0%)
Non-specific	3 (42.9%)	1 (14.3%)	2 (28.6%)	1 (14.3%)	0 (0%)	0 (0%)	0 (0%)
P*	**0.088**					**1.000**	**0.063**

Data is given as the number (n) and percentage (%) of the patients. *: Fisher Freeman Halton Test p<0.05

Table 4. Distribution of lesions in BI-RADS according to pathological diagnosis groups

Histopathological diagnoses	BI-RADS classification			
	4a	4b	4c	5
Fibroadenoma (26)	20 (76.9%)	6(23.1%)	0 (0%)	0 (0%)
Sclerosing adenosis (7)	2(28.6%)	5(71.4%)	0 (0%)	0 (0%)
Fibrocystic changes (17)	8(53.3%)	6 (40%)	1(6.7%)	0 (0%)
Inflammation-mastitis (5))	3 (60%)	2 (40%)	0 (0%)	0 (0%)
Intraductal papilloma (7)	3 (42.9%)	4 (57.1%)	0 (0%)	0 (0%)
Fibrosis (4)	2 (50%)	2 (50%)	0 (0%)	0 (0%)
Atypical ductal hyperplasia (2)	2 (100%)	0 (0%)	0 (0%)	0 (0%)
Fat necrosis (6)	2 (33.3%)	3 (50%)	1 (6.7%)	0 (0%)
Radial scar (3)	0 (0%)	0 (0%)	1 (33.3%)	2 (66.7%)
Non-specific (7)	6 (85.7%)	1 (14.3%)	0 (0%)	0 (0%)
Total (82)	48 (58.5%)	29(35.4%)	3 (3.7%)	2 (2.4%)

DISCUSSION

With the increased use of ultrasonography in routine breast imaging, the BI-RADS system recommended by the American College of Radiology (ACR) has been widely used in order to assess the morphology of the lesions and standardize the terminology of reporting. According to BI-RADS-US lexicon, category 3 assessment represents <2% likelihood of malignancy, while category 5 assessment represents ≥95% likelihood of malignancy. Category 4 represents the wide range of 2-94%. For this reason, category 4 is reported by classifying as 4a (2-10%, low risk), 4b (10-50%, moderate risk) and 4c (50-94%, high risk) in our department, as in many centers.

In our study, the most common benign breast lesion was fibroadenoma. Most of our cases were categorized as 4a, and the incidence of 'fibroadenoma' was found to be statistically high in group 4a. Although 50% of fibroadenomas have smooth-macrolobulated margins, we found that indistinct- irregular margins were the most common type. The least common sonographic findings were the spiculated margin, microcalcification, posterior shadowing and the presence of suspicious axillary lymph nodes.

Solid breast lesions can be classified as benign, intermediate and malignant. Spiculated, angular or microlobuled margins, microcalcifications, marked hypoechogenicity, posterior shadowing and vertical growth have been reported to be highly predictive of malignancy (14). Ellipsoid shape, well-defined margins and the presence of macrolobulation are accepted as predictive features for benign lesions (15). Rahbar et al. demonstrated that the most predictive findings for benign lesions were smooth or macrolobulated margins, rounded or ellipsoid shapes with low inter-observer variability and high rates (16).

Elverici et al. reported the mean lesion size as 10.9±5.57 mm among BI-RADS 4 non-palpable breast lesions in their ultrasonography study (11). They found that 22% of benign lesions were well-circumscribed, 25% had indeterminate borders, 47% had microlobulated, and 7% had angular margins. They recommended that these margins should not be considered as significant signs of malignancy in patients with BI-RADS 4 lesions, especially in oval and small lesions, since microlobulated, indistinct and angular margins were difficult to distinguish.

In our study, 39% of benign lesions were found to have indistinct-irregular margins, 15.9% had angular margins, and 12% microlobulated margins, while 30% of them had smooth-macrolobulated margins. Although the rate of having smooth margins is expected to be high in benign lesions, the indistinct, microlobulated and angular margin characteristics were also detected in benign lesions at remarkable rates, as in our study and the study by Elverici. We believe that as the size of the lesion gets smaller, it becomes difficult to differentiate the margins from from each other, the interobserver variability increases and the experience the experience of the radiologist are effective factors in determining the characteristics of the margins.

In another study that was conducted with patients, who were reported as category 4 by ultrasonography, were diagnosed as benign, and had a mean lesion size of 15 mm, the most common diagnoses were fibroadenoma (38%), sclerosing adenosis (18%) and fibrocystic changes (14%) (17). They described the most common features of margins were indistinct and microlobulated in fibroadenomas, irregular-indistinct margins in sclerosing adenosis, and microlobulated margin and posterior shadowing in fibrocystic changes. On the contrary, we found the most common features of margins as smooth-macrolobulated margins in fibroadenomas, and as indistinct-irregular margins in fibrocystic changes. The indistinct-irregular margin was mostly present in the diagnosis group of fibrocystic diseases; however, we did not find a statistically significant difference between the diagnostic groups.

In our study, among the BI-RADS groups with a higher probability of malignancy, there were 3 patients with category 4c and 2 patients with category 5. In the two patients with category 5, the lesions were described as spiculated margin; however, there were no findings of microcalcification and posterior shadowing. Indistinct-irregular margins were observed in 3 patients in category 4c, and posterior shadowing was observed in 1 patient; and none of them had microcalcifications. In these 5 patients, excision was performed following core biopsy due to radiological-pathological discordance. Two patients with pathological diagnoses of category 5 were reported as radial scar, and 3 patients in category 4c were reported as radial scar, fat necrosis and fibrocystic changes. Since imaging findings of radial scar are in the form of spiculated lesions and structural distortions, it is not possible to distinguish it from cancer by imaging. Fat necrosis is a benign lesion with a spectrum of symptoms ranging from a simple fat cyst to a mass lesion with irregular borders, and it cannot be distinguished from cancer when irregularly border. As in our patients, malignancy should be excluded in these lesions with biopsy. In this study, since the spiculated margins were seen in very few benign lesions and the presence rates of microcalcification and posterior shadowing were low, we believe that these findings are more predictive of malignancy, as mentioned in the literature.

This study has several limitations. First of all, the features of the margins, the presence of microcalcification and posterior shadowing were recorded from the reports due to the retrospective design of the study. Normally, the characteristics of the lesions can be evaluated in more detail with real-time US. Second, we were not able to use the findings of shape, orientation, vascularity and elasticity, which were mentioned in the last version of the BI-RADS atlas, since these data were not reported together in all reports. Other limitations are the inability to analyze interobserver and intra-observer variability due to the

retrospective design of our study, and the small number of cases in some subgroups such as BI-RADS 4c-5.

CONCLUSION

In this study, it was concluded that the possibility of fibroadenoma was higher in lesions defined as BI-RADS 4a, and half of these lesions had smooth-macrolobulated margins. Indistinct-irregular, microlobulated and angular margin features can also be observed significantly in benign lesions, and as the size of the lesion gets smaller, it becomes difficult to distinguish the margin features ; therefore they should be evaluated more carefully.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *This study was planned retrospectively, was checked for compliance with the Helsinki Declaration of Human Rights and was approved by the ethics committee of our hospital before the study (22.03.2021-107/14).*

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Research Article

Does Vitamin D Status Alter the Severity af Preeclampsia? A Single-Center Case-Control Study

D Vitamini Seviyesi Preeklampsinin Şiddetini Değiştirir mi? Tek Merkezli Vaka Kontrol Çalışması

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Abstract

Aim: We aimed to investigate the association between vitamin D deficiency and severity of preeclampsia.
Material and Methods: We conducted a case-control study aiming to evaluate vitamin D serum levels in patients with preeclampsia(PE), severe preeclampsia, eclampsia and HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets). Total number of 69 patients between the ages of 18 and 40 either had a spontaneous vaginal delivery or C-section were included in the study.
Results: The demographic data of the patients were similar, and age was higher in severe PE than in the other groups. When body mass index (BMI) was evaluated, the average BMI of the patients in the severe PE group was found to be significantly higher than PE and similar to the other groups. The average vitamin D levels of all groups was 8.75±3.5 and the mean of severe PE was 6.69±3, which was significantly lower than the other groups. The average vitamin D level in PE was 10.99±2.91, and it was higher than all groups and was significantly higher than patients with severe PE and HELLP syndrome.
Conclusion: We think that there is a significant relationship between the severity of hypertensive disorders that begin during pregnancy and the degree of vitamin D deficiency. We think that the control of vitamin D level and its addition to the treatment will positively affect the course of the disease in order to prevent hypertensive disorders and reduce the severity of disease.

Keywords: Pregnancy, pre-eclampsia, hypertension, vitamin D

Öz

Amaç: D vitamini eksikliği ile preeklampsinin şiddeti arasındaki ilişkiyi araştırmayı amaçladık.
Materyal Metot: Preeklampsi(PE), şiddetli preeklampsi, eklampsi ve HELLP sendromu (Hemoliz, Yüksek Karaciğer enzimleri, Düşük Trombosit) hastalarında D vitamini serum düzeylerini değerlendirmeyi amaçlayan bir vaka-kontrol çalışması gerçekleştirdik. 18-40 yaşları arasında spontan vajinal doğum veya sezaryen olan toplam 69 hasta çalışmaya dahil edildi.
Bulgular: Hstaların demografik verileri benzer olup şiddetli PE de yaş diğer gruplardan yüksek olarak bulundu. BMI değerlendirildiğinde şiddetli PE de hafif pe ye göre anlamlı olarak yüksek olup diğer gruplarla benzer bulundu. Tüm grupların d vit değeri ortalama 8,75±3,5 olup şiddetli PEi nin ortalaması 6,69±3 olup diğer gruplara göre anlamlı olarak düşük bulundu. Hafif PE de d vitamini seviyesi ortalama 10,99±2.91 olup tüm gruplardan yüksek olup.şiddetli PE ve HELLP sendromlu hastalara göre anlamlı olarak yüksek bulundu.
Sonuç: Gebelikte yeni başlayan hipertansif bozuklukların şiddeti ile D vitamini eksikliği derecesi arasında anlamlı bir ilişki olduğunu düşünmekteyiz. Bunları önlemek ve şiddetini azaltmak içim d vitamini seviyesinin kontrolü ve tedaviye eklenmesinin hastalık seyrini olumlu etkileyeceğini düşünmekteyiz.

Anahtar Kelimeler: Gebelik, preeklampsi, hipertansiyon, vitamin D

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INTRODUCTION

Considering the increased consumption vitamin D deficiency is very common during pregnancy and especially during breastfeeding (1) As defined by Endocrine Society level of 25(OH)D below 20ng / ml is vitamin D insufficiency and levels between 21-29ng / ml are Vitamin D deficiency. (2) Vitamin D deficiency is known to have an association with any poor pregnancy consequences including preeclampsia gestational diabetes, preterm birth and low birth weight in newborns (3-5).

Hypertensive disorders of pregnancy including PE and eclampsia cause 14% of maternal deaths (1). PE presents with new-onset hypertension after 20 weeks of pregnancy and often proteinuria in the mother, and a variety of symptoms which can progress to multi-organ dysfunction. The pathogenesis of PE is still debated. It is thought that due to the placental development abnormalities, the maternal inflammatory system gets activated causing the oxidative stress (6). Having an anti-inflammatory effect vitamin D level was investigated in new-onset hypertensive disorders during pregnancy

We aimed to evaluate the relationship between vitamin D deficiency and the severity of pregnancy-related hypertension.

MATERIAL AND METHOD

A total of 69 consecutive patients ages between 18-40 diagnosed with preeclampsia, severe preeclampsia, eclampsia and Hellp syndrome according to the ACOG criteria and followed in the secondary intensive care unit of our obstetrics and gynecology clinic within a 6-month period (January-June 2020) were included in the study. Exclusion criteria were different ethnic origin and skin color, PE diagnosis in previous pregnancies, having chronic hypertension, diabetes melitus, Lupus and other known serious systemic diseases, multiple pregnancy, history of vitamin D replacement intake and not wanting to participate in the study. This study was approved by the research and ethics committee in Istanbul Training and Research Hospital, written informed consent was obtained from all women recruited into the study and conducted in accordance with the declaration of Helsinki.

PE patients were classified as PE and PE with severe features according to ACOG criteria. Group 1 (G1) was PE; Group 2 (G2) PE with severe features. The patients diagnosed with eclampsia were classified as G3, and the patients diagnosed with HELLP as G4.

Age, weight, height, body mass index (BMI) and blood pressure values of the patients were recorded. History of seizure, neurological findings and additional complaints like epigastric pain, abdominal tenderness were questioned and recorded. Liver enzymes (Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Lactate dehydrogenase (LDH), hemoglobin (HB), hematocrit (HCT), platelet count (PLT) , urea, creatinine values and proteinuria levels tested with protein urine dipstick test were evaluated. Negative for urinary proteinuria =<15mg/dl, trace =15-30mg/dL, 1+= 30-100mg/dL, 2+=100-300mg/dL, 3+=300-100 mg/dL and 4+=›1000mg/dL (7).

Venous blood samples were taken from the patients and 25(OH) D3 levels were measured by spectrometry. A 25(OH) level below 20ng/ml was defined as vitamin D insufficiency, between 21-29ng/ml as vitamin D deficiency, and values above 30 ng/ml as normal (2).

Statistical analysis

SPSS version 20 (SPSS inc., MA, USA) package program was used for the statistical evaluation of the data. Continuous variables were given as mean and standard deviation. The Shapiro Wilk test was used to evaluate whether the data were compatible with the normal distribution. One-way ANOVA or Kruskal-Wallis test was used for statistical evaluation between groups. LSD test was used for post-hoc analysis and for all evaluations $P<0.05$ value was considered statistically significant.

RESULTS

The demographic data of the patients were similar and it was observed that the average age in Group 2 was higher than the other groups. BMI values in Group 2 were significantly higher than Group 1 and were found similar to other groups. Gravidity and parity were similar in all groups. Average gestational age was found to be statistically lower in Group 2 than in Groups 1 and 4 (Table 1).

The systolic and diastolic blood pressure measurements were found to be significantly lower in Group 1 compared to the other groups and measurements in Group 3 were found to be higher than the other groups (Table 2). Urinary dipstick values were simiar in Group 1 and 3 and lower than Group 2 and 4. HB and HCT values were lower in Group 2 than Group 3, and they were similar to the other groups. In Group 4 PLT, AST, ALT, LDH values were significantly lower compared to the other groups while these values were similar in the other groups.

Neurological findings were similar in Groups 2 and 3, and significantly more neurological findings were observed in patients in Groups 2 and 3 compared to Groups 1 and 4. In Group 4, the complaint of abdominal pain was significantly higher than in other groups, and it was found to be the least in Groups 1 and 2 (Table 2).

The average vitamin D levels of all groups were found to be 8.75±3.5. The average level of vitamin D of Group 2 was 6.69±3, significantly lower than the other groups while the average level of Group 1 was 10.99±2.91 and found to be significantly higher than Groups 2 and 4 (Table 2).

The average level of vitamin D in Group 4 was 6.8±1.3, similar to Group 2, but significantly lower than the other groups. In addition, a significant correlation was observed between serum vitamin D levels and disease severity ($r=0.598$, $p<0.001$) (Figure 1).

Table 1. Characteristic data of the patients

Parameter	Preeclampsia (n=32)	Severe Preeclampsia (n=29)	Eclampsia (n=3)	HELLP (n=5)	P value ANOVA
Age, Years	26.88±5	29.45±6	31±5	26.4±2	0.249
BMI, kg/m^2	29.15±4	32.83±9	28.33±1	29.20±2	0.100*
Gravidity, n	1.9±0.8	2.2±1.2	2.3±1.1	1.6±0.5	0.504
Parity, n	0.8±0.7	1.8±1.1	1±0.5	0.6±0.9	0.657
Pregnancy Duration, Weeks	33.45±2.9	30.98±3.8	32.97±2.1	34.62±0.7	0.016*.#

*=p<0.05 between group 1 vs group 2, # =p<0.05 between group 2 vs group 4

Table 2. Clinical and laboratory data

Parameter	Preeclampsia (n = 32)	Severe Preeclampsia (n = 29)	Eclampsia (n = 3)	HELLP (n = 5)	P value ANOVA
SAB	157.8±9.4	181.3±18.1	190.0±17.3	186.2±22.9	<0.001
DAB	88.8±5.5	108.0±10.0	123.3±24.6	105.0±23.1	<0.001
Protein urine dipstick	2.5±0.5	2.7±0.4	2.3±0.5	3.0±0.1	0.031∞*
HB	10.3±1.0	10.2±1.5	11.9±1.2	11.5±1.6	0.063°
HCT	31.5±3.4	31.1±3.9	36.0±3.8	34.5±4.4	0.065°
PLT	187.4±96.0	192.2±114.5	156.6±40.4	73.4±21.6	0.106∞
AST	51.8±30.9	71.2±78.3	42.0±5.1	482.2±378.9	<0.001
ALT	54.7±33.6	72.7±59.1	55.0±8.6	619.2±598.4	<0.001
LDH	357.2±101.7	402.9±188.7	367.0±1.7	48.3±2.8	<0.001
URE	46.9±12.9	42.6±12.2	48.3±2.8	45.6±9.9	0.559
KREATİN	0.7±0.2	0.8±0.4	0.9±0.2	0.8±0.3	0.864
Neurological findings	0.2±0.5	1.3±0.7	1.3±0.5	0.4±0.5	<0.001
Seizure	0	0	0,3±0.5	0	<0.001
Epigastric pain	0	0	0.6±0.5	0.4±0.5	<0.001
Vitamin D	10.9±2.9	6.6±3.0	8.2±2.2	6.7±1.3	<0.001

*=p<0.05 between group 1 vs group 2, &=between group 2 vs group 3, ∞between group 1 vs group 4, #=p<0.05 between group 2 vs group 4,°= between group 1 vs group 3 .

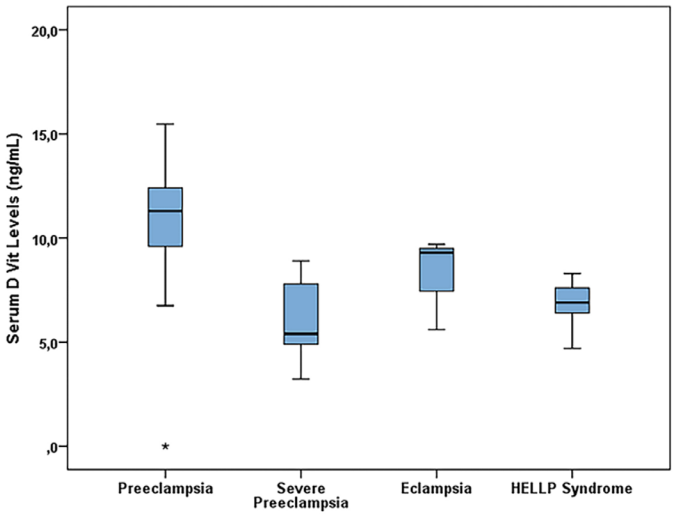

Figure 1. Relationship between vitamin D level and severity of preeclampsia

DISCUSSION

In our study, we concluded that there is a relationship between vitamin D deficiency and the severity of preeclampsia. The average vitamin D level of all groups was 8.75±3.5 which can be classified as deficient. The average of vitamin D values in patients with severe preeclampsia was 6.69±3, which was significantly lower than the other 3 groups.

Many studies have been conducted to determine the maternal risk factors of preeclampsia in pregnant women and to determine the maternal and perinatal effects associated with preeclampsia. Some maternal conditions such as advanced maternal age, obesity, diabetes mellitus, chronic hypertension, antiphospholipid syndrome, chronic kidney disease and systemic lupus erythematosus are known to cause an increased risk of preeclampsia (8,9).

Studies emphasize that prognosis of preeclampsia is negatively affected in elderly patients. English et al showed that effective management of preeclampsia is better achieved in younger patients (10). Similarly, in our study, the mean age of patients with severe PE and eclampsia was found to be higher than the other groups. Nulliparity is thought to be the most common predisposing factor

for preeclampsia, but its cause is not entirely clear (11). Similarly, in our study, gravidity was lower in PE and HELLP patients and higher in eclampsia and severe PE. Preeclampsia can be seen in 4.7% of all pregnancies. Of the PE cases, 47% are nonsevere or unspecified preeclampsia, 37% preeclampsia with severe features/ HELLP, 1.4% eclampsia and 15% superimposed preeclampsia (12,13).

In our study, we evaluated HELLP and severe preeclampsia in different groups and excluded superimposed preeclampsia. The incidence of PE was 46.37%, severe PE 42.02%, eclampsia 4.34% and HELLP 7.24%.

Approximately 25% of severe hypertension and / or one or more of nonspecific symptoms occur in PE. These include persistent or severe headache, visual symptoms, upper abdomen, retrosternal or epigastric pain, mental status change, new onset shortness of breath, orthopnea. In our study, as nonspecific symptoms, headache was recorded in 21%, visual complaints in 18.8%, and abdominal pain in 5.7% of the patients.

The prevalence of vitamin D deficiency in the Turkish population was found to be 51.8% (14). Factors affecting vitamin D levels can be listed as ethnicity, skin color, season, dressing style, age, gender and place of residence (15). In our study, we aimed to exclude these factors by excluding pregnants with different ethnic origin and skin color from the study and including those living in the same region under the same seasonal conditions. All of the patients in the study were living in the Istanbul region witk latitude 41 N 0 and longitude 28 E 58 and were hospitalized in the 6-month period between January and June.

Vitamin D deficiency is also common in women of reproductive age and pregnant women. Maternal vitamin D metabolism changes during pregnancy and this leads to widespread vitamin D deficiency among pregnant women (16,17). Vitamin deficiency is a common problem in Turkey. In a study conducted by Alagöl et al in İstanbul with childbearing age women, vitamin D levels found low in 66,6% of pregnant women (18). In our study, the fact that our patient group consisted of all pregnant women with complicated pregnancy outcomes caused a difference in results. Vitamin D deficiency was recorded in all patients in all groups, and the average vitamin D value was calculated as 8.75±3.5ng / dl.

Vitamin D deficiency may cause poor consequences in pregnant women, including PE, gestational diabetes, and low birth weight in the newborn, and preterm delivery (4). Cordero et al concluded in a meta-analysis in which they examined a total of 55 studies and concluded that vitamin D insufficiency and deficiency were associated with a higher risk of developing preeclampsia (19). Similarly, Serrano Diaz emphasized in their meta-analysis that the preeclampsia prevalence increases as the vitamin D level decreases (20). In a study conducted by Gala et al. it was found that vitamin D levels were low in women who developed severe and early-onset preeclampsia, and vitamin D supplementation had a protective effect against recurrent PE (21).

As a result of the studies, it has been determined that the risk of preeclampsia / eclampsia increases in cases where 25 (OH)-D vitamin falls below 10ng/ml (severe deficiency). For example, in a study conducted in the USA with preganant women in the 15th-20th weeks of gestation, the risk of severe preeclampsia was found 5.41 times higher in pregnant women with insufficient 25 (OH)-D level compared to the control group with the normal level vitamin D (22) In our study, vitamin D value was low in all groups with an average of 8.75±3.5, and there was insufficiency.

Similarly, vitamin D level was found to be significantly lower in the severe PE group. As a result, we came to the conclusion that vitamin D level was correlated with disease severity.

In addition to other factors, overweight during pregnancy causes a lower vitamin D level (23). In our study, it was observed that the vitamin D level was low in Group 2, which had the highest BMI average.

Vitamin D has many effects in the body and also has effects on hematopoietic cells, monocytes, lymphocytes and various precursor cells (24). In their study, Shin et al. emphasized that individuals with vitamin D deficiency may have varying degrees and types of anemias depending on gender (25). In our study, the effect on gender could not be evaluated and the average HB value in severe preeclampsia patients was 10.47 and lower compared to other groups. We think that it may be associated with vitamin D deficiency as a result of nutritional deficiency.

CONCLUSION

We think that there is a significant association between the severity of preeclampsia and low vitamin D level during pregnancy. We think that vitamin D monitoring and replacement is important in the follow-up of pregnancy and in the course of pregnancy-related hypertensive disorders.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *This study was approved by the research and ethics committee in Istanbul Training and Research Hospital, written informed consent was obtained from all women recruited into the study and conducted in accordance with the declaration of Helsinki. (Decision No: 2466).*

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Research Article

Investigation of Perceived Loneliness and Death Anxiety Levels in COVID-19 Patients

COVID-19 Hastalarında Algılanan Yalnızlık ve Ölüm Kaygısı Düzeylerinin İncelenmesi

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Abstract

Aim: The study was conducted to investigation of perceived loneliness and death anxiety levels in COVID-19 patients.
Material and Methods: This cross-sectional and correlational study was carried out in Siirt Education and Research Hospital, located in southeastern Turkey, between January and April 2021. The population of the study consisted of patients who were diagnosed with COVID-19 over the age of 18. The sample of the study consisted of 152 patients who agreed to participate in the study at the time of the study without any sampling selection. The data were collected using an patient information form, the UCLA-Loneliness Scale and the Death Anxiety Scale and evaluated using descriptive statistics, independent samples t test, Mann Whitney-U test, ANOVA, Kruskal-Wallis test, Dunn-Bonferroni post hoc test, and Pearson correlation analysis.
Results: The loneliness and death anxiety mean scores of the patients were 44.26 10.12 and 8.65 3.23, respectively. There was a highly significant positive correlation between their loneliness and death anxiety mean scores ($p<0.05$).
Conclusion: In the study, it was determined that the patients experienced moderate levels of loneliness and death anxiety. It was determined that perceived loneliness increased the fear of death.

Keywords: COVID-19, death anxiety, loneliness

Öz

Amaç: Bu çalışma, COVID-19 tanılı hastalarda algılanan yalnızlık ve ölüm kaygısı düzeylerinin incelenmesi amacıyla yapılmıştır.
Gereç ve Yöntem: Kesitsel ve korelasyonel nitelikte yapılan bu çalışma, Ocak-Nisan 2021 tarihleri arasında Türkiye'nin güneydoğusunda yer alan Siirt Eğitim ve Araştırma Hastanesi'nde gerçekleştirilmiştir. Çalışmanın evrenini, 18 yaş üzeri COVID-19 tanısı konulan hastalar oluşturdu. Çalışmanın örneklemi ise, herhangi örnekleme seçimi yapılmadan çalışmanın yapıldığı tarihlerde çalışmaya katılmayı kabul eden 152 hasta oluşturdu. Veriler, hasta bilgi formu, UCLA-Yalnızlık Ölçeği ve Ölüm Kaygısı Ölçeği kullanılarak toplanmış ve tanımlayıcı istatistikler, bağımsız örneklemler t testi, Mann Whitney-U testi, ANOVA, Kruskal-Wallis testi, Dunn-Bonferroni post hoc testi ve Pearson korelasyon analizi kullanılarak değerlendirildi.
Bulgular: Hastaların yalnızlık ve ölüm kaygısı puan ortalamaları sırasıyla 44.26 10.12 ve 8.65 3.23'tür. Yalnızlık ve ölüm kaygısı puan ortalamaları arasında anlamlı pozitif ilişki olduğu saptanmıştır ($p<0.05$).
Sonuç: Çalışmada, hastaların orta düzeyde yalnızlık ve ölüm kaygısı yaşadığı saptandı. Algılanan yalnızlığın ölüm korkusunu artırdığı belirlendi.

Anahtar Kelimeler: COVID-19, ölüm anksiyetesi, yalnızlık

INTRODUCTION

The corona virus (COVID-19) epidemic, which emerged at the beginning of 2020 and took the whole world under its influence in a short time, caused great concern and fear, while causing millions of people to be infected and many people to die (1,2). This unexpectedly wide spread of the disease and the increased number of COVID-19 patients and deaths cause psychological problems, such as anxiety, loneliness, depression, death anxiety and stress, in patients diagnosed with COVID-19 (1,2).

Unprecedented "social isolation" strategies have been implemented all over the world due to the increased

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number of COVID-19 cases and deaths (3,4). Like many countries such as America, Italy and China (5–7) Turkey has also adopted the quarantine strategy as a containment strategy, and leaving home is only permitted in cases of necessity (8,9). Individuals in social isolation are deprived of most of their usual routine life activities, such as visiting family and friends or attending social gatherings (3,8). As an expected result of social isolation restrictions, people have been forced to be left alone, both to protect vulnerable people and to prevent people diagnosed with COVID-19 from spreading the infection. This extraordinary situation, besides its benefits to public health, caused individuals to be alone (10,11).

Studies have shown that loneliness and social isolation have not equal impacts, but both can have a detrimental effect on health in common and different ways (3,12). Studies have also emphasized that decreased social relations and interactions during the pandemic negatively affects lives, causing them to feel lonely (11,13). Loneliness is an uncomfortable emotional situation where social relations are less than desired or limited, resulting from deprivation and inadequacy. Perceived loneliness has increased among people during the COVID-19 pandemic, worsening their mental health (2,14). A prolonged loneliness has a negative effect on health and well-being (15–17). One study reported that 36% of patients felt alone during the COVID-19 pandemic (18). Death anxiety increases in individuals diagnosed with COVID-19 due to the feeling of loneliness brought by social isolation and the number of symptoms caused by the disease (19,20).

Death anxiety refers to being aware of death attitudes such as negative emotional reactions, fear, grief, restlessness and bereavement (4,20,21). As COVID-19 is an infectious disease, social isolation measures to prevent the infection cause COVID-19 patients to have psychological problems such as death anxiety (2,4,14). Studies of the COVID-19 pandemic have stated that the pandemic took away the feelings of self-control, which is one of the most basic characteristics of individuals, and increased both loneliness and death anxiety by dragging them into uncertainty (12,15). In one study conducted with 175 people to determine their anxiety levels during the pandemic, 85% of the participants had death anxiety (19). Therefore, there is an urgent need to understand the possible psychosocial impact of the COVID-19 pandemic and to identify factors that may reduce its effects on people's psychological health (16,20). Therefore, it is important to determine the levels of loneliness and death anxiety in patients diagnosed with COVID-19 and to take the necessary measures to alleviate the negative mental health consequences in this difficult pandemic process. In this regard, this study was conducted to examine of perceived loneliness and death anxiety levels in COVID-19 patients.

Research questions

What is the level of loneliness in patients diagnosed with COVID-19?

What is the level of death anxiety in patients diagnosed with COVID-19?

Is there a relationship between loneliness and death anxiety in patients diagnosed with COVID-19?

MATERIAL AND METHOD

Study Type

This is a cross-sectional and correlational study.

Study Period and Place

The study was carried out in Siirt Education and Research Hospital, located in southeastern Turkey, between January and April 2021.

Study Population and Sample

The population of the study consists of patients who test positive with COVID-19. The patients who met the inclusion criteria and agreed to participate in the study were recruited. The sample size of the study was calculated using the G-Power 3.1 program. As a result of the power analysis; The sample was found to be sufficient with an effect size of 0.259, a power of 95%, and a margin of error of 0.05. In accordance with the isolation policy in effect in our country at the time the study was conducted, the study was carried out online in order to prevent contamination. The patients who applied to the COVID-19 outpatient clinic for the test were informed about the study face to face and their informed consent was obtained. Contact information of patients who accepted to participate in the study were obtained. Then, the questionnaires were sent online to the patients who tested positive. An online data collection form was prepared using the Google Forms program, and online questionnaires were sent individually via WhatsApp to the patients diagnosed with COVID-19 and kept in isolation for 14 days. Between the study dates, 152 patients who accepted to study and diagnosed with COVID-19 were reached.

Study inclusion criteria

- Being over 18 years old
- Patients who test positive for COVID-19
- Being in a 14-day isolation period
- Having social media accounts to reply to the online form.

Study exclusion criteria

- Being illiterate
- Giving no consent to participate in the study

Data Collection Tools

The data were collected using an online survey form, including an introductory information form, the UCLA-Loneliness Scale and the Death Anxiety Scale and consisting of a total of 44 questions and lasted around 10-

15 minutes.

Introductory Information Form: The form was prepared by the researchers in line with the literature (10,19) and consists of questions about the participants' descriptive features.

Death Anxiety Scale (DAS): The scale was developed by Templer (1970) (22) and adapted into Turkish by Akça and Köse (2008) (23). It consists of 15 items with a yes-no format, where 6 items are scored in reverse. The highest possible score from the scale is 15. The higher the score obtained from the scale, the higher the death anxiety level. A higher scale score refers to greater death anxiety, where 0-4= "low" death anxiety, 5-9="moderate" death anxiety, 10-14="severe" death anxiety, 15="panic level" of death anxiety. The test-retest reliability and reliability coefficient of the scale were 0.79 and 0.75, respectively (23). In this study, the Cronbach's alpha coefficient was found to be 0.74 for the scale.

University California of Los Angeles - Loneliness Scale (UCLA): The scale was developed by Russell et al. (1978) (24), revised by Russell et al (25) and finalized by Russell (1996) (26). It was adapted into Turkish by Demir (1989) (27). In the final version of the scale, half of the items were arranged as positive and the other half as negative. A total of 10 items are scored in reverse. This is a 4-point Likert type, consisting of 20 items to reflect how lonely people describe their lives. The lowest and highest scale scores are 20 and 80, respectively, where 50-64=high loneliness, 35-49 moderate loneliness, and 20-34=low loneliness (27). The Cronbach's alpha internal consistency coefficient of the scale was 0.94 (27). In this study, the Cronbach's Alpha coefficient was found to be 0.84 for the scale.

Ethical Considerations

This study was conducted in accordance with the Helsinki Principles and approved by the Ethics Committee of Siirt University Non-Interventional Clinical Research Ethics Committee (Application date: 31.12.2020 and Approval number:14177). The necessary permissions to conduct the study were obtained from the Ministry of Health and the hospital where the study was conducted. An informed consent was obtained online from all patients included in the study by sending the form containing necessary information about the purpose and method of the study.

Data Evaluation

The data were analyzed using the Statistical Package for Social Science (SPSS 25.0). The Shapiro Wilk test and Q-Q charts were used to test the normality of the data. Parametric tests were used in the normal distribution of the data, and non-parametric tests were used if they were not normally distributed. For those who did not meet the frequency, percentage, mean standard deviation or normality assumption, the ranked scores value was used in descriptive statistics. The data were evaluated using descriptive statistics, independent samples t test, Mann Whitney-U test, Kruskal-Wallis test, One-Way Variance Analysis (ANOVA) and Pearson analysis. Dunn-Bonferroni post hoc test was used among the variables found to be significant as a result of Kruskal-Wallis analysis. A p value less than 0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 26.15±8.67 years. Of them, 67.8% were female, 77.0% were single, 38.8% had bachelor's degree, 20.4 % were workers, 68.4% lived with their parents, 86.2% did not have a chronic disease, 63.8% knew people died from COVID-19 in the immediate vicinity, and 87.5% were not hospitalized due to COVID-19 (Table 1).

Table 1. Characteristic data of the patients

Descriptive Characteristics	n	%
Gender		
Female	103	67.8
Male	49	32.2
Marital Status		
Single	117	77.0
Married	35	23.0
Education		
Primary school	17	11.2
High school	35	23.0
Associate degree	33	21.7
Bachelor's degree	59	38.8
Master's Degree	8	5.3
Occupation		
Unemployed	20	13.2
Worker	31	20.4
Health employee	15	9.9
Officer	20	13.2
Teacher	13	8.6
Housewife	10	6.6
Self-employment	27	17.8
Others	16	10.5
Cohabitants		
Spouse and children	25	16.4
Spouse	10	6.6
Parents	104	68.4
Roommate	8	5.3
Alone	5	3.3
Chronic disease		
Yes	21	13.8
No	131	86.2
Knowing people who died from COVID-19		
Yes	97	63.8
No	55	36.2
Hospitalization due to COVID-19		
Yes	19	12.5
No	133	87.5
Mean Age	$\bar{X}$ **±SD 26.15± 8.67**	

SD: Standard deviation; $\bar{X}$= Mean

The UCLA-LS and DAS scale mean scores of the patients were 44.26±10.12 and 8.65±3.25, respectively (Table 2).

Distribution of patients according to UCLA-LS and DAS levels 53.3% had moderate loneliness and 47.4% had moderate death anxiety (Table 3).

A statistically significant difference was found between the patients' UCLA-LS mean scores according to cohabitants (p=0.04), chronic disease status, death from COVID-19 in their environment, and hospitalization due to COVID-19 (p=0.00). A statistically significant difference was also found between their DAS mean scores according to chronic disease status, death from COVID-19 in their environment, and hospitalization due to COVID-19 (p=0.00). The Dunn-Bonferroni multiple comparison test, which was made to determine which group the difference originated from, suggested a significant difference between those living with their roommates and those living with their parents, where those living with their parents had a higher mean score (p=0.04) (Table 4).

Table 2. Patients' UCLA-LS and DAS Scale Score Levels (n=152)

Scales	Number of Items	Min. - Max. Score	(X) ±SD
UCLA-LS	20	23- 75	44.26±10.12
DAS	15	1- 15	8.65±3.25

SD: Standard deviation; (X)=Mean; Min: Minimum; Max: Maximum; UCLA: University California of Los Angeles- Loneliness Scale; DAS: Death Anxiety Scale

Table 3. Distribution of Patients by UCLA-LS and DAS Levels (n=152)

Scale Score Levels		n	%
UCLA-LS	Low Loneliness (20-34)	27	17.8
	Moderate Loneliness (35-49)	81	53.3
	High Loneliness (50-64)	44	28.9
DAS	Low Death Anxiety (0-4)	17	11.2
	Moderate Death Anxiety (5-9)	72	47.4
	Severe Death Anxiety (10-14)	61	40.1
	Panic Level Death Anxiety (15)	2	1.3

UCLA:University California of Los Angeles- Loneliness Scale; DAS: Death Anxiety Scale

Table 4. Comparison of Patients' UCLA-LS and DAS Scores by Descriptive Characteristics (n=152)

Descriptive Characteristics	UCLA-LS (X+SD) (Mean rank)a	Test and Significance	DAS (X+SD) (Mean rank)a	Test and Significance
Gender				
Female	44.79±10.34	t= 0.92	8.90±3.28	t=1.35
Male	43.16±9.67	p=0.35	8.14±3.14	p=0.17
Marital Status				
Single	45.03±9.66	t=1.71	8.75±3.22	t= 0.65
Married	41.71±11.31	p=0.08	8.34±3.36	p=0.51
Education				
Primary school	44.82±8.95(81.35)x	Z=0.51 p=0.77	9.76±3.15(90.53)x	Z=2.90 p=0.23
High school	47.00±10.99(86.97)x		9.51±3.13(87.50)x	
Associate degree	45.03±7.21(81.12)x		8.45±2.55(73.35)x	
Bachelor's degree	43.54±10.82(72.69)x		8.30±3.56(72.64)x	
Master's Degree	33.37±7.28(29.44)x		6.00±2.50(40.00)x	
Occupation				
Unemployed	45.35±9.84(82.05)x	Z=15.56 p=0.06	8.50±3.76(75.03)x	Z=8.08 p=0.32
Worker	44.41±8.66(75.94)x		8.77±2.85(76.95)x	
Health employee	39.06±8.07(53.17)x		7.20±3.14(57.53)x	
Officer	40.90±6.78(61.58)x		7.70±2.61(63.25)x	
Teacher	42.84±14.85(66.23)x		8.63±4.53(77.12)x	
Housewife	44.60±7.45(81.15)x		10.00±3.36(94.35)x	
Self-employment	46.37±12.92(86.41)x		9.29±2.70(84.48)x	
Others	49.12±10.12(99.91)x		9.37±3.57(86.69)x	
Cohabitants				
Spouse and childrena	41.12±11.49(60.90)x	Z=9.88 p=0.04 d-c*	8.08±3.21(68.36)x	Z=2.78 p=0.59
Spouse b	43.20±11.30(73.00)x		9.00±3.80(79.85)x	
Parentsc	45.59±9.77(82.51)x		8.89±3.19(79.54)x	
Roommated	37.12±6.72(44.00)x		7.12±3.52(58.44)x	
Alonee	46.00±6.04(87.40)x		8.40±3.43(76.10)x	
Chronic disease				
Yes	59.33±7.05	t=9.12	12.23±1.70	U=342.50
No	41.85±8.30	p=0.00	8.08±3.07	p=0.00
Knowing people who died from COVID-19				
Yes	48.29±9.13	t=7.65	9.49±3.17	t=4.47
No	37.16±7.62	p=0.00	7.18±2.84	p=0.00
Hospitalization due to COVID-19				
Yes	58.73±8.12	t=7.89	12.15±1.92	U=358.00
No	42.20±8.59	p=0.00	8.15±3.09	p=0.00

t: Independent samples to test; xMean rank; U: Mann Whitney-U test; Z: Kruskal Wallis Test; UCLA:University California of Los Angeles- Loneliness Scale; DAS: Death Anxiety Scale; p□0.05 is considered statistically significant.;* Dunn-Bonferroni test

In addition, a strong positive correlation was found between the patients' UCLA-LS and DAS mean scores (r:0.763, p=0.00) (Table 5).

Table 5. The Relationship Between Patients' UCLA-LS and DAS Mean Scores

	DAS
UCLA-LS	r= 0.763 p=0.00

Correlation coefficient; Statistical significance was identified if the P-value was lower than 0.001 (p<0.001). UCLA: University California of Los Angeles- Loneliness Scale; DAS: Death Anxiety Scale

DISCUSSION

It is important to protect and maintain mental and physical health during the pandemic. In early 2020, a number of public health measures, from physical distancing to stay-at-home orders, were introduced to prevent further spread of COVID-19 across the world (11,15) Patients diagnosed with COVID-19 and exposed to social isolation may have physical symptoms and psychological problems such as loneliness, fear, death anxiety, and inability to control their own life (15,28).

This study determined that the patients had moderate loneliness (Table 2). Studies conducted in the early days of the COVID-19 pandemic determined that more than one-third of the participants felt lonely (1,16,18). One study found that perceived loneliness increased significantly after an average isolation period of approximately 37 days (8). Different studies have reported that the sense of loneliness increases during the pandemic (2,3,10,28). Studies have also emphasized that negative feelings such as loneliness are an increasingly important factor in the COVID-19 pandemic and stated that loneliness experienced during the pandemic is the main risk factor for some mental conditions such as anxiety and stress (4,12,15,17). In studies similar to our study, it has been observed that patients experience loneliness due to various social isolation measures taken during the pandemic, inability of individuals to meet their daily needs, being separated from their loved ones, and restrictions brought by the disease.

In our study, it was found that the level of loneliness perceived by the patients was significant according to whom they lived with, and in the post-hoc analysis performed to determine which group the difference originated from, there was a significant difference between roommates and those living with their parents, and those living with their parents had a higher mean score. In a study comparing the levels of loneliness, it was stated that the highest feeling of loneliness was in those living alone at home (42.5%), then in a nursing home (23%) and at home with their family (25.5%) (29). Since the mean age of our study was young (26.15± 8.67), the fact that they chatted more with their friends rather than their families might have decreased their perceived loneliness level (Table 4).

Our study determined that the patients with chronic disease had higher loneliness mean score than those without chronic disease (Table 4). Luchetti et al. (2020) observed that the level of loneliness of individuals with chronic diseases in the high-risk group increased during the COVID-19 pandemic (11). Studies of patients infected with COVID-19 have reported that more than 32% of them had a chronic disease (30–32). Studies have also determined that COVID-19 patients with chronic diseases have more severe symptoms during the disease (33). In the studies conducted, it has been determined that those with chronic diseases are more affected by the pandemic process and more disease symptoms are observed in those who have had COVID-19 disease. According to these results, it can be said that it is an expected result that people with chronic diseases have a high loneliness score.

As those with chronic diseases constitute a high-risk group for COVID-19, their perceived loneliness increases because of isolation measures. This study determined that the patients who knew a person died from COVID-19 in their immediate surroundings had higher loneliness mean score than those who did not (Table 4). One study conducted during the pandemic found that knowing people in the family or close circle who died because of the COVID-19 disease increased one's sense of loneliness (13). If patients diagnosed with COVID-19 know dead people in the family or close circle due to the pandemic, this causes them to worry more and their loneliness increases. This result may also be because of their inability to access social support resources due to isolation measures during the disease. In addition, our study determined that the patients who were hospitalized due to COVID-19 had higher loneliness mean score than those who were not hospitalized (Table 4). One qualitative study conducted with individuals who were diagnosed with COVID-19 and stayed in the hospital room alone has determined that their inability to touch and get close to anyone and their inability to recognize healthcare professionals due to the use of protective equipment increased their sense of loneliness (34). This may be because patients who are isolated in line with contact-prevention measures and have limited immobility, are emotionally separated from their loved ones due to visitor restriction (35), therefore they focus on their feeling of loneliness, triggering intense anxiety.

Our study determined that the patients had moderate death anxiety (Table 3). Enea et al. (2021) showed that death obsession increased after an average isolation period of approximately 37 days (8). Another study has reported that 85% of individuals have death anxiety.(19) One qualitative study conducted with 8 COVID-19 patients found that fear of death was among the psychological consequences of this disease (36). The COVID-19 pandemic, which distances social life from its usual boundaries through social isolation measures, increases death anxiety (21). At the time of data collection, mortality rates due to COVID-19 in the world are increasing day by day, and this situation causes death anxiety in COVID-19

patients. In addition, although people's attitudes towards the COVID-19 infection are different, factors such as the publication of death rates every day in the media, around the world and throughout the country, the lack of a complete treatment method for the disease, social isolation measures, and getting away from the routine of life increase death anxiety.

The present study determined that the patients with chronic disease had higher death anxiety mean score than those without chronic disease (Table 4). At the time study data was collected, no effective drug has been developed in the treatment of COVID-19-associated viral pneumonia. The presence of chronic diseases significantly affects the course of the disease in patients infected with COVID-19, increasing the need for intensive care and raising mortality (37). Individuals with chronic diseases constitute a risky group for COVID-19 and publication of the daily number of COVID-19 deaths through social media increases the death anxiety of these individuals. In addition, our study found that the patients who knew a person died from COVID-19 in the close vicinity had higher death anxiety mean score than those who did not (Table 3). One study conducted with healthcare professionals found that 66.3% of them were more concerned about the death of their family members or individuals in their social circles, increasing their death anxiety (19). Another study reported that 42% of those tested positive for COVID-19 first thought about their family and close circles and worried about them, while 17% remembered death (38). Studies of the pandemic found that the fear of COVID-19 and death obsession increased in individuals who thought the deaths of themselves and those around them due to the disease (8,20). In addition to the process of obscurity and uncertainty, it can be said that the death rates are published in the world and in our country every day and witnessing the death of their own relative due to the COVID-19 disease increases the death anxiety in patients diagnosed with COVID-19.

The present study found that the patients who were hospitalized due to COVID-19 had higher death anxiety mean score than those who were not (Table 4). In many studies, it has been determined that hospitalized patients with the diagnosis of COVID-19 during the epidemic experienced psychological problems (34,39). The inability to see one's children and families during the social isolation process, the uncertainty about the end of the disease, the lack of a definitive treatment for the disease, increased number of intubated patients and deaths, disease-related comments on social media, and being exposed to false information about COVID-19 may have led to death anxiety in patients hospitalized with COVID-19. In addition, visitor restrictions, necessity of seeing patients from afar, lack of adequate support for patients, and stigmatization may also increase death anxiety in patients hospitalized with COVID-19.

Our study determined that death anxiety increased as perceived loneliness increased in COVID-19 patients (Table 5). Keskin et al. have found that those who live alone have higher death anxiety (40). In other studies has reported that social isolation of individuals during the pandemic increases their perceived loneliness, whereby they have more death anxiety (8,14). Individuals with COVID-19 feel loneliness more intensely as they focus on their own emotions and feel lonely because of the physical and social isolation measures during the disease, and it can be said that this increases their death anxiety.

CONCLUSION

This study determined that the patients had moderate loneliness and death anxiety and that the perceived loneliness increased the death anxiety. Beyond being a physical disease, the COVID-19 is a pandemic with significant social, psychological and economic effects. Therefore, the psychological aspect of the COVID-19 pandemic, which affects people in all aspects, should be paid sufficient attention. Developing and implementing psychological support programs to cope with stress and strengthen social support resources can alleviate the negative consequences of loneliness and death anxiety in patients with COVID-19.

Limitations

The results of this study cannot be generalized to all patients, as this study consisted of patients who wanted to test for COVID-19 in a single hospital, was conducted online, and consisted of young COVID-19 patients using more social media.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *This study was conducted in accordance with the Helsinki Principles and approved by the Ethics Committee of Siirt University Non-Interventional Clinical Research Ethics Committee (Application date: 31.12.2020 and Approval number:14177).*

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Research Article

Diagnostic Efficiency of Inflammatory Prognostic Index on Pain Scoring for Degenerated Intervertebral Disc

Dejenere Intervertebral Disk için Ağrı Skorlamasında İnflamatuar Prognostik İndeksin Tanısal Etkinliği

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Abstract

Aim: Inflammatory Prognostic Index (IPI), calculated via Albumin, CRP and Neutrophil-Lymphocyte Ratio (NLR), is used in the inflammation related diseases. The study focused the efficacy and predictive effect of the IPI in terms of Visual Analog Scales (VAS) for interpretation of back and leg pain.

Materials and Methods: This multicenter retrospective clinical study was performed by the hospital records of the Degenerated Intervertebral Disc (DIVD) treated between January 2020 and February 2022. IPI value was calculated by the formula of "CRPxNLR/Albumin".

Results: There was a significant difference between VAS-B (2.38±1.74; p=0.0001) and VAS-L (7.09±1.44; p=0.00017) in the comparison of paired VAS values before and after the surgery. Similar change occurred within walking distance after surgery. According to the correlation analysis of the IPI index with DIVD pain scoring, VAS-B(r=0.391; p=0.00017) and delta VAS-B (r=0.422; p=0,00004) showed a positive correlation with the IPI. In the ROC analysis for the diagnostic value of the IPI, the cut-off value of VAS-L above 0.184 showed a diagnostic value as 78.9% sensitivity and 64.3% specificity (UAC:0.702; p:0.003; CI%95: 0.581-0.815).

Conclusion: We showed a strong relationship between IPI and pain scoring of DIVD. The diagnostic value of IPI with VAS-L was very important and can be used by physicians for pain follow-up of DIVD.

Keywords: Inflammatory prognostic index, pain scoring, disc hernia

Öz

Amaç: Albümin, CRP ve Nötrofil-Lenfosit Oranı (NLR) ile hesaplanan İnflamatuvar Prognostik İndeks (IPI), inflamasyona bağlı hastalıklarda kullanılmaktadır. Çalışmamız, sırt ve bacak ağrısının yorumlanması için Görsel Analog Ölçekler (VAS) açısından IPI'nin etkinliğine ve öngörücü etkisine odaklandı.

Materyal ve Metot: Bu çok merkezli retrospektif klinik çalışma, Ocak 2020 ile Şubat 2022 arasında tedavi edilen Dejenere Intervertebral Disk (DIVD) hastalarının hastane kayıtları üzerinden yürütülmüştür. IPI değeri "CRPxNLR/Albumin" formülü ile hesaplanmıştır.

Bulgular: Ameliyat öncesi ve sonrası ikili VAS değerleri karşılaştırıldığında, VAS-B (2.38±1.74; p=0.0001) ve VAS-L (7.09±1.44; p=0.00017) arasında anlamlı fark tespit edildi. Ameliyattan sonra yürüme mesafesinde de benzer bir değişiklik meydana geldi. IPI indeksinin DIVD ağrı skorlaması ile korelasyon analizine göre, VAS-B (r=0,391; p=0,00017) ve delta VAS-B (r=0,422; p=0,00004) ile IPI değeri pozitif korelasyon gösterdi. IPI'nin tanısal değeri için yapılan ROC analizinde, VAS-L'nin 0,184'ün üzerindeki kesim değeri, %78,9 duyarlılık ve %64,3 özgüllük olarak tanısal değer göstermiştir (UAC:0.702; s:0,003; CI %95: 0.581-0.815).

Sonuç: IPI ile DIVD'nin ağrı skorlaması arasında güçlü bir ilişki olduğunu gösterdik. VAS-L ile IPI'nin tanı değeri çok önemliydi ve doktorlar tarafından DIVD'nin ağrı takibinde kullanılabileceğini düşünmekteyiz.

Anahtar Kelimeler: İnflamatuvar prognostik indeks, ağrı skorlaması, disk hernisi

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INTRODUCTION

Low back pain is accepted as a derivative of multi-origin somatic pain with its physical, psychogenic and social aspects, and the problem of degenerated intervertebral disc (DIVD) emerges as the most important source of this pain in the lumbar spine (1). Although clinical results vary, the difficulty of diagnosing objects such as spinal fusion, spondylodesis or arthrodesis, the problematic disc area according to the source and degree of pain is the biggest challenge to be solved today (2). Analyzing the inflammation in the painful area and evaluating the correlation with the pain will be explanatory in the detection and grading of the pain.

The pathophysiology of disc anatomical deterioration is a set of symptoms that develop as a result of inflammatory developments and remodeling of facet joint processes (3). These cytokines and enzymes that break down the matrix disrupt chondrocyte metabolism and thus lead to cartilage transformation (4). In a vicious circle, these changes in cartilage cause extensive pathological remodeling of subchondral bone and stimulate a recurrent inflammatory process (5). In addition to prostaglandins, numerous cytokines such as TNF and IL-6 worsen this picture by causing osteoarthritic alterations. These cytokines and matrix-degrading enzymes disrupt chondrocyte metabolism and thus lead to cartilage transformation (6). In a vicious circle, these changes in cartilage cause intense pathological remodeling in the subchondral bone, stimulating a recurrent inflammatory process (7, 8). Surgeons need novel cheap and practical indexes to maintain and follow pain scoring in DIVD (9). It may be easier to follow these processes clinically to investigate their relevance to pain using indirectly influenced platelet association indices such as neutrophil/lymphocyte ratio (NLR), rather than expensive and difficult-to-measure tests.

Albumin, CRP and NLR, used in routine analyze for inflammatory conditions, are easy to measure, inexpensive, and widely available in clinical practice. Today, the Inflammatory Prognostic Index (IPI), calculated via Albumin, CRP and NLR, is used in the investigation of cancer cases known to be closely related to inflammation and some rheumatological disease. The present study investigated the efficacy and predictive effect of IPI, which has separate effects on DIVD in terms of Visual Analog Scale (VAS) for interpretation of back and leg pain.

MATERIAL AND METHOD

This retrospective clinical study was conducted in the Department of Neurosurgery. Siirt University Faculty of Medicine's Local Ethics Comittee approved the study protochol.(2022/05.06).

Study Design

The patients were treated between June 2021 and February 2022 and were selected from patients undergoing follow-up evaluations. Clinicopathological variables such as age, gender and pain score were recorded with the electronic medical record system. As inclusion criteria, volunteer participants with defined DIVD and complete hospital data were included in the study with their retrospective data. Exclusion criteria included: patients with missing data, who had infection/inflammation, haematological disorder, embolism or infarction, who had a history of active bleeding/ transfusion recently, who had a major drug therapy such as steroid. After assessment of inclusion/ exclusion criteria, 88 of 215 participants were eligible for the present analysis.

Laboratory Data Collection

All laboratory data of the patients were evaluated. The following formula was used to find the IPI value: "CRPxNLR/ Albumin". According to the definition of the World Health Organization (10), anemic, platelet deficiency or disorders in calcium metabolism were evaluated and those with inappropriate results were excluded from the study.

Statistical Analysis

Data analyze was done using SPSS-25.0 software (Chicago,IL,USA). As categorical parameters were presented as number of patients and percentage, mean and standard deviation values were shared in data with normal distribution. Spearmen' correlation test was used to measure the relationships of IPI index with pain scores and outputs of DIVD. The receiver operating characteristic(ROC) curve was used to determine the predictive ability for VAS-L and cut-off value for IPI (Figure-1, Table-3).

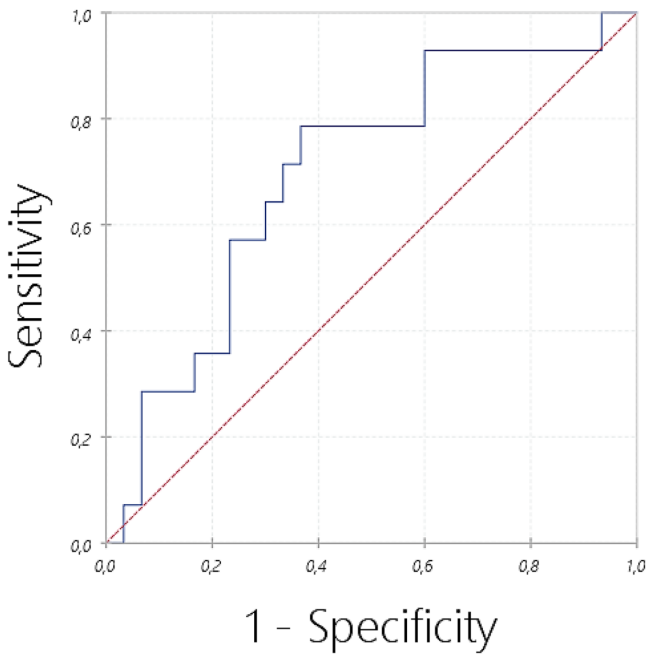

Figure-1. The receiver operating characteristic determining the predictive of IPI for VAS-L

RESULTS

Patient Characteristics

Of the 88 patients included in the study, 54 (61.4%) were

female. The spine levels affected by DIVD were mostly L1 (n:54) and L2 (n:14) spines. Twenty-eight (31.8%) of the patients had high VAS-L values. In terms of VAS-B, it was high in 36 patients (41%). There was a significant difference between VAS-B (2.38±1.74; p=0.0001) and VAS-L (7.09±1.44; p=0.00017) in the comparison of paired VAS values before and after the surgery (Table-1). A similar change occurred within walking distance after surgery (p<0.0001).

Correlations

According to the correlation analysis of the IPI index with DIVD pain scoring, VAS-B (r=0.391; p=0.00017) and delta VAS-B (r=0.422; p=0.00004) showed a positive significant correlation with the IPI value, as given in Table-2. Similarly, follow-up (r=0.308; p=0.003) and hospital stay period (r=0.854; p=0.0001) took longer time when the IPI value increased. Walking distance showed a negative correlation with the IPI (r=-0.355, p=0.001). VAS-B and delta VAS-B values did not show any correlation with the IPI (p>0.05).

ROC Analysis

In the ROC analysis for the diagnostic values of the IPI value in the presence of Leg VAS (Figure-1 and Table-3), the cut-off value above 0.184 showed a diagnostic value of 78.9% sensitivity and 64.3% specificity [UAC:0.702; p:0.003; CI%95: 0.581-0.815). When looking for the Back-VAS values of the IPI value, we did not find a significant cut-off such as Leg-VAS (UAC: 0.529, p:0.647, CI: 0.402-0.656).

Table 1. Paired scale results by before and after the surgery

Variables	Mean	SD	SE	95% CI		Df	P-value
				Lower	Upper		
VAS-L	7.09	1.44	0.19	6.01	7.17	87	0.00017
VAS-B	2.38	1.74	0.22	1.69	2.85	87	0.00011
W-D	-333.5	101.4	14.2	-408.6	-319	87	0.00003

Abbreviations. Leg pain visual analog scale (VAS-L), Back pain scoring (VAS-B), Walking distance (W-D), SE: Standard Error, SD: Standard Deviation, CI: Confidence Interval, Df: Degrees of Freedom

Table 2. Correlation analysis of the IPI index vwith DIVD pain scoring

IPI Comparison	VAS-L	VAS-B	Delta VAS-L	Delta VAS-B	W-D	Stay (day)	Follow-up (month)
Pearson Correlation	0.089	0.391	0.092	0.422	-0.355	0.854	0.308
Sig. (2-tailed)	0.406	0.00017	0.394	0.00004	0.001	0.0001	0.003

Abbreviations. Leg pain visual analog scale (VAS-L), Back pain scoring (VAS-B), Walking distance (W-D)

Table 3. Details of the ROC analyze performed for the prediction of VAS-LEG

Variables	Area	Std. Error	P value	95% Confidence Interval	
				Lower	Upper
IPI	0.702	0.077	0.003	0.581	0.815
NLR	0.430	0.071	0.355	0.292	0.568
CRP	0.511	0.068	0.013	0.577	0.845
Albumin	0.413	0.073	0.253	0.275	0.551

Abbreviations. IPI: Inflammatory Prognostic Index, CRP: C-reactive protein, NLR: neutrophil/lymphocyte ratio

DISCUSSION

As a result of the increase in diagnostic costs in health systems of pandemics worldwide, the need for inexpensive diagnostic parameters in public and private institutions has increased more than ever. Since the IPI index we investigated in the present study is a strong indicator of inflammation and can be used very conveniently and cost-effectively in pain scoring, the results of the study will help us to score pain practically and inexpensively for use in the pre- and postoperative routines of DIVD patients.

Low back pain is accepted as a derivative of multi-origin somatic pain with its physical, psychogenic and social aspects, and the problem of DIVD emerges as the most important source of this pain in the lumbar spine (11, 12). An inflammatory condition in DIVD is a kind of anti-injury response to injury in the skeleton, and it plays a crucial efficiency in the development and worsening of DIVD (13). Platelet generates reactive oxygen species and interleukins. Recently, the inflammatory response was accepted to be a parameter in the weak prognosis of cases with some diseases through hematological indexes (14,15). Under the inflammatory condition, the increased neutrophil count can produce nitric oxide, resulting in worsening the immediate clinical condition (16).

In DIVD patients, we need to assess the inflammation process in terms of pain that radiates to the extremities and beck (17). CRP, which is accepted as a better indicator of inflammation than erythrocyte sedimentation rate (18), responds more quickly to changes in a more sensitive clinical situation than many parameters (18). Albumin, on the other hand, is a negative acute-phase protein, unlike CRP, and its level decreases during sepsis or injuries (19). In addition, albumin reduction is not only closely related to inflammation (20). In this sense, we cannot specifically accept CRP and Albumin. The CRP/Albumin ratio, which is another inflammatory scale examined in combination with CRP, was first studied in some inflammatory-related diseases (21). Patients with a higher CRP/Alb ratio showed a worse overall survival than patients with a lower rate. We think that the NLR parameter, which is obtained by

the ratio of neutrophil and lymphocyte parameters and which has attracted attention recently, can help us in this sense. Some orthopedic studies have presented NLR as a potential marker with prognostic and predictive values in inflammatory conditions (22). In a study performed by Ethemoglu et al., among patients with neck pain, those with non-elevated NLR and CRP levels may have normal neck MR imaging, and in patients with elevated NLR and CRP levels, early protective approaches may play a preventive role in disc degeneration and cervical disc hernia development (23). In our study, we evaluated lumbar disc hernia for the first time, the effect of the IPI value, consisting of NLR, CRP, and albumin, on pain in DIVD patients.

In our study, we found a significant efficiency for IPI in pain scoring of DIVD. There was a significant difference between VAS-B and VAS-L in the comparison of paired VAS values before and after the surgery. Similar change occurred within walking distance after surgery. According to the correlation analysis of the IPI index with DIVD pain scoring, VAS-B and delta VAS-B showed a positive significant correlation with the IPI value. Similarly, follow-up and hospital stay period took longer time when the IPI value increased. Walking distance showed a negative correlation with the IPI. VAS-B and delta VAS-B value did not show any correlation with the IPI. In the ROC analysis for the diagnostic values of the IPI value in the presence of VAS-L, the cut-off value above 0.184 showed a diagnostic value as 78.9% sensitivity and 64.3% specificity.

The present study had some limitations. We collected all the data by retrospective way; therefore, case comparison may be affected by selection bias. Second, the present research included a non-homogenous group, and so we had no restrictions according to some variables such as age. We think that the coefficient of significance evaluation can be increased by reducing the BIAS in studies that will be conducted by creating a higher participation and control group in terms of the number of patients.

CONCLUSION

In the present study, we showed a correlation between IPI and pain scoring of DIVD. We concluded that this correlation is due to the relationship between IPI and inflammation, and it increases in correlation with pain. In particular, the diagnostic correlation between VAS-L values and IPI was very important and can be used by physicians for follow-up of DIVD.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *Siirt University Faculty of Medicine's Local Ethics Comittee approved the study protochol.(2022/05.06).*

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MEDICAL RECORDS-International Medical Journal

Research Article

Microbiological and Antimicrobial Profile of Urinary System Infections in Children in Uşak

Uşak İlinde Çocuklarda Üriner Sistem Enfeksiyonlarının Mikrobiyolojik ve Antimikrobiyal Profili

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Abstract

Aim: One of the most prevalent pediatric diseases is urinary tract infection (UTI), accounting for 3% of all infections among the pediatric population and affect 2% of males and 8% of females by age seven. Bacteria are the most prevalent cause of UTIs, accounting for more than 95 percent of cases. The most prevalent causal bacteria of UTI is Escherichia coli. Antibiotics are included in the treatment of these infections. As a result, determining the correct antibiotic susceptibility is critical in the therapeutic treatment of bacterial infections. This study aimed to analyse the aetiology and antimicrobial resistance characteristics of urinary tract infection among children presenting with symptoms in Uşak.

Material and Method: A total of 1250 urine culture results were retrospectively analyzed from pediatric patients aged 0–16 years who were admitted to Uşak Öztan Hospital as outpatients with symptoms and complaints of urinary tract infection and whose urine analysis and urine culture were taken between January 2018 and December 2020.

Result: Gram-negative microorganism growth was found in 238 (19%) of the 1250 pediatric patients evaluated in our study. There was no growth in the urine cultures of 877 (70%) patients. E. coli was the most isolated microorganism in our study, which was detected in 168 (70.5%) of the patients.

Conclusions: We present the first antimicrobial resistance data for the city of Uşak. Our study showed that amoxicillin/clavulanate is not the best option for the empirical therapy of community acquired UTIs, contrary to current local practice. In addition, ceftriaxone was found to be the second most resistant antibiotic in our study.

Keywords: Pediatrics, urinary tract infections, etiology, antibiotic resistance

Öz

Amaç: En yaygın pediatrik hastalıklardan biri, pediatrik popülasyondaki tüm enfeksiyonların %3'ünü oluşturan ve yedi yaşına kadar erkek çocukların %2'sini ve kız çocuklarının %8'ini etkileyen idrar yolu enfeksiyonudur (İYE). Bakteriler, vakaların yüzde 95'inden fazlasını oluşturan İYE'lerin en yaygın nedenidir. İYE'n de en sık izole eden bakteri Escherichia coli'dir. Antibiyotikler idrar yolu enfeksiyonların tedavisinin temelini oluşturur. Sonuç olarak, bakteriyel enfeksiyonların terapötik tedavisinde doğru antibiyotik duyarlılığının belirlenmesi kritik öneme sahiptir. Bu çalışmada Uşak'ta belirgin İYE semptomları ile başvuran çocuklarda idrar yolu enfeksiyonunun etiyolojisi ve antimikrobiyal direnç özelliklerinin incelenmesi amaçlanmıştır.

Materyal ve Metot: Uşak Öztan Hastanesi'ne ayaktan idrar yolu enfeksiyonu semptom ve şikayetleri ile başvuran, 2018 Ocak-2020 Aralık ayları arasında idrar tahlili ve idrar kültürü alınan 0-16 yaş arası çocuk hastalardan toplam 1250 idrar kültürü sonucu retrospektif olarak incelendi.

Bulgular: Çalışmamızda değerlendirilen 1250 pediyatrik hastanın 238'inde (%19) gram negatif mikroorganizma üremesi bulundu. 877 (%70) hastanın idrar kültüründe üreme olmadı. Çalışmamızda hastaların 168'inde (%70,5) E. coli en fazla izole edilen mikroorganizma E. coli idi.

Sonuçlar: Uşak ili için ilk antimikrobiyal direnç verilerini sunuyoruz. Çalışmamız, mevcut yerel uygulamanın aksine, toplum kökenli İYE'lerin ampirik tedavisi için amoksisilin/klavulanatın en iyi seçenek olmadığını göstermiştir. Ayrıca çalışmamızda seftriakson en dirençli ikinci antibiyotik olarak bulundu.

Anahtar Kelimeler: Pediatri, idrar yolu enfeksiyonu, İYE etiyoloji, antibiyotik direnci

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INTRODUCTION

One of the most prevalent pediatric diseases is urinary tract infection (UTI), accounting for 3% of all infections among the pediatric population. UTI is an infection that causes an inflammatory response in the urinary tract epithelium (1). Because females have a shorter urethra than males, UTIs are more common. (2). UTIs are frequent in children, affecting 2% of boys and 8% of girls by the age of seven. In febrile newborns with no other known cause, the incidence of UTI can reach 7% (3).

Bacteria are the most common cause of urinary tract infections (UTIs), accounting for more than 95 percent of all cases. Escherichia coli is the most prevalent causal bacteria of UTI, accounting for more than 80% of all UTIs; Klebsiella, Proteus, and Enterococci are other responsible pathogens (1). For as long as causative bacterium is antibiotic-resistant, antibiotics are included in the treatment of these infections. As a result, identifying antibiotic susceptibility is critical in the therapeutic management of bacterial infections. Bacteria that have the potential to develop resistance to antibiotics need to be monitored more closely. According to many physicians around the world, microbial resistance is increasing (4). Renal damage in children, such as kidney failure and chronic hypertension, recurrent infection, pyelonephritis, and sepsis, can be significantly reduced by early and effective antimicrobial therapy for UTIs in children (3).

Antimicrobial susceptibility tests of urine specimens are usually concluded in 48 to 72 hours after the specimens are delivered. According to clinical experience, the majority of antimicrobial treatment for UTIs in pediatric patients is given empirically before test results are available. Oral antibiotics for UTI include sulfonamides (trimethoprim-sulfamethoxazole or sulfisoxazole), amoxicillin-clavulanate and cephalosporins (cefuroxime axetil, cefixime, cefprozil, cefpodoxime or cephalexin) (5). Amoxicillin and ampicillin are effective against around half of E. coli germs. Furthermore, increasing rates of E. coli resistance to amoxicillin-clavulanic acid, ampicillin-sulbactam, first-generation cephalosporins (e.g., cephalexin) and trimethoprim-sulfamethoxazole have been seen in some populations. Resistance to extended spectrum cephalosporins (cefotaxime, ceftazidime, cefepime) has been found in children who have been given prophylactic antibiotics (6). In addition to long-term complications that may occur in patients, further diagnostic testing for structural urinary system problems within the scope of 2nd and 3rd level health care services after attending primary health care services before diagnosis and laboratory analysis, along with antibiotic resistance, cause significant economic impacts and indirect costs through loss of time in school for children and parent labor loss (7).

Unfortunately, apart from a few large cities in Turkey, there is limited data about patterns of antibacterial susceptibility of endemic uropathogens in small cities in Anatolia. This study aimed to analyse the aetiology and antimicrobial resistance characteristics of urinary tract infection among children presenting with symptoms in Usak

MATERIAL AND METHOD

The clinical research ethics committee of Usak University Faculty of Medicine approved the study on 02/12/2020 with decision number 102-07-11. A total of 1250 urine culture results were retrospectively analyzed from pediatric patients aged 0–16 years who were admitted to Usak Private Oztan Hospital as outpatients with symptoms and complaints of urinary tract infection and whose urine analysis and urine culture were taken between January 2018 and December 2020. The study included 238 culture growths that met the inclusion criteria. Pathogens and resistance patterns that were isolated from midstream urine culture were analyzed. The study population consisted of infants and pediatric patients under the age of 18 who sought hospital treatment for UTI symptoms. Symptoms included dysuria and lack of bladder control, as well as low back discomfort and cloudy or bad-smelling urine with fever. According to parents, newborns and younger children had fever and hazy or strong-smelling urine. Urine samples were taken in sterile containers after being captured cleanly. For clean pee collection, a plastic bag was affixed to the genital region of babies and non-potty-trained youngsters. From toilet-trained children, a cleanly captured voided midstream urine sample was taken. To reduce contamination, the vaginal region was cleansed first in both cases. Urine collecting methods that were invasive were avoided. Children who received antimicrobial treatment and had a bladder catheterization within 48 hours were excluded from the trial. Asymptomatic bacteriuria patients were also barred from participating in the trial. Antimicrobial susceptibility testing was used to determine empirical antibiotic treatment.

Laboratory analyses of samples

Urine color was assessed macroscopically immediately after collection for contamination signs. Urine samples accepted by the laboratory were taken for examination without waiting. Urine samples were incubated for 24–48 hours in an incubator at 35–37 °C under aerobic conditions with 0.01 ml of the calibrated standard loop on petri plates containing Eocene Methylene Blue (EMB) agar and blood agar base (8). Bacterial growth of 100000 cfu/ml and above was included in the study after incubation (9). The isolated bacteria were identified using conventional methods, and the API ID (BioMérieux, France) system was used for isolates that could not be identified with this method.

Testing for antimicrobial susceptibility

The sensitivity of the detected isolates to various antibiotics was investigated using the Kirby-Bauer disk diffusion technique on Muller-Hinton agar in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria. All detected E. coli and Klebsiella spp. isolates on Mueller-Hinton agar were interpreted using amikacin (30 g), ampicillin (10 g), cephalexin (30

g), cefixime (10 g), cefpodoxime (30 g), co-trimoxazole (1.25/23.75 g), nitrofurantoin (300 g), and ofloxacin (5 g) (HiMedia Pvt (HiMedia Pvt. Ltd., India). E. coli ATCC 25922 was used to check quality control. Multidrug-resistant isolates were those that were resistant to two or more antimicrobial drugs (MDR).

Statistical analysis

SPSS 21 (IBM SPSS, SPSS inc. an IBM Co., Somers, NY) statistical package program was used for statistical analysis. Descriptive statistics are presented as mean ± standard deviation (minimum-maximum) for continuous variables and the number of cases and percent for nominal variables.

RESULTS

Demographics

Gram-negative microorganism growth was found in 238 (19%) of the 1250 pediatric patients evaluated in our study. There was no growth in the urine cultures of 877 (70%) patients, non-gram negative microorganism growth was detected in 63 (5%) patients, and the urine culture results of 72 (6%) patients were evaluated as contamination. There were 145 (61%) females and 93 (74%) males among the 238 patients who were included in the study with gram-negative growth in their urine culture. The difference in mean age between men and women was not statistically significant (male: 2.94 2.19 years; female: 3.22 2.93 years; P>0.05).

Isolated pathogens

E. coli was the most frequently isolated microorganism in our study, which was detected in 168 (70.5%) of the patients. It was followed by Proteus spp. in 38 (16%) patients. These were followed by 23 (9.7%) Klebsiella spp. patients and 9 (3.8%) Pseudomonas spp. patients (Table 1). In male patients, the infection rate for E. coli was 68.8 percent, 14 percent for Klebsiella spp, 12.9 percent for Ptoteus spp., and 4.3 percent for Pseudomonas spp. In female patients, the infection rate for Ecoli was 71.8 percent, 17.9 percent for proteus, 6.9 percent for klebsiella, and 3.4 percent for pseudomonas.

Antibiotic susceptibility

The most commonly isolated E. coli had the highest detected antibiotic resistance for amoxicillin/clavulanate (46%), ceftriaxone (31%), trimethoprim/sulfamethoxazole (30%), fosfomycin and nitrofurantoin (17%). The resistance rates of isolated microorganisms to antibiotics are shown in Table 2.

Compared with susceptible patients in E. coli infections, resistance to Ceftriaxone was found to be 31% in 52 patients, 19 patients 11.3% in amikacin, amoxicillin in 45.8% in 77 patients, 17.3% in 29 patients on fosfomycin, 0 in imipenem, 16.7% in 28 patients on nitrofurantoin, there were 50 patients on Co-trimoxazole, and the rate was 29.8%.

Compared with susceptible patients in Klebsiella spp. infections, resistance to ceftriaxone was found to be 34.8% in 8 patients, 13% in amikacin in 3 patients, 52.2% in amoxicillin in 12 patients, 34.8% in fosfomycin 8 patients, 4.3% in imipenem in 1 patient, and 9 patients for nitrofurantoin 39.1%, Co-trimoxazole was seen in 7 patients as 30.4%.

Compared with susceptible patients in Proteus spp. infections, the rates of resistant patients were 1 patient on ceftriaxone, 2.6%, 1 patient on amikacin 2.6%, 4 patients on amoxicillin 10.5%, 4 patients on fosfomycin 10.5%, 6 patients on nitrofurantoin 15.8%, Co-trimoxazole, 9 patients were 23.7%.

In Pseudomonas spp. infections, resistance was seen only in 4 patients against Co-trimoxazole compared to susceptible patients, and its rate was 44.4%.

Table 1. Distributions of isolated pathogens from urine culture in 238 culture positive samples [n (%)]

Pathogens	n (%)
Escherichia coli	**168 (70.5)**
Proteus spp.	38 (16)
Klebsiella spp.	23 (9.7)
Pseudomonas spp.	9 (3.8)

Table 2. Antimicrobial susceptibility of isolated uropathogenic bacteria [n (%)]

Antibiotic Name	Escherichia coli	Proteus spp	Klebsiella spp	Pseudomonas spp
Amoksisilin-Klavulanat	**77 (44)**	4 (11)	12 (52)	-
Amikasin	19 (11)	1 (3)	3 (13)	0
Trimetoprim-Sülfametoksazol	50 (30)	9 (24)	7 (30)	4 (44)
Piperasilin/ tazobaktam	6 (4)	0	1 (4)	1 (11)
Seftriakson	52 (31)	1 (3)	8 (35)	-
Meropenem	1 (1)	0	0	0
Imipenem	0	0	1 (4)	0
Fosfomisin	29 (17)	4 (11)	8 (35)	-
Nitrofurantoin	28 (17)	6 (16)	9 (39)	-

DISCUSSION

Only 238 of 1250 urine samples tested positive in our study. The positive culture results were determined using a 100,000 CFU/ml threshold. A positivity rate of 19% was found. Lower bacterial counts may be missed as a result. A higher threshold could mean lower positive culture results. Childhood urinary tract infections (UTIs) can result in higher morbidity, hospitalization, and long-term clinical

implications such as renal scarring, hypertension, and chronic kidney disease (3). As a result, children who have UTI should be detected and treated as soon as feasible. Antimicrobial resistance patterns of isolated uropathogens that cause UTIs differ depending on region and race. Most microorganisms are unaffected by the use of ampicillin as an antibiotic for the empirical treatment of suspected UTI or the prevention of recurrent UTI, according to research done across the world. Amoxicillin-clavulanic acid (30%), trimethoprim-sulfamethoxazole (nearly 40%) and first generation cephalosporins all have high rates of resistance (6). Unfortunately, rising antibiotic resistance allows for ineffective empirical treatment. The formation of broad-spectrum lactamases is one of the mechanisms causing this resistance (ESBLs) (10). Therefore, a safe diagnosis of UTI in children is very significant.

In our hospital, E. coli was the most prevalent cause of pediatric UTI, and this genus accounted for 70.5% of all pathogens isolated. E. coli was identified in 71.4% of the 940 subjects with UTIs in a recent study conducted in Iran, which is consistent with previous studies as well as our study (11). The most common pathogens causing pediatric UTIs worldwide and in Turkey were reported to be E. coli and Klebsiella spp. (12-15). Klebsiella had a rate of 9.7% in our study, and it was placed 3rd after Proteus spp. The rate of Proteus was 16% and was higher than the rate in other studies.

The majority of children are treated empirically before test results are obtained both in our and similar clinics to avoid complications. Our antimicrobial resistance study is shown in Table 2. Both Klebsiella spp. and E. coli had high resistance to amikacin, with resistance rates of 45.8% for E. coli, 52.2% for Klebsiella spp., and 10.5% for Proteus spp. in our study. This is in line with the study by Miranda et al. (16). Co-trimoxazole is the oral antibiotic of choice for the treatment of pediatric UTI, but Proteus spp., Klebsiella spp. and E. coli were found to have resistance rates of 23.7%, 30.4% and 29.8% respectively, in our study. In terms of preference, these rates are high.

Low nitrofurantoin resistance was found in urine E. coli isolates from both children and adults throughout the world (17). In our study, nitrofurantoin was found to be effective against most Klebsiella spp. and Proteus spp. Resistance rates were 9% and 6%, respectively. However, this rate was 28% for E. coli. Moreover, studies evaluating childhood UTIs caused by ESBL-producing bacteria reported low rates of resistance to nitrofurantoin among these uropathogens as well. Because of the low tissue concentrations, it is not advised for use in acute pyelonephritis. Based on these data, nitrofurantoin may be suggested for the empirical treatment of lower-tract UTIs (18). Nitrofurans can also be chosen as a cost-effective alternative as they are relatively less expensive. Antimicrobial resistance is related to inappropriate antibiotic usage, poor diagnosis, self-medication, poor quality antibiotics, insufficient doses, males with uncircumcised penis, and bowel and bladder dysfunction (5). Treatment of childhood UTIs aims to eradicate the infection and prevent complications such as prevent recurrence, urosepsis and provide rapid relief for long-term clinical consequences and symptoms such as renal scarring, hypertension, and chronic kidney disease (3). To combat rising resistance rates, it is critical to do a urine culture and employ local antibiograms, treat only when required, and avoid broad-spectrum antibiotics as much as possible. Patients with severe vesicoureteral reflux and hydronephrosis should also be given selected antibiotic prophylaxis (19). Resistance to imipenem was found to be 4.3% in one case against Klebsiella spp., whereas resistance to meropenem was found to be 0.6% in one case against E. coli. Carbapenems should be preferred in the treatment of serious infections caused by ESBL-producing Enterobacteriaceae, as other studies reported low resistance to carbapenems (20). The prevalence of vancomycin-resistant enterococci (VRE) in pediatric patients has increased in recent years, posing a serious threat to children (21). Fortunately, no resistance was found in our study of pediatric urinary tract infections. Shortridge et al. showed that ceftolozane-tazobactam was the most effective cephalosporin against all Enterobacteriaceae, with only meropenem and colistin having greater susceptibility rates. Ceftolozane tazobactam was the most effective lactam against P. aeruginosa, with a susceptibility rate comparable to colistin (22).

Ampicillin and aminoglycoside combinations are also employed in the empirical treatment of acute pyelonephritis at our hospital, particularly in the early baby period. Because third generation cephalosporins are often inefficient in the treatment of UTIs caused by ESBL-producing bacteria, the combination of ampicillin and amikacin looks to be a practical alternative for avoiding unnecessary empirical therapy of patients with acute pyelonephritis. Furthermore, resistance against ESBL-producing bacteria and high costs associated with broad-spectrum antibiotics will be prevented. As a result, we agree with the usage of the combination of ampicillin plus amikacin for the treatment of patients with acute pyelonephritis who have ESBL-positive UTI risk vectors (23).

In a recent study by Kalaitzidou et al., E. coli was the most common uropathogen, followed by Klebsiella spp. and Proteus spp. In our study, E. Coli was the first at 71.4%, Proteus spp. was second at 16%, while Klebsiella spp. was third at 9.7%, and pseudomonas was fourth at 3% (24). According to the findings of Kalatitzidou et al., the most common antibiotic resistance in E. coli isolates was ampicillin, followed by piperacillin, amoxicillin-clavulanate, and trimethoprim-sulfamethoxazole. 4.21 percent of E. coli strains generated extended-spectrum beta-lactamases (ESBLs). Vesicoureteral reflux was discovered to be a substantial risk factor for multidrug resistance (24). The most prevalent antibiotic resistance of E. coli isolates in our study was for amoxicillin-clavulanate, ceftriaxone, and trimethoprim-sulfamethoxazole, in that order. Contrary to current local practice, both our investigation and the study by Kalatitzidou et al. demonstrated that amoxicillin/clavulanate is not the best option for empirical therapy of

community acquired UTIs. In addition, ceftriaxone was found to be the second most resistant antibiotic in our study. The most common reason for this, we think, is the use of ceftriaxone as a single or multiple-dose outpatient parenteral treatment agent in cases with fever of unknown origin and other infections without culture.

CONCLUSION

Our findings showed high antimicrobial resistance among common uropathogens. We present the first antimicrobial resistance data for the city of Usak. For this reason, these findings can be used as a reference for the treatment of UTI in children in the city of Usak. This study will help clinicians to choose proper antibiotics and identify trends in antimicrobial susceptibility, especially in our region.

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Author contribution: *SG designed the study, collected and analyzed the data, and drafted the manuscript reviewed and revised the manuscript and is the corresponding author. MU collected and analyzed the data and reviewed and revised the manuscript. All authors read and approved the final manuscript.*

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Research Article

Theoretical Knowledge Difference Between Internet-Based and Digital Storytelling Education About Breast Cancer

Meme Kanseri Hakkında Internet Tabanlı ve Dijital Hikaye Eğitimi Arasındaki Teorik Bilgi Farkı

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Abstract

Aim: Previous research has identified the theoretical knowledge about breast cancer early diagnosis of nursing students and stated that new methods are needed in education. To evaluate the effect of education on the theoretical knowledge of students through internet-based or digital storytelling.

Material and Method: Quasi-experimental study with comparison groups and pre- and post-measurements. In the internet-based education group 68 and digital storytelling videos 66 undergraduate nursing students have included in the study. Data for the study were gathered, before education and after eight weeks. The percentages were calculated for every measurement, the test was used for the data whose conformity to normal distribution, and was used to detect the statistical significance of changes between measurements.

Results: The increase in knowledge scores was more often statistically significant in internet-based education than in the digital storytelling video.

Conclusion: This research shows that it is possible to create changes in teaching breast cancer early diagnosis methods by using the developing technology.

Keywords: Nursing education, internet-based education, digital storytelling, theoretical knowledge

Öz

Amaç: Yapılan araştırmalar hemşirelik öğrencilerinin meme kanseri erken tanısı konusundaki bilgi donanımlarını artırabilmek için eğitimde yeni yöntemlere ihtiyaç duyulduğunu belirtmektedir. Bu araştırma meme kanseri erken tanı yöntemlerine ilişkin bilgi artırmada internet tabanlı ya da dijital hikaye anlatımının etkisini belirlemeyi amaçlamaktadır.

Materyal ve Methot: Araştırma ön ve son test ölçümleriyle yarı deneysel çalışma niteliğindedir. İnternet tabanlı eğitim grubunda 68 ve dijital hikaye videoları grubunda ise 66 hemşirelik lisans öğrencisi araştırmaya dahil edildi. Araştırmanın verileri eğitim öncesi ve eğitimden sekiz hafta sonra iki aşamalı olarak toplandı. Her ölçüm için yüzdeler hesaplandı. Ölçümler arasındaki değişiklikleri belirleyebilmek için normal dağılıma bakıldı ve istatistiksel olarak anlamlılıkları test edildi.

Bulgular: İnternet tabanlı eğitimde bilgi puanlarındaki artışın dijital hikaye anlatımı videosundaki artıştan daha fazla olduğu ve bu farkın istatistiksel olarak anlamlı olduğu belirlendi.

Sonuç: Bu araştırma meme kanseri erken tanı yöntemlerini öğretmede gelişen teknolojiden yararlanılarak değişiklikler oluşturmanın mümkün olduğunu göstermektedir.

Anahtar Kelimeler: Hemşirelik eğitimi, internet tabanlı eğitim, dijital hikaye anlatımı, teorik bilgi

INTRODUCTION

Different technological products are used in the continuation of nursing education (1). The nurse must know about theoretical and medical technology to work and manage in a highly complex patient care environment (2). For this reason, it is important to provide permanent information and to train nurses who actively use technological products (3). In addition, the use and dissemination of different education methods in nursing education is an attempt to increase the quality of education.

Digital storytelling is one of the most widely used educational tools today (4). In the literature, the process of creating digital storytelling; students' creative

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thinking skills, imagination, research skills, improve their technological competencies, motivation, and academic (5-7), the achievement is supported to support peer learning (8). However, there are limited resources on the use of this method in nursing practice education.

Internet-based education cannot be confronted with different types such as patient education, and game education for students (9). It is seen that it creates the desired effect in the education groups used, they are an easy-to-accept and useful educational tool (10). In addition, it is seen that adding different support products to the information equipment placed in it, it makes the information attractive (11). In this context, it is seen that it is an educational tool that can be used as theoretical training material.

There is no clear information about which of the two training methods are used to achieve which result. Both methods have positive and negative sides themselves and have not been used sufficiently for nursing education. In this context, there is a variety of educational materials used in nursing education, but it is a discussion about which type of education can be used for the desired level. It is one of the limited studies that evaluate different methods that emerged after the use of developing technologies in the health system.

When previous nursing education researches are examined, different technological products are used in nursing education, and education is supported with these products, and knowledge levels are tried to be increased (12,13). This study aimed to evaluate the comparison between internet-based education and digital storytelling video about nurses' theoretical knowledge of breast cancer early diagnosis.

The study hypothesis was: The difference in theoretical knowledge will be higher in the internet-based education program than in digital storytelling education.

MATERIAL AND METHOD

The Research Design

Quasi-experimental study design with comparison groups and pre-and post-measurements was used. Two groups of sophomore year of university second-year constituted the source of data.

Participants

Students in two different groups were invited to the study according to their order of placement at the university. A total of 134 nursing students agreed to participate. To be eligible to participate in the study, the undergraduate nursing student had to have been untrained before in breast cancer. The lottery was used to decide between include how student's internet-based and digital storytelling education groups. In the list created according to the success order, even numbers digital story, odd numbers website created. The sample size was calculated with power analysis using the openepi website (power 0.95). Based on power analysis, 60 undergraduate nurses were needed in both groups.

Creation of Educational Material

Information including early diagnosis methods of breast cancer was prepared in line with the literature. Expert opinions were taken by three academicians and two clinical nurses, and the text content was finalized. The same content was used in both the digital storytelling and the website. The sentence order and expression options of the content are the same.

Creating The Website

The ADDIE model, one of the education system design models, was used in structuring the website. This model includes a systematic approach process that includes Analysis, Design, Development, Implementation, and Evaluation processes in the development of the educational tool. Each of these stages is interrelated and serves as a flexible roadmap for designing an effective training method. These stages contain their tasks and after completion, the next stage is passed. The breast cancer early diagnosis methods training content prepared in line with the literature was converted into a website by the researcher. In the interfaces and page structure to be created in this transformation, attention was paid to the questions of "the type of product that can be used on the website that prevents learning, is there a time limit for completing the training process? How much time is needed for the participant". presented and evaluated. Changes requested during this process were related to font size, background color, and video bouts. These changes were returned to the relevant step in the ADDIE model used in structuring the training material and the process was started again. After completing the whole process, the website was submitted for the evaluation of field experts. In line with the suggestions received from the experts, the final version of the training material is ready for use. In addition, the 2D video prepared by the Ministry of Health for the BSE examination was placed under the relevant title. The animations and pictures used were informative, supportive, summative, and evaluative. care was taken. The website was opened to the use of students with a QR code.

Creation of Digital Storytelling Video

Many programs are used in preparing digital stories. It is noted that it is appropriate to use Movie Maker, PowToon, Photostory3, Imovie, and PowerPoint software to create digital stories (8). The researcher was trained to use these platforms. To prepare the video suitable for the content of the research, it was decided that the animated character should be animated and the expressions should be presented in written form with speech bubbles. Storyboard, one of the limited platforms, was used to prepare this content. The PowToon program was used to transfer the created animated character to the video and complete the video content. Digital story; It was completed using the systematic approach of creating an individual point of view, asking a striking problem, preparing emotional

content, using sound effects, using the power of music, accelerating the digital story, and creating short and understandable stories. Sound plays an important role in the emergence of effective digital storytelling, and it is stated that the points where the emphasis should be made should be determined well while writing the story (14). Support was received from academics who were experts in the field, who had previously trained with digital stories, in the conversion of the validated text content into the scenario, the vocalization, and the selection of background music. A breast care nurse was preferred because the text content should be an instructive voice and pay attention to the emphasis. Care was taken to make the background music a lively one. This music was chosen based on different educational digital stories. Completing these stages, the video was evaluated by 3 clinical nurses and 2 academicians who are experts in the field. It has been restructured taking into account the recommendations for color and video transitions. The resulting video was uploaded to YouTube and made available to students. The link to the related video was given to the students with a QR code. The training was not completed within the requested time and repeated access.

Data Collection

To prevent students from interacting with each other, the research was explained to the students on two different days. It was signed as a contract with the informed consent form that the students who were in their groups did not share the links. Data were collected using a two-part questionnaire developed by the researchers using the literature (12-14). The first part consists of 8 questions about the sociodemographic characteristics of undergraduate nurses. The second part consists of 28 questions containing theoretical information about breast cancer, risk factors, frequency of early diagnosis methods, and application steps. The second part was repeated eight weeks after the training method was presented to the students. Theoretical information in this section is scored on two points ranging from 1 point, defined as knowing, and 0 points, defined as not knowing. A total score was obtained by scoring for each item. According to the scoring system, a minimum of 0 and a maximum of 28 points can be obtained. A high score was interpreted as a high level of theoretical knowledge. Before using the questionnaire forms, expert opinions of five surgical nurses and five academicians were obtained and necessary corrections were made in line with their suggestions. After the questionnaire forms were finalized, the pre-test phase was conducted with ten students, the questions were reviewed and the research started. The Cronbach alpha reliability coefficient (α) of the questionnaire used in this study regarding knowledge and practice was found to be 0.89 for the pre-test and 0.91 for the post-test.

Data analysis

The study data were processed using the SPSS (Statistical Package for Social Sciences) 25.0 program. Data assessment was conducted using percentages, the Mann-Whitney U test, Kruskal-Wallis, One-Way Analysis of Variance, Correlation Analysis, the t-test, and the Kolmogorov-Smirnov test to determine whether or not data followed a normal distribution. Results were considered significant at $p<0.05$ and the confidence interval was set at 95%.

Ethical Considerations

Authorization was obtained from the dean of the related faculty and consent of volunteers was obtained from the participants. Ethical approval was given by the Ethics Committee of the Scientific Research Faculty of Medicine (No.24237859-569).

RESULTS

The mean age of the students participating in the study was 19.93±0.9 (min:18, max:23), of which 84.3% were women. It was determined that 5.2% of the students had breast cancer in their close relatives, mostly in the mother (2.2%) and aunt (2.2%). Students stated that they obtained the source of information about breast cancer from the television program 19.4% and the internet 10.4%. There was no significant difference between the two groups in terms of age, gender, relatives of breast cancer, knowledge of breast cancer, and screening methods (Table 1).

Table 1. Characteristics of participants, N=134

	Digital storytelling education (66)		Web-based education (68)		Analysis
	N	%	N	%	p
Age					
18-19	27	40.9	18	26.5	
20	24	36.4	39	57.4	0.52**
21-23	15	22.7	11	16.1	
Sex					
Women	54	81.8	59	86.8	0.20*
Men	12	18.2	4	13.2	
Breast Cancer					
Relatives	63	95.5	59	86.8	0.51*
No relatives	3	4.5	4	13.2	
Breast Cancer knowledge					
Yes	23	34.8	19	27.9	0.52*
No	43	65.2	49	72.1	
Breast Cancer awareness					
BSE	20	30.3	16	23.5	
CSE Mammography	3	4.5	3	4.4	0.14**
	-	-	-	-	

*Chi-square ** Kruskal-Wallis

After both education methods, it was seen that each breast screening method had a positive effect on education (Table 2). It was observed that there was a significant change in both the first and last test parameters in both of the training types at an advanced level ($p<0.0001$).

The two training methods made a significant difference between the first and last measurements (Table 3). Both methods did not make any difference in the first measurement, and there was a significant difference between them in the last measurement (p <0.05). Internet-based education creates a higher level of knowledge than digital story videos. As educational material, it was found that the internet-based material was rated 9.39±0.67, and the digital story video was rated 9.12±0.77. While the type of education had a 48.5% impact on the BSE application, internet-based education was found to be 73.5% effective. As a result of the regression analysis, it was found that the internet-based education model of the latest knowledge levels was a significant variable (p=.02) and the determination rate was 28% (R2=0.28).

Table 2. Correlation between among two groups' breast cancer early diagnosis methods

	Digital storytelling education				Web-based education			
	FM-sym	FM-BSE	FM-CBE	FM-mam	FM-sym	FM-BSE	FM-CBE	FM-mam
BM-sym	0.261 0.03				0.94 0.009			
BM-BSE		0.32 0.008				0.63 0.03		
BM-CSE			1.000 <0.0001				1.000 <0.0001	
BM-mam				0.38 0.002				0.98 0.003

BM: Baseline measure Sym: Symptom BSE: Breast Self Examination FM: Follow-up measure Mam: Mammography CSE: Clinical Examination

Table 3. Between among two groups' baseline and follow-up measures

	Digital storytelling education		Web-based education		
	Average	(min-max)	Average	(min-max)	p*
Baseline	8.53(SD±3.51)	(3-16)	8.53(SD±3.95)	(1-18)	0.58
Follow-up	16.08(SD±4.31)	(2-20)	14.34(SD±4.52)	(7-20)	0.007
Z	-7.06		-7.17		
p**	<0.0001		<0.0001		

*:Wilcoxon test, **: Mann Whitney-U test

DISCUSSION

Higher education institutions still strive to implement technological learning tools, and too much focus will be put on the technological materials rather than face-to-face interaction (15). It is inevitable to include technological equipment in education these days when active learning methods are emphasized in the education of nursing students (16). With this research, the effect of internet-based education and digital story videos on learning breast cancer early diagnosis methods were compared. This study was carried out as an original study by comparing technological products and evaluating their effects on education.

In the current study, with both training methods, the desired increase in knowledge level regarding breast cancer early diagnosis knowledge was determined. In a different drama-based training study, it was determined that after the training, women made a significant difference in their level of knowledge about breast cancer early diagnosis methods (17). In the other study, the digital story would be the right research to facilitate understanding of complex nursing education by student nurses (18). In another study, nursing education can be increased with internet-based education is effective, but the need for continuous education (19). It is seen that there is a need for a study that determines which method is more educational for nursing education.

In the present study, the students receiving internet-based education got a significantly higher score for breast cancer knowledge scores than those not receiving this education (Table 3). Although there is no study on nursing education where web-based education is compared with digital story videos, there is evidence that web education is used and gives positive results. In an experimental study in Taiwan, undergraduate nursing students getting web-based education has been significantly higher scores for knowledge scores and skills about intramuscular injections (20). In the other study, the nursing students offered web-based education got a significantly higher score for theoretical information than those not offered this education (21).

In this study, when nursing students are asked to evaluate the training materials they use, it is seen that they give more points to internet-based education. The type of education model appeals to students with more points than digital storytelling. This is because students are more likely to visit the site on their smartphones and visit the site for more education in their daily lives. It is known all over the world that the daily video surveillance times increase (22). However, the preference of the video as an educational material may be another topic to be investigated.

When internet-based education and digital story video were compared, it was seen that both of them produced significant changes in educational material. The training material to be used in nursing education may be suitable for both methods. however, it was observed that internet-based education between the two methods produced better results at the level of knowledge compared to the digital story. This suggests that internet-based education should be preferred when it is desired to create training material related to the level of knowledge. The use of technological products in the education of nursing students creates effective results. The use of such products is recommended, especially in the education of social issues such as cancer awareness.

Limitations

Several limitations of this study must be acknowledged. This research measured the level of knowledge eight weeks after the intervention with educational material. it does not include results about the next level of knowledge.

it also does not have information about how much it uses training material. Therefore, repeated use may have caused an increase in the level of knowledge. It is recommended to check the time spent on the site from the web site admin panel in the studies to be planned. In addition, the digital story users' repeated video views should be recorded.

CONCLUSION

The theoretical knowledge among nursing students modifies throughout the nurse education process. It is not yet clear which transfer of information how the material used in nursing education, should be supported by technological products. The research compared internet-based education and digital story education. However, there is still a need for a comparison of different technological products. Therefore, these research results are a reference for future research in other countries. In addition, the preparation of the content of the materials used in nursing education and the involvement of a health educator in the presentation of the technological product is important both in the transfer of the subject and in the preparation of the material in the preparation of effective training material.

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Research Article

The Precise Location of the Stylomastoid Foramen and Clinical Implication for Facial Nerve Block

Foramen Stylomastoideum'un Kesin Konumu ve Fasiyal Sinir Bloğu için Klinik Önemi

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Abstract

Aim: We aimed to develop linear regression formulas for determining the precise localization of the stylomastoid foramen on the base of the morphometric features of the person's own skull.

Material and Method: The study was conducted on 22 stylomastoid foramina (11 skulls). The 10 parameters determined for the stylomastoid foramen were measured on the photographs taken from the skull base and the 17 parameters determined for the morphometric features of the skull were measured on the photographs taken from the anterior plane, lateral plane, and posterior plan using Image J measurement software. The data obtained were evaluated with SPSS 20.0 statistical software.

Results: To determine the morphometric and topographic features of the stylomastoid foramen the equations have been developed such as; P1 (The distance between stylomastoid foramen and root of the zygomatic arch)=18.758+(0.472xP12)-(2.092x P16)+(0.831xP17)−(0.390xP18)−(0.101x P20); Adjusted R^2=0.865, Standard Error of the Estimation=1.389.

Conclusion: Mean values can give misleading information in determining the topographical relationship between the stylomastoid foramen and the surrounding anatomical structures. We have developed regression formulas that will estimate the accurate location of the stylomastoid foramen and the accurate distances between other surrounding anatomical structures, taking into account the morphometric characteristics of the person's own skull.

Keywords: Stylomastoid foramen, facial nerve, facial nerve block

Öz

Amaç: Çalışmanın amacı, kişinin kendi kafatasının morfometrik özelliklerinden yola çıkarak foramen stylomastoideum'un kesin lokalizasyonunu belirlemek için lineer regresyon formülleri geliştirmektir.

Materyal ve Metot: Çalışma, 22 foramen stylomastoideum (11 kafatası) üzerinde gerçekleştirildi. Foramen stylomastoideum için belirlenen 10 parametre kafa tabanından çekilen fotoğraflarda, kafatasının morfometrik özellikleri için belirlenen 17 parametre ise Image J ölçümü kullanılarak ön, yan ve arka plandan çekilen fotoğraflarda ölçüldü. Ölçümlerden elde edilen veriler istatistik yazılımı SPSS 20.0 ile değerlendirildi.

Bulgular: Foramen stylomastoideum'un morfometrik ve topografik özelliklerini belirlemek için; P1 (Foramen stylomastoideum ile arcus zygomaticus kökü arası mesafe)=18,758+(0,472xP12)-(2,092xP16)+(0,831xP17)−(0,390xP18)−(0,101xP20); Düzeltilmiş R^2=0.865, Tahminin Standart Hatası=1.389 şeklinde denklemler geliştirilmiştir.

Sonuç: Ortalama değerler, foramen stylomastoideum ve onu çevreleyen anatomik yapılar arasındaki topografik ilişkinin belirlenmesinde yanıltıcı bilgi verebilir. Kişinin kendi kafatasının morfometrik özelliklerini dikkate alarak, foramen stylomastoideum'un kesin konumunu ve çevredeki diğer anatomik yapılar arasındaki doğru mesafeleri belirleyecek regresyon formülleri geliştirdik.

Anahtar Kelimeler: Foramen stylomastoideum, nervus facialis, fasiyal sinir bloğu

INTRODUCTION

The stylomastoid foramen, the end of the facial canal, is a curved aperture located on the temporal bone's inferior aspect of the petrous part, midway between the styloid process and the mastoid process. The facial nerve, which is the VII. cranial nerve, leaves the skull and the stylomastoid artery, that is a branch of the posterior auricular artery, enters the skull through the stylomastoid foramen (1-3).

The sensory and the motor roots of the facial nerve

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arise from the sulcus bulbopontinus, on the anterior surface of the brain stem, between the pons and medulla oblongata. Both roots enter the internal auditory meatus in the temporal bone's petrosal part, accompanied by the vestibulocochlear nerve in the fossa cranii posterior. In the internal auditory meatus's lower part, the facial nerve gets into the facial canal and runs outward along with the inner ear. The facial nerve enlarges to form the geniculate ganglion and curves sharply posteriorly on the upper side of the promontorium when it reaches the inner wall of the tympanic cavity. It turns downward on the inner side of the entrance to the antrum mastoideum, on the posterior wall of the tympanic cavity, runs downward behind the pyramis, and leaves the temporal bone using the stylomastoid foramen, locates in front of the styloid foramen and the jugular foramen locates medially. After getting out from the stylomastoid foramen, 5-7 mm behind the mandibular ramus, the facial nerve gives off two branches; the digastric nerve and the posterior auricular nerve. After giving those branches the facial nerve, enters the parotid gland (4-7). The facial nerve's motor branches supply the mimetic and facial muscles (8).

The orbicularis oculi muscle around the eye is the sphincter muscle, innervated by the facial nerve. Facial nerve blockade is required to temporarily paralyze the orbicularis oculi muscle in order to prevent the increase in intraocular pressure that may occur due to squeezing of the eyelids during cataract extraction. Good anesthesia is important for safe intraocular surgery (9).

There have been four techniques described in the literature for facial nerve block: 1) Van Lint block, 2) Atkinson block, 3) O' Brien block, and 4) Nadbath block. According to Van Lint's block, the facial nerve's peripheral branches are blocked near the lateral orbital margin at the level of the external canthus of the eye, a point approximately 2 cm behind. In Atkinson's block, the upper branch of the facial nerve is blocked at the lower edge of the zygomatic bone. In O' Brien block, the main trunk of the facial nerve is blocked near the condylar process at the level of the mandibular neck. In Nadbath block, the facial nerve is blocked in the stylomastoid foramen. This technique is also called enhanced O' Brien block (9,10).

The blockage of the facial nerve trunk in the stylomastoid, Nadbath nerve block, is usually preferred because of the advantages in being less painful and preventing ecchymosis of the face, however, the risks of nerve injury and neurological severe complications may arise, also complications related to respiratory and vocal cords may develop as a result of inadvertent injection (11-13).

We aimed to develop linear regression formulas for determining the precise localization of the stylomastoid foramen on the base of the morphometric features of the person's own skull. Also to evaluate the distances between the surrounding anatomical structures, in addition to the mean and standard deviation values given in the literature, and to raise awareness for person-specific application instead of ambient values, on behalf of avoiding the complications.

MATERIAL AND METHOD

The study was conducted on 22 stylomastoid foramina (11 skulls) in the collection of Harran University Faculty of Medicine, Department of Anatomy. The dry skulls were photographed from inferior, lateral, anterior, and posterior plans in a standard position. Anthropometric points to be taken into account in measurements were determined (Figure 1). The 10 parameters determined for the stylomastoid foramen were measured on the photographs taken from the skull base (from inferior plane) (P1-10: Figure 2), and the 17 parameters determined for the morphometric features of the skull were measured on the photographs taken from the anterior plane (P11-18: Figure 3), lateral plane (P19-25: Figure 4), and posterior plan (P26,27: Figure 5) using Image J measurement software (Ver. 1.51 23 April 2018) (12).

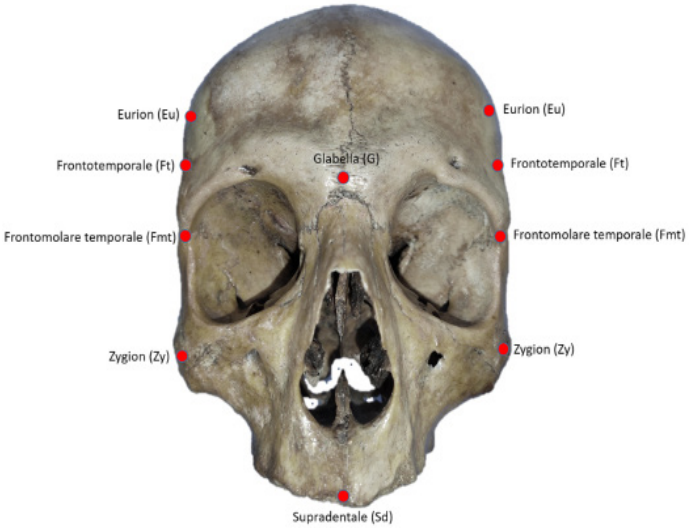

Figure 1. The anthropometric points used as landmark

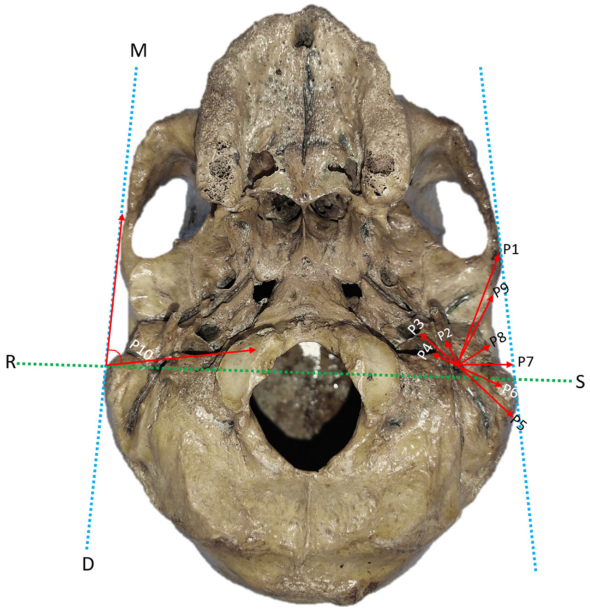

Figure 2. The parameters related to the stylomastoid foramen and surrounding anatomical structures (mm)

Table 1. The results of the descriptive statistics of the parameters related the stylomastoid foramen

Parameters (mm)	Min.	Max.	Mean ± SD
P1. The distance between the center of the stylomastoid foramen and the lateral margin of the root of the zygomatic arch	29.68	45.13	35.66±3.78
P2. The distance between the center of the stylomastoid foramen and the root of the styloid process	2.33	7.38	4.73±1.28
P3. The minimum distance between the center of stylomastoid foramen and the nearest carotid canal margin	5.80	19.53	13.91±2.81
P4. The minimum distance between the center of stylomastoid foramen and the nearest jugular foramen margin	2.95	9.47	6.57±1.69
P5. The distance between the posterior margin of the mastoid process and the center of the stylomastoid foramen	17.66	31.07	24.22±3.43
P6. The distance between the center of the stylomastoid foramen and the tip of the mastoid process	9.03	19.89	13.77±2.68
P7. The distance between stylomastoid foramen and MD line	13.74	21.38	17.54±2.33
P8. The distance between the center stylomastoid foramen and the inferior margin of the external acoustic meatus	6.66	15.08	10.55±1.92
P9. The distance between the center stylomastoid foramen and the lateral margin of the mandibular fossa	18.06	30.89	24.06±3.18
P10. MD-RS angle	54.16	85.99	66.54±9.49

Table 2. The descriptive statistics of the parameters related the skull dimensions

Parameters (mm)	Min.	Max.	Mean±SD
P11. The maximum skull breadth (Eu-Eu)	78.99	103.56	90.53±7.88
P12. The minimum distance between the two frontotemporale (Ft-Ft)	77.05	100.78	88.04±7.25
P13. The upper facial breadth (Fmt-Fmt)	79.94	101.56	92.56±7.25
P14. Orbital breadth	31.42	37.29	34.29±2.13
P15. Bizygomatic breadth (Zy-Zy)	81.37	104.31	93.14±6.88
P16. The orbital height	30.17	40.20	35.05±3.24
P17. The distance between Glabella (G) and supradentale (Sd)	71.57	101.12	84.31±9.43
P18. The distance between the lower margin of the maxilla and the orbit's lower margin	27.67	42.77	35.77±4.67
P19. The maximum antero-posterior breadth of the head (Op-G)	113.62	156.98	135.61±15.48
P20. The distance between the ophistocranion and the tip of the mastoid process	53.98	94.54	73.64±13.72
P21. The distance between the external margin of the external acoustic meatus the tip of the mastoid process	14.95	24.71	19.66±2.714
P22. The distance between the root of the zygomatic arch and the tip of the mastoid process	29.00	39.77	35.50±3.23
P23. The distance between the glabella and the tip of the mastoid process	84.23	106.24	101.59±2.83
P24. The distance between the zygoma ant the tip of the mastoid process	65.79	92.46	79.04±7.36
P25. The distance between the supradentale and the tip of the mastoid process	72.05	90.72	80.41±5.53
P26. The distance between parietal eminences	89.71	147.96	116.54±18.30
P27. The distance between bimastoid line and vertex	103.63	161.33	127.57±16.39

Table 3. The equations for estimating the distances between stylomastoid foramen and surrounding anatomical structures

Equations	Adjusted R^2	Standard Error of the Estimate
P1=18.758+(0.472xP12)-(2.092xP16)+(0.831xP17)−(0.390xP18)−(0.101xP20)	0.865	1.389
P2=-22.398+(0.302xP14)+(0.075xP17)+(0.048xP19)+(0.272xP21)+(0.110xP22)−(0.067xP24)	0.685	0.852
P3=-6.601+(0.497xP12)−(1.137xP16)+(0.368xP17)−(0.308xP18)−(0.087xP20)+(0.711xP21)−(0.309xP22)	0.382	2.206
P4=-24.927+(0.402xP12)−(0.456xP13)+(0.599xP14)+(0.574xP18)+(0.421xP22)	0.545	2.316
P5=22.783+(0.603xP12)−(0.649xP15)−(0.930xP16)+(0.313xP17)+(0.498xP18)−(0.704xP21)+(0.309xP22)	0.665	2.434
P6=9.639+(0.748xP11)−(0.876xP12)+(0.325xP18)−(0.274xP22)+(0.140xP24)	0.543	2.076
P7=79.566−(0.151xP11)−-(1.646xP14)+(0.662xP18)-(1.437xP21)+(0.010xP23)+(0.383xP24)−(0.243xP25)	0.387	1.828
P8=-12.657+(0.338xP15)−(0.071xP20)+(0.400xP21)+(0.452xP21)−(0.166xP25)	0.307	1.605
P9=-69.475+(0.697xP15)+(0.553xP16)−(0.442xP18)−(0.304xP20)+(1.384xP21)+(0.571xP22)	0.754	1.576
P10=-52.265−(3.819xP13)+(4.712xP15)+(0.886xP22)+(0.011xP23)	0.857	3.585

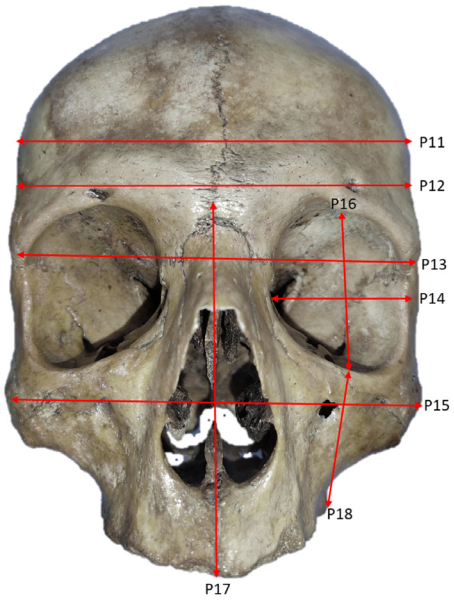

Figure 3. The parameters on the anterior aspect of the skull (mm)

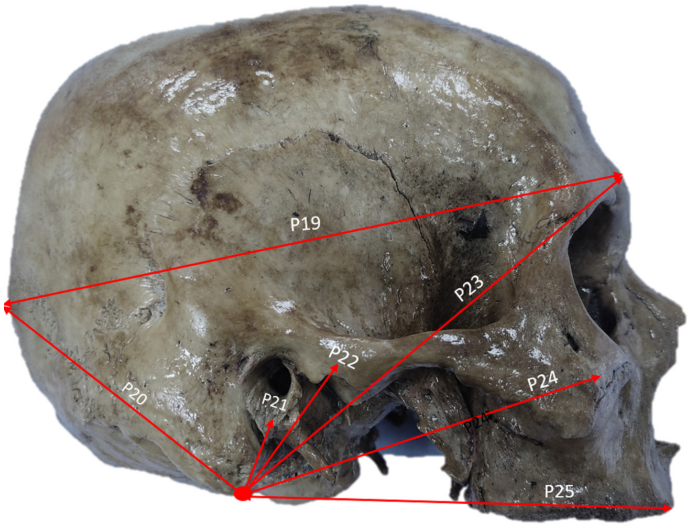

Figure 4. The parameters on the lateral aspect of the skull (mm)

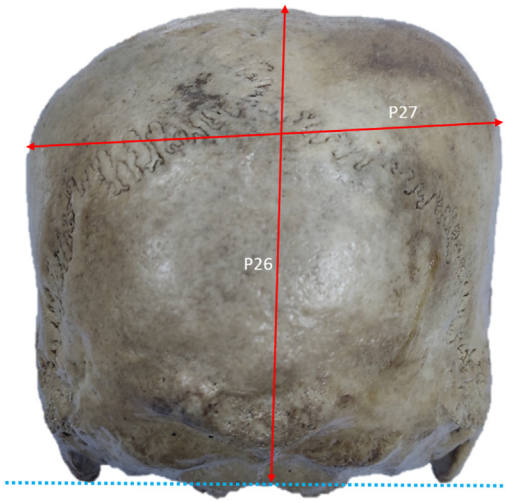

Figure 5. The parameters on the posterior aspect of the skull (mm)

Parameters

P1. The distance between the center of the stylomastoid foramen and the lateral margin of the root of the zygomatic arch

P2. The distance between the center of the stylomastoid foramen and the root of the styloid process

P3. The minimum distance between the center of stylomastoid foramen and the nearest carotid canal margin

P4. The minimum distance between the center of stylomastoid foramen and the nearest jugular foramen margin

P5. The distance between the posterior margin of the mastoid process and the center of the stylomastoid foramen

P6. The distance between the center of the stylomastoid foramen and the tip of the mastoid process

P7. The distance between the center stylomastoid foramen and the MD line (The line between the lateral margin of the zygomatic arch and the lateral margin of the mastoid process)

P8. The distance between the center stylomastoid foramen and the inferior margin of the external acoustic meatus

P9. The distance between the center stylomastoid foramen and the lateral margin of the mandibular fossa

P10. MD-RS angle (The angle between the MD line and RS line)

P11. The maximum skull breadth (Eu-Eu)

P12. The minimum distance between the two frontotemporale (Ft-Ft)

P13. The upper facial breadth (Fmt-Fmt)

P14. The orbital breadth

P15. The bizygomatic breadth (Zy-Zy)

P16. The orbital height

P17. The distance between the glabella (G) and the supradentale (Sd)

P18. The distance between the lower margin of the maxilla and the orbit's lower margin

P19. The maximum antero-posterior breadth of the head (Op-G)

P20. The distance between the ophistocranion and the tip of the mastoid process

P21. The distance between the external margin of the external acoustic meatus and the tip of the mastoid process

P22. The distance between the root of the zygomatic arch and the tip of the mastoid process

P23. The distance between the glabella and the tip of the mastoid process

P24. The distance between the zygoma and the tip of the mastoid process

P25. The distance between the supradentale and the tip of the mastoid process

P26. The distance between parietal eminences

P27. The distance between bimastoid line and vertex

Statistical analysis

As a result of the power analysis, when the effect size was selected as 0.5 (α=0.05) to examine the relationship between dependent variables and independent variables with the regression model, it was determined that approximately 22 (n=22) stylomastoid foramen should be included in the study for a significance level with power 0.80%. We performed statistical analyzes using IBM SPSS version 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). The descriptive statistics values of the parameters related to the stylomastoid foramen and skull were evaluated. Pearson correlation analysis was applied to examine the relationship between the distances of the stylomastoid foramen to the surrounding anatomical structures and skull measurements. Equations to estimate the distances between the stylomastoid foramen and the surrounding anatomical structures were developed by linear regression analysis. The statistical significance level was $p<0.05$.

RESULTS

The results of the descriptive statistics values of the parameters related to the stylomastoid foramen were given in table 1.

The results of the descriptive statistics values of the parameters related to the skull dimensions were given in table 2.

The equations for estimating the distances between stylomastoid foramen and surrounding anatomical structures were given in table 3.

DISCUSSION

Blocking the facial nerve trunk in the stylomastoid foramen is a preferred method, but serious complications may occur due to incorrect injections and nerve injuries. Therefore, examining the morphometry of the stylomastoid foramen and the relationship with anatomical structures nearby is very important to avoid such dangers (9). Lindquist et al. reported that complications such as dysphonia, laryngospasm, unilateral vocal cord paralysis, and feeling of not being able to breathe develop as a result of blockade of the facial nerve trunk due to its proximity to the vagus, glossopharyngeal and accessory nerves (15).

The stylomastoid artery, which emerges from the stylomastoid foramen together with the facial nerve's trunk, masks the facial nerve, making the surgical approach difficult during parotidectomy (16).

The addition of epinephrine to local anesthetics or needle stimulation in the parapharyngeal region may trigger the vascular sympathetic response. As a result, facial nerve palsy may occur due to ischemia of the stylomastoid foramen (17).

Anatomical knowledge of the stylomastoid foramen is important for clinical applications because of its proximity to important neurovascular structures. Any anatomical variation may present with compression symptoms. In addition, the surgical anatomy of the stylomastoid foramen is important (3).

The identified landmarks for the facial nerve trunk should be easy to identify and reliable. Because of their hard and reliable anatomical location, although difficult to palpate the bony structures are more suitable than soft tissue or cartilaginous landmarks (18).

Sharma and Varshney (2015) studied on 100 dry skulls in 2015. They found that 83.51% of the stylomastoid foramen was located anterior to the XY line (The horizontal line passing through the tip of the anterior edge of both mastoid processes), 13.4% along the XY line 3.03% posterior to the XY line (9).

Kutoğlu et al. (2021) studied on 53 temporal bones in 2021 and they found 54.7% of the stylomastoid foramen was located anterior to the XY line, 34% posterior to the XY line, and 13.3% above the XY line (19).

Sharma and Varshney (2015) evaluated the distance between the tip of the mastoid process center and the center of the stylomastoid foramen; and as 15.26±1.4mm on the right side and 14.32±1.8mm on the left side. They found the distance between the jugular foramen and the center of the stylomastoid foramen as 12.28±1.9mm and 12.96±2.1mm (respectively on the right side and left side). They found the angle as 66.57±2.6 and 65.96±1.8 on the right and left sides, respectively, in degree (9).

Jai Rexlin et al., (2019) studied on 40dry human skulls in 2019. They found the distance between the center of the stylomastoid foramen to the center of the jugular foramen as 8.90±1.42mm and 9.34±1.46mm (on the left and right sides respectively). They measured the shortest distance between the mastoid process and the center of the stylomastoid foramen as 13.42±1.97mm on the left side and 13.77±1.64mm on the right side (4).

In the current study, we found the distance between the root of the styloid process and stylomastoid foramen as 4.73±1.28mm, the distance between the jugular foramen and the stylomastoid foramen was 6.57±1.69mm, the distance between the mastoid process and the stylomastoid foramen was 13.77±2.68mm, MD-RS angle was 66.54±9.49 in degree.

CONCLUSION

The size of the range between the minimum and maximum values in the tables (table 1 and table 2) as a result of the

descriptive statistics and the different measurements in between with other studies reveal that the results may vary among the people and also populations. For this reason, mean values can give misleading information in determining the topographical relationship between the stylomastoid foramen and the surrounding anatomical structures. We have developed regression formulas that will estimate the accurate location of the stylomastoid foramen and the precise distances between other surrounding anatomical structures, taking into account the morphometric characteristics of the person's own skull. It is noteworthy that the power of the equations produced for P1 and P10 among the developed formulas is high. We think that the power of the equations related to other parameters will increase with the increase in sample size. We believe that this new technique we have developed will guide anesthesiologists and surgeons in person-specific approaches.

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Ethical approval: *The authors declare that the current study on donated cadaver skulls belonging to the Department of Anatomy was carried out in accordance with the 1964 Declaration of Helsinki. There were no human participants in the study or there was no human/animal experimentation, therefore no ethics committee approval.*

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Research Article

The Correlation of C-Reactive Protein/Albumin, Mii-1 and Mii-2 Indexes With Hospitalization and Mortality in Stanford Type A Aortic Dissection

Stanford Tip A Aort Diseksiyonunda C-Reaktif Protein/Albumin Oranı İle Mii-1 ve Mii-2 İndekslerinin Hastaneye Yatış Süresi ve Mortalite İlişkisi

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Abstract

Aim: In this study we aimed to investigate the relationship between C-Reactive Protein (CRP)/albumin ratio, MII-1 and MII-2 indexes in hospitalization and mortality due to aortic dissection.

Material and Method: Patients who presented to our emergency department with a sudden-onset, sharp and stabbing chest pain and diagnosed with Stanford type A aortic dissection were included in the study. Patients' demographics such as age and gender, hemogram parameters, ratios, indexes, hospitalization and mortality status were recorded. Demographic features, hemogram parameters, ratios and indexes were compared between the survivor and exitus patients.

Results: A total of 71 patients who presented to the emergency department with sudden-onset stabbing chest pain and subsequently diagnosed with aortic dissection were included in this retrospective study. The median age of the patients was negatively correlated with albumin (r=-0.27, p=0.021), hemoglobin (r=-0.28, p=0.019). Hemoglobin values were significantly higher in male than in female patients. The median length of stay in the hospital was found as 10 (7-14) days. In the correlation analysis of the hemogram parameters, indexes and length of stay in the hospital; CRP and CRP/Albumin ratio were significantly correlated with length of stay in the hospital in positive direction.

Conclusion: The results of this study point out a significant correlation between CRP, CRP/albumin ratio and length of stay in hospital. This information might be helpful in rapid decision making process for early diagnosis and treatment of the disease.

Keywords: Aortic dissection, C-reactive protein/albumin, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, multi inflammatory index

Öz

Amaç: Bu çalışmamızda hastanede yatış ve aort diseksiyonuna bağlı mortalitede C-Reaktif Protein (CRP)/albümin oranı, MII-1 ve MII-2 indeksleri arasındaki ilişkiyi araştırmayı amaçladık.

Material and Methot: Acil servisimize akut başlangıçlı, keskin ve saplayıcı göğüs ağrısı ile başvurup Stanford Tip A aort diseksiyonu tanısı alan hastalar çalışmaya dahil edildi. Hastaların yaş ve cinsiyet gibi demografik bilgileri, hemogram parametreleri, oranları, indeksleri, yatış ve mortalite durumları çalışmaya alındı. Taburcu olanlar ve hayatını kaybeden hastalar arasında demografik özellikler, hemogram parametreleri, oranlar ve indeksler karşılaştırıldı.

Bulgular: Bu retrospektif çalışmaya, acil servisimize başvuran ve ardından aort disseksiyonu tanısı konan toplam 71 hasta dahil edildi. Hastaların medyan yaşı albümin (r=-0.27, p=0.021), hemoglobin (r=-0.28, p=0.019) ve prognostik nutrisyonel indeks (PNI) (r=-0.31, p=0.008) ile negatif korelasyon gösterdi. Hemoglobin değerleri erkek hastalarda kadınlara göre anlamlı derecede yüksekti. Hastanede kalış süresi median 10 (7-14) gün olarak bulundu. Hemogram parametrelerinin, indekslerin ve hastanede kalış sürelerinin korelasyon analizinde; CRP ve CRP/Albumin oranı hastanede kalış süresi ile pozitif yönde anlamlı olarak korele idi.

Sonuç: Bu çalışmanın sonuçları, CRP, CRP/albümin oranı ve hastanede kalış süresi arasında anlamlı bir ilişkiye işaret etmektedir. Bu bilgiler hastalığın erken teşhisi ve tedavisi için hızlı karar verme sürecinde yardımcı olabilir.

Anahtar Kelimeler: Aort diseksiyonu, C-reaktif protein/albümin, nötrofil/lenfosit oranı, trombosit/lenfosit oranı, multi-inflamatuar indeks

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INTRODUCTION

Aortic dissection is an uncommon but potentially fatal condition that can be difficult to diagnose and treat in the emergency room. Even when appropriately diagnosed, it has an in-hospital mortality rate of 27% (1). Relatively atypical process of aortic dissection, which mimics other clinical conditions, makes the diagnosis difficult. The diagnosis of aortic dissection in the emergency department is very rare. Patients with aortic dissection mostly manifests a variaty of symptoms. Moreover, aortic dissection may also manifests present with symptoms that are more common in other diseases including heart failure, vascular insufficiency, neurologic deficits and syncope (2). Severe pain with sudden-oenset accompanying with high blood pressure suggests dissection; however lack of these findings does not exclude aortic dissection (3). Prevalence as low as 3.5/1000.000 makes the diagnosis further challenging (4). Because many patients die before arriving to the hospital, the real incidence of aortic dissection is difficult to estimate. Death may be attributed to other causes. Aortic dissection may also be missed during the initial evaluation, resulting in early mortality as a result of misdiagnosis (5).

Taking medical history and physical exam alone are unreliable in making the diagnosis of aortic dissection. Findings of multiple abnormalities on chest radiography can be used as a screening tool to screen for dissections with a sensitivity of 90% (6). In addition, echocardiography and computed tomography are also used to help diagnosis.

The most commonly used classification in aortic dissections are the DeBakey and Stanford classifications. While the DeBakey classification is an anatomical classification, the Stanford classification is more of a functional classification. According to this; Aortic dissections are divided into two types. Regardless of where the primary tear is, all dissections involving the ascending aorta are referred to as type A, and those distal to the left subclavian artery are referred to as type B. The largest part of dissections are Stanford type A and these are commonly related with more increased mortality (4).

On the other hand, researchers have focused on the development of markers and scoring systems to identify aortic dissection cases reliably. Several inflammatory markers have been successfully used to predict various diseases and medical conditions. In an interesting study, Yildiz et al. investigated the correlation of Platelet to Lymphocyte Ratio, Neutrophil to Lymphocyte Ratio and Mean Platelet Volume in Individuals Diagnosed with Gambling Disorder (7). Sevil et al. evaluated the association between the inflammatory parameters and prognosis of Bell's palsy (8). Forrer et al. investigated novel biomarkers for diagnostic work up of acute aortic dissection and reported that IL-10 shows potential as a biomarker for aortic dissection (9). Wen et al. proposed CRP as a biomarker of aortic dissection along with other numerous markers. However, the authors underlined that further studies are needed in order to introduce these biomarkers in emergency settings for rapid diagnosis of aortic dissection. Gao et al. reported that serum albumin levels are associated with in-hospital mortality in aortic dissection (10).

Multi Inflammatory Index (MII) is a new prognostic index composed of MII-1 (Neutrophil-to-lymphocyte ratio [NLR] x CRP) and and MII-2 (Platelet-to-lymphocyte ratio [PLR] x CRP). Gardini et al. used these indexes in patients receiving chemotherapy and reported that the novel MII indexes seem to help determination of prognosis. Boyuk et al. reported that MII-1 and 2 indexes that are are simple, inexpensive, and easy to obtain, these indexes are helpful in distinguishing massive and non-massive pulmonary embolism (PE) (11).

Based on this information from the literature, the objective of this study was to investigate the correlation between CRP/albumin ratio, MII-1 and MII-2 indexes in terms of hospitalization and mortality due to aortic dissection.

MATERIAL AND METHOD

After receiving the necessary ethics approval from the local ethics committee of our hospital, this study was performed retrospectively (Decision No: 2022/30, Date 22/02/2022). Patient consent was waived because of the retrospective design of the study. This study was performed in accordance with the relevant ethical items of the Declaration of Helsinki.

Patients diagnosed with Stanford Type A aortic dissection after computed tomography (CT) seen by their emergency physicians (EP) who applied to the emergency department with sudden onset, sharp and stabbing chest pain between 01 August 2015 and 01 February 2022 were included. Data of the study were obtained from the electronic record system of the hospital with the permission of the hospital management. Patients with ICD-10 code for aortic dissection were analyzed retrospectively. In the case of more than one admission, only the first admission was taken into account. The MII-1 and MII-2 were defined using the following formulas:

MII-1 = NLR (Neutrophil/Lymphocyte Ratio) x CRP

MII-2 = PLR (Platelet/Lymphocyte Ratio) x CRP

Patients' demographics such as age and gender, hemogram parameters, ratios, indexes, hospitalization and mortality status were recorded. Demographic features, hemogram parameters, ratios and indexes were compared between the survivor and exitus patients. Hemogram parameters, ratios, indexes and hospitalization were further compared between genders. Outcomes of the patients were evaluated as hospitalization, exitus our referral to another health care center.

Statistical Analysis

Data obtained in this study were evaluated using SPSS version 23.0 (SPSS, Social Package for Social Sciences, IBM Inc., Armonk, USA). Normality of the data was

evaluated with the Kolmogorov-Smirnov test. Continuous variables are expressed as median and interquartile range and categorical variables are given as frequency (number and percentage). Hemogram and index values of the groups were examined with Mann-Whitney U test. The correlations with length of stay in hospital was examined with Spearman (rho) coefficient. Performances of the hemogram parameters and indexes in predicting mortality and diagnosis were investigated with ROC analysis. p<0.05 values were considered statistically significant.

RESULTS

A total of 71 patients who presented to the emergency department with sudden-onset stabbing chest pain and subsequently diagnosed with aortic dissection were included in this retrospective study. Median age of the patients was 58 years and 74.6% (n:53) male. In the evaluation of hemogram parameters and indexes; a negative correlation was found between age and hemoglobin (r=-0.28, p=0.019), albumin (r=-0.27, p=0.021) and prognostic nutritional index (PNI) (r=-0.31, p=0.008). Hemoglobin values were significantly higher in male than in female patients (Figure 1) (Table 1).

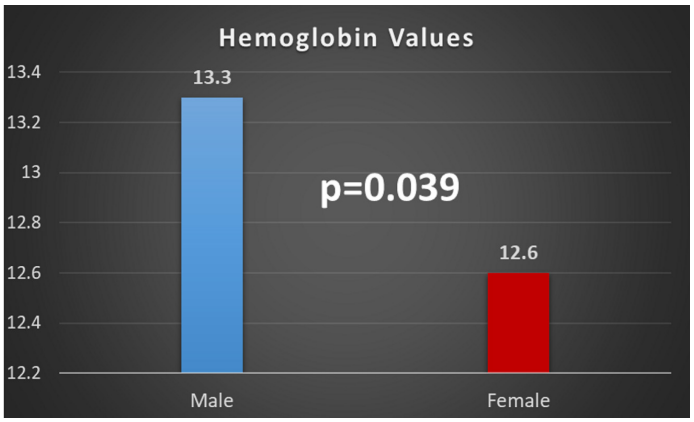

Figure 1. Hemoglobin values according to sexes

Of all patients, 25.4% (n:18) died. No significant difference was found between discharged and died patients in terms of age and gender. There was no statistically significant difference between mortality and hemogram parameters, ratios and indexes (p>0.05, Table 2).

Table 1. Hemogram parameters, ratios, indexes and hospitalization according to demographic characteristics of patients with aortic dissection

	Age		Gender		
	r	p	Female (n=18) Med (IQR)	Male (n=53)Med (IQR)	p
Hemogram					
WBC	-0.17	0.157	11.1 (9.29-14.56)	13.01 (9.5-17.3)	0.358
HGB	-0.28	0.019	12.6 (10.6-13.33)	13.3 (11.6-14.8)	0.039
PLT	-0.06	0.623	219 (180-242.5)	184 (161.5-222.5)	0.193
LYM	-0.19	0.117	1.08 (0.64-2.2)	1.3 (0.87-2.15)	0.379
NEU	-0.12	0.311	9.25 (7.08-12.8)	9.54 (6.49-14.55)	0.781
PDW	0.03	0.771	16.95 (14.65-18.05)	17.1 (12.15-18.5)	0.989
MPV	-0.08	0.488	8.56 (7.02-10.05)	8.6 (7.24-10.25)	0.561
PCT	-0.16	0.182	0.17 (0.14-0.2)	0.16 (0.13-0.2)	0.731
CRP	0.17	0.163	10.9 (1.75-77.38)	5.7 (0.9-22.55)	0.365
ALB	-0.27	0.021	38.75 (32.75-42.13)	38.1 (32.2-42.85)	0.791
Ratios					
NLR	0.09	0.473	9.68 (4.93-12.78)	7.58 (3.27-14.79)	0.534
CLR	0.19	0.113	10.09 (1.48-56.65)	3.74 (0.65-30.46)	0.278
CRP/ALB	0.19	0.119	0.29 (0.04-2)	0.15 (0.02-0.74)	0.341
Indexes					
MI index	0.19	0.119	97.06 (18.6-368.37)	35.92 (7.04-302.94)	0.348
MII index	0.18	0.129	1609.74 (359.9-12047.89)	539.11 (106.33-5282)	0.273
Length of stay*	0.112	0.425	12 (7-14)	10 (7-15.5)	0.892

Statistically significant p values are shown in bold font. IQR: Interquartile range (25^{th}-75^{th} percentiles). Mann-Whitney u test, r: Spearman (rho) correlation coefficient. *: The analysis was made over discharged patients (16 female, 37 male; total 53 patients).

Table 2. Evaluation of demographic features, hemogram parameters, ratios and indexes according to mortality status

	AD		p
	Discharged (n=53)	Exitus (n=18)	
Age, Year, Med (IQR)	57 (49-68)	60 (50.25-72.25)	0.574
Gender - Male, n (%)	37 (69.81)	16 (88.88)	0.130a
Hemogram, Med (IQR)			
WBC	11.7 (8.52-16.7)	13.45 (10.27-16.63)	0.428
HGB	13.1 (11.45-14.2)	13.1 (10.43-14.73)	0.984
PLT	187 (164-231.5)	184.5 (157.5-225)	0.942
LYM	1.22 (0.83-2.18)	1.31 (0.79-2.17)	0.921
NEU	9.16 (6.47-14.85)	10.17 (7.88-13.98)	0.588
PDW	16.9 (12-18.3)	17.4 (16.48-18.7)	0.125
MPV	8.67 (7.26-10.25)	8.03 (6.87-9.9)	0.428
PCT	0.17 (0.13-0.2)	0.17 (0.13-0.2)	0.776
CRP	4.9 (1.1-18.75)	18.5 (0.83-69.95)	0.190
ALB	38.1 (32-42.6)	38.9 (32.78-41.9)	0.802
Ratios, Med (IQR)			
NLR	9.2 (2.8-15.2)	7.4 (5.7-14.2)	0.947
CLR	3.3 (1-21.6)	24.9 (0.3-86.5)	0.229
CRP/ALB	0.1 (0-0.6)	0.5 (0-1.8)	0.224
Indexes, Med (IQR)			
MI index	30.3 (8.6-253)	285.9 (7.3-679.2)	0.191
MII index	539.1 (114.6-4768)	4173.7 (97.4-20223.7)	0.209

Statistically significant p values are shown in bold font. IQR: Interquartile range (25th-75th percentiles). Mann-Whitney U test, a: Fisher's Exact test

Table 3. Correlation analysis of hemogram parameters, indexes and length of stay in the hospital

Indexes	AD (nd=53)	
	r	p
Hemogram		
WBC	-0.09	0.520
HGB	-0.05	0.698
PLT	0.00	0.978
LYM	0.13	0.346
NEU	-0.13	0.341
PDW	-0.16	0.246
MPV	0.16	0.263
PCT	0.11	0.448
CRP	0.29	0.037
Albm	0.05	0.740
Ratios		
NLR	-0.18	0.202
CLR	0.18	0.190
CRP/Alb	0.27	0.046
Indexes		
MII-1 index	0.17	0.231
MII-2 index	0.18	0.201

The median length of stay in the hospital was found as 10 (7-14) days. Age and gender distribution of the discharged patients was similar (p=0.425, p=0.892) (Table 1). In the correlation analysis of the hemogram parameters, indexes and length of stay in the hospital; CRP and CRP/ALB ratio were significantly correlated with length of stay in the hospital in positive direction (Table 3).

DISCUSSION

In our study, in the correlation analysis of hemogram parameters, indices and hospital stay; We found that CRP and CRP/Albumin ratio were positively and significantly correlated with the length of hospital stay. However, MII-1 and MII-2 indices, which have recently been used in the literature, were not significant.

Aortic dissection is a serious medical condition with high rates of morbidity and mortality. Aortic dissection manifests with develops quickly in an intimal flap due to blood streaming into the media and pressing the intima and adventitia apart. The destruction of the ingredients of the aorta is influenced by several risk factors that induce infiltration of inflammatory cells in the aortic wall, apoptosis of vascular smooth muscle cells and inflammatory reaction.

Aortic dissection is a difficult diagnosis for clinicians due to its rarity and the fact that its symptoms are likely to match those of more prevalent illnesses. Especially in the

emergency department the diagnosis of aortic dissection is further challenging, because 20% of aortic dissections presents without chest pain and 6% without any pain (3).

Although chest X-ray and CTA are reliable in the diagnosis, biomarkers might provide valuable information about the course of the disease. Several biomarkers can be found in peripheral blood to help diagnostic and prognostic work up in aortic dissection (12). Studies have proposed cardiac troponins, C-reactive protein (CRP), IL-6, matrix metalloproteinases, smooth muscle myosin heavy chain, creatine kinases, calponin, soluble elastin fragments, D-dimer and pro-brain natriuretic peptide as diagnostic and prognostic biomarkers (13). The concentration of these markers in the blood may be related to symptomatology. The CRP-albumin ratio, rather than either marker alone, may provide a better evaluation of the inflammatory process. The CRP-albumin ratio is a novel inflammatory prognostic indicator in the development of cardiovascular disease, according to several studies (9,10,14).

In the present study, we investigated the relationship between CRP/albumin ratio, MII-1 and MII-2 indexes, length of stay and mortality due to aortic dissection.

CRP is an easy to obtain, inexpensive and simple biomarker used in daily clinical practice. Its role in the immunological pathways in aortic dissection is evidenced by a significant increase in CRP and pro-inflammatory cytokines in patients with aortic dissection (15). Elevated CRP values point out high rates of morbidity and mortality in cardiovascular diseases (16). CRP value has been reported to be significantly increased in patients with complications of acute aortic dissection, including pleural effusion and impaired oxygenation (17). Plasma CRP concentrations > 15 mg/dL have been reported to be an important marker of poor prognosis. Because, CRP levels are rarely raised within several hours after onset, CRP has low diagnostic value in emergency settings (18). Sakakura et al. stated that peak CRP value was a strong predictor od long-term events in aortic dissection (19). In a systematic review, Vrsalović and Presečki showed that there was a significant correlation between elevated serum levels at admission and in-hospital and mid-term mortality (20). In our study, CRP was statistically significantly correlated with length of stay in positive direction (r=0.29, p=0.037). However, no statistically significant correlation was found between CRP and mortality.

Recently, CRP/albumin ratio has been proposed instead of each parameter separately to better predict outcomes in a wide range of conditions including malignancy, sepsis and acute mental illness (21-22). Yazar et al. reported that serum CRP/albumin ratio may be associated with the etiopathogenetic process of idiopathic Parkinson disease (23). Demir et al. proposed that CRP/albumin ratio can be used to indicate lung involvement in COVID-19 patients in whom chest CT is contraindicated (24). Kahraman et al. associated CRP/albumin ratio with increased mortality rate in patients with isolated severe aortic stenosis following aortic valve repair (25). In our study, similar to CRP, CRP/albumin ratio was statistically significantly correlated with length of stay in positive direction (r=0.27, p=0.046). However, no statistically significant correlation was found between CRP and mortality.

It has been suggested that indexes that involve platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and CRP levels have a prognostic value in many clinical situations (11). A novel correlation has been recently reported between multi-inflammatory indexes (MI-1 and MII-2), including NLR, PLR and CRP values and prognosis and severity of inflammatory related cancers (26). In our study, MII indexes were not correlated with length of stay and mortality from aortic dissection. In addition, we could not compare with other studies as this is the first study on this issue in the literature.

Study Limitations

Major limitations of this study are the relatively small number of patients and retrospective design. In addition, it was conducted in a single center. Furthermore, more novel markers could be investigated in regards to aortic stenosis. However, being the first in the literature on this topic increases the strength of our study. We believe that our findings will be encouraging for further more comprehensive prospective studies.

CONCLUSION

The results of this study point out a significant correlation between CRP, CRP/albumin ratio and length of stay in hospital. None of the above parameters were correlated with mortality. This information might be helpful in the rapid decision making process for early diagnosis and treatment of the disease. On the other hand, there is a need for a cut-off value in predicting prolonged length of stay due to aortic stenosis.

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Conflict of interest: *The authors declare that they have no competing interest.*

Ethical approval: *After receiving the necessary ethics approval from the local ethics committee of our hospital, this study was performed retrospectively (Decision No: 2022/30, Date 22/02/2022).*

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MEDICAL RECORDS-International Medical Journal

Research Article

Secret Carbon Monoxide Intoxication Assessments of the Patients Who Presented to Emergency

Acil Servise Başvuran Hastaların Gizli Karbon Monoksit Zehirlenmesi Açısından Değerlendirilmesi

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Abstract

Aim: The primary aim of this study is to evaluate patients who present to the emergency department with atypical symptoms in terms of occult Carbon monoxide (CO) poisoning, and the secondary aim is to compare the invasive and non-invasive values of Carboxyhemglobin (COHb) levels in patients with high CO levels.

Material and Method: This prospective and descriptive study was conducted on 2775 adult patients who visited the Emergency Department (ED) between January 1 and March 31, 2015. The COHb levels of the individuals who applied to the emergency department with non-specific complaints were measured with a non-invasive multiwave pulse oximeter device and the date of application, age, gender, complaint, smoking history, pregnancy status, pulse COHb, blood COHb and blood metHb parameters were recorded in the preformed form. Values under 10% in smokers and under 6.6% in non-smokers were recorded as secret COHb intoxication.

Results: 52.8% of the patients were male and 34.4% were smokers. The rate of pregnant women among female patients was 13.4%. The first three complaints were shortness of breath, chest pain and stomach ache. It was determined that the mean COHb of the patients was 1.44±1.65 in arterial blood gas and 1.75±1.63 in finger measurement. A highly significant positive correlation was found between the two averages. The COHb value measured by both techniques was higher in male patients and in smokers and non-pregnant patients. The rate of latent COHb intoxication was determined as 1% in smokers and 0.1% in non-smokers.

Conclusion: We came to the conclusion that non-invasive COHb measurement can make positive contributions to the diagnosis of secret carbonmonoxyde intoxications.

Keywords: COHb value, emergency department, secret CO intoxication, secret carbon monoxide intoxication

Öz

Amaç: Bu çalışmanın birincil amacı, acil servise atipik semptomlarla başvuran hastaları gizli karbonmonoksit (CO) zehirlenmesi açısından değerlendirmek, ikincil amacı ise yüksek CO düzeyi olan hastalarda Karboksihemoglobin (COHb) düzeylerinin invaziv ve non-invaziv değerlerini karşılaştırmaktır.

Materyal ve Metot: Bu prospektif ve tanımlayıcı çalışma, 1 Ocak-31 Mart 2015 tarihleri arasında Acil Servise (AS) başvuran 2775 erişkin hasta üzerinde yapılmıştır. Acil servise non spesifik şikayetler ile başvuran bireylerin noninvaziv multidalga pulse oksimetre cihazı ile COHb düzeyleri ölçülmüş ve önceden oluşturulan ve başvuru tarihi, yaş, cinsiyet, şikayet, sigara öyküsü, gebelik durumu, pulse COHb, kan COHb ve kan metHb parametlerini içeren forma kaydedilmiştir. Sigara içenlerde %10'un, içmeyenlerde %6.6'nın altındaki değerler gizli COHb intoksikasyonu olarak kaydedildmiştir.

Bulgular: %52.8'i erkek olan hastaların %34.4'ü sigara kullanıyordu. Kadın hastalar arasında gebe olanların oranı %13.4 idi. İlk üç şikayet nefes darlığı, göğüs ağrısı ve karın ağrısıydı. Hastaların COHb ortalaması arteriyal kan gazında 1.44±1.65, parmak ölçümünde 1.75±1.63 olarak belirlendi. İki ortalama arasında yüksek düzeyde anlamlı bir ilişki bulundu. Her iki teknikle ölçülen COHb değeri, erkek hastalarda, sigara içenlerde ve gebe olmayanlarda daha yüksekti. Gizli COHb zehirlenmesi oranı sigara içenlerde %1, içmeyenlerde %0.1 olarak belirlendi.

Sonuç: Non-invaziv COHb ölçümünün gizli karbonmonoksit intoksikasyonlarının teşhisine olumlu katkılar sağlayabileceği kanaatine vardık.

Anahtar Kelimeler: COHb değeri, acil servis, gizli CO intoksikasyonu, gizli karbon monoksit zehirlenmesi

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INTRODUCTION

Carbon monoxide is a gas which makes up less than 0.001% of the gases in atmosphere, it forms as a result of incomplete combustion of fuels such as wood, propane, oil, coal, vinyl plastic. It is a colourless, tasteless, non-irritant gas that can be absorbed by lungs easily. The factors that determine the degree of carbon monoxide intoxication include CO amount in the air, additional diseases, length of stay in the environment and specific self-healing metabolism. Carbon monoxyde is one of the leading agents of morbidity and mortality worldwide (1,2). It is in the top spot in our country when it comes to the rate of intoxication cases resulting in death (3) and according to forensic medicine records, CO intoxication accounts for approximately 100-150 death per year (4,5).

It is easy to confuse it with other diseases because of the fact that clinical symptoms and findings are non-specific. Including nausea and vomiting which are symptoms of a variety of diseases, it can manifest itself with loss of consciousness, choma and death. Central nervous system and cardiovascular system are the ones that are the most affected by CO intoxication. Because they are in a greater need of O2

compared to the other sysytems (6). Acute CO intoxication might mimic symptoms such as epileptic seizure, unstable angina and clouding of consciousness. CO exposure repeated in low concentrations might manifest itself with symptoms such as dizziness, headache, fatigue and nausea that characterize flu (7). For the diagnosis of CO intoxication, suspicion and good history taking is crucially important. In the patients who are suspected to suffer from CO intoxication, COHb level must be checked (8-11). CO level is measured by co-oximeter or arteriel blood gases.

The primary aim of this study is to evaluate patients who present to the emergency department with atypical symptoms in terms of occult CO poisoning, and the secondary aim is to compare the invasive and non-invasive values of COHb levels in patients with high CO levels.

MATERIAL AND METHOD

This study was conducted prospectively between January 1 and March 31, 2015 in the ED of Inonu University Hospital, Turkey. The university's Institutional Review Board approved the study design, and patients or patients' relatives provided written consent. In the study which was based on 24 hour principle, overall 2775 patients who presented were included in the study. Under 18 years olds were not included in the study. At least 6 hours of time period after complaints began to be manifested and getting the approval were set as criterias that would put things into the study. The inclusion criteria were ≥18 years of age and admitted to ED within 24 hours. Patients were excluded if they were admitted to ED after 24 hours and ≤18 yeas of age. Patients were also excluded if they were transferred to our ED from another hospital or transferred to another instution, or if they died during ED management.

The study was conducted through nurses and emergency department doctors with sufficient training on the use of oximeter. COHb levels of the patients who presented to the emergency department with non-specific complaints such as nausea, dizziness, vomiting, headache, shortness of breath and fatigue were measured through non-invasive multi-wave pulse oximeter and they were filled into the form that contained presentation dates, ages, genders, complaints, smoking history, pregnant state, pulse COHb, blood COHb and blood met HB parameters of the patients. In COHb measurement made by non-invasive multi-wave oximeter, which was calibrated, patients were seperated into smokers and non-smokers. The cases where we had 10% COHb level in smokers and 6.6% in non-smokers were put under monitor surveillance. After that for complete blood count, biochemical tests and arterial blood gases, blood samples were taken. In addition to routine parameters, from arterial blood gas samples, blood COHb levels were studied. Smoking patients who had more than 10% COHb levels in both arterial blood gas and measured by pulse oximeter were taken to be suffering from carbon monoxyde intoxication, non-smokers who had more than 6.6% COHb levels were taken to be suffering from carbon monoxyde intoxication. Following this, oxygen masks with reservoir and normobaric oxygen therapy with 100% oxygen were used for the beginning phase of the treatment. Patients who got COHb levels back to normal and were with disappeared symptoms were discharged from the hospital.

Statistical analysis was performed using the software package SPSS for Windows version 16.0 (SPSS, Inc., Chicago, IL, USA). Descriptive statistics were reported, including mean, standard deviation, and frequency. Categorical data were analyzed using the chi-square or Fisher's exact test. The data were summarized using means, standard deviations, frequencies, percentage distribution, Spearman correlation, One-way ANOVA, student's t-test and Mann-Whitney U test. $p<0.05$ was taken statistically significant.

RESULTS

Age averages of the patients who were included in the study were 57±20 and 47% of them were females and 53% of them were males. 34.4% of the patients reported to be smoking. It was detected that 13%-of the female patients were pregnant. Most common complaints of the patients were shortness of breath (27.8%), chest pain (25.8%), abdominal pain (18.1%), fever (4.6%), headache (3.7%), inability to urinate (3.1%) and altered state of consciousness (2.9%).

Table 1 showed that COHb average of the patients was 1.44±1.65,finger COHb levels of the patients was 1.75±1.63 and it was detected that there was a positive and significant co-relation between COHb and finger COHb levels ($p<0.001$).

Table 1. The relationship between COHb and finger COHb values

Parameter	x ± SS	Min - Max	Correlation
COHb	1.44 ± 1.65	-16.4 - 35.5	r=0.850[a]
Finger COHb	1.75 ± 1.63	- 27	p<0.001

[a]Spearman correlation

Table 2 presentation that there was a significant statistical difference between age groups and COHb levels. It was detected that the difference was the case in ≤24 and 25-44 age groups (p<0.05). Moreover, it was detected that COHb and finger COHb levels were significantly higher in male patients compared to female patients, in smokers compared to non-smokers and in non-pregnants compared to pregnants (p<0.001).

Table 2. Socio-demographic characteristics of participants and comparison of COHb and finger COHb averages

Variable	n	%	COHb x ± SS	Test	Finger COHb x ± SS	Test
Age						
≤ 24	171	6.2	1.25±1.30	F=3.458[a]	1.49±1.53	F=2.959[a]
25-44	632	22.8	1.58±2.11	p<0.05	1.83±2.13	p=0.052
≥ 45	1972	71.0	1.42±1.50		1.74±1.45	
Sex						
Female	1309	47.2	1.20±1.37	t=-7.29b	1.48±1.58	t=-8.08[b]
Male	1466	52.8	1.66±1.83	p<0.001	1.98±1.65	p<0.001
Smoking						
Yes	955	34.4	2.21±1.82	t=18.85[b]	2.67±1.78	t=23.67[b]
No	1820	65.6	1.04±1.39	p<0.001	1.26±1.31	p<0.001
Pregnancy (n=1309)*						
Yes	175	13.4	0.61±0.77	t=-6.23[b]	0.74±0.92	t=-6.77[b]
No	1134	86.6	1.30±1.42	p<0.001	1.60±1.62	p<0.001

aOne-way ANOVA bStudent's t-test

Table 3 showed that secret COHb intoxication rate for smokers was 1%. COHb (13.36±2.21). In addition finger COHb average levels in smokers and in the ones with secret COHb intoxication were found to be a significant statistical difference compared to patients with no secret COHb intoxication (p<0.001).

Table 3. The comparison of COHb and toxicity detection and COHb and finger COHb averages in cigarette smoking patients

Hidden COHb Intoxication	n	%	COHb x ± SS	Test	Finger COHb x ± SS	Test
Got intoxication	10	1.0	13.36±2.21	-5.449[a]	12.80 ± 1.81	-5.658[a]
No intoxication	945	99.0	2.09±1.40	p<0.001	2.56 ± 1.44	p<0.001

[a]Mann-Whitney U test

Table 4 presentation that non-smokers, detection of secret COHb intoxication allows us to have COHb and finger COHb level comparisons. Statistical assessment did show that secret COHb intoxication rate for non-smokers was 0.1%. It was detected that COHb average levels (30.55±7.00) and COHb finger levels (21.00±8.48) in non-smokers and in the ones with secret COHb intoxication were found to be significantly higher compared to the patients with no secret COHb intoxication (p<0.05).

Table 4. Comparison of COHb and toxic COHb meaning of hidden COHb intoxication in non-smoking patients

Intoxication	n	%	COHb x±SS	Test	Finger COHb x±SS	Test
Yes	2	0.1	30.55±7.00	-2.449[a]	21.00±8.48	-2.554[a]
No	1818	99.9	1.01±0.97	p=0.014[b]	1.24±1.12	p=0.011[b]

[a]Mann-Whitney U test [b]p<0.05

Table 5 showed that distributions of the complaints of the patients with detected secret COHb intoxication are presented. Presentation complaints of the smokers and of the patients with detected secret COHb intoxication were headache (30%), shortness of breath (30%), dizziness (20%), altered state of consciousness (10%) and syncope (10%). Presentation complaints of the non-smokers and of the ones with no detected secret COHb intoxication were dizziness (50%) and shortness of breath (50%).

Table 5. Distribution of complaints of emergency diagnosis of patients with hidden COHb intoxication

Application Complaint	n	%
Smoking (n=10)		
Headache	3	30.0
Dispnea	3	30.0
Dizziness	2	20.0
Change of consciousness-SVO	1	10.0
Syncope	1	10.0
No smoking (n=2)		
Dizziness	1	50.0
Dispnea	1	50.0

DISCUSSION

CO intoxication coming with non-specific symptoms can mimic a lot of diseases which have wide-ranging and a lot of symptoms such as fainting, newly developed convulsion, flu-like disease, headache, nausea, chest pain (12). In emergency department, 12 patients were detected to have CO intoxication as a result of routine COHb measurents made by non-invasive pulse oximeter. The fact that 12 of 2775 patients were diagnosed CO intoxication via non-invasive method that can be play an important role in the prevention of the wrong diagnosis and treatment of COHb. In ED triage, considering similar studies examining the effectiveness of non-invasive COHb scanning, findings back our study about the success in the diagnosis of secret CO intoxication. Roth and his friends scanned 16108

patients in emergency department triage during a year in a study where they used Masimo Radical 7 CO oximeter and blood gases of 2292 patients were taken and in the study it was reported that 17 patients got diagnosed with CO intoxication (8). Suner et al. reported that there were 28 CO intoxications in their study in which they screened 10856 patients, and they found 11 cases of occult CO poisoning (13). In the light of these findings, it can be said that routine screening with the noninvasive Masimo Radical 7 CO oximeter and another device is effective in detecting occult CO poisoning cases. In the study conducted by Chee et al., COHb levels of 74880 patients who applied to the emergency department were measured with a noninvasive pulse CO-oximeter device. Intoxication criteria was to have more than 10% CO level which is in venous blood gas and determined by pulse oximeter. According to the criterias, 7 patients (0.009%) were detected to have CO intoxication. When taken a look at the presentation complaints of the 7 patients who were taken CO intoxication cases, 3 of them presented to the hospital with headache, 2 of them with dizziness and 2 of them with nausea. As a result of this study, for the diagnosis of the patients presenting to the hospital with non-specific complaints, non-invasive pulse CO oximeter was found to be fit for use (14). In this study, the reason why the rate of poisoning was found to be much higher compared to the study conducted by Chee et al. might be that the study was taken from patients who applied to the emergency department with non-specific symptoms, and in addition, in terms of intoxication criteria, COHb levels were above 6.6% in non-smokers and 10% in smokers. However, according to all these criteria, the high rate of CO poisoning in this patient group is very thought-provoking. This shows that; COHb level measurement using noninvasive pulse CO-oximetry in addition to routine vital signs in emergency department triage; In differential diagnosis, early diagnosis and treatment will also help the clinician. At the same time, it will reduce the cost of many tests from an economic point of view.

In a study conducted by Harduar-Morano et al., it was found that latent CO poisoning occurs most frequently in the 35-44 age group (15). In our study, the comparison of the socio-demographic characteristics of the patients with the COHb and Finger COHb averages was evaluated. In the statistical analysis, it was determined that there was a statistically significant difference between age groups and COHb values. It was determined that the difference was between ≤24 and 25-44 age groups ($p<0.05$). In addition, it was determined that COHb and Finger COHb values were statistically significantly higher in male patients than in female patients, in smokers than in non-smokers, and in non-pregnant patients compared to pregnant patients ($p<0.001$).

Patients who are with carbonmonoxyde intoxication present to the emergency departments with non-specific symptoms, in these patients, the diagnosis of secret CO intoxication can be made with the help of non-invasive pulse CO oximeter. After CO intoxication, diagnosis is generally made by blood gas analysis. But this laboratory technique does not exist everywhere and it is a time-consuming process and that is why we used conventional pulse oximeters. Besides, taking blood gas from every patient was impossible for the fact that it could be difficult for differential diagnosis and economy and for this reason in triage measurements with non-invasive pulse oximeters can lead us to CO intoxication in differential diagnosis. When compared non-invasive COHb-COHb levels of 2775 patients who were analyzed with blood gas, these two levels were found to be well correlated with each other ($r=0.850$). In correlation analysis, it was detected that COHb averages of the patients were 1.44±1.65, finger COHb averages were 1.75±1.63 and there was a highly positive relationship between COHb and finger COHb levels ($p<0.001$). In the study conducted by Suner et al.(13), it was reported that there was a good correlation between noninvasive and venous COHb ($r=0.72$). Barker et al. (16) reported that the correlation coefficient between noninvasive COHb measurement and blood gas was 0.86.

In our study, we questioned the patients if they smoked and according to history taken from patient relatives and from the patients themselves, among 12 secret COHb intoxication patients,10 patients were smokers and 2 patients were non-smokers. In our study, while SpCO sensitivity for non-smokers was 100% for 6% and 10% cut-off levels, in smokers it was 90%. In our study, specificity for smokers was 100% and for non-smokers it was 99.83%. Suner et al. in the non-invasive COHb measurement with their study, while the sensitivity was found to be as high as 96%, as in our study, they found the specificity to be 54% (13) and found it lower than our study. In another study, which found a specificity similar to our study, Touger et al. reported the sensitivity of Rad-57 pulse CO oximeter as 48% and specificity as 99% (17). In a study conducted by Roth et al. (8), which was taken at a value close to our cutoff value (8), the measurement of smokers and non-smokers with non-invasive pulse oximetry was calculated separately, as we did, and the diagnostic performance was tried to be determined. Roth et al accepted the cutoff as 6.6% for all patients, resulting in sensitivity 94% (95% confidence interval; 71%-100%), specificity 77% (95% confidence interval; 75%-79%), positive predictive value was reported as 4% (95% confidence interval 2%-7%). For smokers, when the cutoff is accepted as 6.6%, sensitivity is 89% (95% confidence interval; 52%-100%), specificity is 71% (95% confidence interval; 67%-75%), positive predictive value is 5% (95% confidence interval 2%-10%) and negative predictive value 100% (95% confidence interval; 98%-100%). For non-smokers, when the cutoff is considered to be 6.6%, sensitivity is 100% (95% confidence interval; 63%-100%), specificity is 78% (95% confidence interval; 75%-81%), positive predictive value is 4% (The 95% confidence interval has been reported as 2%-7% and the negative predictive value as 100% (95% confidence interval; 99%-100%) (8). In our study, according to the results of the diagnostic tests, the sensitivity of the reference test in smokers was 90.00% (55.50%-99.75%, 95% CI), and the

specificity was 100.00% (99.61%-100.00%). According to this result, 9 out of 10 individuals with a positive diagnosis from the real test were diagnosed with a positive reference test, while all 945 individuals with a negative diagnosis from the real test were also diagnosed with a negative reference test. The sensitivity percentage of the reference test in non-smokers was found to be 100.00% (15.81%-100.00%, 95% CI), and the specificity percentage was 99.83% (99.52%-99.97%). According to this result, all of the 2 individuals diagnosed as positive by the real test were also diagnosed as positive in the reference test, while 1815 of 1818 individuals diagnosed as negative by the real test were also diagnosed as negative in the reference test.

CONCLUSION

We came to the conclusion that non-invasive carboxyhemoglobin measurement can make positive contributions to the diagnosis of secret carbonmonoxyde intoxications. Non-invasive carboxyhemoglobin measurement can be used for an early diagnosis of CO intoxication and reduce differential diagnosis in triage. It is estimated that early diagnosis and early treatment can reduce mortality and morbidity. It is considered that in winter and profession group distributions, it can be used for the scanning of the patients who present to the hospital with non-specific symptoms.

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Conflict of interest: *The authors declare that they have no competing interest.*

Ethical approval: *Approval was obtained from the Malatya Clinical Research Ethics Committee for the implementation of the study (Decision no: 2015/02). In addition, this research was accepted as a specialization thesis in İnönü University, Department of Emergency Medicine in 2017.*

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MEDICAL RECORDS-International Medical Journal

Research Article

The Relationship Between Sense of Honor and Tendency to Violence in Premarital Couples: A Comparative Study in Terms of Gender

Evlilik Öncesi Dönemdeki Çiftlerde Kadına İlişkin Namus Anlayışı ve Şiddet Eğilimi Arasındaki İlişki: Cinsiyetler Açısından Karşılaştırılmalı Bir Çalışma

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Abstract

Aim: This research was conducted to compare the relationship between the sense of honor towards women and the tendency to violence in premarital couples in terms of genders.

Material and Method: The sample of this cross-sectional and comparative study consisted of 215 (Female=119, Male=96) people who applied to a public health center in eastern Turkey for their wedding ceremony. Data; The Personal Information Form was collected with the "Honor Concept Perception Toward Women Scale" (KINATO) and the "The Violence Tendency Scale" (VTS). In statistical evaluation; mean, standard deviation, percentile distribution, Cronbach's alpha and pearson correlation analysis were used.

Results: It was determined that the total mean score of KINATO was 54.15±15.89 in premarital women and 62.31±13.85 in men, and both genders had an undecided and traditional attitude in terms of honor. It was determined that the total point average and all sub-dimensions of KINATO and the VTS of the men in the premarital period were significantly higher than those of the women ($p<0.05$). In addition, it was determined that there was a negative and weakly significant relationship between the total point average of the KINATO and VTS of women and men in the premarital period, and the level of violence tendency decreased as the level of having an egalitarian attitude towards women in terms of sense of honor increased.

Conclusion: It has been determined that there is a higher tendency to violence in men in the premarital period and that the tendency to violence decreases as the level of egalitarian attitude towards women increases in both genders.

Keywords: Premarital period, sense of honor, violence tendency

Öz

Amaç: Bu araştırma, evlilik öncesi dönemdeki çiftlerde kadına ilişkin namus anlayışı ve şiddet eğilimi arasındaki ilişkiyi cinsiyetler açısından karşılaştırmak amacıyla yapıldı.

Materyal ve Metot: Kesitsel ve karşılaştırmalı nitelikte tasarlanan bu araştırmanın örneklemini, Türkiye'nin doğusunda bulunan bir toplum sağlığı merkezine nikâh işlemleri için başvuran 215 (Kadın=119, Erkek=96) kişi oluşturdu. Veriler; "Kişisel Bilgi Formu", "Kadına İlişkin Namus Anlayışı Tutum Ölçeği (KİNATÖ)" ve "Şiddet Eğilim Ölçeği" ile toplandı. İstatistiksel değerlendirmede; ortalama, standart sapma, yüzdelik dağılım, Cronbach alfa ve pearson korelasyon analizi kullanıldı.

Bulgular: KİNATÖ toplam puan ortalamasının evlilik öncesi dönemdeki kadınlarda 54,15±15,89, erkeklerde ise 62,31±13,85 olduğu ve her iki cinsiyetin namus anlayışı açısından kararsız ve geleneksel tutuma sahip oldukları belirlendi. Evlilik öncesi dönemdeki erkeklerin KİNATÖ toplam ve tüm alt boyutlar ile şiddet eğilim ölçeği toplam puan ortalamalarının kadınlara oranla anlamlı düzeyde daha yüksek olduğu saptandı ($p<0,05$). Ayrıca, evlilik öncesi dönemde bulunan kadın ve erkeklerin KİNATÖ ve Şiddet Eğilim Ölçeği toplam puan ortalamaları arasında negatif yönde zayıf düzeyde anlamlı ilişki olduğu ve kadına ilişkin namus anlayışı açısından eşitlikçi tutuma sahip olma düzeyleri arttıkça şiddet eğilim düzeylerinin azaldığı saptanmıştır.

Sonuç: Evlilik öncesi dönemdeki erkeklerde daha yüksek şiddet eğilimi olduğu ve her iki cinsiyette kadına ilişkin namus anlayışı açısından eşitlikçi tutuma sahip olma düzeyi arttıkça şiddet eğiliminin azaldığı saptanmıştır.

Anahtar Kelimeler: Evlilik öncesi dönem, namus duygusu, şiddet eğilimi

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INTRODUCTION

In a society, loyalty to moral rules and social values, modesty, honesty and integrity are defined as honor (1-3). The sense of honor, on the other hand, varies from society to society and culture to culture, but it is mostly discussed together with female sexuality (3, 4). This sense may also lead to the restriction of women's lives and their punishment when they act contrary to the general judgment (1). Violence, which occurs depending on the way the concept of honor is perceived, negatively affects the health of women throughout their lives and may even result in their death. It is estimated that more than 5000 women are killed in the name of honor killing every year (4). It is emphasized that social culture is influential behind these actions and the importance of youth in the change of cultural dynamics (2). In this context, determining the sense of honor of young individuals who are preparing for marriage is very important in terms of planning education programs that will prevent honor-based violence against women. Studies conducted today, where violence against women and homicides of women are becoming more and more widespread, show that especially the sense of social honor causes domestic/partner violence and murder against women (2,3).

Violence is defined as intentional acts that may result in death, injury, psychological harm, developmental delay or negligence towards oneself, others or a community (5). One of the interaction areas where violence is most common is couple relationships (6). This situation, also called partner violence, has become an increasing social problem (7). The World Health Organization states that partner violence, which is the most common type of violence against women, must be ended within the scope of protecting world health. Within the scope of violence prevention strategies, it recommends family-based programs and trainings on safe and healthy relationship skills for adolescents and young adults. It also states that the issue of violence against women should be integrated into sexual and reproductive health services (8). It emphasizes that healthcare professionals have to be aware of partner violence and know its causes, risk factors, effects and intervention methods (7). Partner violence was also on the agenda in the Turkish Grand National Assembly (TBMM) Violence Against Women Research Commission and a 'Marriage License' proposal was made. However, the application of the Marriage License, in which the current conditions were effective in the occurrence of violence and only the psychological aspect was discussed, was found to be limited. In addition, it was emphasized that determining the violence tendency of individuals is an important factor (9).

It is thought that developing communication and problem-solving skills in the premarital period and having realistic expectations for marriage may help prevent violence (6). In addition, there is a need for studies that allow scientific measurement of attitudes towards honor and violence against women in the name of honor (3,4). When considered from this point of view, it is thought that examining the relationship between the sense of honor towards women and the tendency to violence in premarital couples will contribute to the literature. In this study, it was aimed to compare the relationship between the sense of honor towards women and the tendency to violence in premarital couples in terms of genders.

MATERIAL AND METHOD

Research Design and Sample

In this study, a descriptive and comparative study was conducted in order to compare the relationship between the sense of honor towards women and the tendency to violence in premarital couples in terms of genders. The research was carried out in two separate family health centers located in a city center in eastern Turkey between October 2021 and March 2022. The population of the research consisted of couples who applied to family health centers for marriage procedures. According to the records of the relevant family health centers for 2020, approximately 2269 people applied for marriage procedures. When the sample size was calculated by power analysis, it was determined as at least 154 individuals with 5% level of significance at bidirectional significance level, 95% confidence interval and 80% ability to represent the population (10). Individuals who met the criteria for participation in the study were selected from the relevant population using the improbable random sampling method, and the study was completed with 215 (Female=119, Male=96) individuals.

Participation Criteria

- To be over 18 years old,
- Being literate,
- Not having a communication problem,
- To reside in the city center,
- There is no medical problem in getting married.

Data Collection Tools

The data were obtained with the "Personal Description Form", "Honor Concept Perception Toward Women Scale" (KINATO) and "Violence Tendency Scale (VTS)".

Personal Description Form

It is an 18-question form created by the researcher in line with the literature in order to obtain the socio-demographic characteristics of the people participating in the research, as well as some features that may affect their sense of honor and their tendency to violence (1,11).

The Honor Concept Perception Toward Women Scale (KINATO)

The scale, developed by Gursoy in 2009, is likert type scale and consists of 11 negative (3,5,7,8,10,12,14,17,19,20,25) and 14 positive (1,2,4,6,9,11,13,15,16,8,21,22,23,24) expressions (1). There are 25 items in total. Each item in the scale is scored from 1 to 5 (1=Totally Agree; 5=Totally Disagree). Scale, "Traditional honor concept" (items 3,8,10,12,14,17,19,23,25), "Egalitarian Approach"

(1,2,4,6,9,11,13,15,18,21,24) and "Premarital Sexuality/ Sense of Honor" (items 5,7,16,20,22). Accordingly, the maximum score that can be taken from the "Traditional honor concept" dimension is 45, the minimum score is 9, the maximum score that can be obtained from the "Egalitarian attitude between genders" dimension is 55, the minimum score is 11, the maximum score that can be obtained from the "Premarital sex/honor concept" dimension is 25, and the minimum score is 5'. The lowest score that can be obtained from the overall scale is 25, and the highest score is 125. The highest score obtained from the scale indicates that "egalitarianism" in the understanding of honor regarding women, the lowest score indicates that a "traditional" approach is adopted. Accordingly, it is accepted that students who score between 25-50 for the overall scale have a traditional and gender-discriminatory attitude towards the sense of honor towards women, students who score between 51-75 have an indecisive and traditional attitude, and those who score between 76-125 have an egalitarian attitude. The Cronbach Alpha reliability coefficient of the scale was determined as 0.93 (1). In this study, the Cronbach Alpha reliability coefficient was found to be 0.90.

The Violence Tendency Scale (VTS)

The scale, which was developed by Haskan and Yıldırım in 2012, consists of 20 items. Each item was scored from 1 to 3 (3=always, 2=sometimes, and 1=never) (11).The total score that can be obtained from the VTS varies between 20 and 60. A high score means that the individual has a high tendency to violence. VTS includes four factors. The first factor was "feeling of violence", the second factor was "violence through information technologies", the third factor was "the thought of harming others", the fourth factor was "inflicting violence on others". The Cronbach Alpha reliability coefficient of the scale was calculated as 0.87 (11). In this study, the Cronbach Alpha reliability coefficient was found to be 0.88.

Data Collection

The research data was obtained by the researcher using face-to-face interview method between October 2021 and March 2022. The purpose of the research was explained during premarital counseling to individuals who applied to family health centers for marriage procedures and agreed to participate in the research, and were asked to answer the questionnaires. Data collection took an average of 10-15 minutes.

Data Analysis

Coding and evaluation of the data was carried out in computer environment using SPSS 16.0 package program. The normal distribution of the data was checked with the Kolmogorov-Smirnov Test. In statistical evaluation; percentage distribution, arithmetic average, standard deviation, Cronbach's alpha, t test for independent groups, t test for dependent groups and Pearson correlation test were used. The results were evaluated at the 95% confidence interval and the significance level of $p<0.05$.

Ethical Dimension of the Study

Ethical approval was obtained from Malatya Inonu University Health Sciences Non-Interventional Clinical Research Ethics Committee (No: 2019/329) before the study. In addition, an informed consent form was signed by all individuals before starting the study. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Limitations of the Research

The research is limited to couples who applied to a city center in eastern Turkey for premarital counseling.

RESULTS

In Table 1, the distribution of the introductory characteristics of the couples in the premarital period is given. The average age of the men and women included in the study was 25.57±4.85 and 29.12±5.02, respectively, the average number of siblings was 3.52±1.38, 3.39±1.69, and the duration of marriage decision was 17.02±17.81, 16.65±17.14 months, respectively. It was determined that most of the women and men are working (51.3% and 93.8%, respectively), they are university graduates (68.1%, 65.6%, respectively), their income is equal to their expenses (68.1%, 60.5%, respectively), they have a nuclear family (76.5%, 75.0% respectively).

When the education levels of the mothers and fathers of the women and men are considered, it is observed that most of the mothers of the women were primary school graduates (47.1%), and most of the fathers of the women were high school graduates (30.4%); it was determined that most of the mothers of the men were secondary school graduates (24.0%) and most of fathers of the men were primary school graduates (28.1%). It was determined that the majority of women and men had a sister and/or elder sister (77.3%, 74.0%, respectively), and the majority of women and men had a brother and/or elder brother (79.0%, 75.0%, respectively). Most of the women and men have good family relations (63.0%, 66.7%, respectively), the person who has a say/has a voice in family problems/ issues is mostly both parents (52.1% and 55.2%, respectively), and the majority of parents do not have violence in their families (90.8%,97.0%). respectively). It was determined that most of the women and men started to meet their fiancé/spouse by meeting themselves (47.9%, 57.3%, respectively).

In Table 2, the distribution of the lowest and highest score ranges obtained from the KINATO and VTS for premarital couples is given. It was determined that women got the lowest 9 points and the highest 42 points from the KINATO traditional sense of honor sub-dimension; that women got the lowest 11 points and the highest 36 points from the egalitarian approach sub-dimension; that the women got lowest 5 and the highest 25 points in the sub-dimension of premarital sexuality/sense of honor. In addition, the lowest total score of women in KINATO is 26 points, the highest is 89 points; It was determined that

Table 1. The relationship between COHb and finger COHb values

Descriptive features	Female (n=119)		Male (n=96)	
	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)	Mean±SD (min-max)
Age (years)	25.57±4.85 (18-50)		29.12±5.02 (18-47)	
Number of siblings (pcs)	3.52±1.38 (0-8)		3.39±1.69 (0-13)	
Marriage decision time(months)	17.02±17.81 (1-60)		16.65±17.14 (1-60)	
	n	%	n	%
Employment status				
Yes	61	51.3	90	93.8
No	58	48.7	6	6.2
Level of education				
Primary school	5	4.2	3	3.1
Middle school	9	7.5	8	8.4
High school	24	20.2	22	22.9
Undergraduate and Postgraduate	81	68.1	63	65.6
Living place				
Province	101	84.9	95	99.0
District	18	15.1	1	1.0
Economical situation				
Income more than expenses	35	29.4	37	38.5
Income equals expense	81	68.1	58	60.5
Income less than expenses	3	2.5	1	1.0
Family structure				
Nuclear family	91	76.5	72	75.0
Traditional family	22	18.5	21	21.9
Broken family	6	5.0	3	3.1
Mother's education level				
İlliterate	8	6.7	20	20.8
Literate	12	10.1	13	13.5
Primary school	56	47.1	22	22.9
Secondary school	20	16.8	23	24.0
High school	14	11.8	13	13.5
University and Postgraduate	9	7.5	5	5.3
Father's education level				
İlliterate	1	0.8	4	4.2
Literate	8	6.7	10	10.4
Primary school	33	27.7	27	28.1
Secondary school	26	21.8	22	22.9
High school	36	30.4	21	21.9
University and Postgraduate	15	12.6	12	12.5
Status of having a sister				
Yes	92	77.3	71	74.0
No	27	22.7	25	26.0
Status of having a brother				
Yes	94	79.0	72	75.0
No	25	21.0	24	25.0
State of family relations				
Good	75	63.0	64	66.7
Middle	41	34.5	31	32.3
Bad	3	2.5	1	1.0
Person who has a say in family problems/issues				
Mom	15	12.6	3	3.1
Father	42	35.3	40	41.7
Both of them	62	52.1	53	55.2
Presence of violence in the family				
No violence in the family	108	90.8	93	97.0
There is physical violence	5	4.2	1	1.0
There is psychological/verbal violence	5	4.2	1	1.0
There is economic violence	1	0.8	1	1.0
There is sexual violence	-	-	-	-
How to meet with a engaged				
Arranged	26	21.8	15	15.6
By meeting yourself	57	47.9	55	57.3
Via friend	31	26.1	21	21.9
Via the internet	5	4.2	5	5.2
Total	**119**	**100.0**	**96**	**100.0**

SD: Standard Deviation

women got the lowest 26 points and the highest 89 points from the violence tendency scale. It was determined that men got the lowest 11 points and the highest 41 points from the KINATÖ traditional understanding of honor sub-dimension; that men got the lowest 11 points, the highest 55 points from the egalitarian approach sub-dimension, that men got the lowest 5 points and the highest 25 points in the sub-dimension of premarital sexuality/sense of honor. In addition, it was determined that men got the lowest 30 points, the highest 88 points in the total scores of men from KINATO; and that men got the lowest 20 points and the highest 72 points from VTS.

Table 2. Distribution of the Lowest - Highest Scores of Couples in the Premarital Period from the KINATO and VTS (n=215)

Scales		Female (n=119)	Male (n=96)
	Lowest-highest value receivable	Lowest-highest value received	
KINATO sub-dimensions	Min-Max	Min-Max	Min-Max
Traditional honor concept	9-45	9-42	11-41
Egalitarian attitude between genders	11-55	11-35	11-55
Premarital sex/honor concept	5-25	5-25	5-25
KINATO total score	25-125	26-89	30-88
VTS total score	1-80	12-60	20-72

KINATO: Honor Concept Perception Toward Women Scale, VTS: The Violence Tendency Scale, Min: minimum, Max: maximum

In Table 3, the comparison of the average scores of the couples in the premarital period from the KINATO and VTS is given. It was determined that the average score of KINATO traditional sense of honor sub-dimension for women was 20.61±8.43, and the average score of the men was 25.41±7.43 and the difference between them was statistically significant (t=-4.375; p=0.000). It was determined that the average score of KINATO egalitarian approach sub-dimension for women was 18.78±5.96, and the average score of the men was 23.19±7.75, and the difference between them was statistically significant (t=-4.720; p=0.000). It was determined that the average score of KINATO premarital sexuality/sense of honor sub-dimension for women was 15.97±5.45, and the average score of the man was 62.31±13.85 and the difference between them was statistically significant (t=-2.470; p=0.014). In addition, lit was determined that the total average score of KINATO for women was 54.15±15.89; and the total average scores of KINATO for men was 62.31±13.85 and the difference between them was statistically significant (t=-3.956; p=0.000). It was determined that the average score of the VTS for women was 32.88±6.11 and the average score of VTS for men was 36.39±8.70 and the difference between them was statistically significant (t=-3.469; p=0.001).

Table 3. Comparison of the Mean Scores of Couples in the Premarital Period from the KINATO and VTS (n=215)

Scales	Female (n=119)	Male (n=96)	Test[a] and
	(Mean ± SD)	(Mean ± SD)	p value
KINATO sub-dimensions			
Traditional honor concept	20.61±8.43	25.41±7.43	t=-4.375 p=0.000[b]
Egalitarian attitude between genders	19.40±6.54	22.81±7.92	t=-4.720 p=0.000[b]
Premarital sex/honor concept	15.97±5.45	18.16±4.73	t=-3.107 p=0.002[c]
KINATO total score	54.15±15.89	62.31±13.85	t=-3.956 p=0.000[b]
VTS total score	31.24±6.77	37.04±8.78	t=-3.469 p=0.001[c]

KINATO: Honor Concept Perception Toward Women Scale, VTS: The Violence Tendency Scale, SD: Standard Deviation [a]t=Independent Samples t Test [b]p<0.001 [c]p<0.05

In Table 4, the relationship between the average scores of couples in the premarital period from the KINATO and VTS is given. As a result of the correlation analysis, it was determined that there was a negative and weakly significant relationship between the average scores of the KINATO and VTS of women and men in the premarital period, and the level of violence tendency decreased as the level of having an egalitarian attitude towards the sense of honor towards women increased.

Table 4. The Relationship Between the Mean Scores of the Couples in the Pre-Marriage Period from the KINATO and VTS (n=215)

Female (n=119)	Mean ±SD	Testa and p value	
KINATO	54.15±15.89	r=-0.260	0.004[b]
VTS	31.24±6.77		
Male (n=96)			
KINATO	62.31±13.85	r=-0.368	0.000[c]
VTS	37.04±8.78		

KINATO: Honor Concept Perception Toward Women Scale, VTS: The Violence Tendency Scale, SD: Standard Deviation [a]Test: Pearson Correlation Analyze, [b]p<0.05, [c]p<0.001

DISCUSSION

It was determined that the total average score for KINATO for women was 54.15±15.89 and the total average scores for KINATO for men was 62.31±13.85 and the difference between them was statistically significant. These average scores indicate that the couples have an undecided and traditional attitude in terms of their sense of honor towards women. In the literature review, it was observed the studies indicating that men and women have a traditional attitude towards honor, similar to our finding (12-16). As individuals are brought up according to the traditional moral rules of the society from an early age and

the moral norms learned in childhood can be effective in their future lives, lit is considered normal for individuals to behave a traditional attitude towards the sense of honor. With the influence of the cultural structure and patriarchal society structure, premarital sexual experience does not pose a problem for a man, and sometimes it is possible to encounter supportive approaches against this situation. However, the same cultural structure does not welcome women to have this experience before marriage (12,16). In addition to these, even behaviors such as lifestyle, dressing style, attitude towards men, walking around and talking and laughing have been associated with the honor of women and have caused the sense of honor to be formed. In addition, with the influence of the patriarchal social structure, men were held responsible for the honor of women, and the power to impose sanctions in any situation was given to them (13,16,18).

As a matter of fact, the positive response of 81.9% of male students to the statement that "it is an honor that women have to keep her virginity until marriage" indicates the sense of honor that men have (19). In particular, it has been stated by men that they do not find it appropriate for women to have sexual intercourse before marriage in the sub-dimension of sexuality before marriage (20). Also, it is emphasized in the literature that it is inevitable for individuals to reflect their thoughts and values that they have acquired since childhood to their attitudes (12). When considered from this point of view, the indecisive and traditional attitude of the couples participating in the study in terms of their sense of honor towards women may be explained by the values they have acquired since their childhood and the cultural structure of the society they live in.

Studies in which gender comparisons were made in the literature were examined, and in general, there were studies determined that women exhibit a more egalitarian approach to the perception of honor compared to men (3,13,21-24). In this study, it was determined that although both genders exhibit an indecisive and traditional attitude in terms of honor, men in the premarital period exhibit more egalitarian attitudes than women. The level of egalitarian attitude among men may be related to the rate of working in any job and the rate of living in the city center of premarital men who participated in this study are higher than women. In the literature review, a limited number of studies were found in which men exhibit more egalitarian attitudes than women (15). In addition, the fact that the education level of literate mothers is around 80% in this study can be considered as another important factor in behaving an egalitarian attitude.

It was observed that the average score of VTS of women was 32.88±6.11; and that the total mean score of the men was 36.39±8.70 and the violence tendencies of the men participating in the research were higher than the women. In the literature review, it is said that our study is compatible with the literature (6,25-29).

It has been emphasized by the World Health Organization reports that violence incidents have increased continuously all over the world (5,30). With the effect of having a patriarchal social structure, a higher tendency to violence in men is an expected result. As a general opinion, this social structure is the reason why violent behaviors are accepted as male-specific behaviors and it is considered more normal for men to behave these behaviors compared to women (11,31). It was determined by the study that women were exposed to violence in the first years, including the period of meeting before marriage, and that verbal violence was also included in addition to physical violence (32). It is not desirable that partner violence and violence tendency be high, especially since the premarital period (33). Experiencing violence in the family, which is the basis of the society, will deeply shake/affect negatively the unity of the society and the country, negatively affecting the children growing up in that family and causing the violence to be learned, and it will bring the violence from generation to generation (34). As a matter of fact, studies have stated that individuals who grow up witnessing violence in the family turn into adult perpetrators of violence (35). In addition, in this study, it was determined that as the level of having an egalitarian attitude towards women in terms of sense of honour increased, the level of violence tendency decreased. This finding shows that the concept of honour is an important variable that affects the tendency to violence.

It is seen that the reason for violence against women and honor killings is mostly to protect honor and honor and women are matched (16). When the literature is considered, in the study conducted by Yirmibeşoglu (2007), when asked what should be done in case of any harm to women's honor, 25% of the university students stated that they should be killed and 13% said that they should be punished, and all of these ways lead to violence (12,36). There are limited studies in the literature that reflect the negative attitude towards violence perpetrated by men against women in the name of honor (37-39). Violence in the name of honor deteriorates women's health, paves the way for various diseases and can cause death (1,40). It is thought that enabling individuals to express their thoughts on the concept of honor in the pre-marriage period, improving communication and problem-solving skills, and having realistic expectations for marriage can help prevent violence.

CONCLUSION

In our study, it was determined that the couples in the premarital period had a traditional attitude in terms of the perception of honor towards women. In addition, in this study, it was determined that men experienced more violence tendencies than women. It was determined that as the violence tendencies of individuals in the premarital period increased, their perception of honor towards women changed towards traditional and indecisive attitudes.

In order to establish the marriage union on solid foundations and to maintain the relations in this marriage in a harmonious way, the pre-marital counseling trainings,

which are held to provide information about marriage readiness and marriage relations, should focus on points such as getting to know each other, informing about marriage, improving their relationships when they get married, and strengthening the family. It is an important step to determine the factors that cause violence in marriage life and to develop preventive psychoeducational programs by identifying individuals who tend to violence with scientific methods. Health professionals have to be aware of partner violence and know its causes, risk factors, effects and intervention methods. Women who are exposed to violence on the grounds of honor are expected to be aware and to fulfil their responsibilities professionally during care. With the understanding of honor equals women, which is the dominant perspective of the society in general, it may be fought by increasing the level of education and development. When considered from this point of view, it should be noted that health professionals and midwives have responsibilities such as empowering women, supporting their independence, helping them to know their rights, and providing a safe environment in case of need, as required by their duties of informing and counselling. In addition, it should be ensured that the perception of women is used in the same sense as honor in schools, universities, health institutions and in all areas, and services should be provided with an egalitarian approach in order to prevent gender inequality.

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Research Article

The Relationship between Attitudes of Relatives of Terminal Stage Patients towards Death and Principles about Dying with Dignity

Terminal Dönem Hasta Yakınlarının Ölüme ve Saygın Ölüm İlkelerine İlişkin Tutumları Arasındaki İlişki

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Abstract

Aim: The aim of this study is to determine the relationship between the attitudes of the relatives of terminal stage patients towards death and principles about dying with dignity.

Material and Method: This descriptive cross-sectional study was carried out with 308 patient relatives between 20 December 2021 and 21 March 2022. The data were collected using a "Patient Information Form", 'Death Attitude Profile-Revised (DAP-R)' and 'Assessment Scale of Attitudes towards Principles about Dying with Dignity' (ASAPDD). Descriptive statistics, Student t test, One-Way ANOVA test, Kruskal Wallis test, Mann Whitney-U test, Pearson correlation and regression analysis were used to analyze the data.

Results: The mean age of the relatives of the patients participating in the study was 34.88±2.32, 86.0% were female. 38.6% of the relatives of the patients stated that the patient in the intensive care unit was their mother/father, and 44.1% stated that the patient stayed in the intensive care unit for 3-7 days. The mean DAP-R total score was 107.30±25.1 and the ASAPDD total score was 30.62±10.70. A positive and highly significant relationship was found between DAP-R and ASAPDD.

Conclusions: It was determined that as the attitudes of the relatives of the patients towards death became negative, the level of adopting the principles about die with dignity increased. Health professionals should provide death counseling to the relatives of patients in order to increase the quality of life of patients in the terminal period.

Keywords: Intensive care, patient's relative, death, dying with dignity, attitude

Öz

Amaç: Bu çalışmanın amacı, terminal dönem hasta yakınlarının ölüme ve saygın ölüm ilkelerine ilişkin tutumları arasındaki ilişkinin belirlenmesidir.

Materyal ve Metot: Tanımlayıcı ve kesitsel olarak yapılan bu çalışma,20 Aralık 2021- 21 Mart 2022 tarihleri arasında 308 hasta yakını ile tamamlandı. Veriler, Kişisel Bilgi Formu, Ölüme Karşı Tutum Ölçeği (ÖKTÖ) ve Saygın Ölüm İlkelerine İlişkin Tutumları Değerlendirme Ölçeği (SÖİİTDÖ) kullanılarak toplandı. Verilerin analizinde tanımlayıcı istatistikler, Student t testi, One-Way ANOVA testi, Kruskal Wallis testi, Mann Whitney-U testi, Pearson korelasyon ve regresyon analizi kullanıldı.

Bulgular: Araştırmaya katılan hasta yakınlarının yaş ortalaması 34,88±2,32 olup %86,0'ı kadındır. Hasta yakınlarının %38,6'sı yoğun bakımdaki hastasının anne/babası olduğunu ve %44,1'i 3-7 gündür hastasının yoğun bakımda kaldığını belirtmiştir. Hasta yakınlarının ÖKTÖ toplam puan ortalaması 107,30±25,1, SÖİİTDÖ toplam puan ortalaması 30,62±10,70 idi. ÖKTÖ ile SÖİİTDÖ arasında pozitif yönde ve yüksek düzeyde anlamlı bir ilişki saptandı.

Sonuç: Hasta yakınlarının ölüme ilişkin tutumları negatifleştikçe saygın ölüm ilkelerini benimseme düzeylerinin arttığı saptanmıştır. Sağlık profesyonellerinin terminal dönemdeki hastaların yaşam kalitesini arttırmak için hasta yakınlarına ölüm danışmanlığı yapması gerekmektedir.

Anahtar Kelimeler: Yoğun bakım, hasta yakını, ölüm, saygın ölüm, tutum

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INTRODUCTION

Intensive care units are special areas in hospitals equipped with complex devices, separate from other clinics with their general appearance and atmosphere. The mortality rates of the patients hospitalized in these units are quite high due to their severe illnesses, long-term dependence on invasive procedures and mechanical devices (1). However, with the rapid technological developments and the advancement of diagnosis and treatment techniques, it has become possible to treat deadliest diseases today. With the developing treatment methods, the life expectancy of people has also increased. While technological developments have extended the life expectancy, they have also led to an increase in the number of chronic diseases and patients who need care in the terminal period (2,3).

The terminal period is defined as the last period before death, in which vital functions are expected to end within a certain period, during which holistic care is given to the patient to maintain the quality of life. The term terminal patient mean patient who is in the last days of their life and who is about to die (4). Death is an inevitable life process for every individual. People are aware of death, but they are not aware of how and when it will happen. Although people develop a positive attitude towards death, their attitudes and behaviors towards death are affected by factors such as sociodemographic characteristics, cultural structure and belief systems (5). As attitudes developed against death lose their balance and harmony, the level of anxiety of individuals increases and their adaptation to the environment may become difficult (1).

The diagnosis of terminal illness is a crisis for the patient and their relatives, which is woven with complex emotional reactions. The death process of a patient is a difficult period accompanied by physical and mental distress (6,7). Being with the patient at the time of death and giving care to the dying patient are the most difficult experiences for the family members of the patients as well as the healthcare providers. Undoubtedly, facing the reality of death can be traumatic for healthcare professionals, patients, and their relatives (1,6). The role of the patient's relatives during end-of-life care is too important to overlook.

Reasons such as the inability of patients' relatives to consider death as a part of life, their fear of the death process, their lack of awareness about death, and the lack of knowledge about how to request and provide services when a person is on their deathbed can lead to a worsening of the patients' quality of life and the grieving process (8-11).Individuals who are nearing death want to be prepared for death, to say goodbye to their relatives, to spend time with their relatives, to reconsider their lives, to protect their personal dignity and to die with dignity (12). It is among the important responsibilities of both health professionals and patient relatives that patients can achieve a dignified death, which is a basic human right. For this reason, relatives of patients need to better understand death, accept it and prepare for it with a mature attitude. Relatives of patients should have information about death and be able to talk in order to realize the needs of the patient whose death is approaching. In short, they need to have a positive attitude towards death (8,10,13).

Although there are studies in the literature about health professionals and students in which principles about die with dignity and attitudes towards death are evaluated (1,5,7,14-20), no study has been found on the attitudes of patients' relatives towards "death and principles about dying with dignity. With this study, determining the attitudes of patient relatives towards death and principles about dying with dignity will provide information on increasing the quality of end-of-life care. In addition, in line with the results of the research, it will be able to contribute to the strengthening of the variables that increase the level of adopting principles about dying with dignity", and to the organization of death education programs for the relatives of the patients to provide a respectable death process.

Aim

The aim "of this study is to determine the relationship between the attitudes of the relatives of terminal patients towards death and the principles about dying with" dignity.

Research Questions

1. Do "the sociodemographic characteristics of the relatives of terminal patients affect their level of attitude towards death and principles about dying with dignity?
2. What are the attitude levels of the relatives of terminal patients towards death and the principles about dying with dignity?
3. Is there a relationship between the attitude levels of relatives of terminal patients towards death and principles about dying with" dignity?

MATERIAL AND METHOD

Design and Study Population

This research "was designed as a descriptive and cross-sectional study. The population of the study was consisted of the relatives of the patients who were treated in the intensive care units of Inonu University, Turgut Ozal Medical Center (Internal Medicine, Neurology, General, Anesthesiology, and Reanimation) between 20.12.2021 - 21.03.2022. In the study, the universe was studied (356 relatives of the patients). Sample selection was not made. 308 of these relatives who met the inclusion criteria were included in the study. 48 relatives of patients did not accept to participate in the study, so they were excluded from the study". Study participation rate was 86.5%. The inclusion criteria of the study comprised the following:

- being a relative of a patient who had been on advanced cardiac life support for at least three days at the time of the study and was considered to be in the terminal phase,

- being older than 18 years of age,
- being consanguineous with the patient,
- being able to communicate with the intensive care staff,
- being able to meet the patient's needs one-to-one,
- having no psychiatric disorder
- agreeing to participate in the research.

Instruments

The data were obtained with thePersonal Information Form, the Death Attitude Profile-Revised (DAP-R) Scale, and the Assessment Scale of Attitudes towards Principles about Dying with Dignity (ASAPDD).

Personal Information Form: In the form developed in the light of the literature (5,11,13,15,16,21,22), there were 14 questions questioning the descriptive characteristics of the patients (age, gender occupation, education level, marital status, patient's length of stay in the intensive care unit, closeness with the patient, previous care for another patient in the intensive care unit, frequency of meeting with the patient, frequency of thinking about own death, previous loss of a loved one, sharing thoughts on death, receiving education about death, reaction to death).

Death Attitude Profile-Revised (DAP-R): The scale was developed by Wong et al. in 1994 (23). The Turkish validity and reliability study was conducted by Işık et al. in 2009 (24). The scale consists of 26 items and has three subscales: "Neutral Acceptance and Approach Acceptance", "Escape Acceptance" and "Fear of Death and Death Avoidance". "Neutral Acceptance and Approach Acceptance" subscale contains items of 4,6,8,12,13,14,15,19,21,22,23,25. "Escape Acceptance" contains 5,9,11,20,24th items, and "Fear of Death and Death Avoidance" contains the items of 1,2,3,7,10,16,17,18,26. The Cronbach's Alpha coefficient of the scale is 0.81 in the total scale, 0.82, 0.72 and 0.70 in the subscales, respectively. The expressions of the scale, which is in seven-point Likert type, are between "Strongly Agree" (1 point) and "Strongly Disagree" (7 points). It is evaluated that as the score obtained from the scale increases, negative attitude towards death develops, and as the score decreases, the attitude towards death develops in a positive direction. The Cronbach's alpha value of the scale was 0.81 (24), and this study was 0.84.

Assessment Scale of Attitudes towards Principles about Dying with Dignity (ASAPDD): The scale, which was developed by Duyan (25) in 2014 and includes 12 principles regarding dying with dignity, is in the five-point Likert type. The lowest score is 12 points and the highest 60 points are taken from the scale. A high score on the scale is an indication of high acceptance of the principles of dying with dignity. The Cronbach's Alpha value of the scale was 0.89 (25), and this study was 0.93.

Data Collection

Forms were completed in the rest room by face-to-face interview on the days and hours available to the relatives of the patients who agreed to participate in the study between 20 December 2021 and 21 March 2022. Relatives of the patients were informed about the study and voluntary consent forms were signed. Filling out the forms took approximately 8-10 minutes.

Data Analysis

In the study, the data were analyzed with the Statistical Package for Social Science (SPSS) 24.0 package program. (SPSS) Data distribution was evaluated using the Kolmogorov-Smirnov test. Cronbach's alpha coefficient was calculated for reliability. In independent groups, t test, analysis of variance (ANOVA), Kruskal Wallis test, Mann Whitney-U test, Pearson correlation and regression analysis were used. In the study, the p value was accepted as below 0.05.

Ethical Approval

The Ethical Committee approval (2021-43/18) was obtained to conduct the study. The relatives of the patient have written consent was obtained. Permission to use the above measurement instruments in the study was received from their developers. This study was conducted in accordance with the Good Clinical Practices of the Declaration of Helsinki.

RESULTS

It was determined that 49.3% of the participants were in the 26-32 age groups and average age of all participants was 34.88±2.32 (Table 1). 86.0% of the relatives of the patients were women, 59.4% were single, 70.5% were secondary school graduates, and 63.3% were high school graduates. 38.6% of the patients' relatives were the mother/father of the patient they cared for, while 61.7% of them had previously taken care of patients in the intensive care unit. 65.9% of the patients' relatives saw their patients for 10 minutes or less a day. It was determined that 44.1% of the participants' patients were treated in the ICU for 3-7 days (Table 1).

It was found that individuals, who were male, married, and had a child scored higher on the DAP-R's "Fear of Death" and "Death Avoidance" subscales, and the difference between the groups was statistically significant ($p< 0.05$). Individuals who were the offspring of the patients in ICU scored higher on the DAP-R's "Neutral Acceptance and Approach Acceptance" subscale, and the difference between the groups was statistically significant ($p<0.05$). Individuals aged 40-46 years, male, who had previously taken care of patients in the intensive care unit, who visited their patients between 11-20 minutes daily, and whose patients were treated in the intensive care unit for more than 12 days, obtained higher scores from DAP-R's "Escape Acceptance" subscale compared to other groups.

Accordingly, the difference between the groups was found to be statistically significant (p<0.05). It was found that the individuals who were female, married, were the parents of the patient receiving treatment in the intensive care unit and were previously took care of patients in the intensive care unit scored higher in the DAP-R total score than the other groups, and the difference between the groups was statistically significant (p<0.05) (Table 1).

Table 1. Comparison of the participants' mean total scores according to the information about sociodemographic (n=308)

Variables	n	%	DAP-R	ASAPDD
Age				
26-32	152	49.3	105.78±2.10	30.73±1.94
33-39	99	32.2	107.67±2.06	30.56±1.81
40-46	57	18.5	109.04±2.19	30.00±1.90
p[a]			0.087	0.053
Gender				
Female	265	86.0	107.50±2.02	32.84±1.89
Male	43	14.0	107.27±2.42	29.78±2.05
p[c]			0.094	0.004
Income Level				
Low	25	8.1	108.96±2.71	31.55±2.56
Middle	217	70.5	107.86±2.11	30.80±1.89
High	66	21.4	107.43±1.83	29.40±1.64
P[d]			0.051	0.241
Marital status				
Single	183	59.4	107.90±2.16	28.82±1.94
Married	125	40.6	106.50±0.70	32.00±1.41
p[b]			0.980	0.016
Education Level				
Primary-Secondary School	84	27.3	108.90±2.16	30.80±1.93
High School	195		107.87±2.14	30.86±1.96
University	29	63.3	107.55±2.70	30.03±1.20
p[d]	9.4		0.934	0.780
Relationship with the patient in the intensive care unit				
Mother/Father	119	38.6	107.97±2.09	30.81±1.89
Offspring	20	6.5	106.87±2.19	33.79±1.87
Spouse	94	30.5	108.80±2.36	29.05±2.21
Sibling	75	24.4	107.82±1.91	28.38±1.42
p[d]			0.933	0.009
Previous caring for another patient in the ICU				
Yes	190	61.7	107.74±2.55	29.14±2.49
No	118	38.3	108.82±2.10	31.70±1.84
p[d]			0.073	0.001
Frequency of meeting with the patient (daily)				
10 min and less	203	65.9	108.50±2.55	30.06±2.14
11 min-20 min.	105	34.1	107.79±2.06	30.78±1.90
p[b]			0.802	0.350
Duration of stay of the patient in the ICU				
3-7 days	136	44.1	107.58±2.26	30.35±2.78
7-11 days	100	32.5	106.81±2.11	30.74±1.85
12 days and longer	72	23.4	107.55±2.88	30.00±2.30
p[d]			0.130	0.804

Note: [a] Variance analysis (ANOVA), [b] Independent samples t-test, [c] Kruskal Wallis Test, [d] Mann Whitney U Test, *p<0.05, **p<0.001; DAP-R: Death Attitude Profile-Revised, ASAPDD: Assessment Scale of Attitudes towards Principles about Dying with Dignity; ICU: Intensive Care Unit

It was determined that 52.3% of the participants had lost a loved one before, 51.6% thought about their own death from time to time, 87.3% did not share their thoughts about death, 73.4% did not receive education about death, and 47.7% showed a fear reaction in the face of death.It was found that individuals who think about their own death very often and react with fear in the face of death have a high score in the "Fear of Death and Death Avoidance" subscale of DAP-R, and the difference between the groups is statistically significant (p<0.05) (Table 2).

Obtained data shows that those who received training on death had higher scores from the "Neutral Acceptance and Approach Acceptance" subscale of DAP-R, and the difference between the groups was statistically significant (p<0.05). Those who lost a loved one before and those who had a fearful reaction to death scored higher on the DAP-R total score compared to the other groups, and the difference between the groups was statistically significant (p<0.05). It was found that those who lost a loved one before, those who think about their own death very often, those who share their thoughts about death, and those who receive education about death have higher ASAPDD total scores than the other groups, and the difference between the groups is statistically significant (p<0.05) (Table 2).

In the study, it was determined that the total mean score of individuals from DAP-R was 107.30±25.1. "Neutral Acceptance and Approach Acceptance" subscale mean score of DAP-R is 54.59±12.15, "Escape Acceptance" subscale mean score is 17.20±5.83, "Fear of Death and Death Avoidance" subscale mean score is 46.19±10.16. Individuals' total mean score obtained from ASAPDD was found to be 30.62±10.70 (Table 3).

Table 2. Comparison of the participants' mean total scores according to the information about Death (n=308)

Variables	n	%	DAP-R	ASAPDD
Previous Loss of a Loved One				
Yes	162	52.6	109.90±2.15	33.80±1.92
No	146	47.4	106.50±2.12	28.0±4.24
p[b]			0.005	0.001
Frequency of thinking about own death				
Very often	75	24.4	107.59±2.02	34.20±1.89
Occasionally	159	51.6	106.60±2.31	28.84±1.96
Rarely	74	24.0	107.46±2.90	27.70±1.08
p[a]			0.881	0.001
Sharing thoughts about death				
Yes	39	12.7	107.63±2.00	32.66±1.80
No	269	87.3	107.96±2.22	29.88±1.99
p[c]			0.046	0.001
Education about Death				
Yes	82	26.6	106.59±2.19	33.44±1.78
No	226	73.4	107.95±2.05	27.98±1.96
p[a]			0.224	0.001*
Reaction to Death				
Fear	147	47.7	110.15±2.24	30.02±2.01
Anxiety	120	39.0	105.18±1.77	30.20±1.45
Guilt	41	13.3	107.98±2.13	30.96±2.11
p[d]			0.003*	0.604

Note: [a]Variance analysis (ANOVA), [b]Independent samples t-test, [c] Kruskal Wallis Test, [d]Mann Whitney U Test, *p<0.001; DAP-R: Death Attitude Profile-Revised, ASAPDD: Assessment Scale of Attitudes towards Principles about Dying with Dignity

Table 3. The mean scores of the participants from DAP-R and ASAPDD (n=308)

Scale Subscales	Mean ± SD	Min-Max
Neutral Acceptance and Approach Acceptance	54.59 ± 12.15	24-83
Escape Acceptance	17.20 ± 5.83	4-32
Fear of Death and Death Avoidance	46.19 ± 10.16	29-60
DAP-R Total	107.30 ± 25.1	30-178
ASAPDD Total	30.62±10.70	12-50

Note: Min: Minimum, Max: Maximum, SD: Standard deviation, DAP-R: Death Attitude Profile-Revised, ASAPDD: Assessment Scale of Attitudes towards Principles about Dying with Dignity

In Table 4, in the correlation analysis of the relationship between the attitudes towards death and attitudes towards principles about die with dignity of the relatives of the patients, it was determined that there is a positive and high-level relationship between the DAP-R subscales of "Fear of Death and Death Avoidance", "Neutral Acceptance and Approach Acceptance", "Escape Acceptance", and Assessment Scale of Attitudes towards Principles about Die with Dignity (p<0.05).

As a result of simple linear regression analysis, a significant correlation was found between DAP-R total and subscales and ASAPDD (R=.740, R2=.548, p<.01). Of the selected independent variables, DAP-R total (β:2.175, p=.000), DAP-R Neutral Acceptance and Approach Acceptance (β: 1.505, p=.000), DAP-R Escape Acceptance (β: 0.872, p=.000) and DAP-R Fear of Death and Death Avoidance (β:0.397, p=.000) were found to predict ASAPDD statistically significantly and positively. Accordingly, selected independent variables affect ASAPDD at a rate of 54.8% (Table 5).

Table 4. Relationship between the mean DAP-R and ASAPDD (n=308)

DAP-R	ASAPDD	
	r	p*
DAP-R Total	0.655	0.040
Fear of Death and Death Avoidance Subscale	0.783	0.030
Neutral Acceptance and Approach Acceptance Subscale	0.709	0.021
Escape Acceptance Subscale	0.661	0.039

Note: Pearson correlation, *p<0.05; DAP-R: Death Attitude Profile-Revised, ASAPDD: Assessment Scale of Attitudes towards Principles about Dying with Dignity

Table 5. Simple linear regression analysis between DAP-R ve ASAPDD (n=308)

Variable	B	Std. Error	Beta	t	p
Constant)	114.610	.0408		11.058	.001*
DAP-R Total	1.472	0.521	2.175	6.735	.001*
Fear of Death and Death Avoidance	0.630	0.200	0.397	3.742	.030**
Neutral Acceptance and Approach Acceptance	1.227	0.486	1.505	5.011	.001*
Escape Acceptance	0.934	0.353	0.872	4.899	.038*

Note: * p< 0.01 **p<0 .05 β: Beta; DAP-R: Death Attitude Profile-Revised, ASAPDD: Assessment Scale of Attitudes towards Principles about Dying with Dignity

DISCUSSION

Even though death seems distant to healthy people, for a patient who has passed the terminal stage, it becomes much closer. Death which every living thing will inevitably experience is a complex, incomprehensible and real situation in human life. While the people whose death is approaching experience some emotions in the last stage of his life, at the same time, the emotional state of many people such as their family, environment and health professionals is affected, causing them to develop attitudes and behaviors towards death, and prevents patients from living a dignified death (1,7,19).

In "this study, it was determined that the mean DAP-R score of the relatives of the patients was 107.30±25.1 and they had a negative attitude towards death. In Neutral Acceptance and Approach Acceptance Subscale, patient relatives' attitudes are more negative, while in Fear of Death and Death Avoidance" Subscale, there is moderate acceptance. When the literature is examined, similar results have been reported in the general average and subscales of attitude towards death (1,13,14,26). Death is an abstract concept that extends to whole life. Although death seems like a natural part of life for people, it is also a difficult/undesirable end. It is observed that the relatives of patients who care for terminal patients have a negative attitude towards death due to the fear of losing a relative.

Dignity is a subjective concept and the importance of dignity in the care of the near-death patient cannot be denied. People deserve to receive dignified and respected care at the end of their life. For this reason, it is essential that the relatives of the patients, together with the health personnel, demand and maintain the care that is suitable for the needs of the patient and that will protect their honor and dignity (1). In this study, the average ASAPDD score of the relatives of the patients was 30.62±10.70, which is moderate. When the literature is examined, it has been determined that the ASAPDD averages are high in studies conducted with health personnel and students studying in the field of health (1,3,12,15,22,27). Due to the difference between the results of the study, it can be thought that health professionals have adopted the principles of a respectable death and learned about this issue during their education, since they constantly encounter death in intensive care settings. It is thought that the difference in the attitudes of the relatives of the patients is due to the fear of losing their loved one and their lack of awareness about how to treat the patient during the death process.

In this study, it was "determined that as the attitudes of

the relatives of the patients became negative, the level of adopting principles about dying with dignity increased. As can be understood from this result, the perception of death affects the perception of respectable death. In a study conducted by Çelik (2019) with intensive care nurses, it was determined that as nurses' attitudes towards death become negative, their level of adopting principles about dying with dignity increases (1). In the study conducted by Köse et al. (2019) with physicians and nurses, it was determined that there was no relationship between the attitude towards death and the level of adopting principles" about dying with dignity (12). In the study conducted by Bilgiç (2021), it was determined that the increase in nursing students' perceptions of death positively affected their adoption of principles about dying with dignity (28). In the sub-dimensions of DAP-R, there are expressions such as accepting death objectively and as an approach, escaping from death, fear of death and avoiding death. The negative increase in these attitudes, that is, more fear or avoidance of death, may have caused the relatives of the patients to adopt the principles of respectable death more. Because death is a situation that not only the patients cared for by their relatives, but also all humanity and living things, including themselves. Being aware of this may have a positive effect on the dignity of the individual regarding death. Death, which is a negative thing that the relatives of the patients avoid for themselves, may have caused them to behave more sensitively and respect the family member they care for.

In our study, no correlation was found between the DAP-R scores of the patient's relatives and their sociodemographic characteristics. A significant difference was found between the ASAPDD mean scores of women, married people, those whose children were hospitalized in the intensive care unit, and those who did not care for another patient in the intensive care unit before. In the literature, it has been stated that the ASAPDD scores of women and those who are married are high (3,6,29). Although gender does not directly affect the perception of death, it can affect the approach to respectable death. It is thought that women, married people and people with children develop more values such as care, empathy and compassion, and in this context, they can behave more sensitively towards respectable death.

When death is encountered, with the effect of remembering the losses experienced, feelings such as sadness, fear, and thinking of being saved may occur, while behaviors such as freezing, and crying may occur. In our study, it was determined that the DAP-R scores of those who experienced fear of death were high, and that both the DAP-R and ASAPDD scores of the relatives of the patients who lost a loved one before were high. Ay and Gençtürk (2013) in their qualitative study with midwifery students stated that most students faced death by losing a family member before they were even midwifery students, they were afraid of death, but they had to face death in a dignified manner at home (30). Death experience and fears in individual life can affect people's perceptions of death and their approaches to respectable death. It is thought that the relatives of the patients who have experienced death perceive that death is real and inevitable and they can display a more accepting approach towards death.

In our study, it was determined that the relatives of the patients who think about their own death very often, share their thoughts about death and receive education about death have a higher level of adopting the principles of respectable death. When the literature is examined, it can be seen that physicians and nurses who receive palliative care training, have high palliative care competence, and nursing students who receive training on the care of the dying patient during their education can talk about death and dying more easily, share their thoughts comfortably, adopt the principles of respect death more easily, and improve the quality of care (3,6,15,31). In the study of Chen et al. (2020), they stated that death education facilitates acceptance, increases competency about death, and it is possible to talk about death comfortably (8).Jung et al. (2021) stated that family members of hospice patients make great demands for information about death symptoms before death counseling training, and they need support to ensure a comfortable death after death counseling. In addition, it was determined that the relatives of the patients wanted support to protect their human dignity and sense of well-being until the last moment of their lives (32). The results support our study, and it is thought that when the relatives of the patients receive education about death, they believe that by talking or thinking about death, it will reduce the fear and anxiety of death, thus they accept a dignified death comfortably and the quality-of-care increases.

CONCLUSION

It has been observed that the relatives of the patients who have to care for patients close to death have negative attitudes towards death, and they also adopt the respectable care that should be given to terminal patients. The ability of patient relatives to provide effective and quality care to their terminal patients can be achieved by gaining awareness of their individual feelings and thoughts against death. It is very important that patients who are close to death receive respectable care. In this direction, arrangements are needed to provide adequate social support, as well as to plan a comprehensive and qualified death education by determining the needs of patients' relatives in order to turn their attitudes towards death into a positive one.

Limitations

This study consists of relatives of patients who were treated in the intensive care units of a Medical Faculty in Turkey and accepted to participate in the study and cannot be generalized.

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Research Article

Cytokine Filter Experience in Covid-19 Treatment; A Single Center Study

Covid-19 Tedavisinde Sitokin Filtresi Deneyimi;Tek Merkezli Bir Çalışma

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Abstract

Aim: Several studies state that the primary underlying mechanism of severe COVID-19 cases includes the hyperimmune response triggered following SARS-CoV-2 infections and the subsequent cytokine storm. The study aims to examine the effects of cytokine filters on patients with COVID-19 who developed cytokine storms.

Material and Methods: This is a retrospective, cross-sectional study. All the patients included in the study had tested positive for COVID-19 in their real-time polymerase chain reaction test. The study included patients with COVID-19 who developed cytokine storms and were treated in the ICU. The patients were divided into two groups those who applied cytokine filter or not. The demographic data and laboratory findings of the patients were recorded. The patient outcomes were categorized as discharged or deceased.

Results: The study included 149 patients. Patients' mean age was 56±29 years, and 125 (83.9%) patients were male. A significant decrease was detected in the levels of fibrinogen, ferritin, lymphocyte count, and CRP after cytokine filtration (p <0.001, <0.001, 0.031, and <0.001, respectively). Age, d-dimer, and lymphocyte count were found independent factors for discharge.

Conclusion: The blood filtration method has been found to be useful in the hyperimmune response when administered following early diagnosis in selected cases. When administered following early diagnosis in selected cases, the method can be beneficial in supplementing the effectiveness of primary therapies and preventing secondary cytokine release complications as it controls hyperinflammation.

Keywords: Cytokine storm, COVID-19, therapeutics, interleukin, blood

Öz

Amaç: Yapılan birçok çalışmada şiddetli COVID-19 vakalarının altında yatan ana mekanizmanın, enfeksiyonu takiben tetiklenen hiperimmün yanıt ve ardından gelişen sitokin fırtınası olduğu belirtilmektedir. Çalışmamız sitokin fırtınası gelişen COVID-19 hastalarında, sitokin filtrelerisinin tedavideki etkilerini incelemeyi amaçlamaktadır.

Materyal ve Metot: Çalışmamız retrospektif, kesitsel bir çalışmadır. Çalışmaya dahil edilen tüm hastaların gerçek zamanlı polimeraz zincir reaksiyonu ile COVID-19 testi pozitif olan hastalardan oluşmaktadır. Çalışma, sitokin fırtınaları geliştiren ve yoğun bakım ünitesinde tedavi edilen COVID-19 hastalarını içeriyordu. Hastalar sitokin filtresi uygulanan ve uygulanmayanlar olmak üzere iki gruba ayrıldı. Hastaların demografik verileri ve laboratuvar bulguları kaydedildi. Hasta sonuçları taburcu veya ölen olarak kategorize edildi.

Bulgular: Çalışmaya 149 hasta dahil edildi. Hastaların yaş ortalaması 56±29 yıl olup 125 (%83,9) hasta erkekti. Sitokin filtrasyonu sonrası fibrinojen, ferritin, lenfosit sayısı ve CRP düzeylerinde anlamlı düşüş tespit edildi (sırasıyla p <0,001, <0,001, 0,031 ve <0,001). Yaş, d-dimer ve lenfosit sayısının taburculuk için bağımsız faktörler olduğu tespit edildi.

Sonuç: Seçilmiş olgularda ve erken tanı sonrası kan filtrasyon yöntemlerinin uygulanması hiperimmün yanıt tedavisinde faydalı olduğu bulunmuştur. Seçilmiş vakalarda erken tanının ardından uygulandığında bu yöntem, hiperinflamasyonu kontrol altına aldığı için birincil tedavilerin etkinliğini desteklemede ve sitokin salınımına sekonder gelişen komplikasyonları önlemede faydalı olabilir.

Anahtar Kelimeler: Sitokin fırtınası, Covid-19, terapötik, interlökin, kan

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INTRODUCTION

After the detection of the initial cases of coronavirus disease 2019 (COVID-19) presenting with atypical pneumonia in Wuhan, China in late 2019, the infection was classified as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses on March 2, 2020 (1). Three months following the outbreak of the disease, it was declared a pandemic by the World Health Organization due to its high contagion (2). Since the disease rapidly spread due to its high virulence, it led to a swift increase in the number of cases, exceeding the capacities of health systems and resulting in serious losses of lives, as a specific antiviral treatment with proven efficacy was yet to be developed prior to the completion of vaccine generation (3). Although numerous hypotheses have been proposed concerning the pathogenesis of COVID-19, the certain mechanism of action and underlying causes of its varying clinical presentations are yet to be revealed (4).

Conditions such as infections, malignancies, rheumatological diseases, and certain medications bring about the uncontrolled and excessive release of cytokines, known as a cytokine storm (5). Since proinflammatory cytokines are of critical significance to the inflammatory pathways, they are also important in the generation of cytokine storms (6). It is shown that the primary underlying mechanism of severe COVID-19 cases includes the hyperimmune response triggered following SARS-CoV-2 infections and the subsequent cytokine storm (7). In postmortem studies, patients with severe COVID-19 presented with pulmonary edema, widespread alveolar damage, reactive hyperplasia of type II pneumocytes, fibrinous exudate, and the inflammatory infiltrates of concentrated monocytes and macrophages (8). Following reports stating that one of the aggravating effects of the clinical picture of severe COVID-19 cases was the immune responses caused by uncontrolled cytokine release, the management, and treatment strategies of the disease began focusing on this issue (9,10). Blood purification is also among the methods employed to alleviate the effects of cytokine storm in COVID-19. With previous successful and promising outcomes in cases of sepsis where the method was attempted, blood purification is intended to eliminate the harmful effects of the systemic responses that develop due to the release of pro-inflammatory and anti-inflammatory agents (11,12).

The present study aims to examine the possible effects of blood purification on the outcomes and laboratory findings of patients in the intensive care unit (ICU) with severe COVID-19 who developed cytokine storms.

MATERIAL AND METHOD

Study Design

This is a retrospective, cross-sectional study conducted over a period of 5 months (May–September 2021). All data obtained from Mersin City Hospital. The study included patients with COVID-19 who developed cytokine storms and were treated in the ICU of a tertiary hospital and consequently followed up for COVID-19. The ethical approval for the study was obtained from the Mersin University local ethics committee (approval no. 2021/632; obtained on September 22, 2021), and the study was conducted in accordance with the Declaration of Helsinki.

Patient Selection

All the patients included in the study had tested positive for COVID-19 in their real-time polymerase chain reaction (RT-PCR) test. The criteria for ICU hospitalization were a respiratory rate of ≥30/min, severe respiratory distress (involving dyspnea and use of accessory respiratory muscles), and oxygen saturation at ambient temperature ≤90% (PaO_2/FiO_2 <300 in a patient receiving oxygen). The parameters indicating a hyperimmune response in the patients included prolonged and persistent fever despite treatment, elevated levels of C-reactive protein (CRP) (or CRP progression during treatment), ferritin, and D-dimer, existing lymphopenia and thrombocytopenia, and impaired liver function tests. The patients under the age of 18 years who were not diagnosed with cytokine storm during the hospitalization or follow-ups, those who tested negative in RT-PCR tests, and those whose data were completely or partially unavailable on the hospital information system were excluded from the study. Since interleukin (IL) inhibitors were not yet in supply, they were not among the treatments administered to the patients in the ICU for cytokine storms during the study period. Some of the patients received cytokine filtration treatment along with supportive treatment during the study period, whereas others only received the supportive treatment in the ICU because of disruptions in the supply of the cytokine filter.

CytoSorb (Cytosorbents Inc., New Jersey, USA) blood purification method was applied in the present study. CytoSorb is a blood purification method that removes inflammatory molecules from the blood using blood-coated beads that are highly absorbent and are coated with polyvinylpyrrolidone for biocompatibility (13). The criteria for the selection of the patients on whom cytokine filtration was to be applied were as follows: the presence of elevated levels of serum inflammatory molecules (ferritin >300 ug/L and an increased value during follow-up, lymphocyte <0.6×109/L, D-dimer >1mcg/mL, and CRP >5mg/dl or doubled after 48 hours), Sequential Organ Failure Assessment score >2, lactate levels >2mmol/L in blood gas measurement, vasopressor support in the absence of hypovolemia to keep the average arterial pressure at ≥65mmHg, shock, and appropriate antimicrobial therapy administration. After obtaining the consent of the patients selected for cytokine filtration, a double-lumen venous catheter for venovenous hemofiltration was put in place. The CytoSorb cartridge was used for hemofiltration. The

blood flow rate was planned as 150–200ml/min and the CytoSorb kit was replaced at intervals of 24 hours.

Data Collection

The demographic data (age, gender) and laboratory findings (creatinine, alanine transaminase, fibrinogen, D-dimer, ferritin, white blood cell (WBC), neutrophil, lymphocyte, platelet, CRP, procalcitonin) of the patients were recorded. The patient outcomes were categorized as discharged or deceased. Finally, the total number of cytokine filters applied to each patient was recorded. During the study, no complications related to the device or method were encountered in the treatment group.

Outcome

The primary outcome of the investigation was the effect of cytokine filter application on the laboratory findings of the patients who developed a cytokine storm due to COVID-19. The secondary outcome was to determine the effect of this treatment following patient discharge.

Statistical Analysis

To statistically analyze the findings obtained in the present study, IBM SPSS Statistics 22 (IBM SPSS, Turkey) software was used. Shapiro Wilks test was used to confirm the normal distribution of the parameters. Along with the descriptive statistical methods (mean, standard deviation, median and interquartile range, frequency), Wilcoxon signed-rank test was also used to compare the dependent quantitative variables. Logistic regression analysis was employed to examine the effects of the variables on discharge. The statistical significance was set at $p<0.05$.

RESULTS

The study included 149 patients. Patients' mean age was 56±29 years, and 125 (83.9%) patients were male.

According to the comparison of the laboratory parameters measured before and after cytokine filtration, a significant decrease was detected in the levels of fibrinogen, ferritin, lymphocyte count, and CRP ($p<0.001$, <0.001, 0.031, and <0.001, respectively). In contrary, WBC, neutrophil, and platelet counts were significantly elevated ($p<0.001$, <0.001, and 0.031, respectively). The other values are shown in Table 1.

Cytokine filtration was performed at least once and a maximum of six times on each patient. In 115 (77.2%) patients, a total of three cytokine filtrations were performed. The number of applied cytokine filter median was 3 [3-3].

The logistic regression analysis of the parameters that might affect the discharge outcome revealed that age, D-dimer, and lymphocyte count influenced the discharge. Increased age and D-dimer levels significantly reduce the rate of discharge (odds ratio [OR] = .948, 95% confidence interval [CI; .909–.989] and OR = .749, 95% CI [.604–.928], respectively). Increased lymphocyte levels had a positive effect on discharge. The logistic regression analysis and parameter data are summarized in Table 2.

Table 1. Changes in laboratory parameters before and after cytokine filter application

	Before Treatment	After Treatment	p*
Creatinine	0.78 (0.38 IQR)	0.82 (0.92 IQR)	.079
ALT	50.00 (61.50 IQR)	63.00 (80.00 IQR)	.007
Fibrinogen	560.00 (218.50 IQR)	429.00 (260.00 IQR)	<.001
D-dimer	1.52 (2.78 IQR)	2.96 (7.18 IQR)	<.001
Ferritin	1441.00 (509.50 IQR)	938.00 (855.00 IQR)	<.001
WBC	11000 (7395 IQR)	13410 (6966 IQR)	<.001
Neutrophil	9750 (6730 IQR)	12000 (7000 IQR)	<.001
Lymphocyte	585 (415 IQR)	500 (550 IQR)	.031
Platelet	207000 (109000 IQR)	216000 (124000 IQR)	.031
CRP	10.91 (12.07 IQR)	5.36 (12.64 IQR)	<.001
Procalcitonin	0.20 (0.50 IQR)	0.20 (0.92 IQR)	.270

* Wilcoxon Signed Rank Test was used, IQR: Interquartile Range

Table 2. Logistic regression analysis of patients' parameters in terms of discharge

	Wald	Odds Ratio	95% C.I.	
Age	6.168**	.948	.909	.989
ALT	1.803	1.005	.998	1.012
Fibrinogen	.257	1.001	.997	1.004
D-dimer	6.979**	.749	.604	.928
Ferritin	1.944	1.000	.999	1.000
WBC	2.247	1.000	1.000	1.001
Neutrophil	2.573	.999	.999	1.000
PLT	.893	1.003	.997	1.008
Lymphocyte	6.026**	1.002	1.000	1.003
CRP	.802	.964	.889	1.045
Procalcitonin	3.724	.287	.081	1.020
Number of filter applications	.337	1.205	.642	2.265

Omnibus $\chi 2$ (12) = 63.001 $p<0.001$ R2 = 0.478 (Negelkerke)
**$p<0.05$ C.I.: Confidence Interval

DISCUSSION

Kogelmann et al. used the CytoSorb blood filtration method in sepsis and septic shock patients who were followed up in the ICU. In the study, the patients who had an Acute Physiology and Chronic Health Evaluation II score of >25 and developed two or more organ failures presented with accelerated hemodynamic stabilization and significant decline in blood lactate levels and lower mortality rates. Hence, it was accepted that applying the filtration within the first 24 hours following sepsis diagnosis resulted in significant improvements in the clinical outcomes of the patients, and the benefits reduce especially if the filtration is applied ≥48 hours later (13). Rimmelé et al. reported that

hemoadsorbtion treatments are well tolerated by patients and effective in removing inflammatory molecules and endotoxins from the blood and in increasing hemodynamic stabilization and oxygenation (14). In another study, the researchers found a significant decrease in the IL-6 levels and vasopressor requirements of a patient with septic shock after 4 days of treatment using the CytoSorb method, with no side effects associated with the device or method (15). In a study where Taniguchi et al. examined the efficacy of hemoperfusion therapy in endotoxemia management, the researchers found the method to be successful in removing small and medium protein molecules such as cytokines, enterotoxins, and toxic shock syndrome toxin 1 and reducing mortality by controlling the inflammatory response and recommended the use of the method in selected cases with sepsis clinic (16).

According to a few studies on cytokine filtration conducted in patients with COVID-19, one study examining the efficacy of blood filtration methods in the management of the disease reported that factors such as increased vascular permeability caused by the uncontrolled release of IL-6 in plasma and cardiac dysfunction predominantly affected the mortality rates of COVID-19. Furthermore, the study reported that along with the existing treatment protocols, the early use of blood filtration methods in individuals presenting with cytokine storms may reduce the need for intensive care support (17). In a study by Ruiz-Rodríguez et al., an underlying state of uncontrolled immune response and hyper inflammation in patients with severe COVID-19 was reported and the researchers argued that extracorporeal cytokine adsorption methods were clinically useful in ensuring oxygenation and hemodynamic stability in the patients whose clinical state could not be managed with the standard treatments and who developed cytokine storm (18). In several case reports and series, similar observations have been made, highlighting the positive effects of the method on oxygenation and hemodynamic stability; however, all such studies emphasize that the method is to be considered a supplementary to the primary treatment option for managing the hyperimmune response and the consequent cytokine storm that may occur during the disease (19,20).

On comparison of the laboratory data of the patients before and after blood filtration in the group of patients who were administered with this method, the levels of the clinical markers of a cytokine storm i.e., ferritin, CRP, fibrinogen, and D-dimer, were found to be significantly decreased, whereas the WBC, platelet, and neutrophil counts were significantly elevated in the post-filtration period. It was determined that increased age and D-dimer levels negatively impacted discharge while lymphocyte levels had a positive effect on it. The literature states that this method should be applied following early diagnosis only in selected cases rather than being considered a standard treatment (21). Previous studies have shown that cytokine filtration is associated with hemodynamic stabilization, reduction in vasopressor requirements, a significant reduction in serum lactate levels, and improvement in lung functions, with no serious side effects associated with the device and method being reported (22).

Limitations

This study was a single-center study. More efficient results can be obtained with studies to be carried out with the participation of more than one center. In this study, the effects of the cytokine filter method on mortality were not examined. More comprehensive studies are needed to examine the effects of cytokine filters on mortality.

CONCLUSION

The blood filtration method has been found to be useful in the hyperimmune response that develops during the inflammatory process and reduces inflammatory cytokine release. When administered following early diagnosis in selected cases, the method can be beneficial in supplementing the effectiveness of primary therapies and preventing secondary cytokine release complications as it controls hyperinflammation. However, further studies with a better study design including extensive clinical trials are needed.

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Research Article

Investigation of the Relationship Between of Dependent Personality Trait, Depression, Anxiety, and Stress Levels of Asthmatic and Non-Asthmatic Individuals

Astımlı ve Astımlı Olmayan Bireylerin Bağımlı Kişilik Özelliği ile Depresyon, Anksiyete ve Stres Düzeyleri Arasındaki İlişkinin İncelenmesi

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Abstract

Aim: There is a complex relationship between asthma and psychiatric problems; therefore, it is important to investigate this relationship for optimal treatment. In this cross-sectional and comparative study, it was aimed to examine the dependent personality trait, depression, anxiety and stress levels of asthmatic and non-asthmatic individuals.

Material and Method: 382 individuals with (n=172) and without (n=210) asthma were included in our study. The study data were collected with Identifying Information Form, Personality Belief Questionnaire, and Depression Anxiety Stress Scale (DASS) 21-Short Form. Comparisons between groups were made using the Chi-square test, Mann Whitney-U test, and Pearson correlation test.

Results: The mean age of the participants was 40.80±12.06, 45% of them were asthmatic, and the disease year was 7.92±8.49. It was observed that asthmatic individuals had high dependent personality trait and anxiety levels ($p<0.050$). It was found that there was a weak positive correlation between dependent personality trait and depression, anxiety and stress, and the correlation between dependent personality trait and anxiety and depression was higher in asthmatic individuals.

Conclusion: The incidence of dependent personality trait and anxiety was higher in asthma patients. In asthma management, it is recommended that personality traits and psychiatric symptoms should be handled with care along with pharmacological treatments.

Keywords: Asthma, depression, anxiety, stress, dependent personality

Öz

Amaç: Astım ve psikiyatrik sorunların arasında karmaşık bir ilişki bulunmakta, optimal tedavi için bu ilişkinin araştırılması önem kazanmaktadır. Kesitsel ve karşılaştırıcı desende yapılan bu araştırma ile astımlı olan ve olmayan bireylerin bağımlı kişilik özellikleri, depresyon, anksiyete ve stres düzeylerinin incelenmesi amaçlanmıştır.

Materyal ve Metot: Bu çalışmaya astımlı olan (n=172) ve olmayan (n=210) 382 birey katılmıştır. Veriler Tanıtıcı Bilgi Formu, Kişilik Özellikleri Ölçeği ve Depresyon Anksiyete Stres-21 Ölçeği Kısa Formu ile toplanmıştır. Grupların karşılaştırılmasında Ki-kare testi, Mann Whitney-U testi ve Pearson Korelasyon testi kullanılmıştır.

Bulgular: Katılımcıların yaş ortalaması 40.80±12.06 olup, %45'i astımlı bireylerdir ve hastalık yılı 7.92±8.49'dur. Astımlı bireylerin bağımlı kişilik özelliği ve anksiyete düzeyinin yüksek olduğu görülmüştür ($p<0.050$). Bağımlı kişilik özelliği ile depresyon, anksiyete ve stres arasında zayıf düzeyde pozitif bir ilişki olduğu, astımlı bireylerde bağımlı kişilik özelliği ile anksiyete ve depresyon korelasyonun daha yüksek olduğu bulunmuştur.

Sonuç: Astımlı bireylerde bağımlı kişilik özelliği ve anksiyete daha yüksektir. Astım yönetiminde farmakolojik tedaviler kadar kişilik özellikleri ve psikiyatrik belirtilerin özenle ele alınması önerilir.

Anahtar Kelimeler: Astım, depresyon, anksiyete, stres, bağımlı kişilik

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INTRODUCTION

Asthma is a chronic respiratory inflammatory disease which is affected by psychological, neurological, infectious, environmental and allergic factors (1). Infectious, environmental and allergic factors have been examined in many studies (2,3). In addition, an increasing number of studies have been conducted on psychological factors in recent years (4,5). The symptoms of asthma such as coughing, difficulty in breathing, and mucus secretion have been shown to have worsened in case of suffering from stress, anxiety, and depression. The neurological pathway in stress and psychological diseases occurs through insula, anterior cingulate cortex, and hypothalamic-pituitary-adrenal axis changes. Also, the neuroimmune interactions trigger the asthma exacerbation (6).

Psychosomatic illnesses such as asthma can be a risk factor for mental disorders. On the other hand, mental disorders can emerge along with physical symptoms. Considering the worsening effect of somatization on the control of asthma may be useful for optimal treatment of asthma exacerbation and to prevent longer hospitalization durations. Therefore, it is important to investigate depression, anxiety and stress in asthma patients. In previous studies, a higher incidence of anxiety and depression has been shown in asthma patients than in general population (7-9). In another study, the incidence of psychological stress was found to be higher in young individuals and women with asthma (10). It has been determined that psychological problems are prevalent in asthmatic children, and that behavior problems, anxiety, depression, and emotional problems are frequently observed (11).

Regarding the etiology of asthma and the emergence of psychological problems in asthma, it has been reported that asthmatic individuals experience separation problems in the relation they establish with their mothers starting from childhood, that a dependent relation with the mother in early childhood constitutes the basis for asthma, and that these problems are reflected on adulthood period as dependent personality (12). According to the psychoanalytic theory, the quality of early period mother-child relation and maternal attitudes have an effect on the emergence of asthma disease, and that dependent personality trait is associated with asthma (13). In the study he conducted in Australia, Williams (1975) compared asthmatic and non-asthmatic children in terms of the bond they established with their mothers and found that asthmatic children were more dependent on their mothers in comparison to non-asthmatic children (14). Similarly, in the study in which he examined depression and anxiety in asthmatic children through projective tests, Tanik (2011) determined that asthmatic children had a dependent relationship with their mothers, revealed that asthma disease played a role in this relationship, and demonstrated the existence of basic depression, accompanying processive thought, and intense anxiety (15).

The dominant view today is that asthma is a genetic disease in general, and it is explained with triggers such as pollens, mold, moisture, air pollution, and cigarette smoke. However, in addition to the physical factors that cause asthma, it is important to investigate the psychological factors underlying the problem as well as the environmental factors. Moreover, it is known that psychosomatic diseases such as asthma can lead to the development of mental disorders, and that mental problems can be expressed through physical complaints (12). When asthma and psychiatric problems co-exist, or when the contribution of somatization is not considered, patients are unnecessarily examined, their hospital stay can be extended, and the treatments applied can affect one another. Although there are studies in the literature on psychological problems experienced by individuals with asthma (7-9) and on dependent personality trait in asthmatic children (13-15), it has been deemed necessary to examine these variables in adult individuals in a design with control group. Thus, it will be possible to obtain information for optimal treatment and control of asthma, as well as defining the relationship between asthma in adulthood period and dependent personality trait and psychiatric symptoms.

The research questions are:

- Is there a difference between dependent personality trait, depression, anxiety, and stress levels of asthmatic and non-asthmatic individuals?
- Is there a relationship between dependent personality trait, depression, anxiety, and stress levels of asthmatic and non-asthmatic individuals?

MATERIAL AND METHOD

Purpose and design

The study has a cross-sectional and comparative design. It was aimed in the study to investigate the dependent personality trait, depression, anxiety, and stress levels of asthmatic and non-asthmatic individuals.

Population and sample

The population of the study consisted of adult individuals between 18-65 years old who lived in the province of Kırşehir, Turkey. By using the sampling method with known population, the population number (16) of adult individuals living in Kırşehir was determined as 190.000 and asthma prevalence (17) was taken as 4.3%, and the study sample was determined as a total of 340 individuals (170 with asthma, 170 without asthma) with 5% error margin and 99% confidence interval. Individuals with asthma and without asthma were informed about the study during their application to the Chest Diseases Outpatient Clinic of Kırşehir Training and Research Hospital, and the study was completed with 382 individuals who met the inclusion criteria. The inclusion criteria for asthmatic individuals were being diagnosed with asthma, not experiencing an acute asthma attack, being between 18-65 years old, not having a chronic disease other than asthma, being able to communicate in Turkish, being literate, and agreeing

to participate in the study. The exclusion criteria for non-asthmatic individuals were experiencing an acute asthma attack, being pregnant, having another chronic mental or physical disorder, being illiterate, and not agreeing to participate in the study. The inclusion criteria for non-asthmatic individuals were being between 18-65 years old, not having a chronic disease, being able to communicate in Turkish, being literate, and agreeing to participate in the study. The exclusion criteria for non-asthmatic individuals were being pregnant, having a chronic mental or physical disease, being illiterate, and not agreeing to participate in the study.

Conduct of the study

After the necessary permissions for the study were taken, individuals who presented to the outpatient clinic of Kırşehir Training and Research Hospital between 24.11.2021 and 28.02.2022 were informed about the study, they were told that participation in the study was on a voluntary basis, and they were allowed some time to think before they made a decision. Since asthma exacerbations increase in the spring months, the winter season with the least seasonal allergens such as pollen, dust and sun were chosen, and the data collection process was terminated before the spring months arrived. Care was taken to observe the precautions taken against infection in the pandemic conditions. The questionnaire took approximately 10 minutes to fill out, and a suitable room was reserved for the participants. The study was completed with 382 individuals who met the inclusion criteria and voluntarily agreed to participate in the study.

Data collection tools

Identifying Information From

In this form including the questions prepared by the researchers by reviewing the literature (7-9), 14 questions were asked in order to collect data regarding the individuals' demographic characteristics and disease process.

Personality Belief Questionnaire- Short Form

The original scale was developed by Beck and Beck (1991) in order to determine whether the individuals taking the test had non-functional beliefs regarding personality disorders defined in The Diagnostic and Statistical Manual of Mental Disorders (DSM), and if they had, to identify the degree of their believing in their existing beliefs. The Personality Belief Questionnaire consists of statements that aim to measure the individual's beliefs about themselves, others, and the world, and each statement is related to avoidant, dependent, passive-aggressive, histrionic, narcissistic, antisocial, obsessive-compulsive, schizoid, and paranoid attitudes that are defined in the personality disorders in DSM. The scale, which tests 9 personality traits, is made up of a total of 65 items. In line with the purpose of the present study, 7 questions of the scale which test dependent personality traits were used. Individuals score the statements between 0 (do not believe at all) and 4 (totally believe) as they fit their personality. The score to be obtained from this subscale ranges between 0-28, and dependent personality trait increases as the score obtained increases. The Turkish validity and reliability study of the short form of the scale in university students was carried out by Taymur et al. (2011) (18), and Cronbach's alpha coefficient of the dependent personality subscale was found to be 0.66, while it was determined as 0.74 in the present study.

Depression Anxiety Stress Scale-Short Form (DASS-21)

The 21-item short form of the scale was developed by Henry and Crawford (2005) and was adapted to Turkish on normal and clinical samples by Saricam (2018), and it was seen in the clinical sample that the scale differentiated between individuals who were diagnosed and not diagnosed with depression, anxiety, and stress (19). The depression subscale of the scale consists of items 3, 5, 10, 13, 16, 17, and 21, the anxiety scale is made up of items 2, 4, 7, 9, 15, 19, and 20, and items 1, 6, 8, 11, 12, 14, and 18 of the scale measure the stress subscale. The score to be obtained from the subscales ranges from 0 to 21. As the score obtained from the subscales increases, the severity of the symptom increases. Also, the severity of symptoms is determined as normal, mild, moderate, severe, and extremely severe according to the scores obtained from the subscales. While in the validity and reliability study of the scale, Cronbach's alpha coefficient was measured as 0.68 for depression, 0.66 for anxiety, and 0.61 for stress (19), it was found in the present study as 0.87 for depression, 0.83 for anxiety, and 0.81 for stress.

Data analysis method

The statistical analyses of the study were performed by using Statistical Package for Social Sciences (SPSS) 25.0 for Windows software. In the analysis of the data, descriptive statistics such as number, percentage, mean, and standard deviation were used, and the data were presented as median and minimum and maximum values. Normality assumption and variance homogeneity tests of the data were determined by Kolmogorov-Smirnov test, and it was determined that there was no normal distribution by examining the dependent and independent variables Comparison of asthmatic and non-asthmatic individuals was made by using Chi-square tests, and non-parametric tests of Mann- Whitney U Test and Spearman Correlation Test were used in the analysis. In determining the reliability of the scale and its subscales, Cronbach's alpha coefficient was calculated. In statistical analyses, $p<0.050$ was accepted as the indicator of significant difference.

Ethical Considerations

Before conducting the study, institutional permission from Kırşehir Research and Training Hospital and Kırşehir University Non-interventional Ethics Committee Approval (dated 23.10.2021, numbered 2021-13/188) were taken.

The data were collected in line with the principles of the Helsinki Declaration. Accordingly, each participant was informed with voluntary consent form and their written consent was taken.

RESULTS

The asthmatic group constituted 45% of the study sample and they were mostly older than 35 years (40.80±12.06, min=18, max=65). The demographic data of the participants are presented in Table 1. The participants were mostly female, married, employed, and had college-graduate or higher education status. Their expenses were equal to their income. The participants were also mostly non-smokers. They tended to describe their health status mostly as "moderate" (Table 1).

There were no significant differences in terms of the demographic data such as age, gender, education status, marital status, economic status and employment status (p>0.05). Moreover, in the context of the comparison of socio-demographic data of participants in asthmatic and non-asthmatic groups, it was found that there was no statistically significant difference in socio-demographic data of participants, and hence, the groups were similar. The asthmatic group had been diagnosed for a median 7.92±8.49 (min=1, max=30) of years.

Table 1. Demographic data of asthmatic and non-asthmatic group (N=382)

	Total group		Asthmatic group		Non-asthmatic group		p value
	n	%	n	%	n	%	
Age							
≤ 35	135	35.4	63	36.6	72	34.2	0.634
>35	247	64.6	109	63.4	138	65.8	
Gender							
Male	159	41.6	65	37.8	94	44.8	0.169
Female	223	58.4	107	62.2	116	55.2	
Education Status							
Primary school	103	27.0	51	29.7	52	24.8	
High school	131	34.3	61	34.5	70	33.3	0.075
University or higher	148	38.7	60	35.8	88	41.9	
Economic status							
Income<expenses	75	19.6	30	17.4	45	21.4	
Income=expenses	218	50.1	102	59.3	116	55.2	0.489
Income>expenses	89	23.3	40	23.3	49	23.4	
Marital status							
Single	90	23.6	47	27.3	43	20.5	0.117
Married	292	76.4	125	72.7	167	79.5	
Employment status							
Employed	218	57.1	93	54.0	125	59.5	0.308
Unemployed	164	42.9	79	46.0	85	40.5	
Smoking status							
Smoker	122	31.9	55	32	67	31.9	0.296
Non-smoker	260	68.1	117	68	143	68.1	
Health status							
Bad	94	24.6	45	26.2	49	23.3	
Moderate	188	49.2	92	53.5	96	41.7	0.289
Good	100	26.2	35	20.3	65	35.0	
Total	**382**	**100**	**172**	**100**	**210**	**100**	
Chi-square test							

Table 2. Dependent personality and DASS levels of asthmatic and non-asthmatic groups

	Asthmatic group		Non-asthmatic group			
	Median	(Min-Max)	Median	(Min-Max)	p value	
Dependent personality	6	0-26	4	0-21	<0.001	U:12.900.500
DASS- Depression	5	0-20	4	0-16	0.055	U:16.007.000
DASS- Anxiety	6	0-20	3	0-20	<0.001	U:9.225.500
DASS- Stress	6	0-21	6	0-19	0.130	U:16.439.000
Mann-Whitney U Test, p<0.001						

When the median scores obtained from DASS-21 scale were examined, it was seen that while the anxiety levels of asthmatic individuals were at a moderate level, those of the non-asthmatic individuals were at a mild level. It was also observed that the depression levels of asthmatic individuals were mild, while individuals in the non-asthmatic group had a normal level of depression. As for stress, both groups were found to have normal levels of stress. It was determined that dependent personality trait characteristics of the asthmatic individuals and their anxiety levels were higher compared to the non-asthmatic individuals (p<0.001) (Table 2).

Table 3. The relationship between dependent personality trait and DASS levels in asthmatic and non-asthmatic individuals

		DASS-Depression	DASS-Anxiety	DASS-Stress
Dependent personality (Asthmatic group)	r	0.361	0.312	0.376
	p	<0.001	<0.001	<0.001
Dependent personality (Non-asthmatic group)	r	0.298	0.278	0.375
	p	<0.001	<0.001	<0.001

Pearson Correlation Test, p<0.001

A weak and positive relationship was found between the dependent personality trait and depression, anxiety, and stress levels of asthmatic and non-asthmatic individuals (p<0.001) (Table 3). In the analysis performed, it was seen that the asthmatic individuals had a higher correlation coefficient in terms of the relationship between their dependent personality trait and depression and anxiety levels in comparison to the non-asthmatic individuals.

DISCUSSION

It is known that there is a complex relationship between asthma and psychiatric problems, and that according to the psychoanalytic theory, dependent personality trait has an effect on the emergence of asthma (12). 382 asthmatic and non-asthmatic individuals participated in the present study which aimed to examine the relationship between these variables in adults. In the comparisons made, it was seen that asthmatic and non-asthmatic individuals displayed similarities in terms of descriptive characteristics such as age, gender, education status, economic status, marital status, end employment status (p>0.05).

It was determined in the study that asthmatic individuals' anxiety level was moderate, while non-asthmatic ones had a moderate level of anxiety, that asthmatic individuals had a mild level of depression, while non-asthmatic individuals had a normal level of depression, and that both groups had a normal level of stress. In addition, when the anxiety level of the asthmatic individuals was compared with that of the non-asthmatic individuals, it was seen that the asthmatic group had a higher level of anxiety (p<0.001) (Table 2). Clinical research conducted on asthmatic patients have shown that asthma presents a significant comorbidity with mental health problems (7-9). In a study in which anxiety and depression were examined in asthma patients, it was determined that 44.5% of the patients met anxiety disorder criteria, and that 24.5% met depression disorder criteria, and it was reported that asthma patients with anxiety and depression symptoms had weaker pulmonary function compared to those without these symptoms (20). In a systematic compilation of asthma and anxiety comorbidity 19 studies covering 106.813 participants were included. It was reported that anxiety symptom and anxiety disorders were prevalent in asthmatic individuals, and that anxiety symptom accompanying asthma was 1.89 times higher and comorbid anxiety disorder was 2.08 times higher (21). In another study, 11.2% of 65.342 patients were found to have anxiety, 5.5% depression, and 7.7% both anxiety and depression (22). Although there are studies which reported that depression was a prevalent mental problem in asthmatic patients (23), there are also studies which reported that there was no relationship between asthma and depression (5). It is seen that the study findings are consistent with the literature. While it was seen in the present study that anxiety in asthmatic individuals created a statistical difference, there was no significant difference in the severity of depression, though it was higher compared to non-asthmatic individuals. Anxiety disorder is the only disorder that is significantly related with asthma, and it has been emphasized that asthma symptoms and anxiety have a two-way relationship, which suggests that one can originate from the other, or one can result in the other (25). In studies conducted in recent years by using magnetic resonance imaging, regions of the brain that could play a mechanistic role in asthma and mental health disorders have been investigated. Asthmatic patients displayed abnormal structural connections in bilateral frontal gyri, right temporal and parietal cortices and limbic regions with respect to healthy controls, which suggests that brain region functions change depending on emotions (5). In addition, it has been reported that cytokine levels change especially in depression symptoms (24). It can be stated that in a disorder with a somatic dimension such as asthma, a subconscious coping strategy is used in conflicts experienced by individuals, and that psychiatric symptoms develop more as a result of mitigation of the anxiety that basically emerges with the conflict and expression of mental problems through physical symptoms.

In the study, it was determined that dependent personality trait of the asthmatic individuals was higher compared to non-asthmatic individuals (p<0.001) (Table 2). Studies with children have also been examined, since personality development begins in early childhood and the foundations laid in this period manifest itself as a personality pattern during adulthood. In a study in which asthmatic and non-asthmatic children were examined in terms of the relationship they established with their parents, it was reported that the bond between asthmatic children and their mothers had a dependent quality (14). Similarly, in another study, it was revealed that a relationship of dependent quality between asthmatic children and their mothers existed in early childhood period, and that this relationship had an effect on the development of asthma (15). Although

no personality structure specific to asthmatic individuals has been reported in the literature, it has been argued that asthmatic individuals are generally avoidant, sensitive, and obsessive people who cannot express their feelings, and it has been observed that the families of asthmatic children are more aggressive, anxious, perfectionist, depressive, and worried people (26). In a population-based study conducted in Iran with the participation of 3.175 individuals, a high degree of neuroticism (needing extreme compassion, having difficulty in showing one's feelings to others, lacking self-confidence, restlessness, and hesitation towards social activities, etc.) was shown to increase the risk of anxiety and depression (27). Dependent personality trait is characterized by a personality type which is sensitive towards disruption of interpersonal relations, has exaggerated fears about loss and being abandoned, feels a strong need for love and attention, and has an increased tendency to seek help and support from others especially when encountered with stress. It can be stated that this personality type involves the feelings of loneliness, weakness, and hopelessness, and that these feelings have an important effect on increasing anxiety and depression.

In the correlation analysis performed in the study, a weak and positive relationship was found between dependent personality trait of asthmatic and non-asthmatic individuals and their levels of depression, anxiety and stress, and it was determined that asthmatic individuals had higher correlation coefficients for depression and anxiety ($p<0.001$) (Table 3). When the literature is reviewed, it is seen that there is a positive relationship between asthma and depression, that depression is more prevalent in asthmatic patients (23,24), and that similarly there exists a positive relationship between asthma and anxiety (20,21,28). In a study in which asthma, stress, anxiety, and depression were examined, asthma symptom severity was found to be associated with perceived stress and anxiety, and it was reported that the asthmatic group represented a population who were defenseless against stress and anxiety (29). In another study conducted on patients with bronchial asthma, it was determined that asthmatic individuals were less dominant, more introverted, more worried, and more depressive individuals compared to the control group, and that low dominance or dependent social attitude was associated with low forced vital capacity (30). In a study in which depression and anxiety in children were examined, the presence of a dependent mother-child relation, depression, and extreme anxiety mood were shown in asthmatic children (15). In another research that examined the relationship between the mental status of parents of asthmatic children and asthma symptoms, parent and child depression symptoms were found to be associated with worse asthma control (31). In a community-based study conducted with the participation of 2.168 individuals, it was reported that 13.4% of the participants had been diagnosed with asthma, and that asthma diagnosis and depressive symptoms were interrelated (32). In a systematic compilation study which included 27 studies, a weak correlation was found between somatic symptoms and dependent personality traits and depression (33). In another study conducted on asthma patients, asthma patients were compared with both healthy control groups and psoriasis patient group in order to exclude the effect of chronic process. The asthma patients were found to have a high level of avoiding harm, low scores of searches for innovation and self-regulation, and it was determined that depression and anxiety symptoms were associated with both asthmatic individuals' personality and character dimensions (34). It can be claimed that in understanding the comorbidity of asthma and psychiatric diagnosis, the stress of having a chronic disease additionally increases the likelihood of the development of anxiety and depressive symptoms (35). The research results are compatible with the literature. It can be thought that this is due to the fact that individuals with asthma use somatization more when they are under stress and express themselves, and that anxiety and depression are related to introversion, low dominance or dependent social attitude, which is a natural result of dependent personality traits.

CONCLUSION

There is a close interaction between respiratory system and psychic condition. It was seen that dependent personality trait and anxiety were significantly higher in asthmatic individuals in comparison to non-asthmatic individuals. It was also determined that there was a weak and positive relationship between dependent personality trait and depression, anxiety, and stress, and that the correlation between dependent personality trait and anxiety and depression in asthmatic individuals was high. Dependent personality trait and presence of psychiatric symptoms can negatively affect behavioral factors such as adaptation to treatment, self-assessment, and environmental triggers in the optimal treatment of asthma. Therefore, along with pharmacological treatment, providing supportive treatments for personality characteristics and psychiatric symptoms is recommended.

The limitations of the study can be mentioned as being based on self-report, accessing the sample through a certain hospital, and having a cross-sectional design.

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Research Article

Morphometric and Morphological Evaluation of the Fovea Capitis Femoris

Fovea Capitis Femoris'in Morfometrik ve Morfolojik Değerlendirilmesi

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Abstract

Aim: This study was performed to examine morphometric and morphological characteristics of the fovea for ligament of head of femur (FLHOF) on the dry femur to determine its location and morphological types.

Material and Method: FLHOF was analyzed morphometrically and morphologically on 57 dry adult femora (27 right; 30 left) and their digital images. Dimensions and surface area of the FLHOF were measured using a digital caliper on dry bone and ImageJ software on digital images.

Results: The transverse length of the FLHOF ($p<0.001$) and surface area of the FLHOF ($p=0.007$) were found to be greater in the left femur bones than in the right femur bones. Type 1 localization was the most common localization type of the FLHOF. The most common morphological type was found as oval-shaped FLHOF (43.8%), followed by round (40.4%), triangular (10.5%), and piriform shape types (5.3%).

Conclusion: This study indicates that FLHOF was located mostly posteroinferior quadrant and is usually oval or round in shape. Findings obtained in the present study could provide useful information in both clinical and anthropological practice.

Keywords: Fovea capitis, femur, localization, shape, type

Öz

Amaç: Bu çalışma, fovea capitis femoris'in (FCF) kuru femur üzerindeki morfometrik ve morfolojik özelliklerini incelemek, lokasyonunu ve morfolojik tiplerini belirlemek amacıyla yapılmıştır.

Materyal ve Metot: FCF, 57 yetişkin kuru femur (27 sağ; 30 sol) ve dijital görüntüleri üzerinde morfometrik ve morfolojik olarak analiz edildi. FCF'nin boyutları ve yüzey alanı, kuru kemik üzerinde bir dijital kumpas ve dijital görüntüler üzerinde ImageJ yazılımı kullanılarak ölçüldü.

Bulgular: FCF'nin enine uzunluğu ($p<0,001$) ve FCF'nin yüzey alanının ($p=0,007$) sol uyluk kemiklerinde sağ uyluk kemiklerine göre daha büyük olduğu bulundu. Tip 1 lokalizasyon, FCF'nin en yaygın lokalizasyon tipiydi. En yaygın morfolojik tip oval şekilli FCF (%43,8) olarak bulunurken, bunu yuvarlak (%40,4), üçgen (%10,5) ve piriform (%5,3) tipler izledi.

Sonuç: Bu çalışma, FCF'nin çoğunlukla posteroinferior kadranda yerleştiğini ve genellikle oval veya yuvarlak olduğunu göstermektedir. Bu çalışmada elde edilen bulgular hem klinik hem de antropolojik uygulamada faydalı bilgiler sağlayabilir.

Anahtar Kelimeler: Fovea capitis, femur, lokasyon, şekil, tip

INTRODUCTION

The fovea of the femoral head (HOF) is a rough fovea of the HOF, which has a strong attachment to the ligament of the head of the femur (LHOF). FLHOF transmits vessels via LHOF for supplying blood to the femoral head. It is regarded as a clinically important anatomical structure as it is closely related to avascular necrosis of the HOF, especially in hip fractures and dislocations.

Morphometric and morphological characteristics of the FLHOF are essential for the surgical approaches for preservation or reconstruction of the injured LHOF due to its relationship with this ligament (1,2). It has been reported that the relationship between the morphometry of the FLHOF and its position with the development of dysplasia and osteoarthritis in the hip joint (3,4). Morphological features of FLHOF may provide useful information in clinical practice for objective evaluation of

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the hip joint osteoarthritis and LHOF. Precise information about the position of the FLHOF may help clinicians for the determination of the rotational position of the HOF in femoral neck fractures (5). The FLHOF is an important anatomical structure for proximal femur measurements, radiological evaluation, arthroscopic surgery, and surgical approaches to the hip joint (6-8). The evaluation of the morphology of the FLHOF is also important in anthropological studies, used for sex determination of the individual and distinguishing femur from other long bones (9,10).

Although morphometry, position, and morphological types of the FLHOF are keystones in both clinical and anthropological practice, there have been very few published reports on the morphometric and morphological characteristics of FLHOF. In this study, it was aimed to analyze the morphology and morphometry of the FLHOF on the preserved dry femur to determine its precise position, size, and morphological shape in the HOF.

MATERIAL AND METHOD

Morphometric and morphological measurements were performed on 57 preserved adult femora with unknown sex and age (27 right and 30 left). The bones were collected from the Anatomy Department of Hitit University, Çorum. Samples with deformity of the proximal femur were not included in the study. Morphometric and morphological measurements of the FLHOF performed in the present study were described previously (11,12). The dimensions, location, and morphological types of the FLHOF were analyzed from digital images and dry femur. A digital camera (Canon, Inc, Tokyo, Japan) was used to obtain mediolateral images of the femur bone. The femur bones were placed on the horizontal table by means of both greater trochanter and lesser trochanter were in contact with the table surface. Reference scale bar was placed next to femur bones for calibration of the measurements. The mediolateral images were obtained by taking photos of the femoral head from medial view. All measurements were performed using ImageJ, which is distributed for free by the United States National Institute of Health. Longitudinal length, transverse length, depth, and surface area of the FLHOF was measured (Figure 1). The longitudinal length of FLHOF was measured as the longest diameter of the fovea. The transverse length of FLHOF was measured as the short diameter of the fovea. The depth of the FLHOF was measured by a digital caliper on dry bones. Surface areas of the HOF and FLHOF were measured by tracing the boundaries of these structures. For identification of the position of the FLHOF on head of femur, HOF is divided into four equal quadrants by drawing vertical and transverse straight lines which passing through the central point of the femoral head on mediolateral images. The localization of the FLHOF was classified according to its position within the quadrants. Morphological types of the fovea were also determined in oval, circular, triangular, and piriform according to the morphological characteristics of the fovea. Triangular and piriform morphological types of the FLHOF were identified regarding their geometric appearance (Figure 2). Study data were analyzed using SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA). Categorical variables were analyzed by Pearson's chi-square test. The independent t-test or the Paired t-test was used for comparison of the continuous variables.

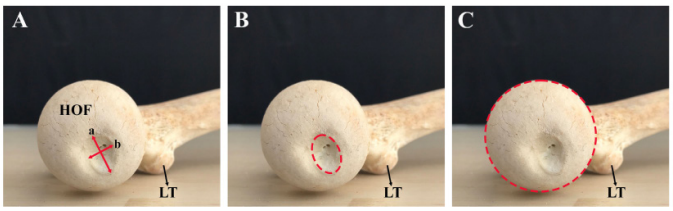

Figure 1. A. The longitudinal length of FLHOF (a); transverse length of FLHOF (b) B. Surface area of FLHOF C. Surface area of HOF. HOF: Head of the femur, LT: Lesser trochanter

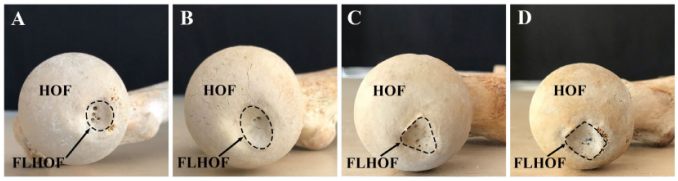

Figure 2. Morphological types of FLHOF A. Round (or circular) type B. Oval type C. Triangular type D. Piriform type

RESULTS

Measurement values of the head of the femur and FLHOF are presented in Table 1. The mean longitudinal length, transverse length, and depth of the FLHOF were 15.01±2.13mm, 10.23±1.52mm, and 2.71±1.09mm, respectively. The mean surface area of the HOF and the FLHOF was 1475.35±195.115mm^2 and 171.51±45.83mm^2, respectively. The transverse length of the FLHOF and surface area of the fovea were observed to be greater in left femora than in right femora ($p<0.001$ and $p=0.007$, respectively). No significant differences were found between the right and left femora in terms of longitudinal length, depth, and surface area of the fovea ($p>0.05$).

The distribution of the types of the fovea in terms of location on the HOF is presented in Table 2. No significant difference was found between the right and left femora in respect of localization of the fovea ($p=0.212$). Type 1 was the most common localization type of the FLHOF at 45.61%, followed by Type 2 (24.5%) and Type 3 (14.1%). The distribution of the morphological types of the FLHOF is given in Table 3. There was no significant difference between the right and left femora regarding localization types of the FLHOF ($p=0.550$). The oval type of FLHOF was the most common morphological type of FLHOF at 43.8%, followed by the round type (40.4%). Triangular and piriform types of FLHOF were found % at 10.5 and 5.3%, respectively.

Table 1. Mean and standard deviations (SD) of the femur and FLHOF parameters

Parameters	Side (mean ± SD)		
	Left (n: 30)	Right (n: 27)	Total (n: 57)
Longitudinal length of the FLHOF (mm)	15.50±2.20	14.47±1.93	15.01±2.13
Transverse length of the FLHOF (mm)	10.88±1.44	9.51±1.27	10.23±1.52
Depth of the FLHOF (mm)	2.84±1.15	2.56±1.01	2.71±1.09
Surface area of the FLHOF (mm^2)	186.53±49.75	154.81±34.85	171.51±45.43
Surface area of the HOF (mm^2)	1491.47±199.01	1457.44±192.84	1475.35±195.11

FLHOF fovea capitis femoris, n number of cases

Table 2. Distribution of the localization types of the fovea capitis femoris (FLHOF)

Side	Localization types of the FLHOF [n (%)]				
	Type 1	Type 2	Type 3	Type 4	Type 5
Left (n:30)	12 (40.0%)	7 (23.4%)	3 (10%)	4 (13.3%)	4 (13.3%)
Right (n:27)	14 (51.85%)	7 (25.9%)	5 (18.51%)	-	1 (3.7%)
Total (n:57)	26 (45.6%)	14 (24.5%)	8 (14.1%)	4 (7.0%)	5 (8.8%)

n number of cases

Table 3. Distribution of the morphological types of the fovea capitis femoris (FLHOF)

	Shape types of the FLHOF [n (%)]			
	Round (or circular)	Oval	Triangular	Piriform
Left (n:30)	10 (33.4%)	15 (50.0%)	4 (13.3%)	1 (3.3%)
Right (n:27)	13 (48.1%)	10 (37.1%)	2 (7.4%)	2 (7.4%)
Total (n:57)	23 (40.4%)	25 (43.8%)	6 (10.5%)	3 (5.3%)

n number of cases

DISCUSSION

The morphometric and morphological characteristics of the FLHOF are crucial in clinical practice (6-8). In the present study, the morphometry, position, and morphological types of the fovea were investigated on dry preserved femora.

There are a few studies in the literature which have investigated the dimensions of FLHOF. Perumal et al. have examined 125 dry isolated femora and reported that the mean longitudinal length and transverse length of the FLHOF were 18mm and 14 mm, respectively. Foveal depth of FLHOF was not evaluated in their study (11). In another study that obtained morphometric measurements from 30 dry femur bones, the length, width, and depth of the fovea of the femur bones were found as 11.17mm, 12.64mm, and 2.80mm, respectively (12). In a recent study by Yarar et al., of the 146 dry femora (146 males, 154 females), the mean longitudinal length, transverse length, and depth of the FLHOF were found to be 15.25mm, 12.00mm, and 2.67mm, respectively (13). The authors reported that there were no significant differences between right and left femur bones in respect of dimensions of the FLHOF. In this study, longitudinal length, transverse length, and depth of the FLHOF were found as 15.01mm, 10.23±1.52mm, and 2.71±1.09mm, respectively, in concordance with previous reports. On the other hand, the transverse length and area of the FLHOF were significantly greater in the left femora than in the right femora. In addition, morphometric features of the FLHOF, right and left side dependent differences in FLHOF morphometry should be taken into consideration when the surgical approach is used in FLHOF of the femur bone. In the present study, we also measured both surface areas of the FLHOF and HOF. Perumal et al. found that areas of the FCF and femoral head were 1.8cm^2 and 10.5cm^2, respectively (11). In another study conducted on 212 femur bones, Bertsatos et al. stated that the area of the FLHOF was larger in males than in females (219mm^2 vs. 177 mm^2) (14). Yarar et al. found that areas of the femoral head and FLHOF were 1587.17mm^2 and 144.43mm^2, respectively (13). In this study, areas of the femoral head and FCF was

found as 171.51mm² and 1475.35mm². Although our results concur with these findings, in the measurement of the surface area of the FLHOF and HOF, methodological differences between previous reports and our findings are noteworthy.

Previous studies have stated that fovea is located posteroinferiorly on the HOF (2,13,15,16). In our study, in concordance with previous studies, FLHOF was located posteroinferiorly on the femoral head. Although FLHOF was mostly located posteroinferior quadrant of the head of the femoris, in the majority of the cases, the FLHOF was also related a little bit to the other quadrants. In 14 cases, FLHOF was related to the anteroinferior quadrant, while in 8 cases it was related to the posterosuperior quadrant. In 5 cases, with mostly located posteroinferiorly, FLHOF was also related other three quadrants of the femoral head. It was reported that FLHOF is more superior position in dysplastic hips, mostly due presence of increased femoral valgus in this condition (3,17). Perumal et al. found, in 123 of 125 bones, the FLHOF was located on the posteroinferior quadrant of the HOF (11). However, the authors did not state if the fovea had a relationship with the other three quadrants. Yarar et al. reported that type 2 localization of FLHOF was the most common localization type (13). Precise information about the position of the fovea is important for radiological evaluation of the images, and to assist diagnostic hip arthroscopic, especially in patients with absent or completely ruptured LHOF (11). Localization of the fovea could provide useful information for the identification of the rotational position of the head of the femur in the fixation approach in femoral neck fractures (5,18).

LHOF is also called the round ligament or ligamentum teres because the distal end of the LHOF is ovoid or round-shaped (19). Previous reports have shown FLHOF is an oval-shaped structure (15,16). Perumal et al. stated that FLHOF has main three morphological types oval-shaped (65.6%), circular-shaped (28%), and triangular-shaped (6.4%) (11). Eliopoulos et al. defined the shape of the FLHOF according to a femoral index of more than 85 as oval-shaped or round-shaped and a femoral index of less than 70 as irregular-shaped or triangular-shaped (9). The authors determined oval-shaped FLHOF was the most common morphological type at 39.73% by followed round-shaped (37.67%), triangular-shaped (11.64%), and piriform-shaped (10.96%) morphological types. The authors determined oval-shaped FCF was the most common morphological type at 39.73% by followed round-shaped (37.67%), triangular-shaped (11.64%), and piriform-shaped (10.96%) morphological types. We found that the most common morphological types were oval (43.80%) and round types (40.40%) in comparison to triangular (10.50%) and piriform (5.30%) morphological types. Our findings are consistent with the reports of previous studies.

The main limitation of the study is that we were not able to evaluate the FLHOF based on sex, age, and ethnicity as lack of demographic data in the present study. Therefore, it is required future studies consist of a morphological evaluation of FLHOF on femur bones with known sex, age, and ethnicity for obtaining information on morphometric and morphological characteristics of FLHOF with age and sex.

CONCLUSION

In conclusion, in the present study, we investigated the morphometric and morphological characteristics of FLHOF. Our findings showed that FLHOF is not only located posteroinferior quadrant of the head of the femoris, in most cases, the FLHOF was also related a little bit to the other quadrants. The transverse length and surface area of the FLHOF exhibited right and left sides dependent differences. Oval types were the most common FCA type, followed by round, triangular, and piriform shape types. Detailed information about the localization and morphology of the FLHOF may help distinguish the FLHOF in both radiographic and arthroscopy images. Findings obtained in the present study could provide useful information in both clinical and anthropological practice.

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Ethical approval: *The authors declare that the current study on donated cadaver skulls belonging to the Department of Anatomy was carried out in accordance with the 1964 Declaration of Helsinki. There were no human participants in the study or there was no human/animal experimentation, therefore no ethics committee approval.*

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Research Article

Comorbidities and the Effect of Comorbidities on Recurrence in Benign Paroxysmal Positional Vertigo

Benign Paroksismal Pozisyonel Vertigoda Komorbiditeler ve Komorbiditelerin Rekürrens Üzerine Etkisi

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Abstract

Aim: Our study aims to investigate comorbidities and the effect of comorbidities on recurrence in posterior canal benign paroxysmal positional vertigo (P-BPPV).

Materials and Methods: Fifty-four patients diagnosed with P-BPPV were included in the study. Demographic characteristics of the patients, smoking, alcohol use, P-BPPV side, comorbid diseases, menopausal status, previous head trauma history, body mass index (BMI) and biochemical parameter results were recorded. Reposition maneuver (Epley) was applied to the patients, and the patients were followed up for six months. Fifty-four patients followed were divided into two groups according to P-BPPV recurrence. Twenty-three patients with relapsed P-BPPV were included in group I, and 31 patients with non-relapsed BPPV were included in group II.

Results: There was no difference between the two groups in terms of age, comorbid diseases, menopausal status, gender, BMI, smoking, alcohol use and biochemical parameters ($p>0.05$). The recurrence rate was lower in P-BPPV patients with right ear involvement ($p<0.05$).

Conclusions: Recurrence is observed less frequently in individuals with P-BPPV whose right ear is affected than in those whose left ear is affected. Our study shows that P-BPPV, comorbid diseases and abnormal biochemical parameters, which are more common in advancing ages, are observed together coincidentally.

Keywords: Benign paroxysmal positional vertigo, vertigo, relapse, comorbid diseases, biochemical parameters

Öz

Amaç: Çalışmamızın amacı, posterior kanal benign paroksismal pozisyonel vertigoda (P-BPPV) komorbiditeleri ve komorbiditelerin nüks üzerindeki etkisini araştırmaktır.

Materyal ve Metot: P-BPPV tanısı alan 54 hasta çalışmaya dahil edildi. Hastaların demografik özellikleri, sigara ve alkol kullanımı, P-BPPV tarafı, komorbid hastalıkları, menapoz durumu, geçirilmiş kafa travması öyküsü, vücut kitle indeksi (BMI) ve biyokimyasal parametre sonuçları kaydedildi. Hastalara repozisyon manevrası (Epley) uygulandı ve hastalar altı ay takip edildi. Takip edilen 54 hasta nüks etme durumuna göre iki gruba ayrıldı. P-BPPV'si nüks eden 23 hasta grup I'e BPPV'si nüks etmeyen 31 hasta grup II'ye dahil edildi.

Bulgular: İki grup arasında yaş, komorbid hastalıklar, cinsiyet, menapoz durumu, BMI, sigara, alkol kullanımı ve biyokimyasal parametreler açısından bir fark yoktu ($p>0.05$). Sağ kulağı tutulan P-BPPV hastalarında nüks oranının daha az olduğu saptandı ($p<0.05$).

Sonuçlar: Sağ kulağı etkilenen BPPV'li bireylerde nüks, sol kulağı etkilenen P-BPPV'li bireylere göre daha az gözlenmektedir. Çalışmamızdan ilerleyen yaşlarda daha sık görülen P-BPPV, komorbid hastalıklar ve anormal biyokimyasal parametrelerin tesadüf olarak birlikte gözlendiği çıkarılabilir.

Anahtar Kelimeler: Benign paroksismal pozisyonel vertigo, vertigo, nüks, komorbid hastalıklar, biyokimyasal parametreler

INTRODUCTION

Benign paroxysmal positional vertigo (BPPV) is the most commonly diagnosed type of vertigo that occurs as a result of the fall of otoconia in the utricle into the semicircular canals (SCC) (1). Displaced otoconia can move freely in SSCs or attach to the cupula. Thus, excitations or inhibitions occur in the head movements in the axis of the affected canal, which abnormally stimulate the vestibulo-ocular reflex. Patients apply to their outpatient clinics

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with the complaint of vertigo, which is triggered by head movements and lasts for seconds. Sudden onset of BPPV and causing severe true-vertigo can be very distressing and frightening for the patient. The type of BPPV and the affected ear are detected by the characteristic nystagmus that occurs with maneuvers such as Dix Hallpike or supine roll. Patients' symptoms often improve with successful maneuvers. However, despite effective treatment in BPPV, recurrences can be seen within months and years. For this reason, researchers have carried out some studies to understand the factors affecting relapse in BPPV and to prevent relapses. Although it was stated in these studies (2-7) that characteristics such as gender and age, and chronic diseases such as hypertension, diabetes mellitus (DM), and cardiovascular diseases, which are common in the community, may be associated with BPPV disease and its recurrence, the findings are contradictory.

This study aims to investigate comorbidities and the effect of comorbidities on recurrence in BPPV.

MATERIAL AND METHOD

This prospective cross-sectional study was carried out on patients aged between 18 and 80 years who applied to the otolaryngology clinic with a complaint of vertigo. Detailed anamnesis was taken from the patients, and otorhinolaryngological examination was performed. In the case of observing characteristic nystagmus for P-BPPV in the applied Dix Hallpike maneuver (Vertical and clockwise rotation in left Dix Hallpike test - vertical and counterclockwise rotation in right Dix Hallpike test), the patients are treated with Epley maneuver was performed. Thirty minutes later, the control maneuver was applied to the patients. The results of previous examinations in the hospital system of the patients who did not have vertigo/nystagmus in the control maneuver and whose complaints improved were checked. Fifty-four patients who had a blood test in the last three months and whose vertigo improved as a result of the Epley maneuver we applied were included in the study. Age, gender, affected side, previous head trauma, smoking-alcohol use, menopausal status, comorbid diseases, height (cm) and weight (kg) of these patients were recorded and body mass index (BMI) was calculated (<18.50kg/m^2 underweight, between 18.50-24.99kg/m^2 normal, 25.00-30.00kg/m^2 overweight and >30 kg/m^2 obese). These patients were followed for six months and were divided into two groups according to their P-BPPV recurrence. 23 patients (42.5%) with P-BPPV recurrence were included in group I, and 31 (57.5%) patients without P-BPPV recurrence were included in group II. Patients with chronic dizziness and vertigo due to another reason and patients with tympanic membrane perforation were not included in the study. Written and verbal consent was obtained from all patients. Permission was obtained from the university's ethics committee for the study (2020/308).

Lab Tests

In the last three months, leukocyte, erythrocyte, thrombocyte and haemoglobin levels were recorded in the hemogram. Biochemistry tests include glucose, urea, creatine, ast, lower, albumin, total bilirubin, direct bilirubin, alkaline phosphatase, sodium, potassium, chlorine, calcium, iron, iron-binding capacity, cholesterol, triglyceride, very low-density lipoprotein (VLDL) and high-density lipoprotein (HDL) levels were recorded. Ferritin, thyroid-stimulating hormone (TSH), free T3 and T4, vitamins D and B12, folate, and HbA1C values were recorded from hormone tests. Values considered normal are shown in Table 1.

Table 1. Normal ranges of parameters and abnormal biochemical parameters by groups

Parameters (Abnormal)	Group I (n:23)	Group II (n:31)	p Value	Normal Range of parameters
Hemoglobin	2 (8.7%)	4 (12.9%)	0.511[b]	(11-16 g/dL)
Leukocyte	5 (21.7%)	3 (9.7%)	0.558[b]	(4-10 10^9/L)
Erythrocyte	1 (5.3%)	3 (9.7%)	0.663[b]	3.5-5.5 10/uL)
Triglycerides	2 (8.7%)	3 (9.7%)	0.545[b]	(0-250 mg/dL)
HDL	2 (8.7%)	2 (6.4%)	0.643[b]	(33-90 mg/dL)
TSH	1 (4.3%)	2 (6.4%)	0.612[b]	(0.35-5.5 ulU/ml)
HbA1C	5 (21.7%)	6 (19.3%)	0.721[a]	(4-6 %)
Vitamin B12	1 (4.3%)	4 (12.9%)	0.362[b]	(211-911 pg/mL)
Vitamin D	5 (21.7%)	8 (25.8%)	0.730[a]	30-100 ng/mL)
Folate	1 (4.3%)	4 (12.9%)	0.362[b]	(5.38-17 ng/ml)
Fe	5 (21.7%)	5 (16.1%)	0.563[a]	(50-175 ug/dL)
TIBC	2 (8.7%)	4 (12.9%)	0.563[a]	(120-370 ug/dL)
Ferritin	7 (30.4%)	10 (32.2%)	0.447[a]	(22-322 ng/mL)
Glucose	7 (40.4%)	11 (35.4%)	0.717[a]	(74-106 mg/dL)
Urea	2 (8.7%)	1 (3.2%)	0.569[b]	(10-49 mg/dL)
Creatinine	3 (13.0%)	4 (12.9%)	0.623[b]	(0.5-1.3 mg/dL)
AST	1 (4.3%)	1 (3.2%)	0.675[b]	(5-34 u/L)
ALT	0 (0%)	1 (3.2%)	0.584[b]	(10-49 u/L)

[a]: Chi Square Test [b]: Fisher Exact test

Statistical analysis

SPSS 21 program was used for data analysis. Descriptive statistics were given with n (%), mean±sd, and median (minimum and maximum). The Chi-square test was used to compare categorical variables. Normality distribution was evaluated with the Shapiro-Wilk test. T-test was used for the data conforming to the normality assumption, and Mann Whitney-U test was used for the data not. P<0.05 was considered statistically significant.

RESULTS

The mean age of group I was 49.03±14.12 (23-76), while the mean age of group II was 51.95±15.05 (22-74). Ten (43.4%) of the individuals in group I were male, and 13 (56.6%) were female, 12 (38.7%) of the individuals in group II were male, and 19 (61.3%) were female. There was no significant difference between the groups regarding age and gender (p>0.05, Table 2).

The most common comorbid diseases in patients with BPPV were 15 (28.3%) hypertension, 12 (22.6%) DM, 6 (11.3%) cardiovascular disease, 6 (11.3%) hypothyroidism, 4 (7.5%) migraine, 4 (7.5%) osteoporosis, 3 (5.6%) hyperlipidemia, 2 (3.7%) chronic obstructive pulmonary disease and 1 (1.8%) hyperthyroidism. There was no difference between the groups regarding comorbid diseases, BMI, menopause, smoking and alcohol use, and previous head trauma (p>0.05, Table 3). However, left ear involvement was higher in relapsed patients than in non-relapsed patients (p<0.05, Table 3). There was no difference between the groups regarding abnormal biochemical parameters (p>0.05, Table 1).

Table 2. Age and gender distributions by groups

	Group I (n:23) Mean±ss	Group II (n:31) Mean±ss	P value
Age (Years)	**49.03±14.12**	**51.95±15.05**	**0.699[a]**
Genger (n)			**0.724[b]**
Female	13 (56.5%)	19 (61.3%)	
Male	10 (43.5%)	12 (38.7%)	

a: T test, b: Chi Square test

Table 3. Comorbid diseases, menopausal status, head trauma status, body mass index (BMI), smoking and alcohol use, and affected side by groups

	Group I (n:23)	Group II (n:31)	p Value
Comorbid Diseases (n)			
Hypertension	7 (30.4%)	8 (25.8%)	0.707[a]
Diabetes Mellitus	4 (17.4%)	8 (25.8%)	0.462[a]
Cardiovascular Disease	1 (4.3%)	5 (16.1%)	0.242[b]
Chronic Obstructive Pulmonary Disease	1 (4.3%)	1 (3.2%)	0.675[b]
Osteoporosis	2 (8.7%)	2 (6.4%)	0.643[b]
Hypothyroidism	3 (13.0%)	3 (9.7%)	0.512[b]
Hyperthyroidism	1 (4.3%)	0 (0%)	0.426[b]
Hyperlipidemia	1 (4.3%)	2 (6.4%)	0.612[b]
Migraine	2 (8.7%)	2 (6.4%)	0.643[b]
BPPV Side (n)			**0.022[a]**
Left	13 (56.5%)	8 (25.8%)	
Right	10 (43.5%)	23 (74.2%)	
Menopause (n)	9 (39.1%)	9 (29.0%)	0.436[a]
Head Trauma (n)	2 (8.7%)	1 (3.2%)	0.569[b]
BMI (n)			0.371[a]
Normal Weight	5 (21.7%)	12 (38.7%)	
Overweight	12 (52.1%)	14 (45.1%)	
Obese	6 (26.0%)	5 (16.1%)	
Smoking	7 (30.4%)	8 (25.8%)	0.707[a]
Alcohol	2 (8.7%)	2 (6.4%)	0.643[b]

a: Chi Square Test b: Fisher Exact test

DISCUSSION

Otoconias falling from the utricle to the SCCs can move freely within the canals (canalolithiasis) or adhere to the cupula of the SCCs (cupulolithiasis). According to the characteristics of the nystagmus that occurs during provoking maneuvers, it can be easily understood whether the otoconia move freely or adhere to the cupula. In the cupulolithiasis form, the latency of nystagmus is very short or absent and lasts longer than in canalolithiasis. In canalolithiasis, nystagmus has a latent period. However, the same cannot be said for the aetiology of BPPV, and it is sometimes difficult to determine the aetiology. In most patients with BPPV, the etiology cannot be determined and it is called idiopathic BPPV. Head trauma, vestibular neuritis, stapes surgery, Meniere's disease and osteoporosis have been implicated in the aetiology of secondary BPPV (8). None of the patients included in our study had Meniere's disease, vestibular neuritis, or stapes surgery histories and findings. Three patients included in our study had a history of head trauma. In our research, BPPV recurrence was detected in 42.5% of the patients. It has been reported in the literature that the recurrence rate of BPPV is between 7% and 50%, similar to our study (9-12).

Kansu et al. (11) examined 118 patients with BPPV in their study and stated that the most common aetiology was idiopathic with 46.6%, and recurrence occurred in 33.1% of the patients. According to this study, patients with a history of head trauma were more likely to relapse than patients with other etiologic causes. Recurrence was observed in 2 of 3 BPPV patients with head trauma who participated in our study. However, there was no difference in terms of head trauma between patients who relapsed and those who did not.

The risk of BPPV increases with advancing age and female gender. However, it is controversial whether there is a relationship between BPPV recurrence and age and gender. In some of these studies, it was stated that relapses were higher in the elderly and females (13,14,15), while in others, it was noted that age and gender were not a factor for recurrence (4,14,16). In our study, 59.3% of the patients were female, 40.7% were male, and the female-to-male ratio was found to be 1.4. However, there was no difference in age and gender between our study's relapsed and non-relapsed groups.

Studies in the literature have reported that right ear involvement is more common in P-BPPV patients (14,17). In the study of Çakır et al. (17), it was found that 67% of the patients habitually took a lateral head position during bed rest, and in 86% of these patients, the side affected by BPPV was compatible with the side-lying on the head during bed rest. In our study, 61.1% of the patients had right ear involvement, which was consistent with the literature, but left ear involvement was significantly higher in patients with relapsed BPPV.

Singh et al. (18) investigated the relationship between cardiovascular risk factors and BPPV in a 4-year follow-up study with 628 patients with BPPV. No significant relationship was found between BPPV recurrence and dyslipidemia, BMI, hypertension and DM in the study. Chen et al. (4) stated that vitamin D deficiency, DM, hypertension and osteoporosis were possible risk factors for BPPV recurrence in a meta-analysis including 14 studies. However, it was reported that age, head trauma, Meniere's disease and migraine should be investigated further. In addition, it was stated in the study that most of these studies were conducted in Asia, and it would be wrong to generalise to the world. Akkoca et al. (7) reported that recurrent attacks were more common in patients with hypertension, with 72 BPPV patients in their study. They did not find a significant relationship between DM and other comorbidities and BPPV attacks. De Stefano et al. (19) evaluated 1092 patients and found a significant correlation between the number of comorbidities and recurrences. In the study, it was reported that when comorbidity increased, recurrence also increased. They suggested that the presence of the systemic disease may cause more frequent otolith rupture. However, there was no difference between the groups in our study in terms of comorbid disorders. In addition, there was no significant relationship between smoking and alcohol use and relapse rates in our research. In the literature, similar to our study, it was stated that there was no relationship between relapse and alcohol use. At the same time, it was reported that smoking significantly reduced the recurrence of BPPV (20). The study stated that smoking protects dopaminergic neurons by inhibiting monoamine oxidase, and dopamine release protects inner ear functions.

In the study by Webster et al. (21), the glucose-insulin test was applied to 72 BPPV patients. According to the results, they divided the patients into groups normal, glucose intolerance, hyperinsulinemia, and hyperglycemia. They found that hyperinsulinemia and hyperglycemia are risk factors for BPPV recurrence, while normal glucose test is protective against BPPV. In the study of Yüceant et al. (22), the bone mineral density of 67 BPPV patients and 78 healthy volunteers were examined. No significant difference was found between the two groups regarding osteoporosis prevalence. In the study, BPPV patients were also divided into two groups according to their relapse status. There was no significant difference between the relapsed and non-recurring groups in terms of osteoporosis prevalence. They stated that the higher incidence of osteoporosis in the elderly than in the normal population might cause BPPV and osteoporosis to be seen together coincidentally.

In the study by Talaat et al. (23), T scores and vitamin D levels of 80 BPPV patients and 100 healthy individuals were compared. T scores and vitamin D levels of BPPV patients were lower than the control group. When analysed according to relapse status, a significant difference was found between the two groups in terms of vitamin D levels. However, no significant relationship was found between T score and relapse. In the meta-analysis of Yang et al. (24), serum vitamin D levels were significantly lower in the group

with BPPV than in the healthy group. In comparing the vitamin D levels of the relapsed and non-relapsed groups, the vitamin D level was found to be significantly lower in the relapsed group. It was concluded that vitamin D is an independent risk factor for BPPV. Unlike these studies, there was no difference between the groups in terms of biochemical parameters in our study.

Ogun et al. (25) analysed 1.377 BPPV patients and showed that perimenopausal women are particularly susceptible to BPPV. They noted that hormonal fluctuations might increase the tendency to develop BPPV. When 32 female BPPV patients included in our study were examined in terms of menopausal status, it was found that 18 patients were in menopause, 9 in the relapsed group and 9 in the non-relapsed group. There was no difference in menopause between relapsed and non-relapsed BPPV patients.

CONCLUSION

Recurrence is observed less frequently in individuals with BPPV whose right ear is affected than in those whose left ear is affected. Our study shows that BPPV, comorbid diseases and abnormal biochemical parameters, which are more common in advancing ages, are observed together coincidentally.

Financial disclosures: *The authors declared that this study hasn't received no financial support.*

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Research Article

Examining the Relationship between the Gender Perception and Psychosocial Health Status of Pregnant Women

Gebe Kadınların Toplumsal Cinsiyet Algıları ve Psikososyal Sağlık Durumları Arasındaki İlişkinin Belirlenmesi

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Abstract

Aim: This descriptive study was conducted to determine the effect of the gender perceptions of pregnant women on their psychosocial health status.

Material and Methods: The study was conducted in the obstetrics service and outpatient clinic of Yozgat Bozok University Hospital between November 2020 and June 2021, and 121 pregnant women were included in the sample. In the study, in which the Individual Identification Form, Pregnancy Psychosocial Health Assessment Scale (PPHA) and the Gender Perceptions Scale (GPS) were used, the data were collected through face-to-face interviews.

Results: The mean age of the pregnant women included in the study was found to be 29.46±6.16. A significant relationship was found between the total mean GPS score of pregnant women and the total mean score of PPHAS. In addition, it was concluded that there was a statistically significant relationship between the mean score of GPS and the subscales of PPHAS, characteristics of spousal relationship, characteristics of anxiety and stress, characteristics of domestic violence, familial characteristics and physical-psychosocial changes related to pregnancy. ($p<0.05$).

Conclusion: Pregnancy is critical period that can negatively affect the woman biopsychosocially. Therefore, in all health screenings, monitoring and evaluations for psychosocial health should be done with a holistic approach.

Keywords: Gender perception, pregnancy, psychosocial health

Öz

Amaç: Bu tanımlayıcı araştırma, gebelerin cinsiyet algılarının psikososyal sağlık durumlarına etkisini belirlemek amacıyla yapılmıştır.

Materyal ve Metot: Çalışma Kasım 2020–Haziran 2021 tarihleri arasında, Yozgat Bozok Üniversitesi Hastanesininin kadın doğum servis ve polikliniğinde yapılmış olup örnekleme 121 gebe dahil edilmiştir. Birey Tanıtım Formu, Gebelikte Psikososyal Sağlık Değerlendirme Ölçeği ve Toplumsal Cinsiyet Algıları Ölçeğinin kullanıldığı çalışmada veriler, yüz yüze görüşmeler ile yapılarak toplanmıştır.

Bulgular: Çalışmaya dahil edilen gebelerin yaş ortalaması 29,46±6,16 olarak tespit edilmiştir. Gebelerin TCAÖ puan ortalaması ile GPSDÖ toplam puan ortalaması arasında anlamlı ilişki tespit edilmiştir. Ayrıca TCAÖ puan ortalaması ile GPSDÖ'nun alt ölçekleri olan eş ilişkisine ait özellikler, kaygı ve strese ait özellikler, aile içi şiddete ait özellikler, ailesel özellikler ve gebeliğe ilişkin fiziksel-psikososyal değişikliklere ait özellikler puan ortalamaları arasında istatistiksel olarak anlamlı bir ilişki olduğu sonucuna varılmıştır ($p<0,05$).

Sonuç: Gebelik, kadın biyopsikososyalini olumsuz etkileyebilecek kritik bir dönemdir. Bu nedenle tüm sağlık taramalarında psikososyal sağlığa yönelik izleme ve değerlendirmeler bütüncül bir yaklaşımla yapılmalıdır.

Anahtar Kelimeler: Gebelik, psikososyal sağlık, toplumsal cinsiyet algısı

INTRODUCTION

Pregnancy is a physiological process that is important for the continuity of the generation, the formation of family integrity, and the transmission of culture from generation to generation (1). A number of physiological, psychological and social changes are experienced in this process, which is a critical milestone in women's life (2,3). Women, who often have difficulties in adapting to these changes, are particularly adversely affected by mental aspects and may experience psychosocial problems such as anger, anxiety, fear, hypersensitivity, irritability, restlessness,

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communication problems (1,4). Various studies indicate that these psychosocial problems occurring during pregnancy are experienced in a way that cannot be compared with other periods of women's life (2,4).

Psychosocial health; It is the condition of a person's adaptation to the social environment and the absence of factors that may adversely affect her health in the social environment she lives in (5). Psychosocial health, which is an important indicator of pregnant women's health; it is directly related to many factors such as age, education level, spouse-family relationship, previous pregnancy experiences, perceived social support, social/ cultural roles and expectations regarding womanhood/ pregnancy (1,3,6,7). Among these factors, social / cultural roles and expectations, which have a decisive place in human life, are also of great importance for pregnant women (8). Social roles and expectations, which can affect women's perception of health, the level of benefiting from health services, and even fertility behaviors, directly affect women's psychological and physiological health (7,9,10,11).

Main role and responsibility in women's life in traditional societies; to be a "good mother" and a "good wife". In these societies, getting married, becoming pregnant, having children (especially male) and caring for the family are considered as indicators of femininity (12). Within the framework of these roles, women are obliged to take care of their children, spouse, if any, the elderly or sick at home and to take care of household chores throughout their lives (13,14). In addition, not being married, divorcing, not having/having a baby is generally seen as a shame and deficiency (15). Women who have grown up with this perception since childhood feel intense pressure, thinking that they will not receive the psychological-social support they need, especially during pregnancy, and will be exposed to threats and violence (9,10). In this context, our study was conducted to determine the effect of pregnant women 'gender perceptions on their psychosocial health status. Especially in the literature, it is seen that studies in this area are insufficient. As a result of our study, it is thought that effective data will be obtained on the subject and will guide preventive and solution-producing studies for the psychosocial health problems of women in pregnancy.

MATERIAL AND METHOD

Purpose and Desing of the Research

The study was conducted descriptively in order to determine the effect of gender perceptions of pregnant women on their psychosocial health status.

Research Sample

The universe of the study consisted of pregnant women who were hospitalized in the obstetrics service or applied to the outpatient clinic of Yozgat Bozok University Hospital between November 2020 and January 2021. The minimum number of individuals to be included in the sample of the study G-power 3.1.3. calculated using the program. The sample size of the study was determined as 111 with 0.05 significance level, 80% power and medium effect (0.30), based on one-way analysis of variance in the G*power statistical program. In order to see the relationship between the variables more clearly, a study was conducted with 121 pregnant women.

The forms of five pregnant women who could not continue the questions because they had pain during the interview and three pregnant women who did not want to continue the interview were not included in the study. The research sample have consisted of 121 pregnant women. While the interviews were conducted with the outpatients in a private room after the examination, they were conducted with the pregnant women in the hospital in their own rooms.

Inclusion Criteria

• Pregnant women,

• Being at the obstetrics service or the outpatient clinic of a university hospital,

• Volunteering to participate in research.

Data Collection

The data were conducted with pregnant women and women who were hospitalized in the gynecology service of a university hospital. The purpose of the study was explained to the individuals who met the inclusion criteria, and their written consents were obtained from the individuals who agreed to participate in the study. Approximately 20 minutes of interviews were held with each participant after the consent was obtained. In these interviews, Individual Description Form, Psychosocial Health Scale during Pregnancy and Gender Perceptions Scale were applied.

Data Collection Tools

Individual Information Form

The form created by the researcher by examining the literature includes questions about the personal characteristics of the participants such as age, educational status, marriage type, economic income, employment status, relationship with spouse or family (1,4,15,16).

Pregnancy Psychosocial Health Assessment Scale (PPHAS)

The PPHAS was developed by Yıldız (2011) for determining the psychosocial health status of the pregnant woman and the factors affecting it (16). The Pregnancy Psychosocial Health Assessment Scale is a 5-point Likert-type scale consisting of 46 items in total. The average value is determined by dividing the total score obtained from the

scale by the number of items, and a result between 1 and 5 is determined. As a result, as both the total score and the subscale scores move away from 5 and approach 1, it indicates that there is a problem in psychosocial health during pregnancy. The sub-dimensions of the scale determine whether there is a problem in terms of factors affecting psychosocial health. On the scale, items expressing "Characteristics of pregnancy and spousal relationship" are (1-8,18-20,32,34); items expressing the first sub-dimension "Anxiety and stress characteristics" are (9-12,36-38,40); items expressing the second sub-dimension "Characteristics of domestic violence" are (21-27,43); items expressing the third sub-dimension "Characteristics of psychosocial support needs" are (16,17,28-30,41,45); items expressing the fourth sub-dimension "Familial characteristics" are (31,33,35,42) and items expressing the fifth sub-dimension and "Characteristics of physical-psychosocial changes related to pregnancy" (13-15,39,44,46) constitutes the sixth sub-dimension. The Cronbach's Alpha coefficient of the " Pregnancy Psychosocial Health Assessment Scale" scale was determined as 0.93. In our study, Cronbach's Alpha coefficient of the scale was found to be 0.925.

Gender Perception Scale (GPS)

GPS was developed by Altınova and Duyan (2013) and it is a five-point Likert-type measurement tool that consists of a single dimension and 25 items (17). 10 of the items were written as positive and 15 as negative. In the scale formed in the form of a five-point Likert scale, individuals are asked to submit a five-degree opinion: "5-I totally agree, 4-I agree, 3-I am undecided, 2-I do not agree, and 1-I completely disagree. Items 2, 4, 6, 9, 10, 12, 15, 16, 17, 18, 19, 20, 21, 24 and 25 are negative and calculated in reverse. Accordingly, the scores that can be obtained from the scale are in the range of 25-125, and high scores indicate a positive gender perception. In Altınova and Duyan's (2013) study, the Cronbach's Alpha coefficient of the scale was found to be 0.872. In our study, Cronbach's Alpha coefficient of the scale was found to be 0.846.

Data Analysis

Number, percentage, mean and standard deviation were used for the descriptive characteristics of the data and descriptive statistics of the scale scores. Compliance of numerical data to normal distribution was determined by Kolmogorow-Smirnow test, Skewness and Kurtosis. T-test, Chi square, One Way Analysis of Variance in the evaluation of data with normal distribution; The ANOVA test, Kruskall Wallis, Mann Whitney-U was used to evaluate data that did not show normal distribution. Statistical significance level was accepted as $p<0.05$.

Ethical Approval

This study was approved Yozgat Bozok University ethics committee (dated: 12-11-2020, no:88148187-900-E.31109). The participants were first given information about this study aims and details, and then their verbal and written consent were obtained. Participations were entirely on a voluntary basis. Participations were also informed that they could contact the research team at any time for questions or to discuss the study.

RESULTS

The average age of pregnant women participating in the study was 29.46±6.16, 57.0% lived in the city center, 28.9% graduated from secondary education, 84.3% did not work in an income generating job, 56.2% was determined that they married willingly and 31.4% had two children. 32.2% of the pregnant women had a high education level, 84.3% had good thoughts about marriage, 71.1% had a good spouse relationship, 84.3% had good family relations and 70.2% had good relations with the family of their spouses.

It was determined that there is a statistically significant difference between the PHASP total score averages of the women included in the study and the age, education level, way of marriage, general thoughts about marriage, spouse relationship, relationship with their family and the relationship of their spouse with their family ($p<0.05$). It was found that there was a statistically significant difference between the total GPS score average of pregnant women and education level, and relationships with their spouse's family ($p<0.05$).

It was found that the mean GPS score of pregnant women in the study was 85.27±13.11 and the mean total score of PHASP was 3.88±0.55. PPHAS subscale mean scores; pregnancy and spousal relationship 3.94±0.64, anxiety and stress characteristics 3.23±0.92, domestic violence 4.49±0.70, psychosocial support needs 3.76±0.69, familial characteristics were determined as 4.13±0.72, and the characteristics of physical-psychosocial changes related to pregnancy were 3.67±0.86. There is a statistically significant correlation between the mean GPS score and the mean PPHAS total score, the characteristics of pregnancy and spouse relationship, the characteristics of anxiety and stress, the characteristics of domestic violence, familial characteristics, and the physical-psychosocial changes related to pregnancy sub-dimension mean scores. It was concluded ($p<0.05$).

Factors affecting the mean GPS score of pregnant women were evaluated by multiple linear regression analysis. In the study, it was concluded that the model created with the factors affecting the GPS score average was statistically significant ($F=7.405$, $p=0.000$). According to the model, GPS score average is 32.5%; The PPHAS total score average is explained by the variables of pregnancy and marital relationships, characteristics of anxiety and stress, characteristics of domestic violence, characteristics of psychosocial support, familial characteristics, employment status, education level, and spouse-family relationship variables.

Table 1. Investigation of the relationship between the participants' mean PPHAS total score and GPS score average

Features	Mean±Ss (min-max) n(%)		PPHAS Mean±Ss	PPHAS F;p/t;p	GPS Mean±Ss	GPS F:p/t;p
Age	29.46±6.16(19-47)		3.88±0.55	F=2.526 p=0.001	85.27±13.11	F=1.440; p=0.102
Place of Residence	City Center	69(57.0%)	3.87±0.58	F=0.281; p=0.839	87.33±15.32	F=1.547; p=0.206
	Town	8(6.6%)	4.00±0.25		79.87±12.98	
	Village	29(24.0)	3.83±0.49		82.34±8.19	
	Other	15(12.4)	3.95±0.69		84.33±7.72	
Education Level	Not literate	6(0.5%)	3.22±0.65	F=5.762; p=0.000	77.0±5.47	F=8.847; p=0.000
	Primary School	28(23.1%)	4.08±0.29		82.0±12.28	
	Secondary School	35(28.9%)	3.94±0.54		82.25±11.0	
	High School	30(24.8%)	3.64±0.69		83.93±13.06	
	University	22(18.2%)	4.05±0.37		98.31±10.96	
Spouse Education Status	Primary School	39(32.2%)	3.89±0.50	F=0.348; p=0.045	77.69±9.27	F=7.269; p=0.000
	Secondary School	19(15.7%)	3.86±0.50		90.52±14.92	
	High School	35(28.9%)	3.83±0.67		85.31±9.30	
	University	28(23.1%)	3.92±0.54		92.03±15.54	
Marriage Type	With flirt	49(40.5%)	3.99±0.51	F=5.844; p=0.004	88.36±14.74	F=2.400; p=0.005
	Arranged Method/ Willingly	68(56.2%)	3.85±0.53		83.04±11.77	
	Arranged Method/ Unwillingly	4(3.3%)	3.05±0.84		85.25±6.25	
Number of Children	0	23(19.0%)	3.70±0.69	F=1.696; p=0.156	89.52±14.67	F=1.107; p=0.357
	1	33(27.3%)	3.97±0.49		86.0±13.31	
	2	38(31.4%)	3.80±0.57		83.47±12.31	
	3 and upper	27(22.3%)	3.88±0.55		83.29±12.35	
General Opinion Against Marriage	Good	102(84.3%)	4.04±0.37	F=54.346; p=0.000	86.13±12.88	F=1.588; p=0.209
	Bad	11(9.1%)	3.29±0.68		82.09±17.93	
	Neutral	8(6.6%)	2.68±0.36		78.62±3.96	
Spouse Relationship	Good	86(71.1%)	4.01±0.37	F=22.94; p=0.000	86.90±12.79	F=2.620; p=0.077
	Bad	26(21.5%)	3.78±0.66		80.34±13.29	
	Neutral	9(7.4%)	2.90±0.69		83.88±13.43	
Relationship with Own Family	Good	102(84.3%)	3.93±0.56	F=9.073; p=0.000	85.54±12.99	F=0.534; p=0.588
	Bad	17(14.0%)	3.73±0.153		84.70±14.56	
	Neutral	2(1.7%)	2.41±0.00		76.00±0.00	
Relationship with Family of Spouse	Good	85(70.2%)	4.06±0.38	F=86.77; p=0.000	87.55±13.36	F=7.248; p=0.001
	Bad	24(19.8%)	3.88±0.34		83.16±10.95	
	Neutral	12(9.9%)	2.60±0.11		73.33±7.54	
Total		121(100%)				

PPHAS: Pregnancy Psychosocial Health Assessment Scale GPS: Gender Perception Scale

Table 2. Investigation of the relationship between participants' mean total score of PPHAS and their mean scores for the sub-dimension of PPHAS and GPS total score average

PPHAS	Mean±Ss (min-max)	PPHAS Score Average F/p
Pregnancy and Spouse Relationship Characteristics Sub-Dimension Average Score	3.94±0.64 (2.46-5.0)	F=3.080 p=0.000
Anxiety and Stress-Related Sub-Dimension Score Average	3.23±0.92 (1.13-4.88)	F=2.238 p=0.001
Characteristics of Domestic Violence	4.49±0.70 (1.75-5.0)	F=1.776 p=0.015
Characteristics of Psychosocial Support Needs Sub-dimension Average Score	3.76±0.69 (2.14-5.0)	F=1.163 p=0.280
Familial Traits Sub-Dimension Average Score	4.13±0.72 (1.75-5.0)	F=2.282 p=0.001
Characteristics of Physical-Psychosocial Changes Related to Pregnancy Sub-Dimension Average Score	3.67±0.86 (1.67-5.0)	F=2.177 p=0.002
Total Score Average	3.88±0.55 (2.41-4.70)	F=1.872 p=0.009
GPS Score Average	85.27±13.11 (62-119)	

PPHAS: Pregnancy Psychosocial Health Assessment Scale GPS: Gender Perception Scale

Table 3. Factors Affecting Gender Perception in Pregnancy

Factors	β	Standard Error	t	p	R2
(Constant)	72,355	14.628	4.946	0.000	0.468
PPHAS Total Score Average	-4.148	13.935	-0.298	0.766	
Features of Pregnancy and Spousal Relationship	10.090	5.209	1.937	0.055	
Anxiety and Stress-Related Sub-Dimension Score Average	2.000	3.613	0.553	0.581	
Characteristics of Domestic Violence	-1.161	3.626	-0.320	0.749	
Characteristics of Psychosocial Support Needs Sub-dimension Average Score	-2.027	3.111	-0.651	0.516	
Familial Traits Sub-Dimension Average Score	-2.027	3.111	0.778	0.438	
Working Status	-9.620	3.100	-3.103	0.002	
Level of education	2.671	1.127	2.370	0.019	
Spouse-Family Relationship	-1.716	2.297	-0.747	0.457	

R Squared = ,375 (Adjusted R Squared = ,325); inf.=information F=7,405 p=0.000 PPHAS: Pregnancy Psychosocial Health Assessment Scale GPS: Gender Perception Scale

DISCUSSION

Pregnancy, known as the period of happiness in women's life for centuries, has turned into a complex process that negatively affects women both physically and mentally in the modern world (18). This long and tense process, which starts with the news of pregnancy, negatively affects women biopsychosocially due to changes in body pattern, social relations and roles that occur over time (19).

According to the results of our study in this context; PPHAS mean score of pregnant women was 3.88±0.55 and the mean GPS score was 85.27±3.11. These data show that psychosocial health and gender perceptions of pregnant women are at a moderate level. When the studies in the literature are examined; It was determined that the psychosocial health levels of pregnant women were between 3.95 and 4.31 points (20,21). The reason for the lower scores in our study; It is thought to be caused by their living in regions with different sociocultural characteristics. It is thought that the cultural characteristics and gender perceptions of our sample, especially from the Central Anatolia region, where patriarchal culture is more dominant,

are influential in these results. Although there are very few data about the effects of gender perceptions on the psychosocial health of pregnant women in the literature, the available information shows that the pregnancy and birth process, which are two important periods for women, are strongly related to gender perceptions (22,23). According to the results of our study, a statistically significant relationship was found between total GPS score average and PPHAS total score average ($p<0.05$). In the patriarchal culture representing the region where our sample lives, women are expected to have a large number of children, since being a mother and gaining status are equated with each other (9,19,23). This idea means that women can exist in society only with their maternal role and turns pregnancy into a means of existence. Pregnancy turns into a serious psychosocial crisis due to this imposition and its accompanying domestic roles (22,24,25). Stress and anxiety caused by the excessive and unrealistic roles/expectations imposed on women by the society (wife, family, etc.) during pregnancy, childbirth and postpartum can disrupt the harmony of the pregnant woman for her entire life (family, work, social, occupational, etc.) (10,23).

From our study results, it was concluded that there was a statistically significant relationship between the mean GPS score and the characteristics of anxiety and stress and the physical-psychosocial changes related to pregnancy sub-dimension mean scores ($p<0.05$). The roles and responsibilities imposed by culture and society on biological sex contribute to the formation of psychosocial problems experienced by pregnant women in various ways. Passive, calm, emotional, silent, dependent, meticulous roles determined by society for women explain psychosocial problems such as depression, anxiety, fear, sadness, and vulnerability, especially during pregnancy (10,23,24). In addition, it is obvious that these symptoms, which have been explained with the biological changes in postpartum and premenstual periods for years, are caused by multiple roles such as being a good mother, good wife, good housewife, good bride and sociocultural impositions associated with these roles (10,24).

When the results of the study are examined, it is seen that the mean PPHAS scores of the group who said that their relationship with their spouse, their family and their spouse's family was bad was significantly lower ($p <0.05$). In addition, it was found that there is a significant relationship between the mean GPS score and the PPHAS pregnancy and spouse relationship sub-dimension and familial characteristics sub-dimension mean scores ($p <0.05$). Pregnancy is an important period for both the woman and her husband and family. It is reported that one of the most important factors that can turn pregnancy into a problematic period and directly affect psychosocial health is the relationship of the pregnant woman with her husband and her environment (26). The fact that pregnant women have a healthy relationship with their spouse and their families enables them to accept pregnancy more easily and adapt to the biopsychosocial changes that occur during pregnancy (27). However, especially in family structures where there is a relationship characterized by pressure, violence and social restrictions, this situation causes the opposite results (9,28). When considered in this context, it is thought that women who live with their husbands and families who have a traditional gender perception experience less happiness, less positive social interaction, more anxiety, stress and problems during pregnancy.

Education level is stated as a prerequisite for women to live productively and to live in high quality and to show behaviors to solve health problems. In many studies, it is stated that as the education levels of pregnant women and their spouses increase, depression, anxiety and stress symptoms, which are the components of psychosocial health, decrease (9,20). In parallel with this, our research results show that as the education levels of pregnant women and their spouses increase, their psychosocial health scores increase significantly. It is thought that this relationship is related to the ability of pregnant women and their spouses with a high level of education to have easier access to information and support mechanisms related to pregnancy and birth. In addition to psychosocial health, gender perception is also affected by the education level of the pregnant woman and her husband (29,30). This result is thought to be due to the fact that pregnant women and their spouses with high educational levels act with a more egalitarian perception of gender.

In the study, the way of marriage was determined as another factor affecting the psychosocial health and gender perceptions of pregnant women. It is known that women raised in patriarchal cultures and families with traditional attitudes generally act with a traditional perception. In these families, women often marry someone who the family deems appropriate (even if they do not want to), because the woman is dependent on others in making decisions, cannot express her wishes as she wishes, and her flirting is not welcome. This situation emerges as a major reason for the couple's lack of harmony with each other (31). Studies in the literature show that women who marry by courtship and willingly have a positive effect on psychosocial health during pregnancy (31,32).

The study has been done on pregnant women who were treated at a university hospital in Turkey. Our study results are limited to the answers given by the pregnant women to the forms. In addition, the lack of studies in the literature on the examining of between the psychosocial health and gender roles of pregnant women is the strength of the study.

CONCLUSION

Our study results show that there is a significant relationship between the gender perceptions of pregnant women and their psychosocial health. In addition, it was determined that many sociocultural factors such as age, education level, marriage type, general thoughts about marriage, spouse relationship, relationship of pregnant woman with her family and relationship of pregnant woman with her

husband's family are also effective in psychosocial health conditions of pregnant women.

Pregnancy, which is a very sensitive period in women's life, has the potential to affect women not only physiologically but also psychologically and socially positively or negatively. For this reason, the spouse of the pregnant woman should be included in the health screenings to be performed during pregnancy, monitoring and evaluations should be made for psychosocial health with a holistic approach, and possible risks should be determined. In these follow-up and evaluations that will turn into routine, groups of younger gestational age, low education level, and poor social relations with their spouses and their environment should be examined carefully. In addition, counseling support should be provided to pregnant women and their spouses on issues such as gender roles, parenting roles, and domestic violence. On the other hand, training programs should be organized in order to increase the knowledge, skills and awareness of all health professionals, including midwives, nurses and physicians working in the field of women's health, about psychosocial health and gender roles, which is one of the most important determinants of pregnancy.

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MEDICAL RECORDS-International Medical Journal

Research Article

Investigation of the Relationship between Serum Ferritin Levels, Lung Involvement and Treatment Methods in COVID 19 Patients: A Retrospective Study

COVID19 Hastalarında Serum Ferritin Düzeyleri, Akciğer Tutulumu ve Tedavi Yöntemleri Arasındaki İlişkinin Araştırılması: Retrospektif Bir Çalışma

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Abstract

Aim: COVID-19 disease was identified as cases of pneumonia of unknown origin in China in 2019. It has been reported that after the Covid 19 virus entered the body, the immune system cell was over-activated and there was an intense release of cytokines and the clinical picture worsened accordingly. In addition there is a relationship between ferritin level and cytokine release. In the present study, it was aimed to examine the relationship between the presence of lung involvement and treatment and ferritin levels in cases diagnosed with Covid 19 in the emergency department.

Material and Methods: Cases aged 18 years and older who applied to the emergency department with positive SARS-CoV-2 PCR analysis were included in the study. Demographic characteristics, serum ferritin levels, lung tomography reports (according to the Co-Rads Classification) and treatment modalities (outpatient treatment, inpatient treatment in the service and treatment in the intensive care unit) of the cases were examined.

Results: It was determined that patients with pulmonary involvement had an increased treated in intensive care (p<0.001). It was determined that the serum ferritin level of the patients treated in the service was significantly higher than those of the outpatients (p<0.001). The serum ferritin levels of the patients treated in the intensive care unit were also found to be significantly higher than the serum ferritin levels of the inpatient group (p<0.001).

Conclusion: Cytokine storm is seen in Covid 19 patients. This situation worsens the clinical condition of the patients and causes an increase ferritin level. Serum ferritin levels are increased in patients with lung involvement and increased with severity of the disease. It is recommended to measure serum ferritin levels in the routine follow-ups of Covid 19 patients.

Keywords: Covid-19, lung tomography, ferritin, Covid 19 treatment

Öz

Amaç: COVID-19 hastalığı, 2019 yılında Çin'de menşei bilinmeyen pnömoni vakaları olarak tanımlanmıştır.
Covid 19 virüsü vücuda girdikten sonra ,bağışıklık sistemi hücreleri aşırı aktif hale gelir, yoğun sitokin salınımına sebep olur ve buna bağlı klinik tablo kötüleştiği bildirilmiştir. Ayrıca ferritin düzeyi ile sitokin salınımı arasında da bir ilişki vardır. Sunulan çalışmada acil serviste Covid 19 teşhisi konulan olguların akciğer tutulumu varlığı, tedavi şekilleri ile ferritin düzeyleri arasındaki ilişkinin incelenmesi amaçlanmıştır.

Materyal ve Metot: Acil serviste SARS-CoV-2 PCR pozitifliği saptanan, 18 yaş ve üzeri olgular çalışmaya dahil edilmiştir. Olguların demografik özellikleri, serum ferritin seviyeleri, akciğer tomografı raporları (Co-Rads Sınıflandırması) ve tedavi yöntemleri (ayakta tedavi, serviste yatarak tedavi ve yoğun bakımda tedavi) bakım ünitesi incelenmiştir.

Bulgular: Akciğer tutulumu olan hastaların yoğun bakımda tedavi edilme oranlarının arttığı belirlendi (p<0,001). Hastanede serviste yatarak tedavi edilen hastaların serum ferritin düzeyi,ayaktan tedavi edilen hastalara göre anlamlı derecede dah yüksek olduğu saptandı (p<0,001). Yoğun bakımda yatarak tedavi gören olguların serum ferritin düzeyleri de serviste yatarak tedavi olan diğer olgulara göre anlamlı derecede yüksek bulundu (p<0,001).

Sonuç: Covid 19 hastalarında sitokin fırtınası görülür. Bu durum hastaların klinik durumlarının kötüleşmesine ve serum ferritin seviyesinin artmasına sebep olur. Akciğer tutulumu olan hastalarda serum ferritin seviyeleri yükselir ve hastalığın şiddeti ile artar. Covid 19 hastalarının rutin takiplerinde serum ferritin düzeylerinin ölçülmesi önerilir.

Anahtar Kelimeler: Covid-19, akciğer tomografisi, ferritin, Covid 19 tedavisi

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INTRODUCTION

COVID-19 disease was identified as pneumonia cases of unknown origin in China in 2019 (1). In a short time, it spread all over the world and became a pandemic. The disease that caused deaths affected more than 200 countries, more than 6,000,000 confirmed cases and more than 370,000 patients were reported (2).

The clinics of those infected with COVID 19 may differ from patient to patient. The treatment of patients is planned according to their clinical status and lung involvement. In cases such as myalgia, fever, sore throat and dry cough that do not impair the general health of the people; are treated on an outpatient basis. It was reported that she was hospitalized in the service in cases accompanied by severe symptoms such as shortness of breath and / or hypoxemia.It has even been reported that they are treated in intensive care units in cases where clinical conditions with high mortality such as septic shock and acute respiratory distress syndrome (ARDS) develop (3).

After the COVID 19 virus enters the body, the immune system cell becomes over-activated, causing the release of intense amounts of cytokines. This situation worsens the clinical picture of the patients. In addition it has been reported that there is a relationship between ferritin level and cytokine release (4). In this direction, the present study aimed to examine the relationship between the presence of lung involvement and treatment (outpatient treatment, inpatient treatment in the service and treatment in the intensive care unit) and serum ferritin levels in cases diagnosed with COVID 19 in the emergency department.

MATERIAL AND METHOD

The presented study is a cross-sectional and retrospective study. Before starting the study, approval was obtained from the Ethics Committee of Ordu University Faculty of Medicine (2022/51 date: 25.02.2022). The study was conducted in accordance with the Declaration of Helsinki.

Patient data were accessed through the patient registration system. Age, gender, serum ferritin levels, lung tomography reports (according to the Co-Rads Classification) and treatment modalities (outpatient treatment, inpatient treatment in the service and treatment in the intensive care unit) of the patients were examined..

Study populastion

Cases aged 18 years and older who applied to the emergency department between 01/03/2020 and 01/06/2021, whose SARS-CoV-2 PCR analysis was positive and whose data were accessed from the patient information system, were included in the study.

Patients whose data could not be accessed from the patient information system, SARS-CoV-2 PCR analysis was not performed, ferritin level and lung tomography examination were not performed, those under 18 years of age, those with a history of liver malignancy, liver failure, cirrhosis, hepatitis, those receiving medical treatment that cause deterioration in liver function tests, pregnant women patients with immunodeficiency and cancer were excluded from the study.

Lung Tomography Analysis

The pulmonary tomography reports of the patients included in the study were recorded retrospectively. In the hospital where the study was conducted, the lung tomography reports of COVID 19 patients were evaluated according to the Corads scoring. Cases reported as having a corads score of 3 and above were accepted as having lung involvement (5).

Co-Rads Classification

Level	Suspicion Level	Findings
CO-RADS 0	Not evaluated	The review is technically inadequate.
CO-RADS 1	Very low	Normal or non-infectious findings (mild or severe emphysema, perifissural nodules, lung tumor or fibrosis)
CO-RADS 2	low	Typical findings for other infections (Budded branch, centrlobular pattern, lobar or segmental consolidation, cavitation)
CO-RADS 3	Medium/ uncertain	Findings in both COVID-19 and other diseases (central ground glass opacities, pulmonary edema, Homogeneous, diffuse ground-glass appearance with interlobular septal thickening or pleural effusion suggestive ground glass nodules that are not centrlobular or adjacent to the visceral pleura)
CO-RADS 4	High	Suspicious / possible findings for COVID-19
CO-RADS 5	Very high	Typical findings for COVID-19 (bilateral and multifocal, including fissure, adjacent to the visceral pleura, with or without consolidation, ground glass opacities)
CO-RADS 6	Definitive diagnosis	RT-PCR** positive patient

Statistical Analysis

Data were collected retrospectively and analyzed with the IBM SPSS for Windows 22.0 Program. Data are given in numbers and percentages are indicated. Demographic information of the patients and the relationship between thorax tomography involvement and treatment method were examined. The relationship between the patients' serum ferritin levels at the time of admission and their pulmonary involvement and treatment modalities was analyzed using the Mann-Whitney U test. Data were tested for normality using analysis first and than descriptive statistics (number of samples, percentage, mean, standard deviation, median, minimum/maximum) were made. Kolmogorov-Smirnov test and Levene test for variance homogeneity were used. $p<0.05$ was accepted as significant in the statistical evaluation.

RESULTS

In the study, 580 cases with positive COVID 19 test in the emergency room were included.

It was determined that 53.4% (n=310) of the patients were female and 46.6% (n=270) were male. Median and IQR values were used because the age group of the patients did not fit normal distribution. The median age of all Covid cases was 46/year (IQR 28), the median age of female patients was 44/year (IQR 27), while the median age of male patients was 48/year (IQR 26). No correlation was found between them according to age groups (p>0.05).

The treatment modalities of the patients were examined; 51.9% (n=301) were treated as outpatients, 44.5% (n=258) were hospitalized in the service and 3.6% (n=21) were in the intensive care unit has been treated.

Lung tomography reports of the patients who applied to the emergency department were reported as corads of 3 and above were considered positive. It was determined that 82.2% (n=477) patients had negative CT scans and 17.8% (n=103) patients had positive CT scans. Treatment modalities according to involvement were analyzed using the chi-square test.

Positive tomography uptakes increased the inpatient treatment requirements of the patients (p<0.001). Tomography involvement was detected in 6.3% (n=19) of 301 outpatients, 25.2% (n=65) of 258 hospitalized patients were treated in the service and 90% of 21 patients treated in the intensive care unit. It was determined that; 5 (n=19) of them had tomography involvement. Accordingly a statistically significant relationship was found between tomography involvement and treatment modalities of covid patients (p<0.05).

Serum ferritin levels were measured in all patient groups. Median values were used because they did not fit the normal distribution. The median serum ferritin was 103.45 ml/l (IQR 210.8).

The relationship between serum ferritin levels and lung tomography involvement of COVID 19 patients was investigated. While the median ferritin level of the patients without lung tomography involvement was 266.9ml/l, the median ferritin level of the patients with lung tomography involvement was 399.8ml/l. It was determined that there was a significant difference between the patient groups with and without lung tomography involvement (p<0.001).

The relationship between serum ferritin levels and treatment modalities of COVID 19 patients was investigated. Ferritin level of the patients receiving outpatient treatment was 229.80ml/l, the serum ferritin levels of the patients treated in the service were found to be 338.57ml/l and there was a statistically significant relationship between them (p<0.001). Serum ferritin levels of patients receiving outpatient treatment and patients receiving intensive care inpatient treatment were 152.79ml/l and 286.33ml/l respectively. It was found that there was a statistically significant relationship between them (p<0.001). In addition, the serum ferritin levels of COVID 19 patients receiving inpatient treatment in the service and inpatient treatment in the intensive care unit were found respectively 133.33ml/l and 221.90ml/l. It was found that there was a statistically significant relationship between them (p<0.001)

DISCUSSION

PIn line with the source information; the mechanism of disease in humans how the disease progresses and the effect of the cases on the immune system are still not fully known. However, some opinions have been focused on. The most common among them; it is thought to be associated with the inflammatory cytokine storm during the period of COVID 19 infection. Cytokine storm is an uncontrolled and dysfunctional immune response due to the immunopathogenic mechanism of COVID-19. Meanwhile, many inflammatory cytokines such as TNF-α, IL-6, IL-12 and IL-8 are released (6). It has been reported that cytokine storm causes negative effects on many tissues in the body. Most affected structure among these tissues is the lung tissue (2). In patients with lung involvement; diffuse alveolar epithelial destruction, hyaline membrane, capillary damage, capillary bleeding, alveolar septal fibrous proliferation and/or pulmonary hypertension may occur (7). It may have an effect on acute respiratory distress syndrome (ARDS) and systemic organ failure and even mortality in the further stages of the disease (8). Another study reported that COVID 19 causes different levels of damage to the lungs depending on the severity of the disease (9). In presented study; the pulmonary involvement status of patients diagnosed with COVID 19 in the emergency department was examined and it was found that a large proportion of 17.8% had lung involvement, similar to the literature. Presence of lung involvement and degree of disease guide the planning of treatment modalities. Treatment modalities also differ from patient to patient. While some cases are treated as an outpatient, some are treated in the hospital COVID 19 service and some are treated in intensive care units (2). The presence of lung tomography involvement is among the important determinants of treatment modalities (10). In a similar

study, it was stated that lung imaging plays an important role in detecting the lung involvement of COVID 19, determining the severity of the disease and even planning the treatment of the patient (11). In another study, it was reported that the co-rads classification is useful in detecting the degree of lung involvement of the COVID 19 disease and in making decisions in the treatment of the disease (12). In the presented study; The relationship between pulmonary tomography involvement and hospitalization was examined. It was found that patients with lung involvement were more likely to receive inpatient treatment (p<0.001).The treatment of patients in the Covid service or intensive care unit while receiving inpatient treatment was examined and a significant correlation was found with lung

involvement (p<0.001). This can be explained by the high rate of treatment in patients with lung involvement in the covid service and intensive care units.

Many systems in the body are affected due to COVID 19 infection. Among these systems, iron homeostasis and ferritin levels were also found to be related (13). It has been reported that serum ferritin levels increase and serum ferritin levels can be used to predict mortality, especially in the case of worsening of the disease due to cytokine storm (14). Ferritin is an iron-storing protein. In clinical practice, it is often used for the diagnosis of iron deficiency anemia as it is associated with serum iron levels (15). Ferritin consists of two different subunits; H and L. In particular, it is known that H-ferritin has both proinflammatory and immunosuppressive functions and even the level of ferritin increases in viral infections as a marker of viral replication (16). Colafrancesco et al. reported that there is a correlation between high ferritin level and disease severity in COVID 19 patients (17). Taneri et al. reported that as the severity of the disease in COVID 19 patients increased the ferritin level also increased (18). Similarly, in the presented study; serum ferritin levels of patients with lung tomography involvement were found to be statistically significantly higher than those of patients without lung involvement (p<0.001). In addition, the patients receiving outpatient treatment and inpatient treatment in the service are compared; it was determined that the serum ferritin level of the group receiving inpatient treatment in the service was significantly higher than the other group (p<0.001). The serum ferritin levels of the patients receiving treatment in the intensive care unit were also found to be significantly higher than the serum ferritin levels of the inpatient group (p<0.001). This situation can be explained as the increase in cytokine storm in patients worsens the clinical condition and causes an increase in ferritin level.

CONCLUSION

In COVID 19 patients, the presence of lung involvement adversely affects the clinical course of the disease.

It has been determined that serum Feritin levels increase in diseases such as COVID 19 in which cytokine storms occur. In addition, it can be said that in cases with lung involvement of COVID 19 serum ferritin levels increase and the severity of the disease increases. It is thought that serum ferritin levels should be checked in the routine follow-ups of COVID 19 patients and the change of serum ferritin levels can give an idea about the course of the disease.

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MEDICAL RECORDS-International Medical Journal

Research Article

Knowledge and Awareness of Health Care Associated Infection Control Measures Among Intensive Care Unit Nurses in Hospitals, Turkey

Türkiye Hastanelerinde Yoğun Bakım Hemşireleri Arasında Sağlık Bakım ile İlgili Enfeksiyon Kontrol Önlemleri Hakkında Bilgi ve Farkındalık

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Abstract

Aim: In this study, we aimed to determine knowledge and awareness of health care associated infection control measures among intensive care unit (ICU) nurses in Turkish hospitals using case-vignettes.

Material and Methods: The questionnaire form used in this study was designed and prepared by the researchers by screening the relevant literature. Informative part of the form consisted of demographic data. The question part included 5 main sections with narrative questions of case vignettes and multiple-choice items related to the vignettes. A total of 285 nurses were accessed through e-mail addresses; the survey link was then sent to the ICU nurses who accepted participation in the questionnaire.

Results: A total of 149 out of 285 nurses completed the questionnaire and sent filled the form online. The number of the nurses who consider screening of patients admitted to the ICUs from another health care institutions in terms of MRSA, VRE and carbapenemase-producing Enterobacteriaceae was 111 (74.4%), 118 (79.1%) and 93 (62.4%), respectively. The number of the nurses who thought that the hands should be rubbed with alcohol-based hand sanitizer and for 20-30 seconds was 90 (60.4%) and 95 (63.8%), respectively. In case of patients with Clostridium difficile diarrhea, the number of nurses gave the answer as the hand hygiene must be provided by washing hands with antimicrobial soap and water was twenty-six (17.4%)

Conclusion: The result of this study indicated that knowledge and awareness of HCAIs among ICUs nurses were not at a desired level. Our results highlight the need for education and training especially on hand hygiene to raise awareness of control of HCAIs in ICUs.

Keywords: Intensive care unit, health care acquired infection, hand hygiene, isolation, nurse, questionnaire

Öz

Amaç: Bu çalışmada, Türkiye'deki hastanelerdeki yoğun bakım ünitesi (YBÜ) hemşirelerinin sağlık hizmetleri ile ilişkili enfeksiyon kontrol önlemleri konusundaki bilgi ve farkındalıklarını vaka vinyetleri kullanarak belirlemeyi amaçladık.

Materyal ve Metot: Bu çalışmada kullanılan anket formu araştırmacılar tarafından ilgili literatür taranarak tasarlanmış ve hazırlanmıştır. Formun bilgilendirici kısmı demografik verilerden oluşmuştur. Soru kısmı ise olgu vinyetlerinin anlatımsal sorularını ve çoktan seçmeli maddeleri içeren beş ana bölümden oluşmuştur. Toplam 285 hemşireye e-posta adresleri üzerinden ulaşılmış ve ankete katılmayı kabul eden ICU hemşilerine anket bağlantısı gönderilmiştir.

Bulgular: Toplam 285 hemşireden 149'u anketi tamamlayarak formu çevrimiçi olarak göndermiştir. ICU'lara başka başka bir sağlık kuruluşundan gönderilen hastaların MRSA, VNE ve karbapenemaz üreten enterobakteriler açısından taranması gerektiğini düşünen hemşirelerin sayısı sırasıyla 111 (%74.4), 118 (%79.1) ve 93 (%62.4)'tür. Ellerin alkol bazlı el dezenfektanı ile ve 20-30 saniye boyunca ovulması gerektiğini düşünen hemşirelerin sayısı sırasıyla 90 (%60.4) ve 95'tir (%63.8). Clostridium difficile diarrhea bulunan hasta olması durumunda ellerin antimikrobiyel sabun ve su ile yıkanmasıyla el hijyeni sağlanması gerektiği şeklinde cevap veren hemşirelerin sayısı 26'dır (%17.4).

Sonuç: Bu çalışmanın sonuçları ICU hemşireleri arasında HCAI bilgi ve farkındalığının istenen düzeyde olmadığını göstermiştir. Bulgularımız ICU'larda HCAI kontrolünün farkındalığını artırmak amacıyla özellikle el hijyeni konusundaki eğitim ihtiyacını vurgulamaktadır.

Anahtar Kelimeler: Yoğun bakım ünitesi, sağlık bakım edinilmiş enfeksiyon, el hijyeni, izolasyon, hemşire, anket

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INTRODUCTION

Health care associated infections (HCAIs) are those infections that patients acquired while receiving health care (1). HCAIs include infections developed in various settings of where patients received care such as family medicine clinics, home care, ambulatory care and long-term care. Studies have reported that the most common adverse events affecting hospitalized patients include HCAIs, adverse drug events and surgical complications (2, 3). HCAIs increase morbidity, mortality and duration of hospitalization, and therefore more research and changes in daily practice are needed to ensure hospital safety and prevent HCAIs (4,5).

The impacts of HCAIs involve prolonged hospital stays, long-term disability, increased resistance of microorganisms to antimicrobials, additional financial burden, high costs for patients and their families and excess deaths (6). Patients at Intensive Care Units (ICUs) are more prone to HCAIs. HCAIs not only negatively affect patients at ICU, but also impose socioeconomical burden by increasing health care costs especially in developing countries (7). According to the 2017 Surveillance of HCAIs and preventions indicators in European ICUs report by the European Union, patients admitted to ICUs are at 5 to 10 fold higher risk of acquiring HCAIs due to both intrinsic (e.g. immune-depression) and extrinsic (e.g. mechanical ventilation) risk factors, because ICUs are often the epicenter of an emerging HCAIs problems and antimicrobial resistance in the hospital (8). This makes knowledge, attitudes and responsibilities of health care workers at ICUs more critical. According to the report of the European Surveillance System (TESSy) in 2014 patients staying in an ICUs longer than two days, 6,995 (8%) presented with at least one HCAIs (9). The utilization of invasive devices and invasive monitoring is an important risk factor for developing HCAIs in ICUs, resulting in a significant increase in morbidity, mortality and health care costs (10).

Nursing workload has been shown to have a significant impact on HCAIs (11). A nurse to patient ratio <1 has been associated with an increased risk of developing HCAIs, prolonged length of stay and costs (12). In the ongoing COVID-19 pandemic, shortage of nurses in ICUs has caused considerable problems in the management of hospitals and coping with HCAIs in addition to the novel coronavirus itself. The COVID-19 outbreak has shown the importance of infection control especially in ICUs and the knowledge and attitudes of nurses towards hygiene. Adherence to infection control guidelines, sound knowledge of the health care workers, including nurses, and simple practices such as hand hygiene have shown dramatic effects on reduction of HCAIs. The objective of this study was to investigate knowledge and awareness of health care associated infection control measures among intensive care unit nurses in Turkish hospitals.

MATERIAL AND METHOD

This study was performed as case-vignettes questionnaire between June 2019 and September 2019. This study was performed as case-vignettes questionnaire between June 2019 and September 2019. Before the beginning, approval was obtained from the Yeditepe University Clinical Research Ethics Committee for the implementation of the study (Decision no:KAEK:991). The study was conducted in accordance with the relevant ethical principles of 1964 Declaration of Helsinki and its later amendments. The study was conducted via e-mail communication with nurses, members of Turkish Society of Intensive Care Nurses (TSICN), and working in ICUs in Istanbul province and other provinces.

Questionnaire Form

The questionnaire form used in this study was designed and prepared by the researchers by screening the relevant literature (Appendix). Informative part of the form consisted of demographic data including gender, city of institution, hospital type, ICU type and duration of working in ICU. The question part included 5 main sections with narrative questions of case vignettes and multiple-choice items related to the vignettes. Q1 consisted of YES/NO options, Q2 multiple-choice answers, Q3 two sub-items, Q4 and Q5 TRUE/FALSE options. The answers given by the participants were compared with an answer key and evaluated. In order to facilitate the analysis and prevent bias, no open ended questions were used. The questionnaire form was entered to the popular questionnaire website SurveyMonkey (www.surveymonkey.com)

The Survey

First, e-mail information of ICU nurses from Istanbul and other provinces was obtained from the TSICN. A total of 285 nurses, members of TSICN were accessed through e-mail addresses and social media platforms. The nurses were trained about infection in detail. The survey link was then sent to the ICU nurses who accepted participation in the questionnaire. A deadline for the completion was sent to the participants. Incomplete forms were excluded from the study. 149/285 nurses completed the survey. The question part included 5 main sections with narrative questions of case vignettes and multiple-choice items related to the vignettes. We selected common clinical cases in terms of health care associated infection control measures.

Statistical Analysis

The answer forms were transferred to the Microsoft Excel software. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequency (n) and percentage (%). As of the nature of the study, we did not perform hypothesis tests and were content with evaluating the questionnaire objectively.

RESULTS

A total of 149 out of 285 nurses completed the questionnaire

and sent filled the form online. At the deadline, all 285 nurses were informed about the completion of the questionnaire. The answers were entered to a computer and sorted. The mean age of the nurses was 29.0±6.1 years. Of all participants, 121 (81.2%) were female and 28 (18.8%) were male. Duration of working in an ICU was longer than 5 years in 99 (66.4%) nurses. The city of institutions was Istanbul in 77 (51.7%) and non-Istanbul in 72 (48.3%) nurses. Distribution of hospital types is shown in Figure 1 and that of ICU types in Figure 2.

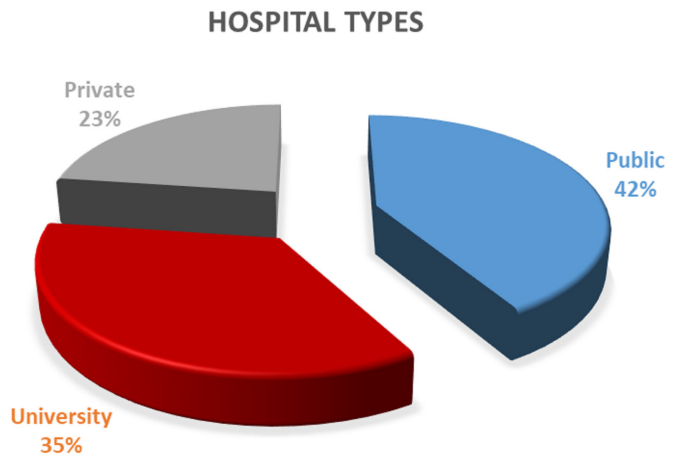

Figure 1. Distribution of the nurses according to hospital types

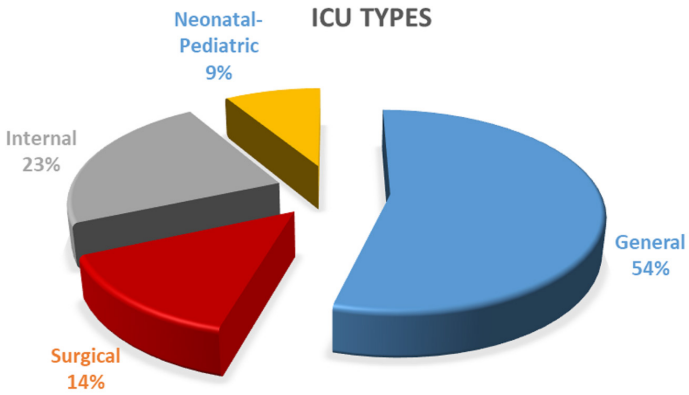

Figure 2. Distribution of the nurses according to ICU types

Evaluation of the Questionnaire

Q1

The number of the nurses who consider screening of patients admitted to the ICUs from another health care institutions in terms of MRSA, VRE and carbapenemase-producing Enterobacteriaceae was 111 (74.4%), 118 (79.1%) and 93 (62.4%), respectively. Seventy (50%) of the nurses gave the correct answer to all three conditions. Distribution of the nurses who gave the correct answer to this question is shown in Figure 3.

Q2

The number of the nurses who gave the correct answer to the Q2 was 119 (79.9%). Distribution of the nurses who gave the correct answer to this question is shown in Figure 4.

Q3

The number of the nurses who thought that the hands should be rubbed with alcohol-based hand sanitizer and for 20-30 seconds was 90 (60.4%) and 95 (63.8%), respectively. Of all nurses, 65 (43.6%) knew both the correct method and the correct duration. Distribution of the nurses who gave the correct answer to the Q3 is shown in Figure 5.

Q4

Only one nurse stated the correct answer during the aspiration of respiratory secretions of patient in intensive care unit regarding the use of personnel protective equipment and hand hygiene.

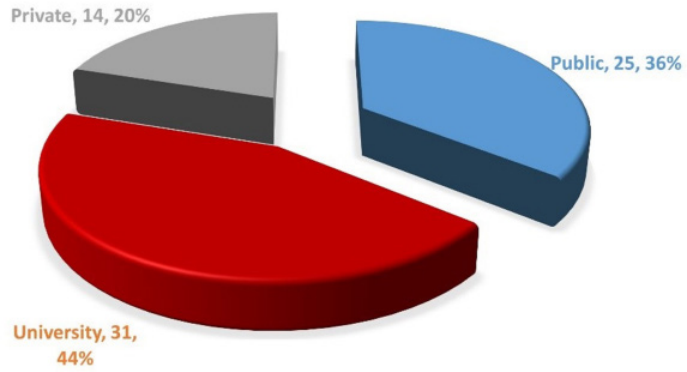

Figure 3. Numbers and percentages of the correct answers to Q1 by hospital type

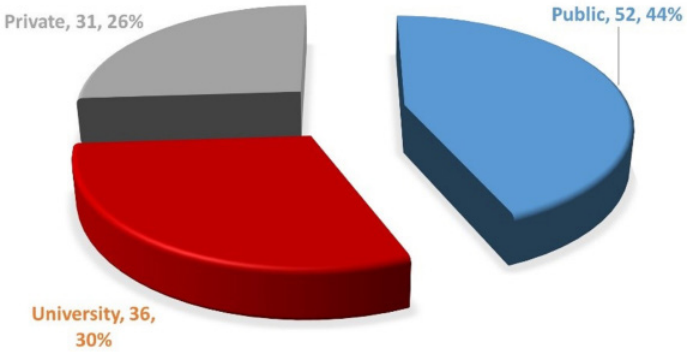

Figure 4. Numbers and percentages of the correct answers to Q2 by hospital type

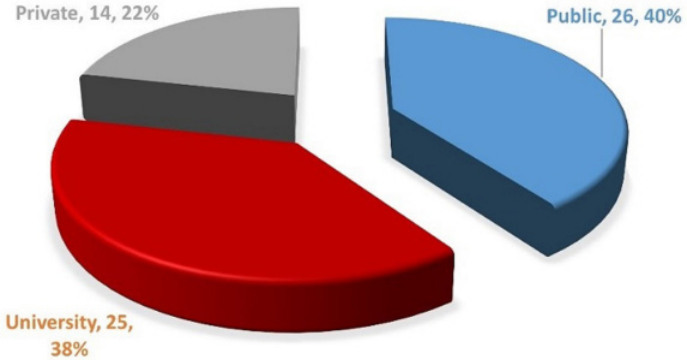

Figure 5. Numbers and percentages of the correct answers to Q3 by hospital type

Q5

In case of patients with Clostridium difficile diarrhea, the number of nurses gave the answer as the hand hygiene must be provided by washing hands with antimicrobial soap and water was twenty-six (17.4%). Distribution of the nurses who gave the correct answer to this question is shown in Figure 6.

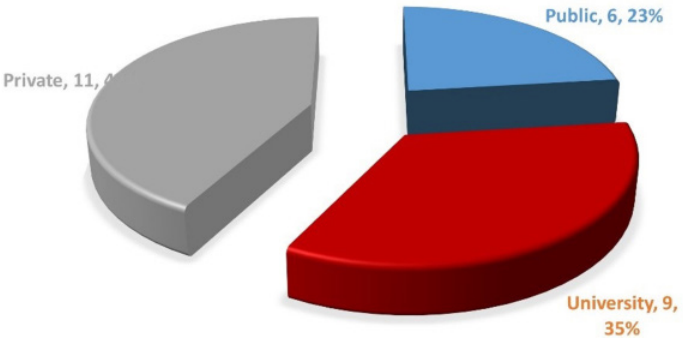

Figure 6. Numbers and percentages of the correct answers to Q5 by hospital type

DISCUSSION

The present study was performed in order to investigate knowledge and awareness of control of HCAIs among Turkish ICU nurses. In the present study, it is seen that results of the case-vignettes are not very satisfactory and there are a lot of things that can be done to close the gaps in the knowledge and awareness of HCAIs among ICUs nurses. As ICUs have a critical place in the control of HCAIs, particularly amidst the -unfortunately- ongoing COVID-19 pandemic, both basic and advanced knowledge of HCAIs is a very current issue from nurses' perspective. Because nurses are in the front line at the fight with the virus at one hand, while they are responsible to deliver optimal-quality of care to protect patients' against HCAIs.

Looking at the other side of the medallion, 38 (25.5%), 31 (20.8%) and 56 (37.6%) nurses stated that they do not consider screening of patients admitted to the ICUs from another health care institutions for MRSA, VRE and carbapenemase-producing Enterobacteriaceae. These facts are very high for such a critical profession working in ICUs where the rate of HCAIs is reported as high as 8% (9). Even higher rates have been reported in the literature. In a study from Greece, the rate of HCAIs was reported as 9.1% with the most common types of HCAIs being lower respiratory infections, bloodstream infections and systemic infections (13). In another study, the rate of HCAIs was reported as 9.4% with the most common types being bloodstream infections, UTIs and pneumonia (14). These rates highlight the importance of knowledge and awareness of HCAIs among healthcare staff, especially those working in ICUs.

In a study from Hungary aiming at measuring nurses' awareness of infection control measures, low HCAI and hand hygiene (HH) scores obtained from the questionnaire were reported to underline the need to enhance infection control training in Hungarian hospitals and to improve nurses' knowledge on infection control (15). In the present study, 30 (20.1%) ICU nurses did not answer the hygiene related question correctly. Furthermore, 59 (39.6%) nurses did not prefer the most effective hand hygiene method as rubbing the hands by alcohol-based hand sanitizer in case of there is no visible dirt, no body fluid belonging to the patient on the hands of nurses. and 54 (36.2%) nurses chose the hand hygiene duration as 40-60 seconds for this situation. Of course these rates are disappointing. The importance of hand hygiene was closely observed once again during the COVID-19 pandemic. Whereas, health care staff and especially nurses have responsibility for being role models for patients in particular and the general population in a wide sense. The situation is not much different in other regions of the world. According to the recommendation from the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC), hand hygiene is the most important and easy way to control HCAIs (16,17). According to the vital role of nurses in preventing HCAIs, they are key members of infection control teams in hospitals. For this reason, one should have sufficient knowledge and skills in the field of infection control.

Unfortunately studies investigating nurses' knowledge about hand hygiene have not reached the same conclusion. In a study about hand hygiene among health care staff, Malekmakan et al. noted that nurses' knowledge about standard precautions is not enough and many nurses believe that there is no need for hand hygiene by wearing gloves (18). In another study by Bulut et al., hand washing of health care staff working in intensive care units of a state hospital were found not to be at a desirable level and also the physical conditions were not sufficient for providing hand hygiene (19). Fox et al. reported that a hand hygiene protocol for patients in the ICU was associated with reductions in HCAIs and improvements in nurses' hand-washing compliance (20).

In our study, the Q4 included one question of three options about isolation of the patients and nine further questions regarding donning PPEs appropriately. Unfortunately, among 149 participants, only one (0.67%) nurse knew all 10 questions correctly, indicating the urgent need for education and training programs especially for nurses working in ICUs. On the contrary, Arli et al. reported that the nurses included in the study have generally good compliance with isolation precautions and scores of the nurses working in an ICU were higher than those of the nurses working in clinics (21).

In this study twenty-six (17.4%) nurses informed hand hygiene by washing hands with antimicrobial soap and water in case of C. difficile diarrhea although alcohol based hand sanitizers are not effective against spores of Clostridium difficile, therefore hand hygiene with antimicrobial soap and water is preffered method for this reason.

Oughton MT et all (22). have shown that handwashing with

antimicrobial soap and water reduced the colony count on the hands by 2.14 log (10) CFU/mL whereas alcohol based handrub had no effect (0.06 log(10) CFU/mL) removing C. difficile from the hands.

Today, there are numerous opportunities to overcome these shortcomings. These facilities include on-line training, periodic educations, congresses, symposiums as well as digital platforms such as YouTube. For example, professional YouTube contents can be uploaded to directly focus on nurses. However, there is not much time to accomplish these improvements because of the disaster named COVID-19 and what will be done without wasting time.

Study Limitations

First, the number of participants is small for such a significant questionnaire. Second, although there are numerous questionnaire studies on HCAIs in the literature, each study applied its own survey form, making a healthy comparison difficult. Third, our study included three major domains as hand hygiene, patient isolation and PPEs. Perhaps including more domains of HCAs nursing management could give more detailed insight. Finally, hand-washing, PPE donning and isolation practices differ among the countries based on sociocultural and developmental factors. Nevertheless, we believe that our results will shed light on the issue and provide guidance for future large-scale studies.

CONCLUSION

The result of this study indicated that knowledge and awareness of HCAIs among ICU nurses were not at a desired level. However, this is also true for many previous studies. Even in the same studies there are significant differences between health centers. Our results highlight the need for training especially on hand hygiene and donning PPEs. In order to achieve training targets, technological tools including social media and video platforms such as YouTube could be effectively used to facilitate these education programs and their effectiveness. Every possible material from ICU protocols to posters could be benefited from to raise awareness of HCAIs in health care staff working in ICUs.

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Conflict of interest: *The authors declare that they have no competing interest.*

Ethical approval: *Before the beginning, approval was obtained from the Yedi Tepe University Clinical Research Ethics Committee for the implementation of the study (Decision no:KAEK:991).*

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MEDICAL RECORDS-International Medical Journal

Research Article

Evaluation of Hepatitis A Seroprevalence in Kastamonu Province, Turkey

Kastamonu İlinde Hepatit A Seroprevalansının Değerlendirilmesi

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Abstract

Aim: Hepatitis A disease is a contagious liver infection caused by the hepatitis A virus (HAV). This study aimed to decide the hepatitis A seroprevalence in all age groups in Kastamonu province, Turkey.

Material and Method: The current study analyzed the anti-HAV antibodies test results of the patients who applied to Kastamonu Training and Research Hospital for various reasons between 2018-2022. The most up-to-date test results of patients sent more than one serum sample were evaluated. The patients were separated into eight age groups: 0-10,11-20, 21-30, 31-40, 41-50, 51-60, 61-70, and ≥71. The anti-HAV IgM and anti-HAV IgG values were determined using the chemiluminescence microparticle immunoassay method in the Abbott Architect i2000SR. The results were evaluated based on the manufacturer's instructions.

Results: There was positivity in 27 (1.3%) of 2083 patients in whom anti-HAV IgM was studied and in 837 (58.2%) of 1439 patients in whom anti-HAV IgG was studied. The anti-HAV IgG positivity in females and males was 55.9% and 61.0%, respectively; anti-HAV IgM positivity was 1.7% and 0.8%. The anti-HAV IgG positivity rate increased with increasing age ($p<0.001$). The age group with the highest rate of anti-HAV IgG positivity (100%) was ≥61, and the age groups with the lowest rate of anti-HAV IgG positivity (26.0% and 33.7%) were determined as 11-20 and 21-30. Also, the anti-HAV IgG positivity in the 0-10 age group was 70.1%.

Conclusion: These data showed that hepatitis A seronegativity was high in the 11-20 and 21-30 age groups in Kastamonu province. Since the prognosis of hepatitis A disease may worsen with increasing age, the HAV vaccine is suggested for the seronegative young population.

Keywords: Age groups, anti-HAV, Hepatitis A, IgG, IgM

Öz

Amaç: Hepatit A hastalığı, hepatit A virüsünün (HAV) neden olduğu bulaşıcı bir karaciğer enfeksiyonudur. Bu çalışmada Kastamonu ilindeki tüm yaş gruplarında Hepatit A seroprevalansının belirlenmesi amaçlanmıştır.

Materyal ve Metot: Çalışmada 2018-2022 yılları arasında Kastamonu Eğitim ve Araştırma Hastanesi'ne çeşitli nedenlerle başvuran hastaların anti-HAV antikor test sonuçları retrospektif olarak değerlendirilmiştir. Birden fazla serum örneği gönderilen hastaların en güncel test sonuçları değerlendirmeye alınmıştır. Hastalar 0-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70 ve ≥71 olmak üzere sekiz yaş grubuna ayrılmıştır. Anti-HAV IgG ve anti-HAV IgM değerleri Abbott Architect i2000SR cihazında kemiluminesans mikropartikül immün assay yöntemi ile çalışılmış ve sonuçlar üretici firmanın önerileri doğrultusunda değerlendirilmiştir.

Bulgular: Anti-HAV IgM çalışılan 2083 hastanın 27 (%1,3)'sinde, anti-HAV IgG çalışılan 1439 hastanın 837 (%58,2)'sinde pozitiflik belirlenmiştir. Kadınlar ve erkeklerdeki anti-HAV IgG pozitifliği sırasıyla %55,9 ve %61,0; anti-HAV IgM pozitifliği ise %1,7 ve %0,8 olarak bulunmuştur. Artan yaş ile birlikte anti-HAV IgG pozitiflik oranının yükseldiği tespit edilmiştir ($p<0,001$). Anti-HAV IgG pozitiflik oranının en yüksek (%100) olduğu yaş grubu ≥61 yaş, en düşük (%26,0 ve %33,7) olduğu yaş grupları 11-20 ve 21-30 olarak saptanmıştır. İlave olarak 0-10 yaş grubunda Anti-HAV IgG pozitiflik oranı %70,1 olarak tespit edilmiştir.

Sonuç: Sonuç olarak 11-20 ve 21-30 yaş gruplarında hepatit A seronegatifliği yüksek oranlarda bulunmuştur. Sonuçlar, hepatit A hastalığının prognozunun artan yaş ile birlikte olumsuz seyretme riskinin yüksek olmasından dolayı, HAV aşısının genç erişkin bireylere de uygulanması gerektiğini göstermektedir.

Anahtar Kelimeler: Anti-HAV, Hepatit A, IgG, IgM, yaş grupları

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INTRODUCTION

Hepatitis A disease is a contagious liver infection caused by the hepatitis A virus (HAV). The infection is present worldwide. However, the virus has the potential to cause epidemics in areas with poor sanitation and unvaccinated populations (1). HAV is usually transmitted from person to person through the consumption of contaminated food and drink. Also, it can be transmitted through a blood transfusion during viremia (2).

Although the hepatitis A infection does not show a chronic course, its symptoms can range from mild to severe. However, it is known that individuals who are unvaccinated and encounter the virus for the first time in adulthood are at risk (3). Moreover, age is considered to be the most significant factor determining prognosis, as the disease advances more severely and the mortality rate is high in advanced age groups (4).

HAV-specific immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies are examined in the patient's serum sample in the hepatitis A diagnosis. The serological profile is interpreted as i) only anti-HAV IgM positivity indicates the early stage of acquired infection, ii) both anti-HAV IgG and anti-HAV IgM positivities indicate late stages of infection, and iii) only anti-HAV IgG positivity indicates acquired immunity (5). Since there is only one serotype of HAV, anti-HAV IgG formed in individuals is permanent for life and is widely used in hepatitis A seroprevalence studies (6).

Knowing the hepatitis A seroprevalence of a population in a region or province can be a guide for taking appropriate preventive measures and establishing vaccination programs against the infection (7,8). It is stated that Turkey has a moderate endemicity level of hepatitis A when compared to the rest of the world (9,10). In addition, hepatitis A seroprevalence in Turkey may vary based on geographical regions and provinces. In the literature, there is no data on hepatitis A seroprevalence in Kastamonu province in the north of Turkey. Therefore, this study aimed to determine the hepatitis A seroprevalence in all age groups in Kastamonu province. The second aim of the study is to compare the data obtained from this study with the results in different regions of Turkey.

MATERIAL AND METHOD

Ethical approval for this study was obtained from the Kastamonu University, Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (Date: 11.05.2022, Decision no: 2022-KAEK-45).

Anti-HAV antibodies test results of the patients who applied to Kastamonu Training and Research Hospital (TRH) for various reasons between January 2018 and January 2022 were analyzed retrospectively using the laboratory database in the current study. The most up-to-date test results of patients sent more than one serum sample were evaluated. The patients were separated into eight age groups: 0-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70, and ≥71. The anti-HAV IgM and anti-HAV IgG values were determined using the chemiluminescence microparticle immunoassay (CMIA) method in the Abbott Architect i2000SR (Abbott Laboratories, Chicago, IL, USA). The results were evaluated based on the manufacturer's instructions, and <1 S/CO and ≥1 S/CO were considered to be negative and positive values, respectively.

Statistical Analysis

The statistical analyses were done using the Pearson chi-square test in SPSS 23.0 for Windows (IBM Inc., Armonk, NY, USA). The statistical significance was accepted as $p<0.05$.

RESULTS

The anti-HAV IgM and anti-HAV IgG tests were studied in 2083 and 1439 patients, respectively, in this study. The anti-HAV IgM and anti-HAV IgG positivity were detected to be 1.3% and 58.2%, respectively (Table 1). The anti-HAV IgG positivity in females and males was 55.9% and 61.0%, respectively; anti-HAV IgM positivity was 1.7% and 0.8%. No statistically significant difference ($p>0.05$) was found for hepatitis A seroprevalence between the genders (Table 2).

Table 1. Seroprevalence of anti-HAV IgG and anti-HAV IgM in the study groups

	Positive [n (%)]	Negative [n (%)]	Total
Anti-HAV IgM	27 (1.3%)	2056 (98.7%)	2083
Anti-HAV IgG	837 (58.2%)	602 (41.8%)	1439

HAV: Hepatitis A virus, IgG: Immunoglobulin G, IgM: Immunoglobulin M, n: Number

Table 2. Comparison of anti-HAV IgG and anti-HAV IgM seropositivity based on gender

		Female [n (%)]	Male [n (%)]	p value
Anti-HAV IgM	Positive	19 (1.7%)	8 (0.8%)	0.067
	Negative	1082 (98.3%)	974 (99.2%)	
	Total	1101	982	
Anti-HAV IgG	Positive	449 (55.9%)	388 (61.0%)	0.052
	Negative	354 (44.1%)	248 (39.0%)	
	Total	803	636	

HAV: Hepatitis A virus, IgG: Immunoglobulin G, IgM: Immunoglobulin M, n: Number

While the mean age of the patients in the anti-HAV IgM study group was 33.0±19.5, the mean age of the patients in the anti-HAV IgG study group was 32.5±19.2. The anti-HAV IgG positivity increased with the age group ($p<0.001$). The age groups with the lowest anti-HAV IgG positivity were 11-20 (26.0%) and 21-30 (33.7%). The anti-HAV IgG positivity rates were over %92 over 41 years of age. The anti-HAV IgG positivity rate was 70.1% in the 0-10 age group. The highest anti-HAV IgM positivity rate was in the 61-70 age group at 2.5% and the lowest in the 0-10, 11-20, and 21-30 age groups at 0.7%. There was no significant difference ($p=0.24$) between the age groups and the anti-HAV IgM positivity rate (Table 3).

Table 3. The distribution of anti-HAV IgG and anti-HAV IgM positivity based on age groups

	Anti-HAV IgM*		Anti-HAV IgG**	
Age Group	Positive [n (%)]	Total (n)	Positive [n (%)]	Total (n)
0-10 years	1 (0.7%)	148	78 (70.1%)	110
11-20 years	3 (0.7%)	413	95 (26.0%)	365
21-30 years	4 (0.7%)	603	119 (33.7%)	353
31-40 years	7 (2.3%)	304	130 (71.0%)	183
41-50 years	4 (2.1%)	190	132 (92.3%)	143
51-60 years	3 (1.9%)	159	122 (98.4%)	124
61-70 years	4 (2.5%)	158	96 (100%)	96
≥71 years	1 (0.9%)	108	65 (100%)	65
Total	27 (1.3%)	2083	837 (58.2%)	1439

HAV: Hepatitis A virus, IgG: Immunoglobulin G, IgM: Immunoglobulin M, n: Number *p=0.24, **p<0.001

Table 4. Hepatitis A seroprevalence in various provinces/cities of Turkey in the last decade (2012-2022).

Study	Period	Province/City	Age	Anti-HAV IgM positivity (%)	Anti-HAV IgG positivity (%)
Çitil et al. (13)	2012-2013	Adıyaman	0-≥81	NA	77.5
Ertürk et al. (14)	2012-2013	Rize	17-70	1.2	75.0
Aşçı et al. (15)	2013-2014	Afyon	0-≥40	NA	69.7
Köroğlu et al. (16)	2012-2014	Sakarya	0-92	4.4	74.7
Bölükbaş et al. (17)	2013	Bolu	0-≥70	NA	76.2
Çalık et al. (18)	2015-2016	İzmir	0-≥55	NA	74.0
Yilmaz (19)	2015-2018	Erzurum	0-93	0.2	87.3
Tuna et al. (9)	2016-2018	Van	0-≥50	NA	48.7
İnci et al. (20)	2016-2019	Karabük	0-≥60	0.1	57.0
Çavuş et al. (21)	2017	Bingöl	16-≥70	NA	97.4
Kader et al. (22)	2017	Yozgat	6->60	NA	79.1
Alkan Çeviker et al. (23)	2017-2018	Samsun	0-≥81	NA	58.9
Kula Atik et al. (24)	2017-2019	Balıkesir	0-≥51	2.6	68.6
Düzenli et al. (10)	2017-2020	Çorum	0->80	0.7	84.4
This study	2018-2022	Kastamonu	0-≥71	1.3	58.2

HAV: Hepatitis A virus, IgG: Immunoglobulin G, IgM: Immunoglobulin M, NA: Not available

DISCUSSION

The World Health Organization estimates that nearly 1.5 million cases of hepatitis A infection occur worldwide every year (11). Although hepatitis A is a vaccine-preventable disease, it remains significant in developing countries. Based on hepatitis A incidence in the world, three different endemicity patterns have been identified high, moderate, and low endemicity (12). Turkey is at a moderate endemicity level of hepatitis A seroprevalence compared to the world, but the rates may differ between geographical regions and provinces.

The existence of anti-HAV IgG in the patient serum is an indicator of acquired immunity. Moreover, since HAV has the only serotype, the immunity is permanent for many years (5,6). Hepatitis A seroprevalence studies conducted in Turkey in the last decade are summarized in Table 4. Briefly, anti-HAV IgG positivity was reported in 48.7-97.4% (9,10,13-24). The current study determined the anti-HAV IgG positivity to be 58.2%. The findings showed that the anti-HAV IgG positivity of Kastamonu province was within the range of the results of other studies conducted in Turkey. However, this rate in Kastamonu was generally low compared to many provinces (except Van and Karabük provinces). On the other hand, the anti-HAV IgG positivity was determined to increase with age groups in this study, which was consistent with the literature. This may be because individuals have more contact with the external environment with increasing age and the possibility of consuming contaminated food and beverages increases. However, the anti-HAV IgG positivity was determined to be higher in the 0-10 age group (70.1%) than in the 11-20 (26.0%) and 21-30 (33.7%) age groups. The hepatitis A vaccine had on the national vaccination calendar in September 2012 in Turkey and started to be administered to children born after March 2011 in two doses at the

18th and 24th months (25). Therefore, the anti-HAV IgG positivity may have been higher in the 0-10 age group than in the 11-20 and 21-30 age groups in this study. The results showed that especially the 11-30 age group in Kastamonu has a high risk of acquiring hepatitis A.

The detection of only anti-HAV IgM in the serum sample indicates acute hepatitis A disease (5,6). The anti-HAV IgM positivity has been reported in the range of 0.1%-4.4% in studies conducted in Turkey in the last decade (10,14,16,19,20,24). The anti-HAV IgM positivity was detected at a rate of 1.3% in 2083 different patients who applied to Kastamonu TRH between 2018-2022 in the present study. The results showed that Kastamonu province is within Turkey's mean in terms of acute hepatitis A.

It was observed that different results were obtained in studies in which gender and anti-HAV IgG positivity were evaluated together in the literature. While no significant difference was found between hepatitis A seroprevalence and gender in many studies (10,13,21,22,24), the anti-HAV IgG positivity was determined to be significantly greater in females or males compared to the opposite gender in some studies. For instance, Yılmaz (19) reported that anti-HAV IgG positivity was statistically higher in males than in females and attributed this to males having more contact with the external environment. However, Tuna et al. and Alkan Çeviker et al. found that anti-HAV IgG positivity in females was significantly higher than in males (9,23). Anti-HAV IgG positivity was higher in males (61.0%) than in females (55.9%), and anti-HAV IgM positivity was higher in females (1.7%) than in males (0.8%) in the present study. However, these differences were not statistically significant (p>0.05).

CONCLUSION

Kastamonu TRH is the central hospital in the province. So, the results provide data about the hepatitis A seroprevalences of Kastamonu province. As a result, hepatitis A seronegativity was high in the 11-20 and 21-30 age groups. The results suggest that these age groups may be the risk group for hepatitis A in Kastamonu. Since the prognosis of hepatitis A disease may worsen with increasing age, the HAV vaccine is suggested for the seronegative young population.

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MEDICAL RECORDS-International Medical Journal

Research Article

Biochemical and Histopathological Investigation of the Protective Effect of Lutein in Rat Kidney Exposed to Cisplatin

Sisplatin'e Maruz Bırakılan Sıçan Böbreğinde Lutein'in Koruyucu Etkisinin Biyokimyasal ve Histopatolojik Olarak İncelenmesi

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Abstract

Aim: The aim of this study was to determine the protection of lutein (L) (100 mg/kg, orally) against kidney damage caused by cisplatin (Cis) (10mg/kg, intraperitoneal).

Materials and Methods: Twenty-eight rats aged 8 weeks were used and divided into four equal groups (n=7): Control, L, Cis, and Cis + L.

Results: As a result of biochemical findings, serum Cr and BUN levels of the Cis group were significantly increased compared to the control group ($p<0.05$). Serum Cr and BUN levels of the Cis + L group were found to be significantly reduced compared to the Cis group ($p<0.05$). In addition, a decrease in MDA level and an increase in GSH, SOD and CAT levels were detected in the Cis + L group compared to the Cis group ($p<0.05$). In the histopathological examinations, in the Cis group kidney tissues; pathological changes such as interstitial mononuclear leukocyte infiltration, tubular degeneration, and tubular necrosis were observed. When the Cis + L group is compared with the Cis group, it can be said that there is a decrease in oxidative stress, an increase in antioxidant activity and a decrease in histopathological changes with the effect of L.

Conclusion: These results show that L is effective in preventing Cis-induced kidney injury. It is also emerging that L is a pharmacological agent with the potential to be used in this damage.

Keywords: Antioxidant, kidney, lutein, cisplatin, rat

Öz

Amaç: Çalışmamızda, sisplatin (Cis) (10mg/kg, intraperitoneal) kaynaklı böbrek hasarına karşı lutein'in (L) (100mg/kg, oral) koruyucu etkisi incelendi.

Materyal ve Metot: Bu çalışma, 8 haftalık 28 adet sıçanla gerçekleştirildi. Oluşturulan 4 grubun her birinde 7 tane sıçan yer aldı: Kontrol, L, Cis ve Cis + L.

Bulgular: Biyokimyasal bulgulara göre, Cis grubunun kontrol grubu ile kıyaslanmasında serum Cr ve BUN seviyelerinin anlamlı düzeyde arttığı görüldü ($p<0.05$). Cis + L grubunda serum Cr ve BUN düzeylerinin Cis grubuna kıyasla anlamlı düzeyde azaldığı tespit edildi ($p<0.05$). Ayrıca Cis + L grubunun Cis grubu ile kıyaslanmasında MDA seviyesinde düşüş, GSH, SOD ve CAT seviyelerinde ise artış kaydedildi ($p<0.05$). Yapılan histopatolojik incelemelerde Cis grubu sıçanların böbrek dokularında interstisyel mononükleer lökosit infiltrasyonu, tubuler dejenerasyon ve tubuler nekroz gibi patolojik değişiklikler gözlendi. Cis + L grubu Cis grubu ile kıyaslandığında L'nin etkisi ile oksidatif streste bir azalma, antioksidan aktivitede bir artma ve histopatolojik değişikliklerde bir azalma olduğu söylenebilir.

Sonuç: Bu sonuçlar L'nin Cis kaynaklı böbrek hasarının önlenmesinde etkili olduğunu göstermektedir. Ayrıca L'nin bu hasarda kullanılma potansiyeli olan bir farmakolojik ajan olduğuda ortaya çıkmaktadır.

Anahtar Kelimeler: Antioksidan, böbrek, lutein, sisplatin, sıçan

INTRODUCTION

Chemotherapy is known as the most common and effective method for cancer treatment. Although chemotherapeutic drugs help to cure cancer, they have been dedected to cause side effects in healthy organs. Many chemotherapeutic drugs are widely used in the treatment of cancer patients (1). Cisplatin (Cis) is used against various tumor types and malignancies as an anti-

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neoplastic drug. Although Cis is widely used in clinical practice, it has many undesirable side effects such as neurotoxicity, ototoxicity and nephrotoxicity (2,3). It has been reported that the most important side effect limiting the use of this drug is nephrotoxicity (4). Nephrotoxic effects have been reported in 20-40% of patients during treatment with Cis (5). In the investigations, it has been reported that histopathological changes such as tubular degeneration, interstitial mononuclear leukocyte infiltration, congestion in inter-tubular blood vessels, and tubular necrosis are formed as a result of the use of Cis (6). At the same time, it has been determined that this drug causes changes in many parameters in different organs such as liver and kidney (7). In addition, it was determined that Cis negatively affects the antioxidant system and produces many harmful radicals that cause oxidative damage (8). Studies have reported that Cis increases free radicals, causes damage to many tissues, and reduces protective activity against the effects of oxidative damage. Therefore, it is hypothesized that Cis-induced nephrotoxicity may result from increased oxidative stress from the increase of free oxygen radicals (9).

As a result of various studies conducted in recent years, it has been shown that some side effects of Cis can be reduced without changing the effects of chemotherapy by applying antioxidants obtained by different methods (10,11). After the nephrotoxic effect of Cis was determined, many agents and compounds with known antioxidant effects were used experimentally for therapeutic purposes (12). In this context, lutein (L), which has antioxidant properties, has been used in many studies. L is a carotenoid synthesized by plants, bacteria, and algae and is not synthesized in the body. It is also known that L is a carotenoid that does not contain vitamin A. At the same time, L is a member of the xanthophyll group obtained by the consumption of various green leafy plants. It can react strongly with free oxygen radicals through its hydroxyl group in the L structure. In this way, it can show an effective free radical scavenging activity (13). In addition, it has been noted that L has an oxidative stress-reducing effect through its antioxidant properties (14). In addition, L has been found to have many different effects as an anti-inflammatory (15) and anti-cancer agent (16). It has also been proven that L protects against stomach lesions (17) and gastrointestinal ulcers (18). Overall, the low toxicity of L makes it advantageous among conventional therapeutic drugs. Therefore, L can be tested against kidney damage due to chemotherapeutic drugs.

Although many studies have been conducted on agents with antioxidant effects to prevent the nephrotoxic effects of Cis, the fact that the protectiveness of L has not been examined in this regard adds originality to our study. Therefore, it was aimed to reveal the protectiveness of L in order to eliminate the pathological changes caused by Cis in kidneys.

MATERIAL AND METHOD

Chemicals

In our study, all chemicals, including Cis, were obtained from Sigma Chemical Co. (St. Louis, MO). L was obtained from Solgar (USA).

Animals

The rats preferred in this study were 210-255 g in weight and 8 weeks old. At the same time, 28 Sprague-Dawley type male rats were determined as needed. These were purchased from Adıyaman University Experimental Animals Research Center. Our research was conducted in accordance with the rules determined by the Ethics Committee (Protocol 2022/036). The temperature of the experimental environment was kept at 22±2°C and the humidity rate was 55±5%. The animals were given free feed and water as much as they could consume (*ad libitum*).

Experiment Protocol

In the experiment, groups were randomly formed and designed to have seven rats (n=7) in each of the 4 groups.

1. Control group: Rats were given 1 ml of saline orally for 7 days.
2. L group: L (100mg/kg/day, gastric gavage) for seven days (19).
3. Cis group: A single dose of Cis (10mg/kg, i.p.) on the 4th day of the study (20).
4. Cis + L group: A single dose of Cis (10mg/kg, i.p.) on the 4th day of the study. L (100mg/kg/day, gastric gavage for seven days).

All experimental applications in our study were completed within 7 days. Then, the rats were anesthetized with xylazine and ketamine and decapitated under anesthesia. Blood and kidney tissues were taken to be used in biochemical and histopathological examinations. The obtained serum was placed at -85°C for use in biochemical analyzes. One of the taken kidneys was placed at -85°C for biochemical analysis, while the other was immersed in fixation solution for histopathological examinations.

Histopathological Analyses

Tissues were placed in 10% neutral buffered formaldehyde for one day and were paraffin embedded after routine histological procedures (21). Tissues cut from 5 µm thick paraffin blocks by microtome (Leica Biosystems RM 2245) were stained with hematoxylin-eosin method after being taken on the slide (22,23). All sections were evaluated using a light microscope (Nikon Eclipse Ni-U), followed by images with a camera (Nikon DS-Fi3).

Biochemical Analysis

Blood Sample Assessment

Creatinine (Cr) and blood urea nitrogen (BUN) (mg/dL) levels were obtained in serum by picric acid method (24). Measurements were performed using Abbott ARCHITECT

c16000 (Abbott Laboratories, Abbott Park, IL) and Roche Diagnostics kits (Mannheim, Germany). BUN and Cr parameters were determined as mg/dl serum.

Renal Oxidative Stress Biomarker Assessment

Our samples were homogenized in ice (IKA, Germany) at 12.000 rpm for 1-2 minutes. Targeted procedures were found to work best at 4°C. Homogenates to be used in biochemical analyzes were prepared as 0.5-1.0g. Kidney tissues were prepared for malondialdehyde (MDA), reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) analyzes and protein level. Results were obtained using the methods of Lowry et al. (1951) to determine protein concentrations (25).

The procedure for evaluating the MDA parameter was performed using the methods of Uchiyama and Mihara (1978). At this stage, thiobarbituric acid reaction was determined to take about 15 minutes at pH 3 and 95°C. Then, as a result of measurements performed at 532 nm and maximum absorption, the formation of pink pigment was achieved (26).

The procedure for the evaluation of the GSH parameter was performed using the Ellman (1959) method. First of all, chemicals were added to the sample and the reaction took place in the environment. After this procedure, a yellow-green color formation was achieved. The evaluation procedure of the GSH parameter was performed using a spectrophotometer at 410nm absorbance (27).

In our study, SOD activity was measured by inhibiting the autoxidation of pyrogallol. These procedures were carried out by applying the method of Marklund and Marklund (1974). Procedures for enzyme activity were performed at 440nm for 180 s(s). In this context, the results obtained are expressed as U/mg Hb (28).

Numerous procedures were used to analyze the CAT parameter. First, 0.9% NaCl was added to 10% tissue homogenates. A phosphate buffer was used to measure the CAT parameter. Analysis of hydrogen peroxide hydrolysis at pH 7.0 was then performed. We observed the maximum absorbance at 240nm. Our results are reported as nmol/mg protein (29).

Statistical Analysis

Statistical analyzes in our study were made with SPSS software (v.21). The data produced were evaluated as mean ± SEM. Normally distributed data were analyzed with the Shapiro-Wilk test. In the biochemical parametric evaluation, comparisons between groups and within groups were made with ANOVA and post-hoc LSD tests. In addition, Kruskal-Wallis test was used for histopathological results. The significance level was determined as 0.05.

RESULTS

Biochemical Serum Parameters

Biochemical analysis results obtained in serum are shown in Table 1. Cr and BUN levels were measured to evaluate kidney function. It was determined that these parameters increased significantly in the rats of the Cis group compared to the control and L groups ($p<0.05$). In the Cis + L group, a significant decrease was observed in Cr and BUN levels compared to the Cis group ($p<0.05$) (Table 1).

Biochemical parameters in tissue

The results of the biochemical parameters in the tissue are shown in Table 1. The kidney tissue MDA parameter results of the control and L groups were similar to each other. The MDA level of the Cis group was significantly increased compared to the control and L groups ($p<0.05$). There was a significant decrease in MDA level in the Cis + L group compared to the Cis group ($p<0.05$) (Table 1).

Similar results were obtained in SOD, CAT and GSH parameters of the control and L groups. On the other hand, when the Cis group was compared with the control and L groups, a significant decrease was found in these parameters ($p<0.05$). SOD, CAT and GSH levels in the kidney tissues of the Cis + L group were significantly increased compared to the Cis group ($p<0.05$) (Table 1).

Table 1. Serum biochemical and renal tissue oxidative stress biomarkers

	Control	L	Cis	Cis + L
Serum biochemical biomarkers				
BUN (mg/dl)	28.19±0.89^{c,d}	35.78±0.19^{c,d}	55.29±0.01^{a,b,d}	39.13±0.11^{a,b,c}
Cr (mg/dl)	0.39±0.12^{c,d}	0.43±0.14^{c,d}	0.55±0.21^{a,b,d}	0.45±0.23^{a,b,c}
Renal tissue oxidative stress biomarkers				
SOD (U/g)	4.42±0.14^{c,d}	4.65±0.14^{c,d}	3.27±0.32^{a,b,d}	4.58±0.24^{a,b,c}
CAT (K/g)	0.17±0.03^{c,d}	0.19±0.12^{c,d}	0.13±0.14^{a,b,d}	0.18±0.08^{a,b,c}
GSH (µmol/g)	0.30±0.1^{c,d}	0.33±0.14^{c,d}	0.23±0.05^{a,b,d}	0.31±0.15^{a,b,c}
MDA (nmol/g tissue)	0.19±0.09^{c,d}	0.21±0.05^{c,d}	0.26±0.03^{a,b,d}	0.22±0.04^{a,b,c}

Data are means ± SEM, n = 7. Cis, cisplatin; L, lutein; Cr, creatinine; BUN, blood urea nitrogen; MDA, malondialdehyde; GSH, glutathione; SOD, superoxide dismutase; CAT, catalase.. [a] Significant difference from control, [b] significant difference from L, [c] significant difference from Cis, [d] significant difference from Cis + L

Histopathological Results

The histological structure of renal corpuscle, other parenchymal structures, and stroma were normal in the kidneys of control and L group rats. Histopathological changes such as interstitial inflammatory cell infiltration, tubular degeneration, epithelial desquamation, tubular dilatation, hyaline casts in the tubules, tubular necrosis, and segmental glomerular necrosis were observed in the kidneys of Cis group rats. No histopathological changes were observed in the kidney tissues of Cis + L group rats other than a slight focal tubular dilatation and degeneration. The histological structure of rat kidneys in this group was almost the same as in the control group (Figure1).

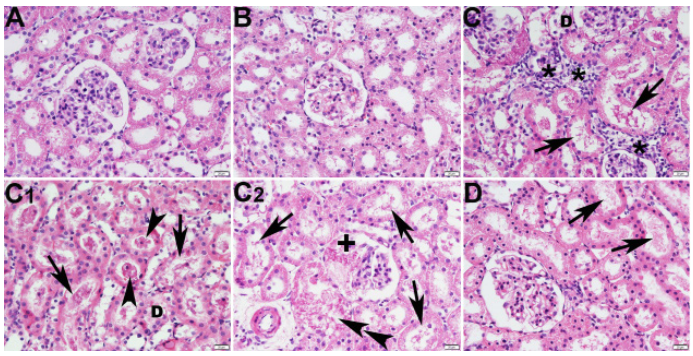

Figure 1. Light microscopic image of kidney sections of control (A), L (B), Cis (C, C1, C2), Cis + L (D) groups. D, tubular degeneration and epithelial desquamation; *, interstitial inflammatory cell infiltration; arrow, tubular dilatation; arrowhead, hyaline casts in the tubules; double arrowhead, tubular necrosis; +, segmental glomerular necrosis. (x 400; H&E)

DISCUSSION

It has been proven that Cis causes nephrotoxicity in patients and various animal species. It is known that Cis-induced nephrotoxicity is a dose-limiting side effect. At the same time, this leads to certain losses in kidney functions (30). The rat model of Cis-induced nephrotoxicity is considered a sensitive and reproducible system. In previous studies, there is evidence that Cis exerts its nephrotoxic effects through the formation of free radicals (31). In addition, it has been reported that harmful oxygen radicals are responsible for the pathogenesis of Cis-induced kidney damage (32). It has also been reported that Cis binds to the sulfhydryl groups of reduced glutathione, thereby reducing the scavenging of free oxygen radicals. Another factor is that the cisplatin-sulfhydryl complex can cause lipid peroxidation and mitochondrial damage by damaging cell membrane and enzyme functions (33). It is speculated that Cis-inducing kidney damage is due to selective uptake from proximal tubule cells. It is known that Cis accumulate at certain rates in other parts of the kidney. It was determined that the Cis concentration was 5 times higher than the extracellular concentration in proximal tubule epithelial cells (34).

In addition, it has been proven in many studies that antioxidant compounds prevent oxidative stress and inflammation in Cis-induced kidney damage (35-38). In this study, increased serum BUN and Cr concentrations, increased MDA levels, decreased antioxidant enzyme activities and GSH levels show that kidney damage occurs as a result of Cis administration. In this model, the application of L as a protective antioxidant was preferred. In our study, Cis-induced lipid peroxide accumulation, as well as depletion of GSH and related antioxidant enzymes, indicate the critical role of oxidative stress in Cis nephrotoxicity. In this study, it was also determined that kidney damage, characterized by increased BUN and Cr, occurred as a result of Cis application to animals. It is estimated that Cis causes nephrotoxicity by decreasing the glomerular filtration rate. In the Cis + L group, kidney damage markers such as BUN and Cr were found to be significantly attenuated. In addition, the approximate values of these parameters in the control group show the protective effect of L.

It has been reported in different studies that Cis causes a decrease in antioxidant parameters (SOD, CAT, GSH) in the kidneys (39). In similar studies, it has been proven that Cis causes lipid peroxidation in renal epithelial cells by decreasing the antioxidant capacity of the kidneys and increasing the MDA level (40). In this study, a decrease in GSH and antioxidant enzyme (SOD, CAT) activities in kidney tissue was determined as a result of Cis nephrotoxicity. This may lead to a decrease in the kidney's ability to clear toxic hydrogen peroxide and lipid peroxides. In addition, an increase in antioxidant capacity and a decrease in MDA levels were noted in the Cis + L group. This result indicates that L provides protection against Cis-induced nephrotoxicity in rats.

In the present study, histopathological changes such as tubular degeneration, hyaline cast formation in tubules, interstitial mononuclear leukocyte infiltration, and tubular necrosis were observed in the kidney tissue of Cis group. It is understood that these changes are similar to the results of studies in the literature (6-8) and confirm the nephrotoxic effects of Cis. In the Cis + L group, the nephrotoxic effects of Cis on the kidneys were greatly reduced. These results showed that L is a pharmacological agent that can be used as a preventative against the nephrotoxicity of Cis in kidney tissue.

Previous studies have shown that many pharmacological agents with antioxidant effects can be used successfully to prevent the toxic effects of anticancer drugs (Cis, paclitaxel) in non-target tissues (4-6,22,38). L, which has antioxidant effects, probably protects the kidney tissue from the harmful effects of oxidative stress by preventing the oxidative stress-increasing effects of Cis thanks to these effects. In our study, it was determined that BUN and Cr concentrations decreased, GSH, SOD and CAT levels increased, and MDA level decreased as a result of L administration. Reversal of Cis-induced oxidative stress has also been reported. Therefore, these observations support the hypothesis that the nephrotoxicity mechanism is related to the depletion of the antioxidant defense system.

CONCLUSION

In conclusion, our results showed that L scavenges harmful radicals, activates antioxidant defense systems and reduces histopathological changes, thanks to its strong antioxidant effects. When the results obtained in this study are evaluated together, it can be said that the application of L together with Cis can reduce the undesirable effects of Cis on the kidney tissues, and thus it can be ensured that the cancer treatment continues effectively and uninterruptedly.

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Research Article

MRI Evaluation of Anterolateral Ligament and Associated Lesions of the Knee

Anterolateral Ligament ve Dizdeki İlişkili Lezyonlarının MRI ile Değerlendirmesi

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Abstract

Aim: This study aimed to evaluate the anatomy of the anterolateral ligament (ALL), ALL injuries and the relationship between ALL injuries and other knee ligaments injuries, meniscal tears, bone injuries by retrospectively scanning patients' knee magnetic resonance imaging (MRI).

Material and Methods: Our study was designed as a retrospective, non-randomized, and single-center clinical study. We included knee MR images of 320 patients who applied to our tertiary care institution and underwent knee MRI between August 2021 and March 2022.

Results: A total 320 knee MRI's [female;163 (50.9%), mean age; 39.60±14.16 years, range; 21-77 years, left knee; 172 (53.7%)] were included study. At least one component of ALL was visualized in 319 (99.7%) cases [whole components: 276 (86.3%), meniscal: 311 (97.2%), femoral: 314 (98.1%), tibial: 280 (87.5%)]. Of the 182 ALL-injured knee, 182 (100%) had anterior cruciate ligament (ACL) injury, 116 (63.7%) had lateral meniscal injury, and 103 (56.6%) had bone injury. ACL (p=0.001), lateral meniscus (p=0.001), and bone injury (p=0.001) were more frequently in ALL-injured as compared with ALL-intact knee.

Conclusion: There is a statistically significant relationship between acute ACL rupture, lateral meniscus, bone injury, and ALL injury. When evaluating MRI in patients with ACL, lateral meniscus, and bone injury, ALL evaluation should also be performed.

Keywords: Anterolateral ligament, ALL, anterior cruciate ligament, ACL, MRI

Öz

Amaç: Bu çalışmada anterolateral ligament (ALL) yaralanmalarının anatomisi ve ALL yaralanmaları ile diğer diz bağ yaralanmaları, menisküs yırtıkları, kemik yaralanmaları arasındaki ilişkinin hastaların diz manyetik rezonans görüntülerinin (MRI) retrospektif olarak taranmasıyla değerlendirilmesi amaçlanmıştır.

Materyal ve Metot: Bu çalışma retrospektif, randomize olmayan ve tek merkezli bir klinik çalışma olarak tasarlandı. Üçüncü basamak kurumumuza başvuran Ağustos 2021 ile Mart 2022 arasında diz MRI çekilen 320 hastanın diz MR görüntülerini derlendi.

Bulgular: Toplam 320 diz MRI [kadın;163 (%50.9)), ortalama yaş; 39,60±14,16 yıl, yaş aralığı; 21-77 yıl, sol diz; 172 (%53,7)] çalışmaya dahil edildi. 319 (%99.7) olguda ALL'nin en az bir komponenti görüldü [bütün komponentler: 276 (%86.3), menisküs: 311 (%97.2), femoral: 314 (%98.1), tibial: 280 (%87.5)]. ALL yaralanmalı 182 dizden 182'sinde (%100) ön çapraz bağ (ÖÇB) yaralanması, 116'sında (%63.7) lateral menisküs yaralanması ve 103'ünde (%56.6) kemik yaralanması vardı. ÖÇB (p=0.001), lateral menisküs (p=0.001) ve kemik yaralanması (p=0.001) ALL-intakt diz ile karşılaştırıldığında ALL-yaralılarda daha sıktı.

Sonuç: Akut ÖÇB rüptürü, lateral menisküs, kemik yaralanması ve ALL yaralanması arasında istatistiksel olarak anlamlı bir ilişki vardır. ÖÇB, lateral menisküs ve kemik yaralanması olan hastalarda MRI değerlendirilirken ALL değerlendirmesi de yapılmalıdır.

Anahtar Kelimeler: Anterolateral ligament, ALL, ön çapraz bağ, ÖÇB, MRI

INTRODUCTION

Anterolateral ligament (ALL) was first described by Segond as a "pearly, resistant and fibrous" band (1). ALL has been given various names such as capsule-osseous layers, short lateral ligament (2-4), lateral capsular ligament (5), and mid-third lateral capsular ligament (6). Vincent et al. identified and described a structure they called the 'anterolateral ligament' in 2012 (7).

ALL has an important function in femorotibial internal rotation. Therefore, it supports the thesis that ALL is a secondary restriction that stabilizes internal tibial rotation

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with increased flexion (8). Following anterior cruciate ligament (ACL) reconstruction, ALL may limit pivot shift and tibial internal rotation. In addition, this has developed ACL surgery that helps limit this pivot shift (9).

In 2014, Caterine et al. first reported the appearance of ALL on MRI (10). There is no standard protocol for the evaluation of ALL with MRI. There are variable results in studies investigating ALL with MRI. Few MRI studies are showing the relationship between ALL and ACL. Studies investigating ALL and its accompanying findings and possible associations between them are still insufficient. Studies are needed on this subject.

Our aim in the study is to evaluate the anatomy of ALL, especially in the axial and coronal planes, with the standard MRI knee examination sequences. It was aimed to evaluate where the ALL originates and where it ends, which parts are not visible, the rate of adhesion to the meniscus region, femoral - tibial band lengths, thickness, and width of ALL measured from the femoral level, and comparing this with the literature. Also to investigate the presence, shape, and localization of ALL injuries. To reveal whether there is a relationship between ALL damage and ACL, lateral collateral ligament (LCL), medial cruciate ligament (MCL), posterior cruciate ligament (PCL) injuries, meniscal tears, bone injuries, and fluid in the joint space.

MATERIAL AND METHOD

Our study was set up as a retrospective, non-randomized, and single-center study. The data was collected through the hospital information system. The age, gender, and knee MRI of the patients were examined from the patient files. The information system and picture archiving and communicating system (PACS) of the University. Hospital were used to evaluate the ALL and the other structures of the knee.

Patients' selection

We studied 320 MRI scans of the knee executed in our institution between August 2021 and March 2022. Patients with a history of fracture or bone procedure, suspected tumor in the knee region, patients with previous knee ligament surgery or injury, patients with MRI scans with poorer image quality, and patients under 16 years of age were excluded from the study.

MRI protocol

All the images were executed on two 1.5-T magnets (MAGNETOM Amira, Material Number 10836777, Serial number 174075 Siemens Healthcare, Erlangen, Germany 2019) with a dedicated knee coil.

Imaging parameters at 1.5 T included: PD TSE FS Sagittal 320 (TR/TE=4500/41 ms, BW 155), T1 TSE Sagittal 320 (TR/TE=4500/41 ms, BW 155), PD Turbo FS Coranal (TR/TE=4500/41 ms, BW 153), PD TSE FS trans axial (TR/TE=4500/41 ms, BW 154). All images were acquired with FOV 150 mm, slide 25, slide thickness 3.5mm, average 1, and phase 100. (FOV=field of view, RT=repetition time, TE=echo time)

MRI analyses

ALL was reviewed on all plans. The location and presence of tibial, femoral and meniscal adhesions were determined.

According to the location in the coronal and axial plane, the femoral insertion was classified into three types. These are anterodistal to the lateral epicondyle, the lateral epicondyle, and posteroproximal to the lateral epicondyle (6,9).

The meniscal attachment pattern of ALL was divided into four types in the coronal plane. These are central, complete, inferior-only, and bipolar.

The vertical distance of the tibial insertion of the ALL below the articular line was measured from the center of the tibial insertion of the ligament to the subchondral bone surface on coronal images. This measurement was elected to provide a correlation with former anatomical, surgical, and MRI studies. ALL thickness was measured at the subchondral bone level of the femur on coronal images. The plan that best shows the thickness of the ligament is the coronal sections. In Figure 1, the length and thickness measurement of ALL is presented.

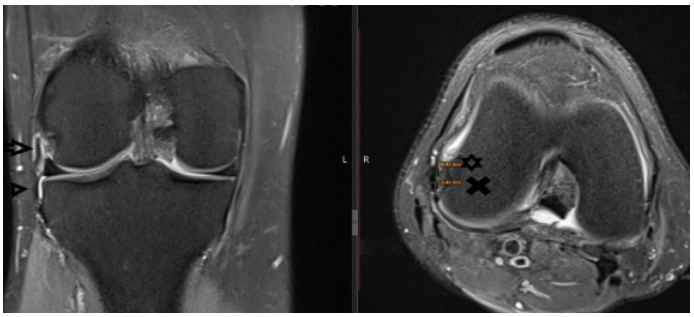

Figure 1. a. Coronal T2 image ALL femoral length (open arrow), ALL tibial length (arrow head) b. ALL width (star), and ALL thickness (cross)

Thickness is the size measurement in the segment where the femoral component is observed in the coronal section. The width is the size measurement of the femoral component on the side of the femoral component traced to the middle segment in the axial section.

We measured the femoral and tibial components. The most important point here is that we did not measure the meniscal segment, but only the femoral and tibial components.

We took care not to include the parts involved in the measurement at the level of the femoral collateral ligament (FCL) and the iliotibial band (ITT).

Other findings or accompanying findings such as ACL injury, MCL injury, LCL injury, PCL injury, MM (medial meniscus) anterior injury, MM posterior injury, LM (lateral meniscus) anterior injury, LM posterior injury, bone injury, fluid and synovial cyst hypertrophy were reviewed on MRI.

Statistical analysis

Statistical analysis was performed by Statistical Program in Social Sciences 25 program. Shapiro Wilk test was

used to check whether the data included in the study fit the normal distribution. The significance level (p) for comparison tests was taken as 0.05. Since the variables did not have a normal distribution (p>0.05), the analysis was continued with non-parametric test methods. Comparisons in independent pairs; since the assumption of normality was not provided, the Mann-Whitney U test was used. In the analysis of categorical data, chi-square analysis was performed by creating cross tables. Correlation coefficients are criteria that give information about the degree and direction of the relationship between the variables. The correlation coefficients range from -1 to +1. The signs show the direction of the relationship. The strength of the relationship increases as it approaches -1and+1, and decreases as it approaches 0. Values that are frequently used in the evaluation of the findings; 0.00–0.19 no relevance, 0.20–0.39 weak relevance, 0.40–0.69 moderate relevance, 0.70–0.89 strong relevance, and 0.90–1.00 is interpreted as a very strong relevance. Since the variables included in the study showed normal distribution, the spearman rank correlation coefficient was used.

RESULTS

The study reviewed a total of 320 knee MRI images of the patients, including 163 (50.9%) female and 157 (49.1%) male patients. The mean age of patients was 39.60±14.16 years (range, 21-77 years). Of these patients, the mean age of female patients was 44.74±13.54, (range, 21-77) years. The mean age of male patients was 34.27±12.76 years, ranging from 21 years to 71 years.

Of the 320 knee MRI images, 148 (46.3%) were right knee and 172 (53.8%) were left knee. While the mean ALL femoral length, ALL tibial length, width, and thickness were 18.29±1.76, 11.05±1.77, 8.02±0.59, 3.32±0.76, respectively. A statistically significant difference was found between males and females according to the measurements of ALL femoral length (p=0.001), ALL tibial length (p=0.001), and thickness (p=0.006). There is a low level of statistically significant positive correlation between thickness and age (p=0.001). There was no statistically significant relationship between age and ALL femoral length (p=0.409) and ALL tibial length (p=0.260).

Anatomical features of ALL and ALL injuries (types and location) are represented in Table 1. When the meniscal insertion site of ALL was evaluated, it was found to be complete type in 138 (43.1%) patients, central type in 37 (11.6%) patients, bipolar type in 142 (44.4%) patients, and inferior type in only 3 (0.9%) patients.

Table 1. Anatomical features of ALL and ALL injuries (types and location)

Variable			n	%
The meniscal insertion site of ALL	Complete		138	43.1
	Central		37	11.6
	Bipolar		142	44.4
	Inferior only		3	0.9
The femoral origin point of ALL	None (not monitored)		6	1.9
	Lateral femoral		298	93.1
	Anterodistal to lateral femoral		15	4.7
	Posteroproksimal to lateral femoral		1	0.3
Visualization of ALL	Whole (F and or M and or T)	None	44	13.8
		There is	276	86.3
	Partial (F+M or M+T or F+T)	None	276	86.3
		There is	44	13.8
	Femoral (F)	None	6	1.9
		There is	314	98.1
	Meniscus (M)	None	9	2.8
		There is	311	97.2
	Tibial (T)	None	40	12.5
		There is	280	87.5
Localization of ALL injury	None		138	43.1
	Femoral		79	24.7
	Tibial		51	15.9
	Both		52	16.3
Type of ALL injury	None		138	43.1
	Partial		153	47.8
	Total		29	9.1
			Minimum	Maximum
Measurements of ALL (millimeter)	Femoral length		14.6	23.7
	Tibial length		3	17
	Thickness		1,4	5.8
	Width		6.5	9.3

When the femoral origin of ALL was evaluated, it was found that it was lateral femoral in 298 (93.1%) patients, anterodistal to lateral femoral in 15 (4.7%) patients, posteroproximal to lateral femoral in 1 (0.3%) patient, and it could not be monetarized in 6 (1.9%) patients. When visualization of ALL was investigated, it was detected in 276 (86.3%) patients as femoral and or meniscal and or tibial. This rate was 13.8% (44) for partial, 98.1 (314) for femoral, 97.2 (311) for meniscal and 87.5% (280) for tibial.

The localization of ALL damage was investigated. The femoral type was observed in 79 (24.7%) patients, tibial type was in 52 (15.9%) patients, and both femoral and tibial types were 52 (16.3%). It was determined that 153 (47.8%) patients had partial and 29 (9.1%) patients had total ALL damage. There were 138 (43.1%) patients without any damage.

Other findings or accompanying findings detected on MRI are represented in Table 2. It was determined that 30 (9.4%) patients had a total, 82 (25.6%) patients had subtotal, 175 (54.7%) partial injuries and 33 (10.3%) patients did not have an ACL injury.

Partial MCL injury was 19.7% (63) while subtotal MCL injury was 1.9% (6). These rates were 17.8% (57) and 2.5% (8), respectively, in PCL injury. Total, partial, and mild anterior MM injuries were determined as 3.1% (10), 15.6% (50), and 41.6% (133), respectively.

Total, partial, and mild anterior LM injuries were found to be 6.6% (21), 25.9% (83), and 17.5% (56), respectively. The bone injury was not detected in 171 (53.4%) patients, but 26 (8.1%) patients had the femoral bone injury, 21 (6.6%) patients had the patellar bone injury, 16 (5.0%) patients had the tibial bone injury, 15 (4.7%) patients had the femoral and patellar bone injury, 37 (11.6%) patients had the femoral and tibial bone injury, 2 (0.6%) patients had the tibial and patellar bone injury, and 26 (8.1%) patients had the subchondral cysts. Baker's cyst was observed in 46 (14.4%) patients.

The association between ALL injury and injury of other ligamentous structures, meniscus, and lesions is demonstrated in Table 3.

In patients with ALL damage; The incidence of ACL injury, MCL injury, LCL injury, PCL injury, anterior MM injury, posterior MM injury, anterior LM injury, posterior LM injury, bone injury, fluid and synovial cyst hypertrophy was found 100% (182), 31.3(57), 8.2%, (15), 31.9% (58), 70.3% (128), 95.6% (174), 63.7% (116), 52.2% (95), 56.6% (103), 87.4% (156), 7.1% (13), respectively.

According to ALL injury, there is not a statistically significant difference between ALL injury and MCL, LCL, and PCL injury (p>0.05). According to ALL damage, there is a statistically significant difference between ACL, lateral meniscus, and bone injury (p=0.001).

Table 2. Accompanying findings detected on MRI

Associated lesions	Group	n	%
ACL injury	None	33	10.3
	Partial	175	54.7
	Subtotal	82	25.6
	Total	30	9.4
MCL injury	None	251	78.4
	Partial	63	19.7
	Subtotal	6	1.9
LCL injury	None	305	95.3
	Partial	15	4.7
PCL injury	None	255	79.7
	Partial	57	17.8
	Subtotal	8	2.5
MM anterior injury	None	127	39.7
	Mild	133	41.6
	Medium	50	15.6
	Total	10	3.1
MM posterior injury	None	24	7.5
	Mild	40	12.5
	Medium	96	30.0
	Total	160	50.0
LM anterior injury	None	160	50.0
	Mild	56	17.5
	Medium	83	25.9
	Total	21	6.6
LM posterior injury	None	189	59.1
	Mild	74	23.1
	Medium	44	13.8
	Total	13	4.1
Bone injury	None	171	53.4
	Femoral (F)	26	8.1
	Patellar (P)	21	6.6
	Tibial (T)	16	5.0
	F+P	15	4.7
	F+T	37	11.6
	T+P	2	0.6
	F+T+P	6	1.9
	Subchondral cyst	26	8.1
Fluid	None	67	20.9
	Retro patellar	127	39.7
	Lateral	18	5.6
	Total	108	33.8
Synovial cyst hypertrophy	None	257	80.3
	Baker's cyst	46	14.4
	Other	17	5.3

Table 3. The association between ALL injury and injury of other ligamentous structures, meniscus, and lesions is demonstrated

Factors associated with ALL injury		ALL injury	
		Yes	No
ACL injury	Yes	182 (100)	105 (76.1)
	No	0 (0)	33 (23.9)
MCL injury	Yes	57 (31.3)	12 (8.7)
	No	125 (68.7)	126 (91.3)
LCL injury	Yes	15 (8.2)	1 (0.7)
	No	167 (91.8)	137 (99.3)
PCL injury	Yes	58 (31.9)	8 (5.8)
	No	124 (68.1)	130 (94.2)
MM anterior injury	Yes	128 (70.3)	65 (47.1)
	No	54 (29.7)	73 (52.9)
MM posterior injury	Yes	174 (95.6)	122 (88.4)
	No	8 (4.4)	16 (11.6)
LM anterior injury	Yes	116 (63.7)	44 (31.9)
	No	66 (36.3)	94 (68.1)
LM posterior injury	Yes	95 (52.2)	36 (26.1)
	No	87 (47.8)	102 (73.9)
Bone injury	Yes	103 (56.6)	46 (66.7)
	No	79 (43.4)	92 (33.3)
Fluid	Yes	159 (87.4)	94 (68.1)
	No	23 (12.6)	44 (31.9)
Synovial cyst hypertrophy	Yes	13 (7.1)	4 (2.9)
	No	126 (69.2)	131 (94.9)

ACL – anterior cruciate ligament; MCL – medial cruciate ligament; LCL – lateral collateral ligament; PCL – posterior cruciate ligament; MM – medial meniscus; LM – lateral meniscus

DISCUSSION

ALL is a ligamentous structure that can be clearly distinguished from the femoral joint capsule. Histopathologically, it is in a ligament structure. ALL originates from the femoral epicondyle near the lateral collateral ligament. It attaches in two places. One is the tibial plateau and the other is the lateral meniscus. MRI shows the oblique and intracapsular course of the ligament (11). ALL has three components. These are femoral, meniscal, and tibial components (8).

Evaluation of ALL only with MRI coronal images may have entrapment effects in distinguishing the blended image of the ligament with surrounding structures (10-14). Despite the proximity of the fibular collateral ligament and the iliotibial band on MRI, the coronal and axial planes help us differentiate ALL (16,17). There is no clinical examination yet to identify ALL injuries. Its intracapsular and oblique course is demonstrated by MRI. The incidence of ALL injuries in patients with acute ACL-knee injury have been investigated. Therefore, MRI has a very important role in the diagnosis and treatment of ALL (8).

It is accepted that ALL is best observed on coronal sections (16,17). In our study, all segments of ALL could not be shown in a single plane in coronal or axial sections. Femoral and or tibial and or meniscal segments were observed in 276 patients, but all segments were observed in a single plane in only 4 of these patients (1.25%) (Figure 2). The main reason for this is the course of the ligament. In our opinion, the other reasons why the entire course of ALL is not seen are as follows; section thicknesses (3.5-4mm) on MRI, the resolution strength of MRI, regressed tears that occurred before the shooting, or congenital agenesis.

Figure 2. Three components of ALL in a coronal view; femoral (arrow), meniscal (star), tibial (arrowhead)

Claes et al. and Kosy et al. divided the femoral origin of ALL adjacent to the LCL into three (9,12,18). These are lateral femoral, anterodistal to lateral femoral, posteroproximal to lateral femoral. In our study, it was found to be 93.1% lateral femoral, anterodistal to lateral femoral 4.7%, posteroproximal to lateral femoral lateral 0.3%. The rate of not being seen is 1.9%. These data are compatible with the literature.

In anatomical and MRI studies of ALL, the incidence of whole components was between 21.3-97.5%, partial or any part of it was between 37-97.4%, the femoral component was 59-89.7%, the meniscal component was 0-94%, and the tibial component was 39.3-94.8% (9,12,13,15,18,19). In our study, the incidence of whole components was 86.3%, partial 13.8%, femoral 98.1%, meniscal 97.4%, and tibial 87.5%. In our study, the incidence of partial was low.

According to meniscal adhesion patterns, complete type (42.5%) and bipolar type (44.4%) were most frequently observed in our study (Figure 3). In Kosy et al.'s study, inferior only was 31.9%, which was quite high compared to our series (9). The central type was 5.32% in Kosy et al. and 11.6% in our case, which was close.

Figure 3. Meniscal attachment types in coronal images: a. complete type meniscal attachment (arrow) b. central type meniscal attachment (arrow), c. bipolar type meniscal attachment (arrow) and accompanying genicular artery and vein (star), d. inferior only type meniscal attachment (arrow)

In the MRI study, Cleas et al. (12) did not state that they could not clearly distinguish ALL from the proximal lateral capsule and distally from the iliotibial band. However, in their anatomical study (18), they stated that they found no connection between ALL and ITB. Considering the length measurements of eight anatomical or MR-based studies, the length was measured 33.2-59mm, width 1.9-8.3mm, and thickness 1.3-5.6mm (7,8,13,15,18). In our study, lengths were measured by excluding the parts that interfere with the femoral collateral ligament in the proximal ALL segment and with the iliotibial band distally. The length measurement was 29.34±1.77mm, and the width was 8.02±0.59 mm. Contrary to the studies above, the thickness was made from the femoral band and was found to be 3.33±0.76 mm. As stated above, considering the length of the involved components of ALL, the measurements were evaluated in accordance with the literature.

The incidence of ALL injuries in patients with acute ACL-knee injury has been investigated. This ratio was determined by Barera et al. (16), Claes et al. (12), Kow et al. (19), Song et al. (20) Ferretti et al. (21) they were found to be 88.2%, 79%, 46%, 38.9%, and 88.2%, respectively. They suggested that these injuries often share a common mechanism of injury, characterized by excessive internal tibial torque (12,16,19-20). They assessed that a clinical ACL injury might often be accompanied by a concomitant ALL injury (12,19).

In our study, 182 patients (56.9%) with ALL damage (partial+total) and 287 patients (89.7%) with ACL damage (partial+subtotal+total) were detected. The coexistence of ALL and ACL damage (Figure 4) at the same time was 84.6%, in our study.

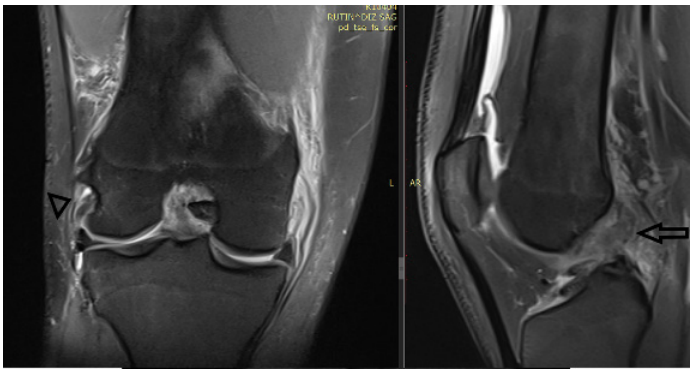

Figure 4. ALL femoral component tear (arrowhead) is seen in the coronal view. ACL rupture (arrow) is seen in the sagittal view

In most of the publications, the association of ALL damage with lateral meniscal tears was not found statistically significant (8,15,16,18). Vieira et al. stated that ALL is closely related to the lateral meniscus. ALL is important in lateral meniscus stability even in the absence of ACL damage. It can prevent anteroposterior rotation and meniscal tear during knee flexion (17). Dyck et al. found a significant association between ALL injury and tears of the lateral meniscus in their study (22). Monaco et al. suggested that if a patient with ACL tear has ALL injury, radiologists should carefully investigate whether there is a lateral meniscal tear (23).

In our study, anterior horn predominant lateral meniscus damage was detected in 162 patients (50.3%). The association of ALL damage with the lateral meniscus anterior horn (Figure 5) was found to be approximately 55.2% and this was statistically significant ($p<0.003$).

Figure 5. In the coronal image, comminuted tear (arrow) and accompanying grade 3 lateral meniscus tear (star) are observed in ALL

Some studies have found that knees with abnormal ALL have more frequent bone injuries compared to healthy knees. Interestingly, a significant correlation was found between ALL injuries and posteromedial tibial bone contusions in these studies (5,7,12). Coup or countercoup bone lesions and contusions were observed.

In our study, bone contusional damage was observed in 123 patients (38.5%). The incidence of bone damage with ALL injuries was 52.8%. This rate was found to be statistically significant (p=0.001).

In previous studies, no statistically significant relationship was found between ALL injury and MCL, LCL, PCL injury, and other structures (15,19,22). No significant relationship was found in our study either.

Our study has some limitations. The main reason for the limitation is the retrospective design of our study. We performed our MRI evaluation according to the routine departmental protocol without acquiring thin-sliced, volumetric, or oblique sequences. In the results we obtained, there is no direct correlation with MRI arthrography, the anatomical dissections of specimens, or surgical results in the patients.

However, our study may guide further clinical studies including the correlation between ALL findings and clinical instability findings in possible knee lateral ligament injuries.

CONCLUSION

There is a statistically significant relationship between acute ACL rupture, lateral meniscus injury, bone injury, and ALL injury. When evaluating MRI in patients with an ACL injury, ALL evaluation should also be performed.

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Conflict of interest: *The authors declare that they have no competing interest.*

Ethical approval: *This study was approved by the Institutional Ethics Committee of Malatya Turgut Ozal University Medicine Faculty Training and Research Hospital (20 August 2021, protocol no.,2021/66). The patients' consent was not required.*

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MEDICAL RECORDS-International Medical Journal

Research Article

Comparison of Prognostic miRNA Signature in Patients with Acute and Chronic Myeloid Leukemia by Bioinformatic Analysis

Akut ve Kronik Miyeloid Lösemili Hastalarda Prognostik miRNA İmzasının Biyoinformatik Analiz ile Karşılaştırılması

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Abstract

Aim: In this study, differentially expressed miRNA profiles were determined using high-throughput expression data from samples of AML and CML patients to identify miRNAs involved in the therapeutic response.

Material and Methods: miRNA microarray datasets GSE142699 and GSE90773 were downloaded via the GEO database and analysis was performed with the online analysis tool GEO2R. Data no. GSE142699 was made with 24 control and 24 newly diagnosed AML patients, data no. GSE90773 was made with 8 control and 10 newly diagnosed CML patients. After the analysis, they were grouped according to fold change (FC) values and $p<0.05$. Potential target genes regulated by differentially expressed miRNAs were predicted using the miRDB and TargetScan databases. Target genes enrichment analysis was performed GO function and KEGG pathway analysis using the DAVID program. Then, hub genes were detected using the regulatory network Cytoscape over the target genes.

Results: There were 27 unique miRNAs whose expression increased and 161 decreased in the AML group. In the CML group, 52 unique miRNAs with increased expression and 122 unique miRNAs with decreased expression were found. After clustering analysis between the AML and CML groups, 11 miRNAs with decreased expression and 5 miRNAs with increased expression were found. 7 miRNAs that were similar but differently expressed in the two groups were filtered out. A total of 2525 predicted target genes were found from 7 miRNAs. It was revealed that differently expressed miRNAs affect 22 common signaling pathways, especially the pathways in cancer, MAPK signaling, and PI3K-Akt signaling.

Conclusion: Our findings demonstrated that the same miRNAs are involved as different regulators in human leukemia development. Different miRNA signatures in myeloid development may be candidates for biomarkers for clinical diagnosis and differentiation, prognosis, and treatment of myeloid leukemias.

Keywords: Bioinformatic analyses, GEO, leukemia, AML, CML, miRNA

Öz

Amaç: Bu çalışmada, terapötik yanıtta yer alan miRNA'ları belirlemek için AML ve KML hastalarının örneklerinden alınan yüksek verimli ekspresyon verilerini kullanarak diferansiyel miRNA ekspresyonunu analiz ettik.

Materyal ve Metot: miRNA mikrodizi veri setleri GSE142699 ve GSE90773, GEO veritabanı aracılığıyla indirildi ve çevrimiçi analiz aracı GEO2R ile analizi yapıldı. GSE142699 nolu data, 24 kontrol ve 24 yeni teşhis edilmiş AML hastası, GSE90773 nolu data ise 8 kontrol ve 10 yeni tanı konmuş KML hastası ile yapılmıştır. Analiz sonrası kat değişimi (FC) değerlerine ve $p<0.05$'e göre gruplandırıldı. TargetScan ve miRDB veritabanları, diferansiyel olarak eksprese edilen miRNA'lar tarafından düzenlenen potansiyel hedef genlerini tahmin etmek için kullanıldı. Hedef genler DAVID programı kullanılarak, aday hedef genlerin zenginleştirme analizi GO fonksiyon ve KEGG yolu analizi gerçekleştirildi. Daha sonra hedef genler üzerinden düzenleyici ağ Cytoscape kullanılarak hub genler tesbit edildi.

Bulgular: AML grubunda ekspresyonu artan 27 ve azalan 161 benzersiz miRNA bulundu. KML grubunda ekspresyonu artmış 52 ve ekspresyonu azalmış 122 benzersiz miRNA bulundu. AML ve KML grupları arasında kümeleme analizinden sonra ekspresyonu azalmış 11 miRNA ve ekspresyonu artmış 5 miRNA bulundu. Benzer olan ancak iki grupta farklı eksprese edilen 7 miRNA filtrelenmiştir. 7 miRNA'dan toplam 2525 tahmin edilen hedef gen bulundu. Farklı eksprese edilen miRNA'ların 22 ortak sinyal yolunu, özellikle kanserdeki yolları, PI3K-Akt sinyalini ve MAPK sinyalini etkilediği ortaya çıkmıştır.

Sonuç: Bulgularımız, aynı miRNA'ların insan lösemi gelişiminde farklı düzenlenleyiciler olarak rol aldığını göstermiştir. Miyeloid gelişimindeki farklı miRNA imzaları, miyeloid lösemilerin klinik teşhisi ve ayrımı, prognozu ve tedavisi için kullanılabilecek birer biyobelirteç adayı olabilir.

Anahtar Kelimeler: Biyoinformatik analiz, GEO, lösemi, AML, CML, miRNA

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INTRODUCTION

Over the past decade, it has become clear how important microRNAs (miRNAs) are, both in normal conditions and in disease states. Gene expression, RNA maturation, and protein synthesis are all regulated by miRNAs (1, 2). miRNAs are 18-25 nucleotide long, non-protein-coding RNA fragments. They play a role in various cellular functions such as cell growth, differentiation, and development through post-transcriptional regulation of target genes (3, 4). The microRNA binds to the untranslated region at the 3' end of the target mRNA or the open reading frame region of the target mRNA (5). Many distinct mRNA transcripts, many of which have similar activities, can be inhibited by one miRNA and control multiple signaling pathways (6). In contrast, numerous miRNAs can target the same mRNA transcript (7).

miRNA expression dysregulation has been linked to a variety of diseases and cancers. Nearly half of miRNAs are located near or in cancer-related genes (8). miRNA genes have been determined to be localized in regions of loss of heterozygosity and fragile regions or in regions of common chromosomal breakpoints, which can lead to cancer if damaged (9-10). They are found stably in tissues and body fluids. The unique expression patterns of miRNAs have been proposed as biomarkers for various diseases, making them ideal diagnostic and therapeutic agents (11-13).

miRNAs can acquire oncogenic or tumor suppressor properties depending on the molecular level properties of the mRNA they target. It has been reported that some of the miRNAs inhibit the translation of protooncogenes in normal tissues. Its function is to control the expression of an oncogene. miRNAs are known as "tumor suppressor miRNAs" (TSmir) (14). MiRNAs regulate normal hematopoiesis by regulating myeloid differentiation, cell cycle, proliferation, apoptosis, and gene methylation (15, 16). MiRNA can operate as a tumor suppressor or an oncogene/oncomiR in hematological malignancies originating from hematopoietic stem and progenitor cells (15,17). miRNAs show promise as a biomarker to discriminate between cancers as well as between Chronic myeloid leukemia (CML) and acute myeloid leukemia (AML). Only the K562 cells revealed higher expression of miR-20a in a transcriptome comparison of AML and CML cell lines. This shows that higher levels of miR-20a expression could be used to distinguish CML from AML (18). Other research has found that miR-29a/b is downregulated in both CML and AML patients, and that these two miRNAs play an important regulatory role in myeloid cells (19).

The roles of miRNAs in leukemia pathogenesis are currently being explored, and various studies have proposed miRNA expression profiles as biomarkers for a leukemia diagnosis, prognosis, and response to therapy. The advantage of determining miRNA profiles over mRNA profiles is that miRNAs can classify poorly differentiated cancer types that mRNA profiles cannot distinguish.

This study aimed to discover the function of miRNAs in the pathogenesis of AML and CML patients. As a result, in silico research was performed to better understand the RNA silencing mechanism of miRNAs with similar or dissimilar roles in AML and CML. Target genes of miRNAs and their related biological pathways were explored in this work to determine the therapeutic potential of miRNAs in AML and CML. MiRNA profiles that are similar or dissimilar can be used as prognostic and differential diagnostic markers in AML and CML.

MATERIAL AND METHOD

The study is a bioinformatics study and raw data was used. The database for which we use the data, Gene Expression Omnibus (GEO), is a public database and therefore ethical approval is not required. GEO is a public, functional genomic data repository that supports minimal information about a microarray experiment (MIAME) compliant data submissions where Array and array-based data are accepted (https://www.ncbi.nlm.nih.gov/geo/)

Dataset Collection

The GEO database was used to derive gene expression profiles for datasets GSE142699 and GSE90773. The dataset of GSE142699 was analyzed with GPL19066 and GSE90773 was analyzed with GPL26945. GSE142699 contains 24 controls and 24 newly diagnosed AML patients. GSE90773 includes 4 control and 5 newly diagnosed CML patients containing Lin- CD34+CD38+ and Lin-CD34-CD38- cells isolated from peripheral blood.

Analyzing the Differential Expression of miRNAs

For the analysis of differentially expressed microRNAs, the R-based GEO online tool GEO2R online tool was used. It performs comparisons between sets of samples in the dataset to identify differentially expressed miRNAs (DEMs). $P<0.05$ and $|$ fold change$| \geq 0$ were used as screening thresholds for the GSE142699 and GSE90773 datasets. Comparisons between gr AML and CML groups were first compared with their healthy group and then with each other goups are made by applying log 2 transformation and Benjamini & Hochberg method. MiRNAs and DEMs that were similar and different between groups were obtained using the Venny online tool.

Target Gene Prediction Analysis

The online databases miRDB (http://miRdb.org/) and TargetScan (http://www.targetscan.org/) were used to determine miRNA target genes. The two databases found identical genes in both databases that were used as target genes. Prognostic miRNAs linked to both AML and CML had common target genes.

Functional Analyses of Common Genes

To describe the biological processes involved in common genes, we used DAVID (https://david.ncifcrf.gov/) to apply the Kyoto Encyclopedia of Genes and Genes (KEGG) Pathway enrichment and Gene Ontology (GO) functionality. Pathways with $P<0.05$ and highest gene

counts were considered important pathways, such as enriched KEGG pathways and functional processes of with GO. Gene ontology was investigated in 3 categories as a biological process (BP), cellular component (CC), and molecular function (MF).

PPI Network Construction and Hub Gene Screening

Interactions between common genes were analyzed with the STRING (http://string-db.org) online visualization tool. The PPI network was constructed with common genes with the highest confidence score of 0.9, and then data from the STRING database were analyzed in Cytoscape (version 3.9.2 https://cytoscape.org/) for visualization. Hub genes were identified with the Cytoscape cytoHubba plugin by scoring with MCODE functional modules and using the MCC algorithm. Selection criteria for MCODE functional modules are cutoff degree =2, node score cutoff =0.2, k-core=2, and max. depth=100.

RESULTS

Differentially Expressed miRNAs (DEMs) Analysis

Raw data of AML and CML patients, GSE142699 and GSE28825, were downloaded from the GEO database and analyzed separately with GEO2R. After the analysis, they were grouped according to fold change (FC) values and p<0.05, and and the gene numbers obtained in AML and CML in Venny were compared. Volcanoblot graphs of differently expressed miRNAs belonging to the groups are given in figure 1. There were 27 unique miRNAs whose expression increased and 161 decreased in the AML group. In the CML group, 52 unique miRNAs with increased expression and 122 unique miRNAs with decreased expression were found (Figure 2A-B).

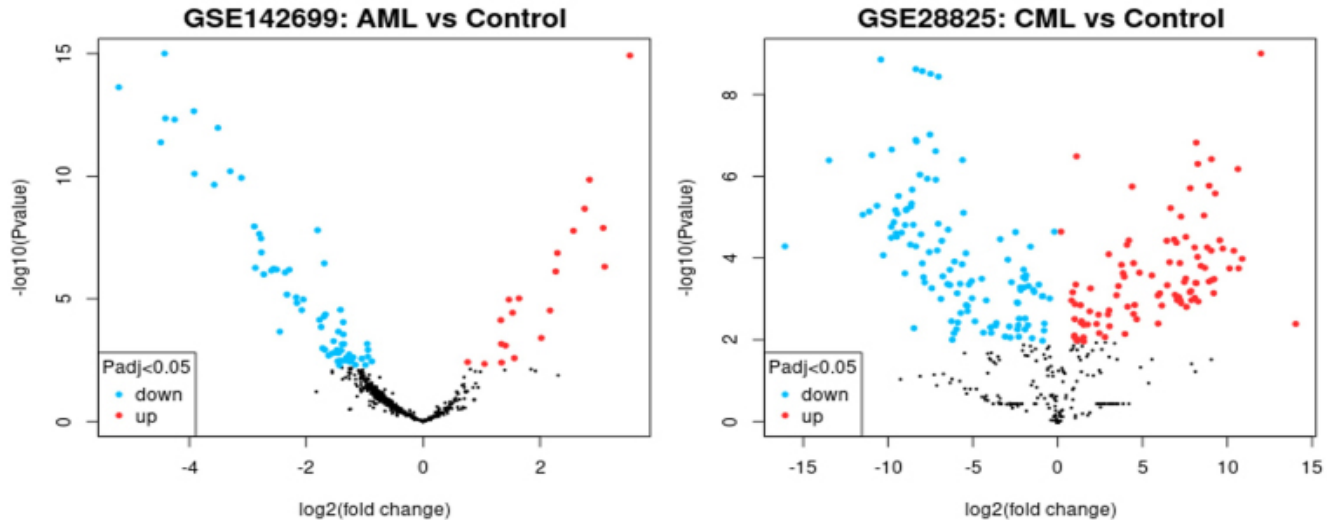
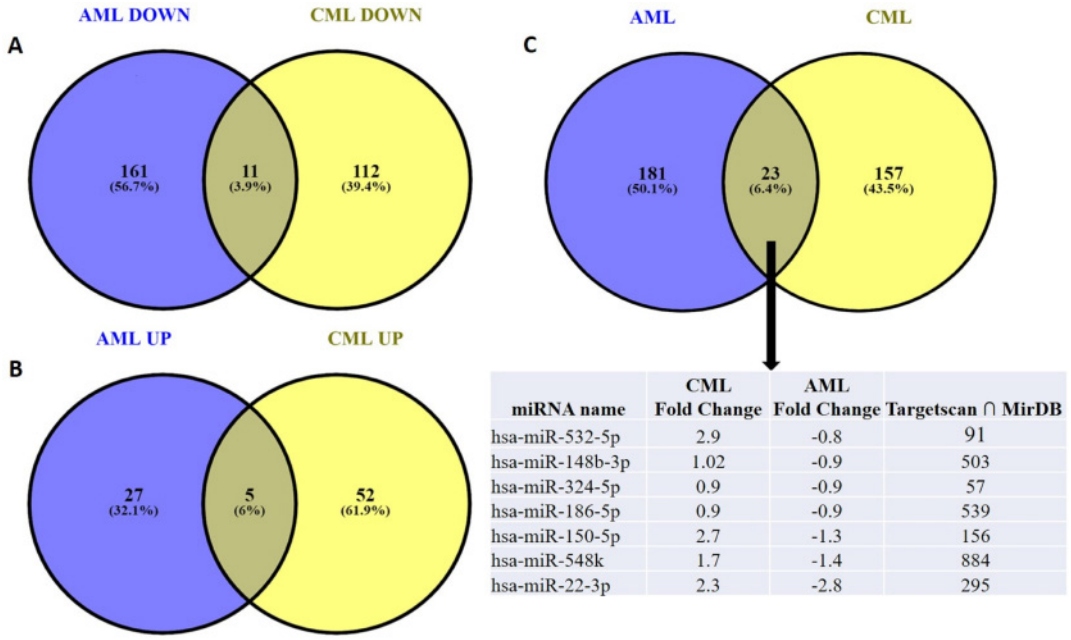


Figure 1. Volcano plot of differentially expressed genes based on GSE142699 and GSE28825, respectively



miRNA name	CML Fold Change	AML Fold Change	Targetscan ∩ MirDB
hsa-miR-532-5p	2.9	-0.8	91
hsa-miR-148b-3p	1.02	-0.9	503
hsa-miR-324-5p	0.9	-0.9	57
hsa-miR-186-5p	0.9	-0.9	539
hsa-miR-150-5p	2.7	-1.3	156
hsa-miR-548k	1.7	-1.4	884
hsa-miR-22-3p	2.3	-2.8	295

Figure 2. Using the Venny to obtain common miRNAs in AML and CML. A. Common downregulated miRNAs in AML and CML B. Common upregulated miRNAs in AML and CML C. Different expressions of miRNAs in AML and CML

A total of 23 common mirnas were found between the two groups (Figure 2C). After clustering analysis between the AML and CML groups, 11 miRNAs with decreased expression and 5 miRNAs with increased expression were found. 7 MiRNAs that were similar but differently expressed in the two groups were filtered out. 7 MiRNAs were found to be the same in the two groups but expressed differently, that is, increased in CML and decreased in AML (hsa-miR-532-5p, hsa-miR-186-5p, hsa-miR-148b-3p, hsa-miR-324-5p, hsa-miR-150-5p, hsa-miR-548k, hsa-miR-22-3p) (Figure 2C).

Prediction of Target Genes with DEMs

The target genes of the DEMs common to AML and CML were found using the targetscan and mirDB databases. Using both tools, common target genes were selected and analyzes were continued with these genes. A total of 2525 predicted target genes were found from 7 overlapping miRNAs.

GO ve KEGG Enrichment Analysis of Target Genes

Gene ontology and KEGG pathway analyzes were performed using the DAVID database for data enrichment on predicted target genes. It was revealed that differently expressed miRNAs affect 22 common signaling pathways, especially the pathways in cancer (108 genes), PI3K-Akt signaling (76 genes) and MAPK signaling (61 genes) (Table 1).

In GO analysis, 660 overlapping genes involved in many biological processes (BP) such as protein phosphorylation, cell division and regulation of transcription are involved. In molecular function (MF), 891 genes were found to be involved in RNA polymerase II transcription factor activity, metal ion binding, ATP binding, sequence-specific DNA binding, and sequence-specific double-stranded DNA binding processes. In terms of cellular components (CC), 290 is enriched in chromatin, receptor complex, RNA polymerase II transcription factor complex, and ribonucleoprotein complex processes. Other enriched processes are shown in Figure 3.

Construction of PPI Network

Target genes predicted by differentially expressed miRNAs were generated by the STRING database, and hub genes were selected using the network analyzer and MCODE interfaces of Cytoscape software to generate the target gene network map from the results from STRING. Genes with degree >25 TP53, EP300, MAPK1, SMAD3, PIK3CA, HDAC2, STAT3, KRAS, ESR1, CREBBP, NRAS, SOS1, MAPK14, ITGAV, FYN, PTEN, UBE2D1, HIF1A, NCOR1, CREB1, EIF4E, MTOR, emerged as important genes (Figure 4). Modules and genes with scores >4 after MCODE cluster analysis are given in the table (Table 3). As it is mostly associated with disease pathogenesis, nodes formed by hub genes in biological networks contain very important proteins.

Table 1. Major KEGG pathways related to miRNAs differentially expressed in AML and CML

	KEGG PATHWAYS	Count	PValue
1	hsa05200:Pathways in cancer	108	1.18E-09
2	hsa04151:PI3K-Akt signaling pathway	76	5.07E-08
3	hsa04010:MAPK signaling pathway	61	4.17E-06
4	hsa05206:MicroRNAs in cancer	57	2.95E-04
5	hsa04014:Ras signaling pathway	50	1.22E-05
6	hsa04510:Focal adhesion	45	1.32E-05
7	hsa04550:Signaling pathways regulating pluripotency of stem cells	37	2.99E-06
8	hsa04150:mTOR signaling pathway	35	1.37E-04
9	hsa04068:FoxO signaling pathway	34	7.57E-06
10	hsa04140:Autophagy - animal	32	2.25E-04
11	hsa04390:Hippo signaling pathway	31	0.003064
12	hsa04310:Wnt signaling pathway	29	0.02364
13	hsa01521:EGFR tyrosine kinase inhibitor resistance	28	7.43E-08
14	hsa04066:HIF-1 signaling pathway	28	6.88E-05
15	hsa04012:ErbB signaling pathway	25	1.73E-05
16	hsa04350:TGF-beta signaling pathway	24	2.83E-04
17	hsa05220:Chronic myeloid leukemia	23	2.52E-05
18	hsa04512:ECM-receptor interaction	23	2.75E-04
19	hsa04110:Cell cycle	23	0.027655
20	hsa05235:PD-L1 expression and PD-1 checkpoint pathway in cancer	21	0.002123
21	hsa05221:Acute myeloid leukemia	17	0.003
22	hsa04115:p53 signaling pathway	15	0.035079

Table 2. Hub genes resulting from the MCODE score for predicted target genes of DEMs.

Cluster	Score	Nodes	Edges	Hub Genes
1	10	10	45	CYCS, PPP3CA, PPP1R12A, WDR82, PPP1CC, PPP1R15B, PPP1R9B, PPP1CB, PPP3CB, PPP4R2
2	9.9	21	99	UBE2D1, HDAC2, SCML2, UBE2W, PHC1, PHC3, UBE2Q2, UBE2N, UBAP2L, UBE2E1, UBE2R2, UBE2B, PCGF5, COMMD3-BMI1, UBE2A, UBA6, BMI1, UBE2D3, SUZ12, UBE2J1, UBE2K
3	7	7	21	ADAMTS18, ADAMTS5, ADAMTS19, ADAMTS15, ADAMTS1, THSD7A, POFUT2
4	6	6	15	KLHL9, GAN, KBTBD8, KLHL3, KLHL13, ENC1
5	5.964	56	164	INO80D, ITGB8, NRIP1, IL6ST, CD28, CUL4A, YIPF6, YY1, PICALM, ITGAV, IKZF3, POU2F1, COPS5, TFRC, NUP35, ZEB1, NECAP1, DICER1, NRAS, IL6R, RORC, NUP107, SUMO2, IL2, PIK3C2A, RAN, SNX2, DDX6, RORA, KRAS, YWHAQ, CEBPD, KITLG, CPD, DCP2, PDGFA, HDAC4, GAB1, CREB1, NUP153, SORT1, SP1, MAPK14, ESR1, YWHAB, KIT, COPS7B, IGF1, ITGA11, ITGA5, EP300, ITGB6, INO80, SOS1, INO80E, AP4E1
6	5.6	6	14	CERS6, UGT8, UGCG, CERK, SGMS2, SGPP2
7	5.6	6	14	SNAP25, LIN7A, CASK, SYT1, RIMS1, LIN7C
8	4.8	6	12	WNT1, FZD3, WNT10B, FZD7, WNT5A, WNT4
9	4.5	5	9	PDS5A, NIPBL, PDS5B, STAG2, SMC3
10	4.444	28	60	DCP1A, TNRC6C, AR, RRAGD, MECP2, CREBBP, DYNC1I1, CNOT7, GTF2B, NCOA1, CNOT6L, MAX, CNOT6, PRKAA2, TOB1, UPF1, PRKAA1, DYNC1I2, PABPC1, TNRC6B, PRKAG2, CPEB3, DYNLL2, AGO4, EDC3, CNOT11, AGO1, KMT2A
11	4	4	6	CDK8, MED28, MED6, CDK19
12	4	4	6	TCP1, BBS2, BBS1, BBS7
13	4	4	6	ARMC8, RMND5A, WDR26, GID8

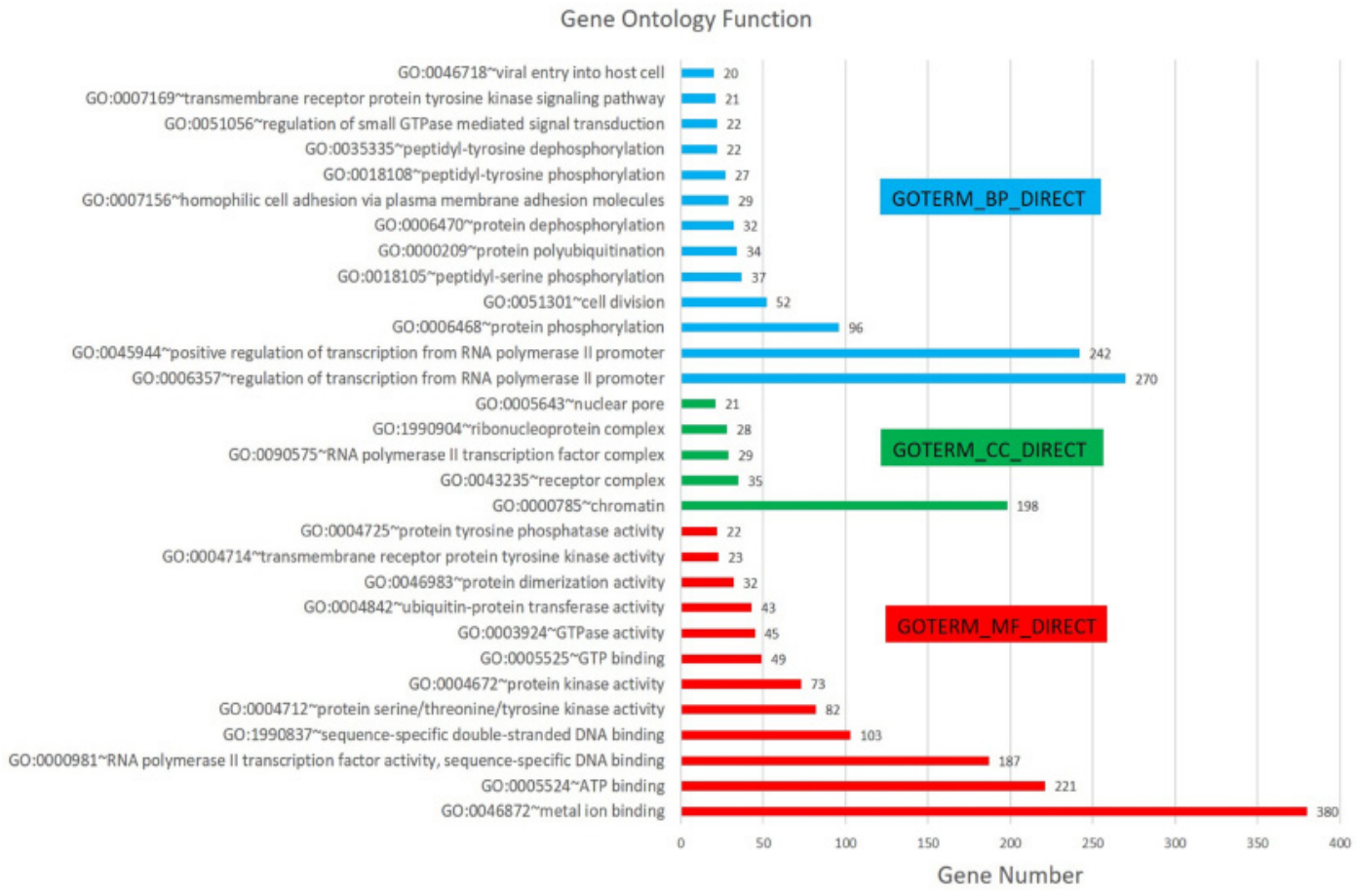


Figure 3. GO terms of down- and upregulated target genes of miRNAs, including BP, CC and MF

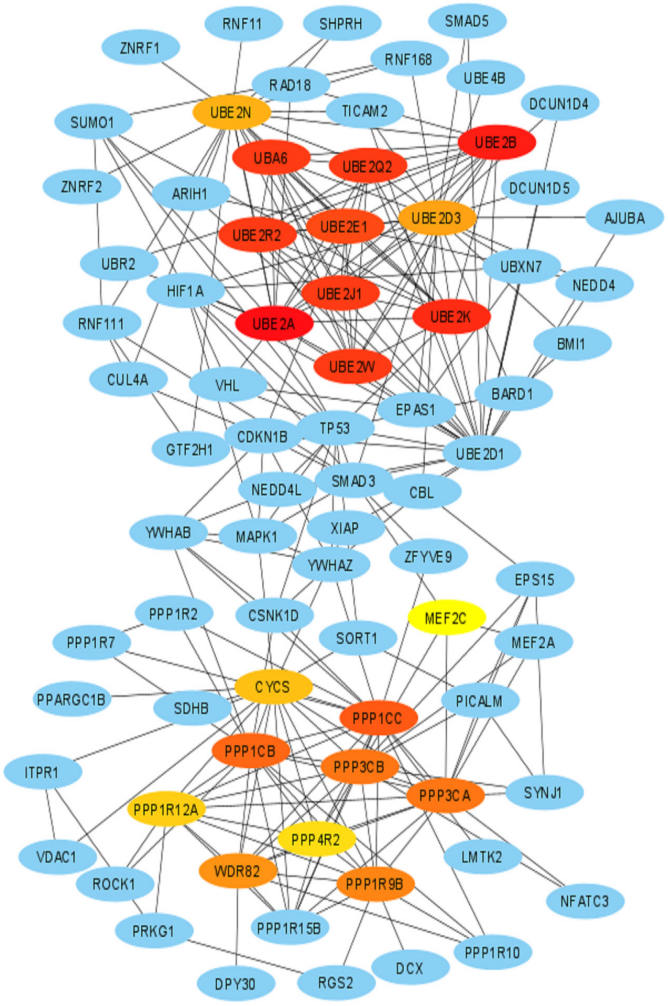


Figure 4. Cytoscape plug-ins cytoHubba analysis of hub genes after PPI analysis

DISCUSSION

Leukemia is a clonal malignant hematopoietic stem cell disease that affects both blood and bone marrow. Excessive cell proliferation of immature blood cells characterizes this disorder. Leukemia is the sixth most common disease and accounts for 4% of all cancers, according to research. Despite the scarcity of remedies, current therapeutic techniques have some drawbacks. As a result, new therapeutic alternatives must be discovered and developed. The identification of distinct cellular and molecular pathways involved in the etiology of leukemia is a crucial step in the quest for new treatment medicines (20).

MiRNAs have emerged as essential participants in the etiology of leukemia among numerous cellular and molecular targets. These molecules are epigenetic regulators that function as tumor suppressors or oncogenes in a variety of cancers, including leukemia. As a result, they can be used as diagnostic, prognostic, and therapeutic biomarkers at various stages of leukemia. Furthermore, growing evidence suggests that miRNAs could be used as markers in diagnosis and treatment in the early stages of the disease or following chemotherapy (21,22).

Using bioinformatics analyses, we identified several miRNAs that could be used as new differential therapeutic targets in the treatment of AML, and CML. MiRNAs have the potential to be used as therapeutic candidates in the treatment of leukemia patients. Creating novel miRNAs for AML, and CML to aid in diagnosis and prognosis, and also open the path for the creation of new treatment platforms for leukemia patients.

In this study, miRNAs between the two leukemia types were compared using AML, and CML data numbered GSE142699 and GSE28825. In the AML group, 161 unique miRNAs were found, 27 of which were increased in expression. In the CML group, 122 unique miRNAs were found with increased expression and 52 decreased expression. In common between AML and CML, 11 miRNAs with decreased expression and 5 miRNAs with increased expression were found. Interestingly, apart from these miRNAs that act as regulators between AML, and CML, 7 miRNAs that were similar but differently expressed in the two groups were detected. 7 differentially expressed miRNAs (hsa-miR-532-5p, hsa-miR-186-5p, hsa-miR-148b-3p, hsa-miR-324-5p, hsa-miR-150-5p, hsa-miR-548k, hsa-miR-22-3p) increased in CML and decreased in AML. GO and KEGG analyses of target genes of these miRNAs were found to be enriched in pathways in cancer, PI3K-Akt signaling, MAPK signaling, and miRNAs in cancer pathways.

miR-148 was associated with poor prognosis in previous studies (23), but it was emphasized that miR-148 inhibited proliferation of AML cells by disrupting CDK expression in AML and targeting miR-148 could be used in the effective treatment of AML (24). While miR-150 was associated with a good prognosis in both, it was found to be expressed differently in our study (23). While studies have shown increased expression of miR-532-5p in AML, it has not been previously identified in CML (25).

According to our findings, the level of miR-186 expression in AML was significantly lower than in normal controls and predicted a poor prognosis in AML patients. In CML cells, however, EAD box polypeptide 43 (DDX43) is overexpressed and DDX43 upregulates long non-coding RNA-H19, increasing cell proliferation and inhibiting apoptosis. miR-186 functions as a negative regulator of DDX43 in CML (26). It has an increased expression in our study and is used as a differential marker between AML and CML, associated with poor prognosis. The miR-548k and miR22-3p miRNAs have not previously been associated with AML and CML and can be suggested as a diagnostic and prognostic marker for AML and CML.

The predicted target genes of 2550 genes were found by 7 miRNAs that were differentially expressed between the two groups. After PPI analysis with these genes, TP53, EP300, MAPK1, SMAD3, PIK3CA, HDAC2, STAT3, KRAS, ESR1, CREBBP, NRAS, SOS1, MAPK14, ITGAV, FYN, PTEN, UBE2D1, HIF1A, NCOR1, CREB1, EIF4E, MTOR, 20 key

genes, including the NOTCH1 gene, emerged as important genes. These key genes, which include many tumor suppressors and oncogenes, show that they regulate biological mechanisms by DEMs in AML and CML.

CONCLUSION

In this study, we analyzed differential miRNA expression using high-throughput expression data from samples of AML and CML patients to identify miRNAs involved in therapeutic response. Our findings will be used to investigate the role of microRNAs in human malignant transformation and hematopoietic development in the future. Different miRNA signatures could also be possibilities for myeloid leukemia clinical diagnosis, prediction, and treatment. Differentially expressed miRNAs representing these two forms of myeloid leukemia will provide insights into CML and AML differentiation and myogenic regulatory control. The results revealed that the same miRNAs have different effects in AML and CML. The miRNAs and their target genes identified in this study are associated with various biological pathways, suggesting that they can serve as distinctive biomarkers in the diagnosis and treatment of the two types of leukemia.

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Conflict of interest: *The authors declare that they have no competing interest.*

Ethical approval: *The study was conducted with the decision of the local ethics center of Sivas Cumhuriyet University Non-Interventional Research Ethics Committee dated on 10.03.2021 and decision number 2021-03/27.*

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MEDICAL RECORDS-International Medical Journal

Research Article

Menstruation Impact Scale Development

Menstruasyon Etki Ölçeği Geliştirilmesi

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Abstract

Aim: Although there are many measurement tools in the literature to measure menstruation attitudes and symptoms, there is a need for a specific measurement tool that measures the impacts of menstruation alone on women's life, independent of premenstrual syndrome and dysmenorrhea. Our aim was to create a scale so that we could measure the impacts of menstruation in the study.

Materials and Methods: It is a methodological research. The sample consisted of 615 female university students. Menstrual Impact draft scale, which is developed by the researchers, subscale of Menstrual Symptom Questionnaire Negative impacts/ somatic complaints and introductory information form have been used as data collecting forms.

Results: After the factor analysis, a 14-item scale, consisting of physical and psychosocial impact subscales, was developed. The scale is a 5 point Likert type scale evaluated between "5" Strongly Agree and "1" Strongly Disagree. The minimum and maximum scores to be obtained from the overall scale are 14 and 70 respectively. As the score increases, the participant's degree of being affected by menstruation increases as well. The total explained variance of the scale is 54.92%. The Cronbach's alpha coefficient of the scale was 0.87.

Conclusion: The literature has been earned a valid and reliable measurement tool to specifically measure the impacts of menstruation in women's life. Menstrual Impact Scale (MIS) is a short, practical, and easy-to-apply scale. Its validity and reliability in different cultures should be tested.

Keywords: Menstruation, reliability and validity, scale

Öz

Amaç: Literatürde mensturasyon tutumlarını ve belirtilerini ölçmeye yönelik bir çok ölçüm aracı olsa bile premenstrual sendrom ve dismenoreden bağımsız olarak menstruasyonun tek başına kadın yaşamına etkilerini ölçen spesifik bir ölçüm aracına ihtiyaç vardır. Araştırmada menstruasyon etkilerini ölçmeye yönelik bir ölçek geliştirmek amaçlanmıştır.

Materyal ve Metot: Metodolojik bir araştırmadır. Örneklemini üniversitede öğrenim gören 615 kız öğrenci oluşturmuştur. Veri toplama formu olarak araştırmacılar tarafından geliştirilen taslak Menstruasyon Etki Ölçeği ile Menstruasyon Semptom Ölçeği Negatif etkiler/ somatik yakınmalar" alt boyutu ve tanıtıcı bilgi formu kullanılmıştır.

Bulgular: Faktör analizi sonucu fiziksel ve psikososyal etki alt boyutlarından oluşan 14 maddelik bir ölçek geliştirilmiştir. Ölçek, "5" Kesinlikle Katılıyorum ve "1" Hiç Katılmıyorum arasında değerlendirilen 5'li likert tipi bir ölçektir. Ölçekten alınabilecek toplam puan 14 ile 70 arasında değişmektedir. Puan arttıkça katılımcının mensturasyondan etkilenme durumları artmaktadır. Ölçeğin, açıklanan toplam varyansı %54.92'dir. Cronbach's Alfa katsayısının ise 0.87 olduğu saptanmıştır.

Sonuç: Literatüre kadın yaşamında spesifik olarak mensturasyonun etkilerini ölçmeye yönelik geçerli ve güvenilir bir ölçme aracı kazandırılmıştır. Menstruasyon Etki Ölçeği (MEÖ), kısa pratik ve uygulaması kolay bir ölçektir. Farklı kültürlerde geçerlilik ve güvenilirliği sınanmalıdır.

Anahtar Kelimeler: Mensturasyon, geçerlilik ve güvenirlik, ölçek

INTRODUCTION

Menstruation is characterized by the evacuation of blood and mucosal tissue from the uterus. The age at menarche, the first menstruation, usually ranges between 11 and 14 (1). In addition to this, to date, the current literature discusses menstruation as a private and sensitive issue (2). Social and cultural stereotypes on menstruation play an important role in determining the menstrual experience (3). Menstruation also affects women emotionally in addition to physical ailments (4,5). The issue to be taken into consideration during the studies is the multidimensional

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psychosocial aspect of the menstrual experience. These dimensions include experiences of embarrassment, fear, nuisance, and discomfort in participating in other activities during menstruation (6).

Therefore, there is an opportunity to add information to the current literature by further investigating both the physical and psychological aspects of menstruation, which is surrounded by taboos (2). To minimize the negative impacts of menstruation, these impacts must be determined and measured. There is a need for standard measuring instruments to measure the impact of menstruation. These measurement tools vary in international studies (7). Premenstrual Symptoms Screening Tool (8), Menstrual Attitude Questionnaire (9), Menstrual Distress Questionnaire (10), Menstrual Symptom Questionnaire (11), Premenstrual Assessment Form (12) and Adolescent Menstrual Attitude Questionnaire (13) all confront us as the measurement tools which are being frequently used all over the world.

Despite all these useful measurement tools, the development of a specific measurement tool that measures the impact of menstruation can be a guide for better understanding and research of the subject. For this reason, it has been thought that developing a measurement tool that focuses on the impact of menstruation on women's lives can contribute to the literature. In this research, we aimed to create a scale so that we could measure the impacts of menstruation on women's lives.

Research question

Is the Menstrual Impact Scale (MIS) really a valid and reliable measurement tool?

MATERIAL AND METHOD

Research Design

The research has a cross-sectional and methodological structure. In this research, we aimed to create a scale so that we could measure the impacts of menstruation on women.

Population and Sample of The Research

The research population consists of female students at a public university in Burdur. The International Test Commission (2018) stated that the minimum sample size should be 200 in order to reveal the psychometric structure of a scale (14). Again, recommended sample calculations were used for scale development studies. Accordingly, 5-30 observations per item are recommended (15). Based on the expert opinion, the number of the items in the scale was reduced to 34 and 615 participants were reached for this scale. The scale especially aims to specifically measure the impacts of menstruation. Therefore, it was important to exclude participants with dysmenorrhea from the scope of the study. Because it is aimed to measure menstruation specifically, free from the impacts of dysmenorrhea. We excluded those who did not want to take part in the study, who did not fill in the data collection tools completely, who did not have menstruation regularly, who had dysmenorrhea, and who were under the age of 18 from the study. Research data were collected based on participants' self-reports.

Data Collecting Tools

The Descriptive Information Form, Menstrual Impact Scale, and Menstrual Symptom Questionnaire were used for data collection,

Descriptive Information Form

The researcher created the form according to the literature. In addition to sociodemographic characteristics such as age and education, the form includes additional questions about menstruation characteristics such as the age at menarche and the duration of menstruation.

Menstrual Symptom Questionnaire (MSQ)

The MSQ was developed by Chesney and Tasto in 1975 to assess menstrual pain and symptoms. In 2009, it was updated by Negriff et al. after being reassessed for the factor structure and usability on adolescents. The scale adapted into Turkish by Guvenc et al. includes 22 items whose responses are rated on a five-point Likert-type scale. Each interval of items namely 1-13, 14-19, 20-22 consecutively refers to the "Negative impacts/somatic complaints" subscale, "Menstrual pain" subscale and " methods of coping with menstrual pain." subscale. Cronbach's Alpha value is 0.86. An increase in the mean score in the subscales indicates an increase in the severity of menstrual symptoms belonging to that subscale (7). Since dysmenorrhea was not questioned in this study, similar scale validity was tested through the "Negative impacts/somatic complaints" subscale of the MSQ. In this study, the Cronbach's Alpha value was 0.81.

The Draft Menstrual Impact Scale (MIS)

A 51-item pool was created by the researchers. Developing the scale to measure the impacts of menstruation was planned. The draft scale is a 5-point Likert type. As the score the participants obtain from the scale increases, so does their level of being affected by menstruation. Before the implementation phase of the scale, a 34-item scale whose content validity was already performed in line with expert opinions was administered to the participants. After the validity and reliability analysis was conducted after the implementation, the draft MIS was finalized to consist of 14 items.

Data analysis

Descriptive Data Analysis

Numbers, Arithmetic Mean, Percentages, standard

deviation, minimum and maximum values were used in the analysis of the descriptive data.

The Stages of Developing the MIS and the Analysis

Scales used by researchers in menstruation studies and studies examining the impacts of menstruation have been reviewed. During the item pooling phase of the draft scale, the current literature was used. Thereafter, the draft scale was examined by 5 academicians who have at least a doctorate degree in the field. Furthermore, it was reviewed by 1 linguist and 1 assessment & evaluation specialist. Then a pilot study including 30 volunteer participants was performed. After the feedback, some stylistic changes were made to increase the clarity of the items. During the validity phase of the scale; 1. expert opinions were used to test content validity, 2. construct validity was tested through the factor analysis, 3. the mean scores obtained from the overall MIS and its subscales were used to examine the menstruation symptom scale, 4. the correlation results between the scores of the Negative Impacts/Somatic Complaints subscale were used to test Criterion-related validity. The sufficiency of the sample size used in the evaluation of the scale for factor analysis was evaluated through Kaiser-Meyer-Olkin (KMO) and Bartlett tests, prior to conducting factor analysis itself. During the reliability phase of the scale; 1. the internal consistency reliability coefficient of total and subscales, 2. Spearman and Guttmann values and item-total score correlation was evaluated to test internal consistency; 3. correlation results were evaluated with Test-retest reliability analysis to test invariance-over-time. SPSS 15.0 program was used in the analysis.

Ethical aspect of research

Before the study was carried out, ethics committee approval was obtained from the ethics committee of Mehmet Akif Ersoy University where the study would be fulfilled (Decision no: GO2017/84). Written and verbal information was provided for the participants.

RESULTS

The Participants' Descriptive Characteristics

The participants' mean age and age at menarche were 20.53±1.88 and 13.64±1.24 years respectively. The majority of the participants (33.5%) were students of first class.

Validity Analysis Results

Content Validity Index

Whether the items in the scale were suitable and valid was determined by consulting the experts. For the first version of the scale, which consisted of the items in the final form, the CVI/CVC ≥0 condition was met, and the content validity was statistically significant (16). Finally, 17 items were eliminated and a 34-item draft MIS was administered to the participants.

Construct Validity

The result of the KMO test performed to determine sampling adequacy was .90. The result of Bartlett's sphericity test was 3649.0 (p<.001). These two findings denote that the sample size used in the research is sufficient and the data are suitable for factor analysis. In this research, no restrictions were placed on the number of factors and factors having an eigenvalue greater than 1.00 were included in the scale. The eigenvalue is taken into consideration while the variance explained by the factors is calculated, and the number of important factors is decided. In factor analysis, factors having an eigenvalue of 1 or greater are considered important factors (Figure 1). Starting from that point, it was decided that the number of factors in the scale could be limited to two.

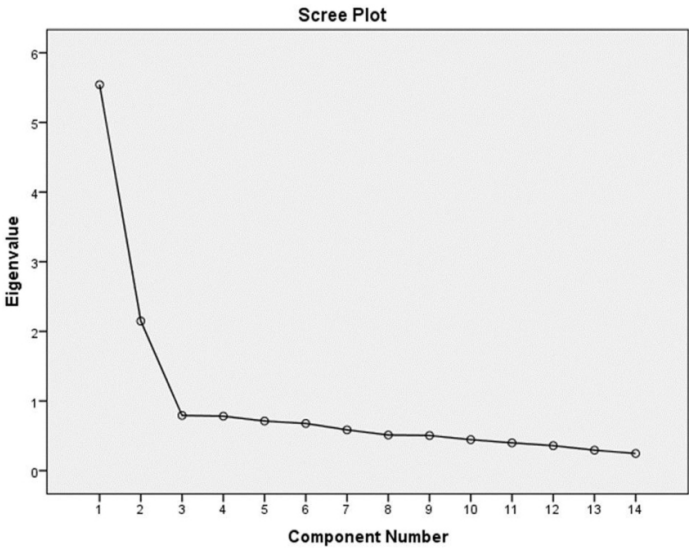

Figure 1. Scree plot of MIS

Variance Ratios Explained by the Subscales of the Menstruation Impact Scale

In Table 1, the eigenvalues of the subscales obtained after the factor analysis and the amount of variance they accounted for are presented. The sub-factor dimensions were named by examining the scale items in each factor. The first factor was named as "physical impact dimension" and the second factor as "psychosocial impact dimension" (Table 1). As seen in Table 2; while the first factor (subscale) with an eigenvalue of 5.54 accounted for 31.83% of the variance, the second factor with an eigenvalue of 2.14 accounted for 23.09% of the variance. The two factors accounted for 54.92% of the total variance.

Table 1. By Subscales of the Menstruation Impact Scale Explained Variance Ratios

Subscales	Eigen Values	Variance (%)	Cumulative Variance (%)
Physical Impact Subscale	5.54	31.83	31.83
Psychosocial Impact Subscale	2.14	23.09	54.92

Factor Loads of the Items Constituting the subscales of the Menstruation Impact Scale

The results of the three-stage factor analysis revealed that the factor loads of some items were below 0.40 or that they had high load values in both factors. Based on these criteria, 20 items (items 7, 8, 12, 13, 14, 15, 18, 20, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34) were removed from the scale and the factor analysis was performed again. After the analysis, the "Menstruation Impact Scale" consisting of 14 items and 2 subscales took its final form. After factor rotation, the physical subscale of the scale included seven items (items 1, 2, 3, 4, 5, 6, 16) and the psychosocial subscale consisted of seven items (items 9, 10, 11, 17, 19, 21, 29). As seen in Table 2; the factor loads of the items in the physical subscale vary from 0.578 to 0.844, and the factor loads of the items in the psychosocial subscale vary from 0.502 to 0.770.

Table 2. Subscales of the Menstruation Impact Scale Factor Loads for Items

Item (I) number	Common Factor Variance	Factor Loads	
		Physical Impact Subscale	Psychosocial Impact Subscale
I1	.629	.793	---
I2	.648	.788	---
I3	.380	.578	---
I4	.615	.768	---
I5	.730	.844	---
I6	.680	.801	---
I9	.596	---	.745
I10	.624	---	.770
I11	.600	---	.766
I16	.571	.711	---
I17	.524	---	.695
I19	.283	---	.502
I21	.461	---	.678
I29	.348	---	.554

Reliability Analysis Results

After the analysis performed to find out the internal consistency reliability of the Menstruation Impact Scale, the Cronbach's Alpha values for the overall MIS and it physical impact and psychosocial impact subscales were calculated as α=0.87, α=0.89 and α=0.80 respectively. Besides determining the Cronbach's Alpha coefficient, the split-half reliability coefficients obtained by dividing the items into two equivalent halves were also calculated. Accordingly, the Spearman value was calculated as r=0.77 while the Guttman value was calculated as r=0.76. For the first group, obtained from the two halves that have been formed within the estimation process of the Spearman and Guttman, the Alpha coefficient was found to be α1=0.85 while it was calculated as α2=0.76 for the second group.

The Spearman value of the physical impact subscale was calculated as r=0.86 and the Guttman value was determined as r=0.85. The alpha coefficient for the first group obtained from the two halves that have been formed within the estimation process of the Spearman and Guttman was found to be α1=0.80, while the alpha coefficient for the second group was α2=0.84.

The Spearman value of the psychosocial impact subscale was calculated as r=0.77 and the Guttman value was r=0.68. For the first group, obtained from the two halves that have been formed within the estimation process of the Spearman and Guttman, the Alpha coefficient was calculated as α1= 0.80, and the alpha coefficient for the second group was α2=0.70 as well.

Findings obtained via the Item Analysis of the Menstruation Impact Scale (Item-Total, Item-Remaining, and Distinctiveness)

As also seen in Table 3, the results of the "Pearson Multiplication Momentum Correlation Analysis" performed for item-total and item-remaining correlations demonstrated that the relationship between all the items in the inventory and the total score was statistically significant at the p<.001 level. Additionally, the results of the "independent group t-test" administered to find out the distinctiveness of the items demonstrated that the difference between the averages of the lower and upper groups for all the items was statistically significant at the p<.001 level.

Table 3. Item Analysis Results for the Menstruation Impact Scale (Item Remaining, Item Total, Item Discrimination)

Item (I) number	Item remaining		Item total		Item discrimination		
	r	p	r	p	t	SD	p
I1	.869	0.000	.537	0.000	15.88	330	0.000
I2	.864	0.000	.638	0.000	23.35	330	0.000
I3	.870	0.000	.504	0.000	15.78	330	0.000
I4	.865	0.000	.615	0.000	21.08	330	0.000
I5	.863	0.000	.656	0.000	22.45	330	0.000
I6	.863	0.000	.670	0.000	24.18	330	0.000
I9	.868	0.000	.550	0.000	20.01	330	0.000
I10	.868	0.000	.549	0.000	19.00	330	0.000
I11	.871	0.000	.501	0.000	16.72	330	0.000
I16	.864	0.000	.633	0.000	19.83	330	0.000
I17	.870	0.000	.520	0.000	15.92	330	0.000
I19	.874	0.000	.427	0.000	11.87	330	0.000
I21	.877	0.000	.390	0.000	12.78	330	0.000
I29	.874	0.000	.431	0.000	11.72	330	0.000

Another dimension of the reliability study in the scale adaptation study is to apply the adapted scale to the same group in a certain time interval (between the 2nd and 4th weeks) and to review the relationship.between. them by using the "Pearson Product Moments Correlation"

coefficient technique (17). For this purpose, the same test was administered twice at an interval of two weeks and the outcomes of the statistical operations on the results obtained are as seen in table 4.

Test-Retest Results Based on General and Subscales of the Menstruation Impact Scale

The analysis of the relationship between the results of the first and second administrations of the Menstruation Impact Scale in Table 4 demonstrated that the relationship was r=0.987 p<.001 for the overall Menstruation Impact Scale, r=0.987 p<.001 for the physical subscale and r=0.983, p<.001 for the psychosocial dimension.

Correlation Results between General and Subscale Scores of Menstruation Impact Scale and those of Menstruation Symptom Scale

A moderate and significant positive linear relationship was determined between the scores for the overall Menstruation Impact Scale, and the scores for the negative effect/somatic complaint subscale of the Menstruation Symptom Questionnaire (r=0.341, p<.001).

Table 4. Test-Re-Test Results Based on General and Subscales of the Menstruation Impact Scale

	Variables	First Evaluation					
		Menstruation Impact Scale Total Score		Physical Impact Subscale Total Score		Psychosocial Impact Subscale Total Score	
		r	p	r	p	r	p
Second Evaluation	Menstruation Impact Scale Total Score	.987	.000	***	***	***	***
	Physical Impact Subscale Total Score	***	***	.987	.000	***	***
	Psychosocial Impact Subscale Total Score	***	***	***	***	.983	.000

DISCUSSION

As a result of the study, the 14-item structure of MIS, together with its physical and psychosocial subscales, was found to be valid and reliable. Likewise, Test-retest reliability, parallel form reliability and internal consistency values were at acceptable levels. To confirm the content validity of the MIS, a detailed outline is created containing the dimensions of the feature to be examined. In the next process, the researcher should determine how the items covering the feature to be examined should be formed, their content and structure (18). In line with the literature, the scope and content structure of the items to be included in the draft scale were determined, and 51 items were obtained prior to consulting the expert opinion during the MIS development phase. In the first stage of the validity study of the scale, the content validity was examined. Within the scope, the relevance/validity levels of the items in the scale were determined by consulting the field experts' opinions. Experts were asked to evaluate each item and convey correction suggestions if any. Those that were found to be statistically insignificant among the CVRs obtained for the items were eliminated. The Content Validity Index (CVI) was calculated by averaging the total CVRs of these items (16). As the result, 17 items out of 51 were removed from the scale, and the process continued with the remaining 34 items.

Factor analysis in the scale and the suitability of the data are evaluated through Kaiser Meyer Olkin (KMO) and Barlett tests. With KMO, whether the distribution is suitable for factor analysis or not is checked. KMO value above 0.60 is accepted (19, 20). The KMO value for the MIS is 0.90, which suggests that the sample size is adequate for the factor analysis. It is tested with the Barlett test that the data come from the multivariate and normal distribution. Along with the Barlett test, the hypothesis that the "correlation matrix is equal to the unit matrix" is tested. Due to the rejection of the hypothesis, it is understood that the correlation between the variables is different from 1.00, which means that the concept we measure is multivariate in the universe parameter. The higher the result of the Bartlett's test is, the more likely it is to be significant (19,20). Bartlett's test value of the MIS was determined as 3649.0 (p<.001). This result indicates that the data are suitable for the factor analysis.

Exploratory factor analysis was performed to confirm the construct validity of the scale and the "Varimax Rotation Method" was used. One of the most commonly used statistical methods, to ensure construct validity in validity-reliability studies, is factor analysis. The Eigenvalue is used to determine the factors during exploratory factor analysis. Factors whose eigenvalue is ≥1 are used (21, 22)). The eigenvalue is taken into consideration while the variance explained by the factors is calculated, and the number of important factors is decided. In factor analysis, factors whose eigenvalue is ≥1 are considered important. In the present study, the eigenvalue was assumed as 1.00, and six factors were determined. When the eigenvalue line graph of the factors given in Figure 1 is examined, a breakpoint is seen in the second factor and a smooth distribution is observed after this point in the graph. Here, it was decided that the number of factors in the scale could be limited to two. As demonstrated in table 2, the first factor with an

eigenvalue of 5.54 accounted for 31.83% of the variance, and the second factor with an eigenvalue of 2.14 accounted for 23.09% of the variance. The two factors accounted for 54.92% of the total variance. It has been reported in the literature that the total explained variance should be at least 40% during the scale development phase. As this value gets higher, the strength of the factor structure increases as well (23). In this case, it has been assumed that the total variance value explained MIS had a strong factor structure. The factor loading value explains the relationship between the items and the subscales. According to the literature, factor loadings ranging from 0.30 to 0.40 can be taken as the lower cut-off point in factor pattern formation. If an item is included in more than one factor, the item is transferred to one having a higher loading value. But in such a case, there should be a difference greater than 0.10 between the two loading values. In this study, 0.40 was accepted as the lower cut-off point (19). The review of the results of the three-stage factor analysis demonstrated that the factor loading value of some items was below 0.40 or they had high loading values in both factors and the difference was smaller than .10. Based on these criteria, 20 items (items 7, 8, 12, 13, 14, 15, 18, 20, 22, 23, 24, 25, 26, 27, 28, 30, 31, 32, 33, 34) were deleted and the factor analysis was performed again. After the analysis, the "Menstruation Impact Scale" including two subscales and 14 items took its final form. After factor rotation, the first subscale of the scale included seven items (items 1, 2, 3, 4, 5, 6, 16) and the second subscale, the psychosocial dimension, included seven items (items 9, 10, 11, 17, 19, 21, 29).

Internal consistency, which is used to test the reliability of the scale, is checked in Likert-type scales by using the Cronbach alpha coefficient for the overall MIS and its subscales. A high Cronbach's alpha coefficient indicates that the items in the scale are inter-consistent and that they measure the same variable, whatever the variable being measured (24). The accepted lower limit of the Cronbach alpha coefficient is 0.60 (22). Again, Spearman and Guttman values are also checked in the calculation of the reliability coefficient. These values are called "internal consistency coefficients." Reliability coefficients should be above 0.60 (25, 26). Dealing with MIS, the Cronbach alpha coefficients obtained from the factors and the sum of the scale, the Spearman and Guttman values were all greater than the lower limit of 0.60. These results showed that the items in the subscales were inter-related, and the subscales consisted of the items which evaluate the same feature. Another way to calculate internal consistency is to perform "discriminant analysis" through the calculation of the "item-total score and item-remaining correlations". "Item-total correlation" is based on investigating the relationship between the score obtained from each test item (variance of each test item) and the total score obtained from the test. As usually accepted in the literature; 1. if the corrected "item-total correlation coefficient" is .30 and above, then the item is an agreeable one, 2. if the same coefficient has a value between 0.20 and 0.30 then the item can be included in the measurement tool, 3. if the coefficient is below 0.20 then the item should be removed from the measurement tool (27,28). As for the item-remaining correlation, the relationship between the score obtained from a certain item and the score obtained from the entire test in the exclusion of that item is examined. The way to calculate the discrimination analysis is to perform the value discrimination of the scale and the t-test analysis which is used for unrelated groups. The higher the scale value coefficient, the more distinctive value the relevant item has. Moving into the t-test, the distinctiveness is determined not by how big the t coefficient (critical ratio) is, but by the high level of significance (24). Within this scope, item-total, item-remaining and discrimination analysis were fulfilled to calculate the internal consistency of the Menstruation Impact Scale. The results of the "Pearson Product Moment Correlation" analysis performed for item-total and item-remaining correlations indicate a statistically significant relationship between all the items in the inventory and the total score at the p<.001 level. In addition, the results of the independent group t-test performed to determine the distinctiveness of the items indicate that the difference between the averages of the lower and upper groups for all the items was statistically significant at the p<.001 level. The results confirm that the items are distinctive in terms of the feature they measure and that each item is in the same structure. Based on these results, we concluded that all the items were reliable.

In the adaptation study of the MIS, another dimension of the reliability study is to administer the adapted scale to the same group at a certain interval (between the 2nd and 4th weeks) and to investigate the relationship between them using the "Pearson Product Moments Correlation coefficient" technique. In other words, it is the coefficient of correlation between the previous and subsequent measurements. This technique, which is the most applied one in practice, is more commonly known as the "test-retest" technique (17). The analysis of the relationship between the results of the first and second administration of the Menstruation Impact Scale in terms of the overall score demonstrates a statistically significant relationship at the level of (1) r=0.987, p<.001 for the relationship between the first and second administrations of the Menstruation Impact Scale, (2) r=0.987, p<.001 for the relationship between the first subscale and first-and-second administrations, (3) r=0.983, p<.001 for the relationship between the second subscale and first-and-second administrations.

In equivalent scale validity a moderate and significant positive linear relationship was determined between the scores for the overall Menstruation Impact Scale, and the scores for the negative effect/somatic complaint subscale of the Menstruation Symptom Questionnaire (r=0.341, p <.001). According to this result, as the general scores of the MIS increase, the negative effects/somatic complaints subscale scores of the MSQ also increase. "Convergent-divergent validity" is based on the assumption that the scale's dimension score, which concerns a certain area, is

highly correlated with the same dimension of another similar scale, which is claimed to question the same concept, or with some other parameters that show the same thing (29). Since there is no other scale that measures exactly the same feature here, the subscale of Negative effects/somatic complaints in the MSQ was chosen as a similar scale. Negative effects/somatic complaints" subscale is similar to MIS although it does not measure the same feature. In this case, a moderate correlation between MIS and Negative effects/somatic complaints subscale was thought to be an expected result.

Limitations

The reliability and validity study of the MIS was conducted only in Turkish. The validity and reliability of the MIS should be tested in different cultures and introduced to the literature.

CONCLUSION

The measurement tool developed to measure the effects of menstruation in this methodological study is considered as a valid and reliable tool. The MIS is a short, practical and easy-to-apply scale. Our findings show that menstruation affects women's lives both physically and psychosocially. We expect that this scale we developed adds a novelty to the literature since no other measurement tool measures the effects of specific menstruation on women's life, independent of dysmenorrhea and premenstrual syndrome. In future studies, conducting descriptive studies to investigate the relationship between the effects of menstruation with many concepts such as anxiety, depression, personality traits, sexual attitude, gender and introducing them to the literature is of great importance. More importantly, randomized controlled experimental studies such as psychoeducational practices to reduce the effects of menstruation may be valuable in terms of bringing evidence-based practices to the literature.

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MIS (The Menstrual Impact Scale)

Physical impact subscale

1. I get restricted in my physical activities when I am on my period.
2. I avoid staying out long when I am on my period.
3. I try not to wear tight clothes when I am on my period.
4. I avoid activities such as running that require physical effort when I am on my period.
5. I cannot perform my daily routine activities as easily as usual when I am on my period.
6. I have difficulty participating in social activities when I am on my period.
7. My period may prevent me from being physically active.

Psychosocial Impact subscale

8. It is embarrassing for me if people around me realize I am on my period.
9. I try to hide that I am on my period.
10. I do not want my male friends to know that I am on my period.
11. I hesitate to tell the people around me that I am on my period.
12. I feel sluggish when I am on my period.
13. I hesitate to purchase menstrual pads/bumpers.
14. When I need to change my menstrual pad, I carry it in a way that those around me will not see it.

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Research Article

Determination of Anthropometric Measurements that may be Associated with Difficult Intubation in Children

Çocuklarda Zor Entübasyon ile İlişkili Olabilecek Antropometrik Ölçümlerin Belirlenmesi

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Abstract

Aim: Difficult tracheal intubation is a fundamental cause of perioperative morbidity and mortality. The frequency of difficult intubation is thought to be higher in the pediatric age group due to the different anatomical and physiological structures, and it may not be easy to detect this beforehand. Anthropometric measurements were evaluated before the elective operation and the relationship of some parameters with difficult intubation.

Material and Method: This prospective cross-sectional study was conducted on 90 pediatric patients aged 2-14 who underwent elective surgery under general anesthesia. All patients' age, gender, height, weight, body surface area (BSA), and body mass index (BMI) records were recorded before the operation. Mallampati scoring, head and neck circumference, thyromental distance measurements, and head circumference/neck circumference ratio were performed. Cormack-Lehane (CL) scoring and endotracheal intubation were applied during direct laryngoscopy of the operated patients. Children with easy intubation (CL grade 1 and 2) group 1; children who underwent difficult intubation (CL grade 3 and 4) were defined as group 2.

Results: There was no significant relationship between Groups I and II in terms of age, height and weight values. There was no significant relationship between the two groups with BSA and thyromental distance measurements. Mallampati scores were found to be grades 3 and 4 (3.3%) in three of the 90 patients, and CL scores of 3 and 4 (4.4%) in four patients. A significant correlation was found between Mallampati scoring and CL scoring. A statistically significant difference was found between the two groups regarding head/neck ratios and BMI.

Conclusion: In our study, head circumference/neck circumference ratio and BMI were found to be helpful while predicting difficult intubation in children with normal physical characteristics, 2-14 years of age, who underwent elective surgery. Our findings can be supported by further studies that will be planned and include more patients.

Keywords: Difficult intubation, head/neck ratio, body mass index, Cormack-Lehane score, Mallampati score

Öz

Amaç: Zor trakeal entübasyon, perioperatif morbidite ve mortalitenin önemli bir nedenidir. Pediatrik yaş grubunda anatomik ve fizyolojik yapıların farklı olması nedeniyle zor entübasyon sıklığının daha fazla olduğu düşünülmekte olup, bunu önceden saptamak kolay olmayabilir. Elektif operasyon öncesinde değerlendirilen antropometrik ölçümler ve bazı parametrelerin zor entübasyanla ilişkisi değerlendirilmiştir.

Materyal ve Metot: Bu kesitsel prospektif çalışma, genel anestezi altında elektif cerrahi uygulanan, 2-14 yaş arasındaki 90 çocuk hastada yapılmıştır. Operasyon öncesinde tüm hastaların yaş, cinsiyet, boy, kilo, vücut yüzey alanı (VYA) ve vücut kitle indeksi (VKI) kayıtları yapıldı. Mallampati skorlaması, baş ve boyun çevresi, tiromental mesafe ölçümleri, baş çevresi/boyun çevresi oranlaması yapıldı. Operasyona alınan hastaların, direk laringoskopi işlemi sırasında Cormack-Lehane (CL) skorlaması ve endotrakeal entübasyon uygulandı. Kolay entübasyon uygulanan çocuklar (CL grade 1 ve 2) Grup 1; zor entübasyon uygulanan çocuklar (CL grade 3 ve 4) Grup 2 olarak tanımlandı.

Bulgular: Grup I ve II arasında yaş, boy ve kilo değerleri açısından anlamlı ilişkisi saptanmadı. İki grup arasında, vücut yüzey alanı ve tiromental mesafe ölçümleriyle de anlamlı ilişki saptanmamıştır. 90 hastanın 3 tanesinde Mallampati skoru grade 3 ve 4 (%3.3), 4 tanesinde CL skoru 3 ve 4 (%4.4) saptandı. Mallampati skorlaması ile Cormack-Lehane skorlaması arasında anlamlı bir ilişki saptandı. İki grup arasında, baş/boyun oranları ve VKI açısından anlamlı fark saptanmıştır.

Sonuç: Çalışmamızda, elektif ameliyat edilen, normal fiziksel özellikteki, 2-14 yaş çocuk hastalarda, baş çevresi/boyun çevresi oranı ve VKI zor entübasyonu öngörmede prediktif olabileceği bulunmuştur. Bulgularımız, yeni planlanacak ve daha çok sayıda hastayı içeren farklı çalışmalarla desteklenebilir.

Anahtar Kelimeler: Zor entübasyon, baş/boyun oranı, vücut kitle indeksi, Cormack-Lehane skoru, Mallampati skoru

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INTRODUCTION

Difficult tracheal intubation is a common problem in clinical practice and is an important cause of perioperative morbidity and mortality (1). It has been reported that difficult intubation is encountered in 1.5-13% of patients undergoing general anesthesia (2). Due to the different anatomical and physiological structures, it may not be easy to determine difficult intubation in the pediatric age group. Studies report that the difficult intubation frequency is higher in children (3,4). When difficult intubation is encountered in the pediatric age group, arterial oxygen saturation decrease rapidly, leading to a decrease in the opportunity for intubation and a life-threatening situation such as brain damage and cardiac arrest (5). Therefore, anesthesiologists need to detect difficult airways in advance, prepare special equipment, and have good experience in airway management in the pediatric age group.

Studies on parameters and tests evaluated in predicting difficult intubation were mainly conducted in the adult patient group. Mallampati and modified Mallampati tests are widely used in clinical practice. In addition, some measurements help predict difficult intubation in adult patients (6-12).

There is insufficient data for predictive factors for difficult intubation in pediatric patients, and there is no complete consensus on parameters that may be associated with difficult intubation (5,13,14). This study evaluated the relationship between anthropometric measurements, thyromental distance, head circumference/neck circumference ratio, and difficult intubation in children aged 2-14.

MATERIAL AND METHOD

This prospective study was conducted at İzmir Bakırçay University Çiğli Training and Research Hospital. İzmir Bakırçay University approved the study plan, Non-Interventional Clinical Research Ethics Committee (Date: 08.04.2021, Decision No: 240, Research No: 221). Consent was obtained from the parents of all patients. Ninety patients aged 2-14 years, who underwent elective surgery under general anesthesia, underwent endotracheal intubation, and with physical status, ASA I-II were included in the study. Those who did not accept to participate in the study, those who developed complications during surgery, those who had a mass in the head and neck region, who had previously undergone a surgical operation in the head and neck region, and/or those who received radiotherapy and cases of surgical emergencies were not included in the study.

Age and gender records, height, and weight measurements for all patients before the operation were done by the same medical staff. Body surface area (BSA) and body mass index (BMI) calculations were made. Mallampati scoring was done while the patient was in the sitting position. Head circumference, neck circumference, and thyromental distance were measured in the supine position with a non-flexible tape measure. Head circumference was measured at the widest part of the head, passing over the glabella, occipital protuberance, and ears. Neck circumference was measured at the level of the cricoid cartilage. The head circumference/neck circumference ratio was calculated. Thyromental distance was measured with the patient's head fully extended and mouth closed. The distance between the thyroid cartilage protrusion and the midpoint of the chin tip was measured.

Before the operation, standard monitoring of the patients in the operating theatre (electrocardiogram, blood oxygen saturation, non-invasive blood pressure measurement) was performed. For the induction of general anesthesia, intravenous 1-2mcgr/kg fentanyl, 2-3mg/kg propofol, and 0.5-0.6 mg/kg rocuronium were administered. Patients were ventilated with a balloon mask for 1.5-2 minutes by giving 100% oxygen. An experienced anesthesiologist performed Cormack-Lehane (CL) scoring and endotracheal intubation during the direct laryngoscopy procedure. The same anesthesiologist performed all procedures.

CL classification: grade 1; glottis fully visible, grade 2; glottis partially visible, grade 3; only the epiglottis visible, grade 4; defined as no epiglottis visible. Group I, 'easy intubation' (CL grades 1 and 2); group II was defined as children who underwent 'difficult intubation' (CL grade 3 and 4) (13,15).

Statistical analyses were performed using the IBM SPSS statistics 22 package program. The mean and standard deviation of descriptive statistics were used. The Kolmogorov-Smirnov test was used to check whether each data group conformed to the normal distribution. An Independent sample t-test was used to compare groups with normal distribution, and the Mann-Whitney U test was used to compare paired groups without normal distribution. Fisher Chi-square independence test was used to compare categorical data, and $p<0.05$ was considered significant.

RESULTS

Of the 90 children participating in the study, 25 were girls, and 65 were boys. There were 83 children in group I and 7 children in group II.

Average age; 6.51/year in group I and 8.14/year in group II. Average height measurements were 119.26cm in group I and 125.14cm in group II. The mean weight measurements were 27kg in group I and 40.14 kg in group II (Table 1). No significant correlation was found between groups I and II, which showed the degree of intubation difficulty in terms of age, height, and weight ($p=0.161$, $p=0.417$, $p=0.053$; respectively). BSA averages; are 0.93/m2 in group I and 1.17/m^2 in group II. The mean thyromental distance measurements were 5.60cm in group I and 5.63cm in group II (Table 1). There was no significant relationship between the two groups with BSA and thyromental

distance measurements (p=0.116, p=0.716; respectively). Mallampati scores were grades 3 and 4 (3.3%) in three of the 90 patients, and CL scores of 3 and 4 (4.4%) in four patients. A significant correlation (dependence) was found between Mallampati scores and CL scores (p=0.014).

Head circumference was 51.74 cm in group I, 23.24cm in group II; neck circumference was 29.31 cm in group I and 32cm in group II (Table 1). While no significant difference was found between the groups in the mean head circumference ratios (p=0.136), a significant difference was found in the mean neck circumference (p=0.024). The head circumference/neck circumference ratio follows the normal distribution (p=0.200 in group I, p=0.200 in group II by Student's t-test). The mean head/neck ratio was 1.77 in group I; 1.67 was detected in group II. A statistically significant difference was found between the head/neck ratios and the two groups showing the risk of difficult intubation (p=0.023). In children with a large neck circumference, the head/neck ratio is reduced, the CL score and the risk of difficult intubation increase.

BMI was calculated as 17.61 kg/m² in group I and 24.21kg/m² in group II (Table 1). A significant difference was found between the two groups in terms of BMI (p=0.006). It was determined that the risk of difficult intubation increased as the BMI increased.

Table 1. Demographic and Anthropometric Characteristics of the Patients

Variable	Mean±SD		P value
	Group I	Group II	
n	83	7	
Age (years)	6.51±3.44	8.14±2.85	0.161
Height (cm)	119.26±22.42	125.14±22.32	0.417
Weight (kg)	27±14.72	40.14±17.24	0.053
Body surface area (m^2)	0.93±0.33	1.17±0.37	0.116
Body mass index	17.61±3.43	24.21±5.90	0.006
Thyromental distance (cm)	5.60±0.69	5.63±0.43	0.716
Head circumference (cm)	51.74 ±2.82	53.24 ±2.08	0.136
Neck circumference (cm)	29.31±2.75	32±2.94	0.024
Head/neck circumference ratio	1.77±0.11	1.67±0.11	0.023

Data are expressed as the mean ± SD

DISCUSSION

Although the incidence of complications in airway management in children is higher than in adults, the number of studies to identify predictors of difficult intubation is less. Airway management may become more difficult in craniopharyngeal and mandibular abnormalities due to various syndromes and congenital abnormalities. In this study, predictors of difficult intubation were compared in normal children aged 2-14 years without additional abnormalities and syndromes. The incidence of difficult intubation was around 3-5%, similar to many previous studies (2). We did not have any patients who could not be intubated. Our study was conducted with CL and Mallampati scores, shown in previous studies to be associated with difficult intubation and predict difficult intubation. Therefore, we think our study is more valuable than predictive studies with a single scoring system.

Vieira Santos et al. evaluated the correlation between the Mallampati scores, which were evaluated as a preanesthetic, and the CL scores, which were evaluated after anesthesia induction, in 108 pediatric patients aged 4-8 years who did not have congenital, genetic, and cognitive impairments that could cause difficult intubation. They showed that the two scoring systems were correlated and the applicability of the Mallampati score in this age group (16). In our study, children aged 2-14 years were evaluated, and in our findings, it was found that the two scoring systems were correlated with each other.

Kim WH et al. evaluated the relationship between neck circumference/thyromental distance ratio in adult patients and difficult intubation in obese patients. BMI, Mallampati score, Wilson score, neck circumference, thyromental distance, sternomental distance, the width of mouth opening, and history of difficult intubation were also included in the study. In obese patients, neck circumference/thyromental distance ratio, Mallampati score, and Wilson score have been reported as predictive parameters for difficult intubation (17). Unlike this study, our study was conducted on pediatric and non-obese patients. Although some of the parameters we evaluated were similar to those in this study, the head circumference/neck circumference ratio and BMI, which we found to be essential parameters in predicting difficult intubation in our patient age group, were not evaluated in this study. We think that these two parameters are significant findings.

Shirgoska et al. evaluated the CL and Mallampati scores, predictive tests for difficult intubation and airway, in 600 adults and 150 pediatric patients. They found Mallampati score of grades 3 and 4 in 3.2% of all patients and CL scores of 3 and 4 in 35%. They reported that evaluation of several parameters such as BMI, head and neck movement, tooth condition, upper lip bite test, incisor gap, and thyromental distance would be more effective and reliable for an effective and reliable estimation of difficult intubation (13). In our study, it was determined that Mallampati and CL scores were correlated with each other. However, it would be an essential advantage if other measurements supporting these two parameters were predictive in this challenging patient group. The head/neck circumference ratio can be evaluated for this purpose.

Mansano et al. evaluated the relationship between difficult intubation with some anthropometric measurements in 446 pediatric patients under 12 years of age, divided into three according to age group. Height, weight, neck circumference, BMI, the distance between incisors, thyromental distance, sternomental distance, distance from the frontal plane to the chin, and Mallampati score were determined. These

parameters were correlated with the CL score. CL scores of 3 and 4 were found in 3.58% of patients. In these patients, difficult intubation was significantly associated with short incisor distance, a considerable distance from the frontal plane to the jaw, thyromental distance, sternomental distance, and Mallampati score (14). Although some of the parameters evaluated in our study and this study are similar, there are also different parameters. Head/neck circumference ratio, which was not evaluated in this study, and BMI, which was not significantly correlated, were found to be associated with difficult intubation in our study. It may be because a significant number of patients under the age of two were also included in this study. Neither study found a relationship between the thyromental distance and difficult intubation.

Liu et al. evaluated parameters associated with difficult intubation in 96 infants with Pierre-Robin syndrome. BSA, gender, and weight were associated with difficult intubation. A correlation was also found between difficult tracheal intubation and the throat region (18). Our study was carried out in normal children who do not have additional problems and between the ages of 2-14; gender, weight, and BSA were not associated with difficult intubation in our study either. In addition, head circumference and thyromental distance, which we evaluated, were not evaluated in this study.

Shahhosseini et al. evaluated some parameters to predict difficult intubation in children under two years of age. 405 patients who underwent general anesthesia with elective surgery and endotracheal intubation were included in the study. Age, height, weight, sternomental distance, mouth opening, neck circumference, acromio-axillo-suprasternal paddy index, and intubation difficulty scale score were evaluated. They reported that age, height, weight, and sternomental distance could be significant predictors for difficult intubation. The age group in this study is entirely different from our patient group. In this study, parameters such as mouth opening, and neck circumference were not significant with difficult intubation due to the inability to fully evaluate the patients because they were under two years of age (5). We think that the head/neck circumference ratio and BMI parameters, which were not evaluated in this study, may be important indicators for our study.

CONCLUSION

In conclusion, head circumference/neck circumference ratio and BMI may predict difficult intubation in children aged 2-14 years with normal physical characteristics who underwent elective surgery. It can be used simultaneously to predict difficult preoperative intubation. Parameters such as gender, age, height, weight, and thyromental distance, which had different results in previous studies and our study, can be evaluated in the group of pediatric patients who are similar to each other in terms of various characteristics.

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Conflict of interest: *The authors declare that they have no competing interest.*

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Research Article

Determination of the Frequency of Gastric Intestinal Metaplasia and Its Association with Helicobacter Pylori

Gastrik Intestinal Metaplazi Sıklığı ve Helikobakter Pilori ile İlişkisinin Belirlenmesi

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Abstract

Aim: Gastric intestinal metaplasia (IM) is a precancerous lesion in the pathway to gastric cancer. Helicobacter pylori (HP) is a bacterium that has been associated with an increase in the development of non-cardia gastric cancer and is involved in the development of gastric IM and atrophic gastritis. In this study, we aimed to determine the frequency of IM and its relationship with HP in patients undergoing endoscopic examination with the indication of dyspepsia.

Material and Method: The study included 2530 patients who underwent upper gastrointestinal system endoscopy and had gastric biopsy at the Karadeniz Technical University Farabi Hospital Gastroenterology Clinic due to dyspepsia between January 2019 and January 2020. Demographic characteristics of the patients such as age and gender, biopsy findings (presence of IM, HP, atrophy, dysplasia) were evaluated retrospectively.

Results: A total of 2530 cases, 1344 (53.1%) women and 1186 (46.9%) men, with a median age of 53 (18-93) years were included in the study. HP was detected in 27.8% of the cases and IM was detected in 26.8%. The median age of 677 patients with positive IM was 59 (19-92) years, and 29.7% (n=352) were male. While no significant difference was found between the sexes in terms of median age within the IM positive and negative groups (p=0.584, p=0.642, respectively), the median age and male sex ratio were higher in patients with IM positive than those with IM negative (p<0.001, p=0.002, respectively). While the rate of HP positivity among male patients was 31% (n=368), the same rate was 24.9% (n=334) among female patients (p=0.001). The male gender was significantly higher in HP positive patients (52.4% vs. 47.6%), and the median age was significantly lower in HP positive patients (p<0.001). There was no significant difference in HP positivity between IM positive and negative patient groups (p=0.341).

Conclusion: IM was more common in older and male patients. HP positivity was found more frequently in male and young patients. No significant difference was found in the frequency of IM and HP.

Keywords: Intestinal metaplasia, helicobacter pylori, gastric atrophy

Öz

Amaç: Gastrik intestinal metaplazi (IM) mide kanserine giden yolda prekanseröz bir lezyondır. Helikobakter pilori (HP) non-kardia mide kanseri gelişiminde artış ile ilişkilendirilen, gastrik IM ile atrofik gastrit gelişiminde rol alan bir bakteridir. Bu çalışma ile dispepsi endikasyonu ile endoskopik inceleme yapılan hastalarda IM sıklığını ve HP ile ilişkisini belirlemeyi amaçladık.

Materyal ve Metot: Çalışmada Ocak 2019-Ocak 2020 tarihleri arasında dispepsi nedeni ile Karadeniz Teknik Üniversitesi Farabi Hastanesi Gastroenteroloji Kliniği'nde üst gastrointestinal sistem endoskopisi yapılıp mide biyopsisi alınan 2530 hastanın yaş ve cinsiyet gibi demografik özellikleri ile biyopsi bulguları (IM, HP, atrofi, displazi varlığı) retrospektif taranarak değerlendirildi.

Bulgular: Çalışmaya median yaşı 53 (18-93) yıl olan 1344 (%53,1) kadın ve 1186 (%46,9) erkek toplam 2530 olgu dahil edildi. Olguların %27,8'inde HP ve %26,8'inde de İM tespit edildi. İM pozitif olan 677 hastaların median yaşı 59 (19-92)yıl idi ve %29,7'si (n=352) erkekti. IM pozitif ve negatif gruplar içinde cinsiyetler arasında median yaş açısından anlamlı farklılık saptanmazken (Sırasıyla p=0,584, p=0,642), IM pozitif saptanan hastalarda median yaş ve erkek cinsiyet oranı IM negatif olanlara nazaran daha yüksekti (Sırasıyla p<0,001, p=0,002). Erkek hastalar arasında HP pozitiflik oranı %31 (n=368) iken aynı oran kadın hastalar arasında %24,9 (n=334) (p=0,001) idi. HP pozitif hastalarda erkek cinsiyet belirgin olarak daha yüksek idi (%52,4'e karşılık %47,6) HP pozitif olanlarda median yaş anlamlı olarak daha düşük idi p<0,001). IM pozitif ve negatif saptanan hasta grupları arasında HP pozitifliği açısından anlamlı farklılık saptanmadı (p=0,341).

Sonuç: IM ileri yaşlarda ve erkek hastalarda daha fazla bulundu. HP pozitifliği erkek ve genç hastalarda daha fazla bulundu. IM ve HP sıklığı açısından anlamlı farklılık saptanmadı.

Anahtar Kelimeler: İntestinal metaplazi, helikobakter pilori, gastrik atrofi

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INTRODUCTION

Gastric cancer ranks third among cancer-related deaths in the world (1). Gastric intestinal metaplasia (IM) is a precancerous lesion found in Correa's cascade, a model on the pathway to gastric cancer, and is histologically defined as the alteration of the oxyntic and antral mucosa to the intestinal mucosa consisting of panin, absorptive, and goblet cells (2) (Figure 1).

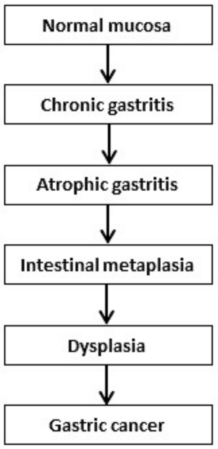

Figure 1. Correa's cascade

Gastric IM rarely causes specific symptoms. It is usually discovered incidentally in patients undergoing upper gastrointestinal endoscopy for dyspepsia.

Helicobacter pylori (HP) is a gram-negative bacterium classified by the World Health Organization (WHO) as a type 1 carcinogen, associated with a 3-fold increase in the development of non-cardia gastric cancer, and involved in the development of gastric IM and atrophic gastritis (3,4). It is estimated that nearly half of the world's population is infected with this pathogen (5). The Maastricht IV guidelines recommend HP infection treatment (6).

In this study, we aimed to determine the frequency of IM and its relationship with HP in different age and sex groups who underwent endoscopic examination with the indication of dyspepsia.

MATERIAL AND METHOD

The Ethics Committee of the Faculty of Medicine of Karadeniz Technical University approved the study under the number 2020/192. In the study, the data of 2530 patients who underwent upper gastrointestinal tract endoscopy (GIT) due to dyspepsia in the Endoscopy Department of Gastroenterology Clinic of Karadeniz Technical University Farabi Hospital, and who underwent gastric biopsy were retrospectively analyzed. Patients under 18 years of age and patients who had undergone gastric surgery were excluded from the study. First-time endoscopy results of patients with repeat endoscopies were included in the study, and subsequent endoscopy results were not included in the study (Figure 2).

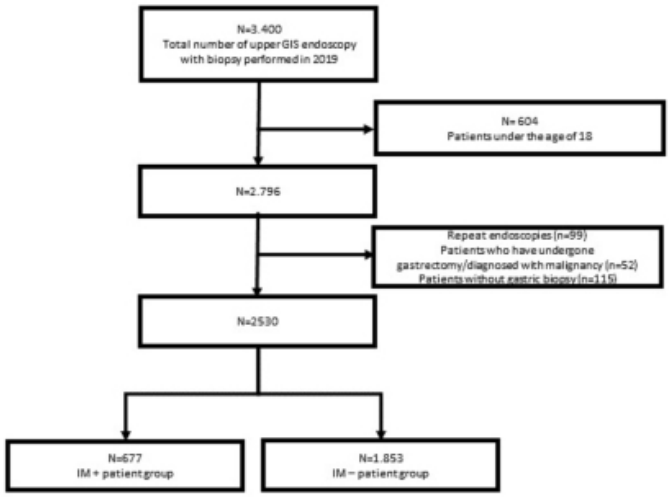

Figure 2. Flowchart of patients included in the study

Patient demographic characteristics such as age and sex, the regions where the gastric biopsy was taken (antrum, corpus, fundus, cardia), and biopsy findings (presence of IM, HP, atrophy, dysplasia) were evaluated.

Pentax, Olympus, or Fuji fiberoptic gastroscopes were used for the upper GI endoscopic procedures performed with sedoanalgesia after at least 8 hours of fasting. During the procedure, 2 biopsies were taken from at least one region of the antrum, corpus, fundus, and/or cardia of the stomach and placed in containers containing 5 ml formalin. The biopsy material was analyzed by the Giemsa method for HP and by the histochemical reaction PAS / AB pH 2.5 for IM.

Statistical analysis

Statistics 22.0 (IBM Corp., Armonk, NY, USA) for Windows package program was used for statistical tests. Continuous variables were evaluated with the histogram and Q-Q plot in terms of normal distribution, while they were evaluated with Shapiro-Wilk or Kolmogorov-Smirnov tests, depending on the number of variables. Normally distributed continuous variables were presented throughout the study as mean ± standard deviation, and the t-test for independent variables was used to compare the two groups. Other continuous variables were presented as median (minimum-maximum or IQR), and the nonparametric Mann-Whitney U test was used to compare the groups. Categorical variables were presented as frequency and percentage, and the Pearson chi-square test or Fischer's exact probability test was used to compare the groups. Tests with a p-value of 0.05 or less at the 95 percent confidence interval were considered statistically significant.

RESULTS

A total of 2530 cases, 1344 (53.1%) women and 1186 (46.9%) men, with a median age of 53 (18-93) years, were included in the study. HP was detected in 27.8% of cases and IM in 26.8% (Table 1).

Table 1. Sex, HP, and IM status of cases	
	Number of patients (%)
Total	2530 (100)
Female	1344 (53.1)
Male	1186 (46.9)
HP +	702 (27.8)
HP -	1828 (72.2)
IM +	677 (26.8)
IM -	1853 (73.2)

The median age of the 677 patients with positive IM was 59 (19-92) years, and 29.7% (n=352) were male (Table 2). While there was no statistically significant difference in median age between male and female sexes in IM positive and negative groups (p=0.584 and p=0.642, respectively), median age and male sex ratio were significantly higher in IM positive patients than in IM negative patients (p<0.001 and p=0.002, respectively) (Table 2).

Table 2. Relationship between IM status and gender and age				
	Total	IM +	IM -	p
Female, n (%)	1344 (100)	325 (24,2)	1019 (75.8)	0.002
Male, n (%)	1186 (100)	352 (29.7)	834 (70.3)	
Total	2530	677	1853	<0.001
Age (min-max)		59 (19-92)	50 (18-93)	
*IM: Intestinal metaplasia				

HP was positive in 27.7% (n=702) of patients. While the rate of HP positivity in male patients was 31% (n=368), the same rate in female patients was 24.9% (n=334) (p=0.001). Among HP-positive patients, the male gender was significantly more prevalent (52.4% vs. 47.6%). The median age was significantly lower in HP positive patients (p<0.001) (Table 3).

Table 3. Relationship of HP with gender and age				
	All patients	HP +	HP -	P
Total	2530 (100)	702 (27.7)	1828(72.3)	0.001
Male, n (%)	1186 (46,9)	368 (31)	818 (69)	
Female, n (%)	1344 (53.1)	334 (24.9)	1010 (75.1)	<0.001
Age, median (IQR)		48 (23)	55 (22)	
*HP: Helicobacter pylori				

HP was positive in 26.3% (n=178) of the 677 patients who tested positive for IM. While no statistically significant difference was found between genders in HP positivity for this subject (p=0.162), the median age was significantly lower in HP positive patients (p<0.001) (Table 4).

HP was positive in 28.3% (n=524) of patients in whom IM was negative. While the HP positivity rate was 32% (n=267) in IM-negative men and 25.2% (n=257) in women, the HP positivity rate was significantly higher in men than in women (p=0.001). The median age of HP-positive patients was significantly lower (p<0.001, median age 46 in HP-positive patients, 53 in HP-negative/positive patients) (Table 4).

Table 4. Gender and age relation according to HP positivity/negativity of intestinal metaplasia positive or negative patients				
		HP +	HP -	p (IM +/-)
IM +, n (%)		178 (26.3)	499 (73.7)	
	Female	77 (23.7)	248 (76.3)	0.162
	Male	101 (28.7)	251 (71.3)	
IM -, n (%)		524 (28.3)	1329 (71.7)	
	Female	257 (25.2)	762 (74.8)	0.001
	Male	267 (32)	567 (68)	
IM +, Age (IQR)		54 (20)	61 (19)	<0.001
IM -, Age (IQR)		46 (24)	53 (23)	<0.001
*IM: Intestinal metaplasia, HP: Helicobacter pylori				

There was no significant difference between IM positive and negative patient groups in terms of HP positivity (p=0.341) (Table 5). There was no significant relationship between dysplasia and Helicobacter positivity and male/female gender (p=0.374 and p=0.283, respectively).

Table 5. Relationship between HP and intestinal metaplasia				
	All patients	IM +	IM -	p
HP +	702 (27.7)	178 (25.4)	524 (74.6)	0.341
HP -	1828 (72.3)	499 (27.3)	1329 (72.7)	
Total	2530 (100)	677 (26,8)	1853 (73.2)	
*IM: Intestinal metaplasia, HP: Helicobacter pylori				

In the cases in which atrophy could be evaluated as pathologic, the frequency of atrophy was 0.9%. As expected, the frequency of atrophy was significantly higher at older ages (median (IQR) 62 (17), 53 (24), p=0.022, respectively). There was no significant difference between genders in terms of the frequency of atrophy (p > 0.05).

Dysplasia was significantly higher in patients with IM positive than in negative patients (p=0.004). 1.3% (n=9) of patients with IM positive had dysplasia and 1.2% (n=8) had atrophy, while atrophy could not be assessed in 31.8% (n=215). Dysplasia was found in 0.3% (n=5) of IM negative patients, while atrophy was found in 0.3% (n=6) and could not be assessed in 39.8% (n=737). Median age was higher in patients with dysplasia (median age (IQR) 66 (8), 53 (23), p<0.001, respectively).

DISCUSSION

Gastric cancer, the incidence of which is gradually decreasing, was the leading cause of cancer-related deaths in many European countries about 50 years ago (7,8). Although the incidence of gastric cancer has decreased because of the focus on diagnosis and eradication of HP after it was recognized as a type 1 carcinogen by the WHO it still causes more than 700,000 deaths per year in the world (9). Early diagnosis and treatment of HP play an important role in preventing the development of gastric cancer, as

some studies have shown that the development of chronic atrophic gastritis, IM, dysplasia, and carcinoma takes 16-24 years from the onset of HP-induced chronic active gastritis (10). Although it is said that the most important risk factor for the occurrence of IM is HP, discussions on this topic continue due to conflicting publications. There are different data from our country and different regions of the world about the incidence of IM, HP, and atrophy.

In the study conducted by Kösekli in the Denizli region, the frequency of IM was 16%, the frequency of atrophy was 0.2%, and IM and atrophy were observed more frequently in males ($p < 0.001$ and $p=0.006$, respectively) (11). In the study conducted by Tosun et al. in the Şanlıurfa region, the frequency of IM was 8.9% and atrophy 5.1% (12), while Özdil et al. found the frequency of IM to be 17.8% (13). In one study, the frequency of IM was found to be 18.1% in Konya (14), 8.62% in Istanbul, and more frequent in men (15). In our study, the frequency of IM was 26.8%, the frequency of atrophy was 0.9%, and IM and atrophy were more common in males ($p=0.002$).

Considering the frequency of IM and atrophy in relation to age, Tosun et al. found that the mean age of cases was significantly higher at IM (12). In contrast, Kösekli et al. found that the frequency of IM and atrophy was higher in patients older than 40 years (11), and Kesici et al. found that the frequency of IM was higher in patients older than 65 years ($p < 0.01$) (15). In our study, the median age of patients with IM and atrophy was significantly higher ($p < 0.001$), lwhich is consistent with the literature.

While Kösekli found the frequency of HP to be 71% (11), Tosun et al. 43.9% (12), Bor et al. 75.7% (16), Kesici et al. 34.61% (15), Korkmaz et al. 40% (14), Özdil et al. 71.3% (13). In the 2010 study by Erkut et al., the frequency of HP in the Trabzon region was reported to be 40.4% (17). Interestingly, the frequency of HP in our study was 27.7%, which was lower than that reported in the literature. The fact that no data could be obtained on whether patients had previously received HP eradication treatment and the increased frequency of patients who had received possible eradication treatment based on the recent history of our study may explain the low rate of HP positivity.

When the association between HP and gender was investigated, no significant gender difference was found in the study by Kösekli (11). In contrast, Kesici et al. found that the frequency of HP was higher in men (15). Our study observed HP more frequently in males ($p=0.001$).

When we look at the relationship between HP and age, the median age of HP-positive patients was significantly higher than that of HP-negative patients ($p<0.001$). In their study, Kesici et al. found that the prevalence of HP was lower at the age of 65 years compared to other age groups ($p<0.01$) (15).

In the study conducted by Tosun et al. it was found that the rate of atrophy was high in IM positive patients ($p<0.01$) (12). In our study, it was found that the rate of atrophy was higher in IM positive patients ($p=0.034$).

In the literature, there are publications with different results about the relationship between HP and IM. Tosun et al. and Topal et al. found no significant association between IM and HP ($p > 0.05$) (12,18). Studies by Crannen et al. and Aydın et al. found that IM was higher in HP positive cases than in negative cases (10,19). In contrast, Kesici et al. found that the frequency of IM was higher in HP -negative patients than in HP -positive patients (15). In our study, no statistically significant difference was found between HP and IM ($p=0.341$).

The main limitations of our study are that it was a single-center and retrospective study. In addition, the IM subgroups were not specified in the histopathology reports, and atrophy could not be assessed in some patients due to inadequate biopsy. Despite all this, we believe that such studies are necessary and useful to collect local data on HP and IM and to perform general evaluation and planning. Our study has once again demonstrated the need for multicenter prospective studies that address these limitations and provide standardization in the endoscopic and histopathologic evaluation (Sydney classification) of the biopsy and also consider potential risk factors and comorbidities. We hope that our study will not only enrich the local data in our country but also be a positive stimulus in this regard.

CONCLUSION

IM was more common in older and male patients. HP positivity was found more frequently in male and young patients. There was no significant difference in HP frequency in IM positive and negative patients. Atrophy was more common in IM positive patients.

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Ethical approval: *The Ethics Committee of the Faculty of Medicine of Karadeniz Technical University approved the study under the number 2020/192.*

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MEDICAL RECORDS-International Medical Journal

Research Article

Web-Based Bibliometric Evaluation of Robotic Radical Prostatectomy in Prostate Cancer: Analysis of Turkey Data

Prostat Kanserinde Robotik Radikal Prostatektominin Web Tabanli Bibliyometrik Değerlendirilmesi: Türkiye Verilerinin Analizi

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Abstract

Aim: Prostate cancers are the second most commonly diagnosed cancers in men. The developments in robotic surgery brought along a period in which all number of articles were written. This study, we researched the field and contribution of articles written in the world and in Turkey on robot assisted radical prostatectomy with bibliometric analysis in a web-based software.

Material and Methods: In our study, 1434 original articles in the world and 57 original articles in Turkey, which met the criteria, were scanned in ISI Web of Knowledge-Science (WoS) data base by using the keywords 'robot, prostate cancer, radical prostatectomy'. The parameters, country of the article, publication year of the article, WoS category of the article, the name of the journal where the article was published, type of the article (Original), language of the article (English) and WoS index (SCI-E), were evaluated with bibliometric analysis method.

Results: Analysis of countries points out that the United States of America ranked the first with 563 (39.2%) articles, while Turkey ranked in the 11th place with 57 (3.9%) articles. According to publication year, it was found that the highest number of articles published in the world was in 2020 with 173 (12.06%) articles, while it was in 2021 with 10 (17.5%) in Turkey. With respect to field categories in WoS data base, the world was found that the field of Urology-Nephrology ranked the first with 1042 (72%) articles, while similarly Urology-Nephrology ranked the first with 35 (61.4%) articles in Turkey. According to journal name, BJU International was the journal in which the highest number of articles were published in the world with 157 (10.9%), while Journal of Endourology was the journal in which the highest number of articles were published in Turkey with 10 (17.5%) articles. In the citations and H-index rates of articles by year, it was 78 in the world and 15 in Turkey which show rising curve over the last two decades.

Conclusion: Current developments in robotic surgery have a significant place in world scientific publication performance. Turkey has made valuable contributions to literature since 2014 with increasing number of articles and citations.

Keywords: Prostate cancer, robotic radical prostatectomy, bibliometric analyze

Öz

Amaç: Prostat kanserleri erkeklerde en sık teşhis edilen ikinci kanser türüdür. Robotik cerrahideki gelişmeler,çok sayıda makalenin yazıldığı bir dönemi beraberinde getirmiştir. Bu çalışmada robot yardımlı radikal prostatektomi konusunda Dünya'da ve Türkiye'de yazılmış olan makalelerin web tabanlı bir yazılımda bibliyometrik analiz yöntemi ile bilimsel literatürdeki durum ve katkıları araştırılmıştır.

Materyal ve Metot: Çalışmamızda kriterleri karşılayan dünyada 1434 orijinal makale ve Türkiye'de 57 orijinal makale ISI Web of Knowledge-Science (WoS) veri tabanında 'robot, prostat kanser, radikal prostatektomi' anahtar kelimeleri kullanılarak tarandı. Parametreler, makalenin bulunduğu ülke, makalenin yayın yılı, makalenin WoS kategorisi, makalenin yayınlandığı derginin adı, makalenin türü (Orijinal), makalenin dili (İngilizce) ve WoS indeksi (SCI-E), bibliyometrik analiz yöntemi ile değerlendirildi.

Bulgular: Ülkeler Wos veri tabanında bibliyometrik analizle incelendiğinde, Amerika Birleşik Devletleri 563 (%39,2) makale ile ilk sırada yer alırken, Türkiye 57 (%3,9) makale ile 11. sırada yer aldı. Yayınlanma yılına göre bibliyometrik analizde, Dünya'da en fazla yayınlanan makale sayısının 173 (%12,06) ile 2020 yılında, Türkiye'de ise 10 (%17,5) ile 2021 yılında olduğu tespit edildi. WoS veri tabanındaki alan kategorilerine göre Dünya'da Üroloji-Nefroloji alanının 1042 (%72) makale ile ilk sırada yer aldığı, benzer şekilde Türkiye'nin Üroloji-Nefroloji alanında 35 (%61,4) makale ile ilk sırada yer aldığı görüldü. Dergi adına göre yapılan bibliyometrik analizde, BJU International 157 (%10,9) ile Dünya'da en fazla makalenin yayınlandığı dergi olurken, Journal of Endourology 10 makale ile Türkiye'de en fazla makalenin yayınlandığı dergi olduğu gözlendi (%17.5). Makalelerin yıllara göre atıf ve H-indeks oranlarında son yirmi yılda yükselen bir eğri göstererek Dünyada H-index 78, Türkiye'de H-İndex 15 olarak değerlendirildi.

Sonuç: Robotik cerrahideki güncel gelişmeler, Dünya bilimsel yayın performansında önemli bir yere sahiptir. Türkiye 2014 yılından itibaren artan makale ve atıf sayısı ile literatüre değerli katkılar sağlamıştır.

Anahtar Kelimeler: Prostat kanseri, robotik radikal prostatektomi, bibliyometrik analiz

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INTRODUCTION

Prostate cancer is the second most common cancer in men (1). It is estimated that approximately 1.4 million men were diagnosed with prostate cancer in the world in 2020. Mortality rates in the world are higher in African origin populations than America and Central Asia (1,2). Rapid developments in diagnosis and treatment due to technological innovations have shown an increasing momentum in the last two decades. In the meantime, robotic assisted prostatectomy (RARP) has become an increasingly used surgical option in the treatment of prostate cancer in the last decade (3). The rates of erectile dysfunction and urinary incontinence inherent in radical prostatectomy play an important role in preferring robotic surgery (4). Positive developments in the diagnosis and treatment of prostate cancer attract the attention of urologists, and thus it provides a lot of written articles with in a period of the last 10 years.

Scientific publications are important areas where scientific academic activities of countries are evaluated. The effectiveness of scientific publications is evaluated with a large number of factors such as the country of the publication, name of the journal, impact factor of the journal and Q classification of the journal (5). Web of Science (WoS), which belongs to Clarivate Analytics®, is a database that analyzes scientific publications consisting of citation indexes and covers scientific journals with high impact around the world (6). Science Citation Index (SCI) was introduced in 1961 for bibliographic access for journals to provide and publish a large data base in their analysis. Science Citation Index Expanded (SCI-E) was expanded by adding various parameters (7). The concept of citing articles is the use of data such as articles, reports and statistics of other studies conducted by other researchers to benefit from different opinions about the subject of the relevant article and to strengthen the study. H-Index (Hirsch Index) is an internationally valid numerical indicator which measures the efficiency, productivity and citation impact of publications by scientists (8).

In this study, our aim was to investigate the place and contribution of Turkey in world literature by evaluating articles on robot-assisted radical prostatectomy in WoS data base with bibliometric analysis method.

MATERIAL AND METHOD

This study was conducted by using WoS database after 674 numbered and local ethics committee approval was taken on 28/07/2022. In order to analyze prostate cancer and robotic radical prostatectomy data, the country of the article, publication year of the article, WoS category of the article, the name of the journal where the article was published, type of the article (Original), language of the article (English) and WoS index (SCI-E) parameters were searched in ISI Web of Knowledge-Science data base. In addition to these parameters, the cities in which the articles were written were also added to study data as a separate parameter. The year of 1998, in which Da Vinci robotic system developed by Intuitive® was started to be used in the field of medicine, was considered as the starting date, the keywords 'robot, prostate cancer, radical prostatectomy' were scanned retrospectively in WoS between 1998 and 2022 and it was found that 1434 original articles were suitable for bibliometric analysis. Of these articles, 57 original articles published in Turkey meeting the criteria were evaluated with bibliometric analysis. Exclusion criterion was more than one published in the same clinic with the same name but different method. In addition, articles which were not written in English, those the full-text of which were not accessed, those which were not SCI-E, those which were not original and those which were multinational were not included in the study.

The data collected in the study were evaluated with SPSS 26.0 (IBM Inc., Armonk, NY, US) program. As descriptive statistical method, the parameters were shown as number and percentage.

RESULTS

In our study, conducted in WoS data base of countries in the bibliometric analysis, it was found that United States of America made the highest contribution to literature with 563 (39.2%) articles, while Turkey contributed to world literature in the 11th place with 57 (3.9%) articles. The contributions of countries to world literature in this field are shown in Figure 1.

When the articles were analyzed bibliometrically according to publication year (between 1998 and 2022) in WoS data base, it was found that the highest number of articles published in the world was in 2020 with 173 (12.06%) articles, while it was in 2021 with 10 (17.5%) articles in Turkey (Figure 2).

When the articles were analyzed with respect to field categories in WoS data base, it was found that the field of Urology-Nephrology ranked the first with 1042 (72%) articles, while similarly Urology-Nephrology ranked the first with 35 (61.4%) articles in Turkey (Figure 3).

When the articles were analyzed according to journal name in WoS data base, it was found that BJU International was the journal in which the highest number of articles were published in the world with 157 (10.9%), while Journal of Endourology was the journal in which the highest number of articles were published in Turkey with 10 (17.5%) articles (Table 1).

In the bibliometric analysis of the cities in which 57 articles conducted in Turkey were published in WoS data base, it was found that Istanbul was the city in which the highest number of articles was published with 30 (53%) articles (Table 2).

The citations and H-index rates of the articles by years were analyzed bibliometrically in WoS data, and the number of citations, which started in 2000 and increased by year until 2022 and H-index were summarized in Figure 4 and Figure 5. It was found that while the H-index of articles published in the world was 78 (Figure 4), the H-index of articles published in Turkey was 15 (Figure 5).

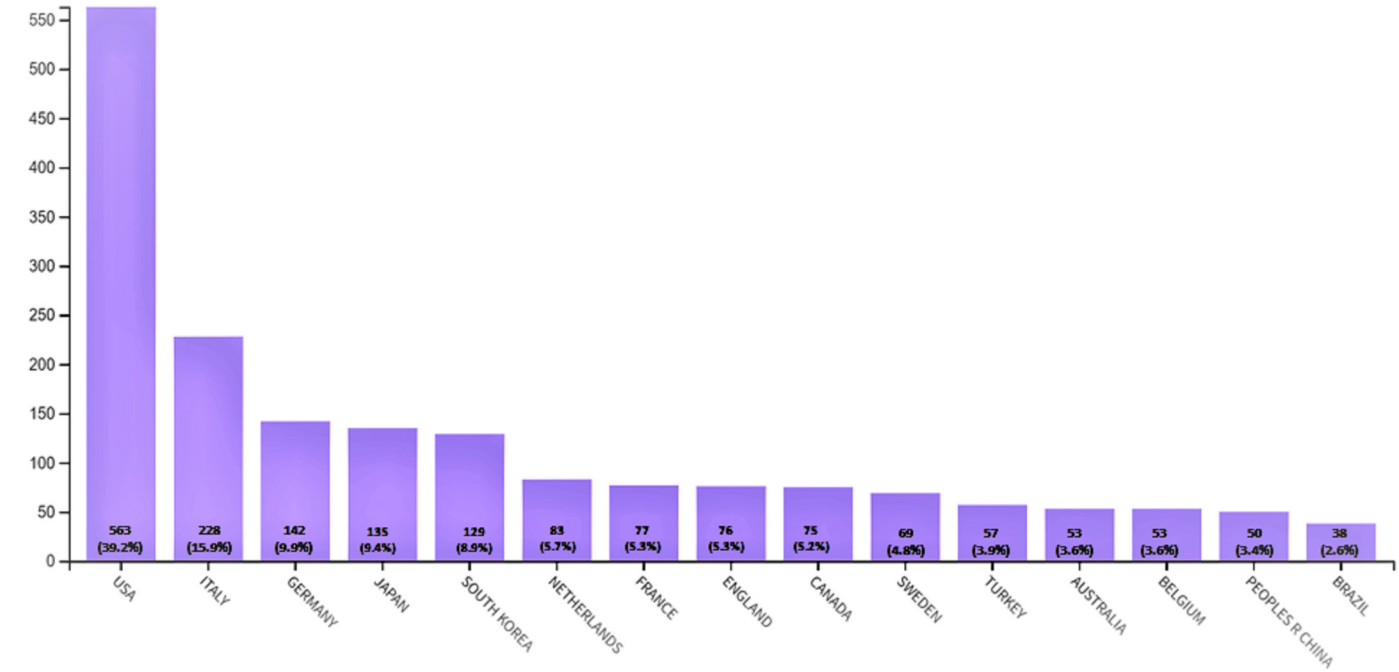


Figure 1. Distribution of articles published by countries on robotic radical prostatectomy in world literature according to WoS data base

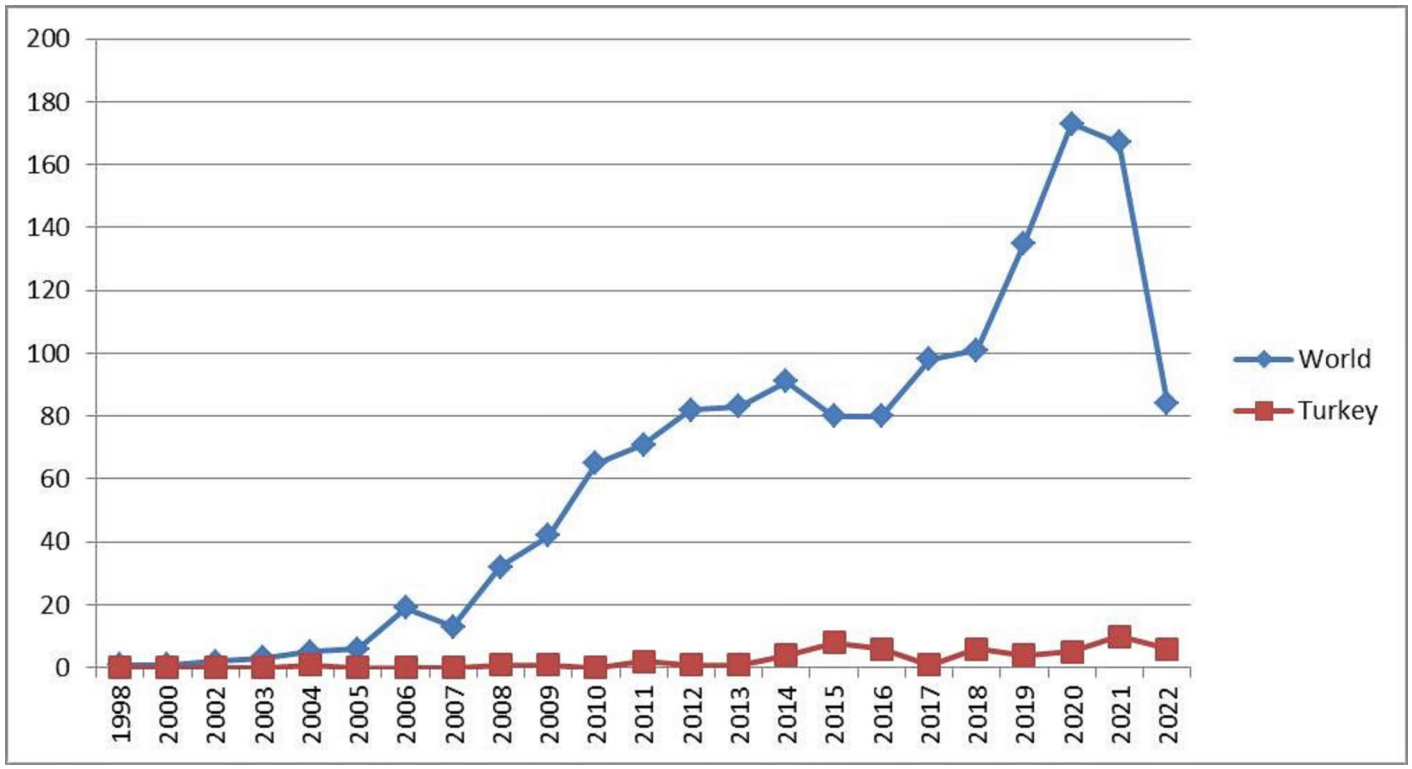
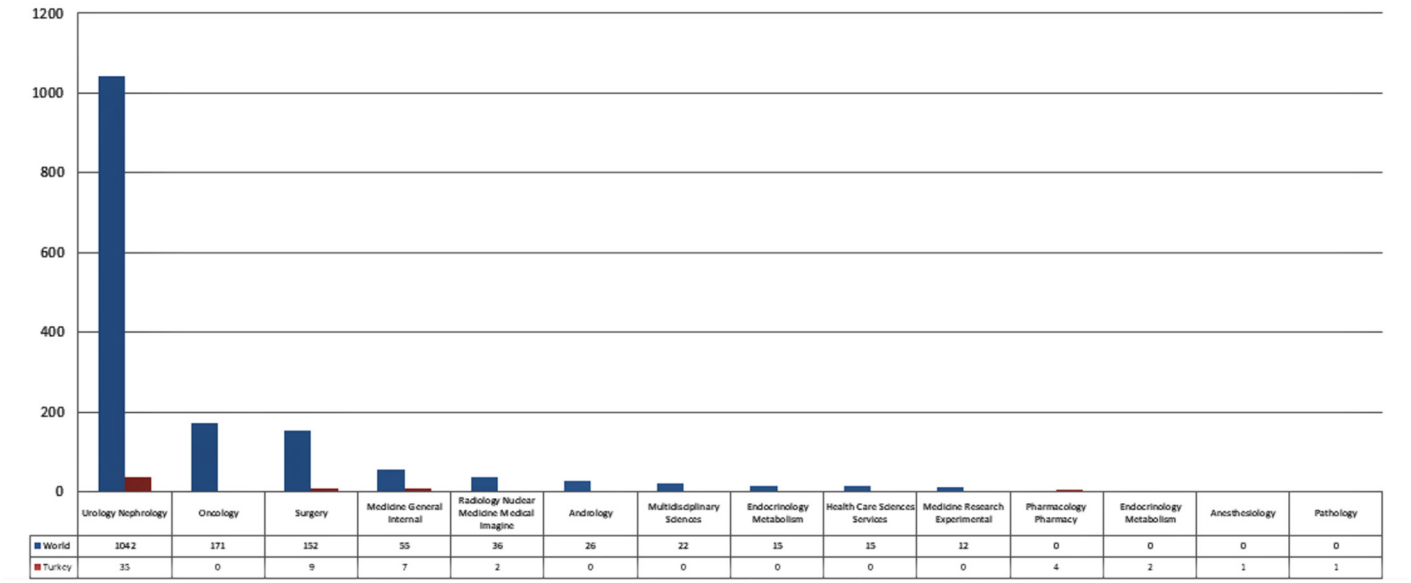


Figure 2. Distribution of number of articles published in the world and Turkey on robotic radical prostatectomy according to WoS data base by years



	Urology Nephrology	Oncology	Surgery	Medicine General Internal	Radiology Nuclear Medicine Medical Imagine	Andrology	Multidisciplinary Sciences	Endocrinology Metabolism	Health Care Sciences Services	Medicine Research Experimental	Pharmacology Pharmacy	Endocrinology Metabolism	Anesthesiology	Pathology
World	1042	171	152	55	36	26	22	15	15	12	0	0	0	0
Turkey	35	0	9	7	2	0	0	0	0	0	4	2	1	1

Figure 3. Distribution of number of articles published in the world and Turkey on robotic radical prostatectomy according to WoS data base by field category

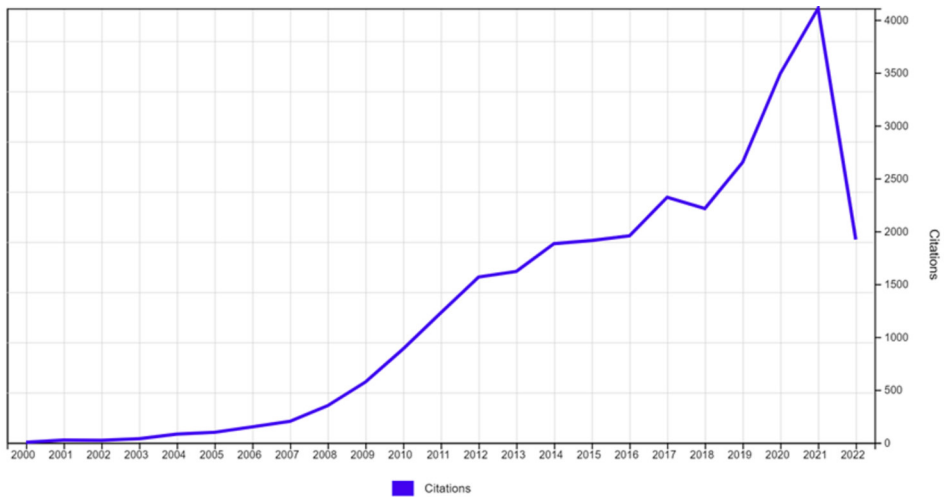


Figure 4. The distribution of citation numbers of articles published in the world on robotic radical prostatectomy according to WoS data base

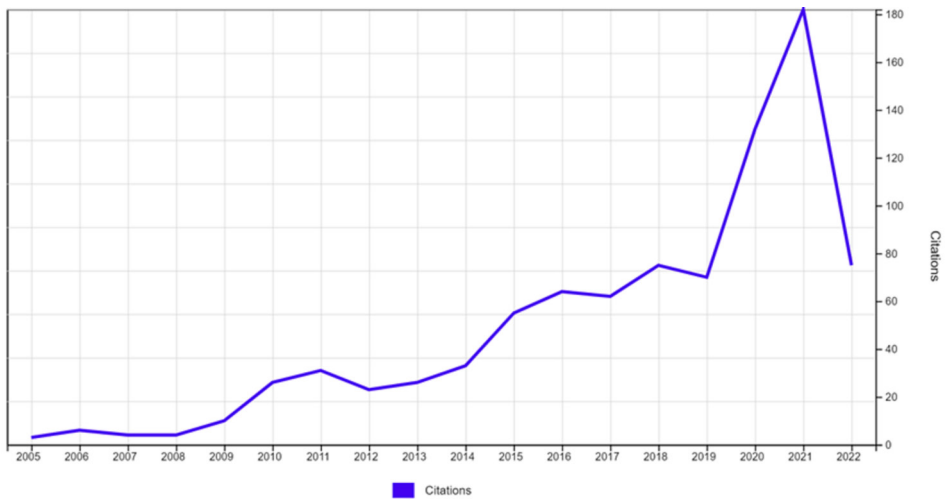


Figure 5. The distribution of citation numbers of articles published in Turkey on robotic radical prostatectomy according to WoS data base

Table 1. Distribution of number of articles published in the world and Turkey on robotic radical prostatectomy according to WoS data base by the names of journals

Journal	n	%
Journals publishing by authors from World		
BJU International	157	10.9
Journal of Endourology	151	10.5
European Urology	106	7.4
World Journal of Urology	70	4.9
Urology	64	4.5
Journals publishing by authors from Turkey		
Journal of Endourology	10	17.5
Archivos Espanoles de Urologia	4	7
European Urology	4	7
Journal of The Society of Laparoendoscopic Surgeons	4	7
Journal of Laparoendoscopic Advanced Surgical Technique	3	5.3
World Journal of Urology	3	5.3

Table 2. Distribution of number of articles published in Turkey on robotic radical prostatectomy according to WoS data base by the cities in which they were published

Cities	n	%
Istanbul	30	53
Ankara	19	33
Izmir	4	7
Other	4	7

DISCUSSION

In this study, we evaluated the articles in Turkey which used the data of cases who underwent robot-assisted radical prostatectomy for prostate cancer by using bibliometric analysis method in WoS data base and researched their place in world literature. To the best of our knowledge, this is the first bibliometric study conducted in Turkey evaluating articles written and published by Turkish authors based on robotic radical prostatectomy in prostate cancer.

As of July 2022, total number of Da Vinci Robotic Surgical Systems installed in the world is 7135. As of the end of year 2021, the number of minimal invasive robotic surgeries performed in the world so far is over 10.000.000. As of July 2022, total number of Da Vinci Robotic Surgical Systems installed in Turkey is 39. These 39 systems are in 7 cities. Robotic surgery system was first used in Turkey in 2004 at "Şişli Florence Nightingale Hospital". Robotic surgery data began to be collected in Turkey as of 2004 and Turkish authors contributed to world literature as co-authors in 2004, 2008 and 2009. The first urological article sent from Turkey was published in "Journal of the Society of Laparoendoscopic Surgeons" in 2011 (9-11).

It can be seen that the data in Turkey began to be collected with the use of robotic radical prostatectomy in prostate cancer in 2004 and since 2011 with the publication of articles using these first data, contributions have been made to world scientific literature with an increasing speed in recent years.

When the articles were examined by publication year, it was found that the number of articles in the world increased rapidly in the last 5 years, with the highest number of articles in 2021. A similar situation can be observed in Turkey, too. In parallel with the increasing data, the highest number of articles published was in 2021.

When the citation and H-index of articles is examined by year, it can be seen that the world and Turkey show a similar graph and there is an increase especially in 2021. However, a decrease was found in the number of articles and citations in 2022. We think that this decrease was caused by decreasing in the number of data due to Covid-19 Pandemic which caused a serious recession in world health sector.

When the articles were evaluated in WoS category, it was found that in the world authors in this field were mostly interested in journals of Urology/Nephrology category, which is their field of science. A similar tendency can be seen in Turkey and journals in Urology/Nephrology category come to the fore.

When all data were evaluated as a whole, it can be said that the number and rates of robot acquisition in Turkey over the years, the spread of robotic surgeries, creation of data and publication of qualified articles that contribute to literature has shown an increasing momentum. Turkish authors have not only taken a position in the world according to technological developments, but they have also contributed to literature with an increasing number of articles and citations.

Especially North American and European publications are examined, multicentred articles can be seen. It can be said that multicentered studies can be planned in Turkey, thus the number of studies can be increased and more contributions can be made to literature.

Limitations of our study included the fact that robotic surgical procedures performed with a single brand were evaluated since only Da Vinci robotic surgical model exists in the world and in Turkey and robotic surgical systems of other brands are not in clinical use. Another limitation is the fact that since it is an expensive treatment modality, it is not applied in all cities in our country and sufficient number of surgeons cannot perform this procedure. We believe that these limitations are other factors that play a role in the decrease in numbers of data and articles in Turkey.

CONCLUSION

Information and analyses of internet data based software which evaluate scientific activities of countries are followed with interest and attention in the academic world. Turkey has been making valuable contributions to literature especially since 2014 with increasing number of articles

and citations. Considering the scientific cyclical structure of its geography, Turkey is moving towards becoming an important country in the field of robotic urological surgery.

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Conflict of interest: *The authors declare that they have no competing interest.*

Ethical approval: *In order to carry out the research, ethical approval was obtained from the Non-Invasive Clinical Research Ethics Committee of the İzmir Bakırçay University (No: 28.07.2022/674).*

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MEDICAL RECORDS-International Medical Journal

Research Article

Evaluation of Cervical Endurance by Craniocervical Flexion Test in Patients with Subacromial Impingement Syndrome: A Preliminary Study

Subakromiyal Sıkışma Sendromlu Hastalarda Servikal Dayanıklılığın Kranioservikal Fleksiyon Testi ile Değerlendirilmesi: Ön Çalışma

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Abstract

Aim: The aim of the study is to evaluate deep cervical flexor endurance in patients with subacromial impingement syndrome (SIS) and compare it with norm values proven in the literature in asymptomatic individuals.

Materials and Methods: The patients' age, weight, height, duration of complaints and dominant side information were recorded. 35 patients (25 female, 10 male) diagnosed with SIS by physicians participated in the study. Pain intensity was evaluated by numerical rating scale at rest, during elevation and at night. Craniocervical flexion test (CFT) is used for evaluating cervical endurance. "Stabilizer Pressure Biofeedback" device is used for this test. Two types of points are obtained as a result of this test. One is the CFT activation score, which expresses the activation level of the deep cervical muscles, and the other is the CFT performance index, which expresses the endurance of the deep cervical muscles.

Results: Both the activation score (3.9±1.9) and the performance index (31.4±14.2) of CFT were significantly different in patients with SIS when compared with those of asymptomatic individuals.

Conclusion: Cervical endurance is reduced in patients with SIS. Treatments including cervical stabilization should be planned in these patients.

Keywords: Cervical endurance, craniocervical flexion test, subacromial impingement syndrome, subacromial pain, cervical stabilization

Öz

Amaç: Çalışmanın amacı, subakromiyal sıkışma sendromu (SSS) olan hastalarda derin servikal fleksör dayanıklılığı değerlendirmek ve literatürde asemptomatik bireylerde kanıtlanmış norm değerlerle karşılaştırmaktır.

Materyal ve Metot: Hastaların yaşı, kilosu, boyu, şikayet süresi ve dominant taraf bilgileri kaydedildi. Çalışmaya hekimler tarafından SSS tanısı konulan 35 hasta (25 kadın, 10 erkek) katıldı. İstirahatte, gece ve elevasyon sırasındaki ağrı yoğunluğu sayısal derecelendirme ölçeği ile değerlendirildi. Servikal dayanıklılığı değerlendirmek için kranioservikal fleksiyon testi (KFT) kullanılır. Bu test için "Stabilizer Basınç Biofeedback" cihazı kullanılmaktadır. Bu test sonucunda iki tür puan elde edilir. Biri derin servikal kasların aktivasyon seviyesini ifade eden KFT aktivasyon skoru, diğeri ise derin servikal kasların dayanıklılığını ifade eden KFT performans indeksidir.

Bulgular: SSS'li hastalarda KFT'nin hem aktivasyon skoru (3,9±1,9) hem de performans indeksi (31,4±14,2) asemptomatik bireylerinki ile karşılaştırıldığında anlamlı olarak farklıydı.

Sonuç: SSS'li hastalarda servikal endurans azalır. Bu hastalarda servikal stabilizasyonu içeren tedaviler planlanmalıdır.
araştırılmalı, FM'nin kardiyovasküler riske katkısını azaltmak için farmakolojik ve nonfarmakolojik tedavi yöntemleri uygulanmalıdır.

Anahtar Kelimeler: Servikal endurans, kranioservikal fleksiyon testi, subakromiyal sıkışma sendromu, subakromiyal ağrı, servikal stabilizasyon

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INTRODUCTION

Subacromial impingement syndrome (SIS) is one of the most common problems of the shoulder, caused by mechanical compression of the rotator cuff and biceps long head tendons in the subacromial space. Compression occurs during the 60-120 degrees elevation of the arm which is defined as the painful arc (1). Pain around the shoulder joint, painful arc during shoulder elevation, crepitation, limitation of joint movement, muscle weakness, scapular dyskinesis and functional disability are the common symptoms of SIS (2,3).

The etiology of SIS is multifactorial. These factors can be divided into intrinsic and extrinsic factors. Intrinsic factors include changes in bony structures, muscle degeneration and anatomical anomalies. Extrinsic factors are related to muscle imbalance, abnormal scapulohumeral kinematics, tightness of soft tissues and postural problems (1).

Postural problems in the upper body such as forward head posture, rounded shoulders and thoracic kyphosis have been suggested as a possible etiologic component in the development of SIS. In the presence of these problems, forward and downward rotation of the scapula may cause depression of the acromion and change the orientation of the glenoid fossa. As a result of this change compression may occur during elevation (4).

Deep cervical muscles play an essential role in maintaining upper body posture. The decrease in the strength and endurance of these muscles causes reduction of stability of the spine (5,6). The spine is in direct relationship with the shoulder by its muscle, tendon, and fascial connections. Because of this relationship, care should be taken to spinal dysfunctions to prevent injuries and ensure full functionality of the shoulder (4).

It has been reported that the activity of the scapular muscles decreases with the change of cervical posture in some cervical problems (7-9). For this reason, in addition to the decrease in the activation of the scapular muscles in SIS, the stability of the cervical region may also be negatively affected due to the relationship of the shoulder and spine.

For a correct treatment approach, it should be determined whether the problem in SIS is directly related to the shoulder or the spine. To determine this, cervical endurance, which is an important criterion for the cervical region, was evaluated in our study.

The aim of the study is to evaluate deep cervical flexor endurance in patients with SIS and compare it with norm values proven in the literature in asymptomatic individuals.

MATERIAL AND METHOD

This study was approved by Karabuk University Faculty of Medicine Non-Interventional Clinical Research Ethical Board numbered 77192459-050.99-E10731 at October 2019. 35 patients (25 female, 10 male) diagnosed with SIS in the orthopedics and physical medicine outpatient clinic participated in the study. The procedure of the study was explained to all participants, and they signed an informed consent form. Inclusion criteria were presence of shoulder pain limiting activity for more than 6 weeks and diagnosed with Stage 1 or 2 SIS in the shoulder. Exclusion criteria were cervical radiculopathy, a history of surgical intervention or degenerative joint disease of the shoulder joint complex, any diagnosed rheumatic, systemic or neurological diseases. Also, people with heart attack and using pacemakers, a history of shoulder dislocation or fracture, and passive joint movement limitation (frozen shoulder) are excluded.

The patients' age, weight, height, duration of complaints and dominant side information were recorded.

Pain intensity was evaluated by numerical rating scale at rest, during elevation and night. In this scale, patients are asked to mark the number that determines their pain intensity on a scale numbered between 0-10 (0 no pain, 10 severe pain) (10).

Craniocervical flexion test (CFT) is used for evaluating cervical endurance. "Stabilizer Pressure Biofeedback" device is used for this test. This device consists of three compartment pressure cell, manometer, and pressure pin. In the evaluation, the upper limit of the pressure cell is placed to the lower border of the occiput without being inflated. At a neutral starting position in supine hook lying, the pressure cell is inflated to 20 mmHg without increasing cervical lordosis. Then, the patient is asked to push her/his chin towards her neck (head nodding) enough to create a pressure of 2 mmHg and to maintain this position for 10 seconds. It consists of 5 progressive stages (22, 24, 26, 28, and 30 mm Hg). At each stage, cervical flexion is repeated for 10 seconds and 10 repetitions. Two types of points are obtained as a result of this test. One is the CFT activation score, which expresses the activation level of the deep cervical muscles, and the other is the CFT performance index, which expresses the endurance of the deep cervical muscles. Activation score is the pressure level that the patient can maintain for 10 seconds with 10 repetitions. For the CFT performance index, the pressure level at which the patient could not maintain it for 10 seconds was taken as the criterion. The CFT performance index is calculated by multiplying the pressure level with the duration that the patient can maintain the pressure. The performance score is calculated by multiplying the pressure level with the duration that the patient can maintain the pressure (11,12).

Statistical Analysis

The analysis of the data obtained from the patients was performed with the Statistical Package for Social Sciences (SPSS) Version 21.0 statistical analysis program. The normality of the variables was determined by the skewness and kurtosis coefficients. The skewness and kurtosis coefficients in the range of -1 to 1 indicate that the data are normally distributed (13). One-sample t-test was used

to compare CFT scores of patients with the norm value obtained from previous studies (11,12,14).

Age, body mass index (BMI), duration of complaints, pain intensity and CFT scores are given as mean and standard deviation values. Dominant and affected side shoulder information is expressed as frequency.

Post-hoc power analysis was performed on 35 individuals using the G*Power 3.1 program. In the post-hoc power analysis based on the CFT Activation score data, the power of the study was found to be 99%, with an effect size of 1.82 and an error score of 0.05 (15).

RESULTS

35 patients (25 female, 10 male) with SIS included in the study. All the patients' dominant side were right. The affected arm of 29 (%82.9) patients were on the dominant side and 6 (%17.1) of them were non-dominant side. Descriptive and clinical data of the patients are presented in Table 1.

Table 1. Descriptive and clinical data of the patients (n=35)

	X±SD (min-max)
Age	43.86±12.71(25.0-65.0)
BMI	27.57±5.49(16.65-37.78)
Duration of complaints (m)	6.09±2.81(3.0-12.0)
Pain at rest	1.86±2.24(0.0-5.0)
Pain at elevation	4.71±2.50(0.0-10.0)
Pain at night	5.34±2.57(0.0-10.0)

X: Mean; SD: Standard deviation; BMI: Body mass index; m: months

CFT activation score and CFT performance index were compared between patients with SIS and norm values of asymptomatic individuals. Significant difference was found (p=0.00). Comparison results are given in Table 2.

Table 2. Comparison of CFT scores between patient with SIS and asymptomatic individuals

	Patients with SIS X ± SD	Asymptomatic Individuals X ± SD	skewness	kurtosis	p
Activation score	3.9±1.9	7.6±2.1	-0.724±0.398	-0.362±0.778	0.00
Performance index	31.4±14.2	65.8±27.5	0.781±0.398	-0.044±0.778	0.00

X: Mean; SD: Standard deviation; SIS: Subacromial impingement syndrome

DISCUSSION

It was aimed to investigate if there was any difference in the endurance of deep cervical muscles between patients with SIS and asymptomatic subjects by using CFT in this study. And it was found that deep cervical endurance was reduced in patients with SIS. Both the activation score (3.9±1.9) and the performance index (31.4±14.2) of CFT were significantly different compared to asymptomatics (respectively 7.6±2.1; 65.8±27.5) (p=0.00).

One of the important structures that provide cervical postural alignment is the deep cervical flexor muscles. Inadequate endurance in deep cervical flexors can lead to impairment of spine and upper body posture (1,16). Based on this idea, Zedan et al. used cervical stabilization exercises in individuals with SIS. They applied only shoulder stabilization exercises to control group and shoulder and cervical stabilization exercises to the experiment group. They evaluated shoulder proprioception and concluded that shoulder proprioception developed in the experimental group (17). On the other hand, Lee et al. investigated the effect of cervical stabilization exercises on the activity of shoulder stabilizer muscles in their study. They showed that there was a significant increase in activity of the upper trapezius, lower trapezius, and serratus anterior muscles in the cervical stabilization exercises group (18). Pheasant used cervical retraction exercises in the case study, he presented and suggested that shoulder muscle pathologies in individuals with SIS may be related to the cervical spine (16).

These studies, which proved the effect of cervical stabilization exercises in patients with SIS, did not evaluate the endurance or strength of the deep flexor muscles (16-18).

CONCLUSION

In conclusion, it was determined in our study that cervical endurance decreased in patients with SIS compared to asymptomatics. This preliminary study demonstrated the need for cervical stabilization due to decreased endurance in these patients. For this reason, the authors planned a study in which cervical stabilization exercises will be performed in these patients.

The study is the first to evaluate cervical endurance in patients with SIS. However, the weakness of our study is that only flexor endurance was evaluated. Comprehensive studies are needed to evaluate extensor endurance.

Studies involving the evaluation and treatment of the cervical region in SIS are needed in the literature.

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Research Article

An Overview of the Glycemic Control of Diabetes Mellitus Patients Before and During the Pandemic

Diabetes Mellitus Hastalarının Pandemi Öncesi ve Pandemi Sırasında Glisemik Kontrolüne Genel Bir Bakış

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Abstract

Aim: Diabetes Mellitus is a chronic disorder characterized by high blood glucose and affects millions of people around the world with its complications. We believe that several factors during the pandemic have negatively affected the glycemic control of the patients. This study aimed to compare the glycemic controls of the patients admitted to the family health clinic of Incesu State Hospital before and during the pandemic.

Material and Methods: Demographic data, HbA1c values, durations between the two admissions, and body mass indices of a total of 203 patients admitted to the family medicine clinic were assessed. Frequency, mean and standard deviation values were used in the analysis of the data.

Results: A total of 203 patients who had HbA1c test before and during the pandemic were included in the study. Mean age of the patients was 60.87±15.24. Of the patients included in the study, 52.7% were female. Mean HbA1c value tested before the pandemic was lower than the mean HbA1c value tested during the pandemic.

Conclusion: Increase in time spent at home, decrease in physical exercises and the presence of forcing psychological factors as a result of the measures taken have caused the glycemic control of the patients to impair. The individuals with chronic diseases can be supported by health authorities, which may help to solve the problems.

Keywords: SARS- CoV-2, diabetes mellitus, pandemic, HbA1c

Öz

Amaç: Diabetes Mellitus kan glukozu yüksekliği ile seyreden, dünya üzerinde milyonlarca insanı etkileyen ve komplikasyonları olan kronik bir hastalıktır. Pandemi döneminde birçok faktörün hastaların glisemik kontrolünü olumsuz yönde etkilediğini düşünmekteyiz. Bu çalışma ile İncesu Devlet Hastanesi aile hekimliği polikliniğine başvuran hastaların pandemi öncesi ve esnasında glisemik kontrollerini karşılaştırmayı amaçladık.

Materyal ve Metot: Aile hekimliği polikliniğine başvuran toplam 203 hastanın demografik verileri, HbA1c değerleri, iki başvuru arasında geçen süreleri, beden kitle indeksleri değerlendirildi. Verilerin analizinde frekans, ortalama ve standart sapma değerleri kullanıldı.

Bulgular: Pandemi öncesi ve esnasında HbA1c değeri bakılan toplam 203 hasta dâhil edildi. Hastaların yaş ortalaması 60,87±15,24 idi. Çalışmaya dâhil edilen hastaların %52,7'si kadındı. Pandemi öncesi bakılan HbA1c değerlerinin ortalaması, pandemi esnasında bakılan HbA1c değerlerinin ortalamasından düşüktü.

Sonuç: Uygulanan tedbirler kapsamında; evde geçirilen sürenin artması, fiziksel egzersizin azalması, zorlayıcı psikolojik faktörlerin olması, hastaların glisemik kontrolünün bozulmasına sebep olduğu düşünülmüştür. Kronik hastalıkları bulunan kişilerin sağlık otoriterleri tarafından desteklenmesi sorunların çözümünde yardımcı olabilir.

Anahtar Kelimeler: SARS- CoV-2, Diabetes mellitus, pandemi, HbA1c

INTRODUCTION

Acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) from the Coronavirus family is an infectious disease first detected in People's Republic of China (1). Affected millions of people and caused a pandemic. Diabetes Mellitus is a chronic disorder characterized by high blood glucose and affects millions of people around the world with its complications (2). Several factors such as age, gender, education, marital status, obesity, smoking, exercises, additional diseases, drugs used, and psychological state affect the glycemic control (3,4). Moreover, the effects of SARS-CoV-2 are more severe in individuals with diabetes

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mellitus (5). We believe that several factors have negatively affected the glycemic control of the patients during the pandemic. We aimed to evaluate the glycemic controls of patients who applied to the family health clinic of Incesu State Hospital before and during the pandemic.

MATERIAL AND METHOD

This study was designed as a retrospective and descriptive study. The patients who were diagnosed with diabetes mellitus and admitted to the family medicine clinic of Incesu State Hospital were included in the study. Incesu is distrinct of Kayseri and the first SARS-CoV-2 case in Kayseri emerged on the 16th of March 2020. A total of 203 patients who were re-admitted to the family medicine clinic within one year before the pandemic and one year after the pandemic emerged were assessed. The patients' demographic data, HbA1c values, duration between the two admissions, and body mass index were assessed with file scanning method by using the data of the clinic.

Data Analysis

Frequency, mean and standard deviation values were used in descriptive data analysis.Chi-square test was used in comparison of categorical data. Student T test was used for numerical data in normally distributed two groups and Mann Whitney U test was used in non-normally distributed groups. Before and after data in normally distributed two groups were assessed with Paired Student T test. Spearman's Correlation analysis was used to assess the correlation between numerical data. p<0.05 was accepted as the statistically significant value. The data obtained were analyzed using the computer IBM SPSS 22.0 software program.

Ethics

The institutional consent for the study was obtained from Kayseri Provincial Health Directorate and the ethical approval was obtained from the Ethics Committee of Kayseri city training and research hospital City Training and Research Hospital (Decision Number:438, Date:14/07/2021).

RESULTS

A total of 203 patients who were re-admitted before and during the pandemic were included in the study. Of the patients, 52.7% were female. Mean age of the patients was 60.87±15.24. Mean age of the male patients was 63.03±16.9 and mean age of the female patients was 58.93±13.36. Mean ages by gender were similar (p:0.056). Mean HbA1c value tested before the pandemic was lower than the mean HbA1c value tested during the pandemic (p<0.01) (Table 1).

HbA1c values increased significantly in both genders. (p<0.001, p<0.001) (Table 2).

Body Mass Index (BMI) significantly increased in both genders before and during the pandemic (p<0.001, p<0.001) (Table 3).

Table 1. Assessment of HbA1c Values Before and During the Pandemic

	HbA1c before Pandemic	HbA1c during Pandemic	p
Mean	6.41	7.36	<0.001
Std. deviation	1.75	1.98	

Table 2. HbA1c Values according to Gender

Gender		Mean	Std. Deviation	p
Male	HbA1c before pandemic	6.31	1.65	<0.001
	HbA1c during pandemic	7.22	1.85	
Female	HbA1c before pandemic	6.49	1.83	<0.001
	HbA1c during pandemic	7.48	2.09	

Table 3. Assessment of BMI Before and During the Pandemic according to Gender

Gender		Mean	Std. Deviation	p
Male	BMI before pandemic	27.41	4.17	<0.001
	BMI during pandemic	27.81	4.34	
Female	BMI before pandemic	24.08	3.86	<0.001
	BMI during pandemic	24.76	3.89	

Patients' mean duration until the follow-up was 7.67±1.95 months. The duration until the follow-up was longer in women than in men (p:0.005) (Table 4).

Table 4. Comparison of Durations until Follow-up according to Gender

	Gender	Mean	Std. Deviation	p
Duration until Follow-up (Month)	Male	7.27	2.15	0.005
	Female	8.03	1.68	

While mean difference between the HbA1c values of the patients aged under 65 before and after the pandemic was 0.76±2.09 it was 1.57±1.84 in patients aged 65 and above. The increase in HbA1c values was higher in patients aged 65 and above (p:0.004).

There was no correlation between HbA1c values and BMI before the pandemic (r:-0.065, p:0.355). There was a positive but weak correlation between HbA1c values and BMI during the pandemic (r:0.140, p:0.046).

Table 5. Correlation between HbA1c and BMI

		BMI before pandemic
HbA1c before pandemic	r	-0.065
	p	0.355
		BMI during pandemic
HbA1c during pandemic	r	0.140
	p	0.046

DISCUSSION

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia caused by abnormalities in insulin release and/or insulin metabolism. Long-lasting hyperglycemia causes chronic organ damage and dysfunction (6).

As known, the infectious diseases impair glycemic regulation (7). Although SARS-CoV-2 is a viral infectious disease the only reason for the impaired glycemic control is not that it is an infectious disease, it also brings about several forcing factors. In addition, SARS-CoV-2 is known to be more fatal in patients with diabetes mellitus (8,9).

In a study on glycemic control during the pandemic in our country, 56% of the patients were male while most of the patients in our study were female (10). Another study was similar to this literature. Mean age of the patients was 55 in the mentioned study and 45 in the study by Fernandez et al. (11). Mean age was 57 in our study, which is similar to the findings in literature.

HbA1c levels of the patients during the pandemic were higher compared with the values before the pandemic. In the study by Onmez et al., HbA1c values of the patients increased compared with the period before the pandemic.10 According to a study performed in France, postprandial blood glucose levelof the individuals and insulin dose used during the pandemic were higher compared with the period before the pandemic (12). Moreover, HbA1c values of female patients and patients at the age of ≥65 in our study increased more. In a study performed in Japan, HbA1c values significantly increased in women and patients at the age of ≥65 and similar results with our study were obtained (13). We considered that their glycemic controls could be more impaired because the institution where we carried out the study was in a more rural area, women participated in the work life less and had to spend longer time at home due to the restrictions.

In the follow-up of the patients with diabetes mellitus, HbA1c values should be followed up at least 3 to 6-month intervals if the decision of the physician is not different (14) In our study, the patients' mean duration until the follow-up was 7.72 months. The studies have revealed that the longer the duration until the follow-up the more impaired the glycemic control (15).

Due to the pandemic, physical activity and dietary habits of the individuals have changed (16). For instance, high calorie fast food products were ordered more and the consumptions of convenience food increased more (17,18). Physical activity decreased as the individuals had to stay at home for a long time. All of these have resulted in weight gain (19,20). In our study, there was a significant increase in BMI before and during the pandemicin both genders. In addition, the individuals could not see even their relatives due to the long-lasting restrictions, which resulted in the increased psychological stress load and impaired glycemic regulation (21). There are also studies revealing that glycemic regulation was maintained in individuals who were followed up with remote access and who continued their physical activity at home during the pandemic (22,23).

Difficulties occurring in health systems, absence of outpatient service or limited service or giving importance to critical patients due to the pandemic may have extended the durations of patients' visits to a health institution for follow-up (24).

It has been observed that using web-based systems to contact the individuals helps to maintain the regulation better (25,26). A fine glycemic control and physical activity will contribute to the immune system (27). Therefore, regularly following up the patients with chronic diseases such as diabetes mellitusis is crucial.

Limitations

The limitations of the study were as follows: It was a retrospective study and fasting blood glucose measurements of the individuals were not included in the study.

CONCLUSION

Increase in time spent at home, decrease in physical exercises and forcing psychological factors experienced as a result of the measures taken due to the pandemic have caused the glycemic control of the patients to impair. The individuals with chronic diseasescan be supported by health authorities in terms of giving psychological support, increasing their exercises and providing their medicines on time, which may help to solve this problem.

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Conflict of interest: *The authors declare that they have no competing interest.*

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Research Article

Gastrointestinal Bleeding In COVID-19 Infection: A case-control study

COVID-19 Enfeksiyonunda Gastrointestinal Kanama: Vaka- Kontrol Çalışması

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Abstract

Aim: Since the gastrointestinal tract contains ACE-2 receptors, gastrointestinal symptoms, including gastrointestinal bleeding (GIB), are frequently seen during COVID-19 infection. In addition, the risk of GIB increases not only due to the virus but also to the drugs used during the treatment of infection. In this study, we aimed to determine the frequency of GIB in patients being treated due to COVID-19 infection in the intensive care unit (ICU), and to examine the effects of anticoagulant, antiaggregant, corticosteroid, antibiotic, and antiviral treatments on bleeding risk.

Material and Methods: This retrospective study included a total of 189 patients hospitalized due to the COVID-19 infection in the intensive care unit. Patients were analyzed according to the presence of GIB. The duration and doses of treatment with steroid, pulse steroid, anticoagulant, antiaggregant, and proton pump inhibitors were also analyzed. Intubation need and mortality rates were compared between GIB and without GIB.

Results: GIB developed in 34 (18%) patients followed in the COVID-19 -ICU. Patients with GIB had longer use of steroids and anticoagulants than those without GIB ($p<0.001$ and $p=0.005$). The mortality rate was higher in those with GIB (73.5% vs 51%, $p=0.027$)

Conclusion: It has been shown that the risk of GIB in patients hospitalized in the COVID-19 ICU is associated with the duration of anticoagulant and steroid therapy. Therefore, we think that patients receiving these treatments should be followed up for the risk of GIB.

Keywords: COVID-19, gastrointestinal bleeding, intensive care unit, anticoagulant, proton pump inhibitor

Öz

Amaç: Gastrointestinal sistem, ACE-2 reseptörü içermesinden dolayı COVID-19 enfeksiyonu sırasında gastrointestinal kanama dahil olmak üzere gastrointestinal semptomlar sıklıkla görülür. Ayrıca sadece virüs nedeniyle değil enfeksiyonun tedavisinde kullanılan ilaçlar nedeniyle de gastrointestinal kanama riski artmaktadır. Bu çalışmada COVID-19 nedeni ile COVID-19 yoğun bakım ünitesinde tedavi edilen hastalarda gastrointestinal kanama sıklığının saptanması ve antikoagülan, antiagregan, kortikosteroid, antibiyotik ve antiviral tedavilerin kanama riski üzerine etkilerini incelemeyi amaçladık.

Materyal ve Metot: Çalışma retrospektif bir çalışmadır. Çalışmaya COVID-19 yoğun bakım ünitesinde takip edilen 189 hasta dahil edilmiştir. Hastalar gastrointestinal kanama varlığına göre analiz edildi. Hastaların steroid, pulse steroid, antikoagülan, antiagregan ve proton pompa inhibitörü tedavisi alıp almaması, tedavi süresi ve tedavi dozları incelendi. Gastrointestinal kanama olan ve olmayan hastalarda entübasyon ihtiyacı ve mortalite oranları karşılaştırıldı.

Bulgular: COVID-19 yoğun bakımda takip edilen hastaların 34 (%18)'ünde gastrointestinal kanama geliştiği gözlendi. Gastrointestinal kanaması olan hastaların, kanaması olmayanlara göre daha uzun süre steroid ve antikoagülan tedavi kullanımına sahip olduğu gözlendi ($p<0.001$ ve $p=0.005$). Gastrointestinal kanama geçirenlerde mortalite oranı daha yüksek izlendi (%73.5 vs %51, $p=0.027$)

Sonuç: COVID-19 yoğun bakım ünitesinde yatan hastalarda gastrointestinal kanama geçirme riskinin, antikoagülan ve steroid tedavisinin süresi ile ilişkili olduğu gösterilmiştir. Bu nedenle, bu tedavileri alan hastaların gastrointestinal kanama açısından takip edilmesi gerektiğini düşünmekteyiz.

Anahtar Kelimeler: COVID-19, gastrointestinal kanama, yoğun bakım ünitesi, antikoagülan, proton pompa inhibitörü

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INTRODUCTION

Coronavirus disease 2019 (COVID-19) started in Wuhan in December 2019 and caused 5.5 million deaths as of January 2022, according to World Health Organization (WHO) data (1). It has been observed in several studies that COVID-19 does not only affect the respiratory system but also affects extrapulmonary systems such as the cardiovascular, central nervous, and gastrointestinal systems (2-4).

Gastrointestinal bleeding (GIB) is one of the common causes of emergency consultations in COVID-19. It is thought that many mechanisms cause this situation. Firstly, the SARS-CO-2 virus enters the cell through the ACE-2 receptor. Since the ACE-2 receptor is found in the lungs, gastrointestinal tract, heart, and kidneys, these systems may be affected (5). Gastrointestinal system findings include diarrhea, nausea, vomiting, abdominal pain, abnormal liver function tests, and GIB (6,7). GIB is not common but may be seen in patients with COVID-19 infection (7). Secondly, the drugs used in the treatment increase the risk of bleeding. It is known that corticosteroids, which are drugs used in the treatment of COVID-19, may also increase the risk of bleeding and perforation (8). In addition, anticoagulant therapy is commonly used according to the clinical status and laboratory findings of the patients due to the increased thromboembolic risk of COVID-19 infection (9). That is also an additional factor increasing the risk of GIB (10).

In this study, we aimed to analyze the frequency of GIB in patients diagnosed with COVID-19 treated in an intensive care unit, and compare the duration and doses of corticosteroid, anticoagulant, antiaggregant, antibiotic, and antiviral therapy.

MATERIAL AND METHOD

Study Design and Settings

This retrospective study was approved by the Health Science Ethics Committee of Muğla Sıtkı Koçman University (14.04.2021- 60). This study was conducted with patients hospitalized in the intensive care unit due to COVID-19 infection. It was carried out in a COVID-19 intensive care unit with a capacity of 14 patients in a secondary hospital. The study included a total of 189 patients between September 1, 2020, and February 1, 2021. Indications for the intensive care unit were planned according to the patient management guide of the Ministry of Health (11).

Selection of the Participants

Patients over the age of 18 were included. Both COVID-19 polymerase chain reaction (PCR) positive and negative patients who were admitted to the intensive care unit with typical radiological findings of COVID-19 were also included. The exclusion criteria in this study were the patient's referral to an external center for any reason or due to the inability to follow up on the last condition of the patient. GIB symptoms are accepted as hematemesis, melena, hematochezia, and presence of the fecal occult blood.

Measurements and Outcomes

Patients hospitalized in the COVID-19 intensive care unit were examined in terms of PCR results and thorax CT findings. Comorbidities and previous GIB of the patients were noted. The duration ve doses of steroid, pulse steroid, anticoagulant, antiaggregant, antibiotic, and antiviral treatments given to the patients were examined. INR, hemoglobin, and platelet counts were examined on the day of hospitalization and the day of GIB. Hospitalization days, length of the intensive care stay, and mortality status were examined.

Statical Analysis

In the summary of data, descriptive statistics are tabulated as mean±standard deviation or median, minimum and maximum depending on the distribution for continuous (numerical) variables. Categorical variables were summarized as numbers and percentages. The normality of numeric variables; was checked with Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling Tests.

In the comparison of two independent groups; the Independent Samples T-Test was used when numerical variables showed normal distribution, and the Mann Whitney U test was used they show no normal distribution.

Pearson Chi-Square was used in 2x2 tables with expected cells 5 and above, Fisher's Exact Test was used in tables with expected cells below 5, and Fisher Freeman Halton test was used in RxC tables with expected cells below in the comparison of differences between categorical variables according to groups.

Statistical analyzes "Jamovi project (2020), Jamovi (Version 2.0.0) [Computer Software] (Retrieved from https://www.jamovi.org) and JASP (Version 0.14.1.0) (Retrieved from https://jasp-stats.org) programs and the level of significance was taken into account as 0,05 (p-value) in statistical analysis.

RESULTS

A total of 189 patients were included in the study. The study group consisted of 108 male (57.1%) and 61 female (42.9%) patients with a mean age of 67.6±16.1 years. Previous GIB was positive in three patients (1.6 %). Hypertension was present in 105 patients (55.6 %) and was the most common comorbid disease. Positive COVID-19 PCR results and typical thorax CT findings for COVID-19 were detected in 118(62.1%) and 180 (95.2%) patients, respectively (Table 1).

GIB was developed in 34 (18%) of patients in the study. GIB developed in 8.5 days (2-37 days) after hospitalization. The median values of INR, hemoglobin, and platelet count on the day of admission were within the normal range. As laboratory tests, were performed on the day of bleeding, INR and platelet count were found to be within the normal range. The median hemoglobin value was 8.5g/dL (Table 2).

Table 1. Demographic and clinical characteristics of patients

	All patients (n=189)
Age†	67.6±16.1
Gender‡	
Male	108 (57.1)
Female	81 (42.9)
Previous gastrointestinal bleeding. yes‡	3 (1.6)
Comorbidites‡	
Diabetes mellitus	69 (36.5)
Hypertension	105 (55.6)
Coronary Artery Disease	59 (31.2)
Chronic Obstructive Respiratory Disease	17 (9.0)
Asthma	10 (5.3)
Chronic Kidney Disease	24 (12.7)
Cancer	12 (6.3)
COVID 19 PCR positive‡	118 (62.4)
COVID 19 Thorax CT positive‡	180 (95.2)

†:mean ± standard deviation‡: n (%)

Table 2. Features of GIB

		All patients (n=189)
Presence of GIB ‡		34 (18.0)
Day of hospitalization where GIB develop§		8.5 [2.0–37.0]
Laboratory findings §		
Hospitalization day	INR	1.1 [0.8–3.6]
	Hemoglobin (g/dL)	12.3 [6.1–151.0]
	Platelet count (x10^9)	216.0 [24.0–662.0]
Day of the GIB	INR	1.0 [1.0–1.1]
	Hemoglobin (g/dL)	8.5 [5.9–11.5]
	Platelet count (x10^9)	206.5 [26.0–547.0]

‡: n (%), §: median [min-max]

The details of treatment were presented in Table-3. While steroid treatment was used in 82.5% of the patients, pulse steroid treatment was needed in 33 patients (17.5%). Anticoagulant and antiaggregant treatments were used in 92.6% and 11.6% of patients. Proton pump inhibitors (PPI) drugs were administered to 183 patients (96.8%). PPIs were used in 59% of these patients daily.

The median duration of hospitalization and intensive care unit stay were 12 and 7 days. At the end of the treatment, the overall mortality rate was 55% (Table 4).

Patients with and without GIB were compared in Table 5 in terms of demographic and general characteristics. No significant difference was detected between the two groups.

Table 3. Distribution of treatment

		All patients (n=189)
Steroid treatment ‡		156 (82.5)
Steroid treatment day		9.5 [1.0 – 35.0]
Pulse steroid treatment‡		33 (17.5)
Pulse steroid treatment day		4.0 [1.0–9.0]
Anticoagulant treatment‡		175 (92.6)
Anticoagulant treatment day		11.0 [1.0–55.0]
Anticoagulant dosage‡		
	0.4 ml, 1/day	1 (0.6)
	0.4 ml, 2/day	35 (19.9)
	0.6 ml, 1/day	82 (46.6)
	0.6 ml, 2/day	22 (12.5)
	0.8 ml, 1/day	35 (19.9)
	0.8 ml, 2/day	1 (0.6)
Antiaggregant treatment ‡		22 (11.6)
Antiaggregant treatment day		5.5 [1.0–31.0]
Proton pump inhibitor treatment‡		183(96.8)
Proton pump inhibitor treatment day		11.0 [1.0–62.0]
Proton pump inhibitor treatment dosage‡		
	1/day	61 (33.3)
	2/day	110 (60.1)
	3/day	10(5.5)
	4/day	2 (1.1)
Regular daily use PPI treatment ‡		111 (59.0)
Antiviral ‡		169 (89.4)
Antibiotic ‡		187 (98.9)

‡: n (%), §: median [min-max]

Table 4. Treatment outcomes and mortality details

	All patients (n=189)
Need for intubation‡	109 (57.7)
Total days of hospitalization§	12.0 [0.0–65.0]
Intensive care unit length of stay (days) §	7.0 [1.0–48.0]
Intubation in the presence of GIB‡	**15 (50.0)**
Prognosis‡	
Survivor	85 (45.0)
Exitus	104 (55.0)

‡: n (%), §: median [min-max]

There was a significant difference between the groups in terms of hospitalization hemoglobin value (p=0.022). The median hospitalization hemoglobin value of patients with GIB was significantly lower than those without GIB (11.4 and 12.6 g/dL)(Table 6).

It was determined that steroid and anticoagulant drugs were used for significantly longer periods in patients with GIB than in patients without GIB (p<0.001 ve p=0.005)(Table 7). The dosage and frequency of the anticoagulant drug used did have no significant effect on GIB (p=0.261). The

Table 5. Comparison of patients with and without GIB in terms of demographic and general characteristics

	GIB (-) (n=155)	GIB (+) (n=34)	p
Age†	66.9 ± 15.9	70.7 ± 16.7	0.227
Gender‡			
Male	92 (59.4)	16 (47.1)	0.262
Female	63 (40.6)	18 (52.9)	
Previous GIB. yes‡	2 (1.3)	1 (2.9)	0.450
Comorbidities‡			
Diabetes mellitus	53 (34.2)	16 (47.1)	0.225
Hypertension	84 (54.2)	21 (61.8)	0.539
Coronary Artery Disease	46 (29.7)	13 (38.2)	0.441
Chronic Obstructive Respiratory Disease	14 (9.0)	3 (8.8)	0.999
Asthma	9 (5.8)	1 (2.9)	0.693
Chronic Kidney Disease	20 (12.9)	4 (11.8)	0.999
Cancer	10 (6.5)	2 (5.9)	0.999
COVID 19 PCR positive‡	99 (63.9)	19 (55.9)	0.499
COVID 19 thorax CT positive‡	147 (94.8)	33 (97.1)	0.999

†: mean ± standard deviation‡: n (%)

Table 6. Comparison of patients with and without GIB in terms of laboratory values during hospitalization

	GIB (-) (n=155)	GIB (+) (n=34)	p
INR §	1.1 [0.8–3.6]	1.1 [0.9–1.6]	0.702
Hemoglobin (g/dL)§	12.6 [6.1–151.0]	11.4 [6.1–16.5]	0.022
Platelet Count (x10^9)§	213. 0 [25.0–645.0]	234.5 [24.0–662.0]	0.758

§: median [min-max]

Table 7. Comparison of patients with and without GIB in terms of treatment characteristics.

	GIB (-) (n=155)	GIB (+) (n=34)	p
Steroid treatment‡	125(80.6)	31 (91.2)	0.224
Steroid treatment day	8.0 [1.0–30.0]	14.0 [2.0–35.0]	**<0.001**
Pulse steroid treatment‡	25 (16.1)	8 (23.5)	0.435
Pulse steroid treatment day	4.0 [1.0–9.0]	4.0 [1.0–8.0]	0.882
Anticoagulant treatment‡	142 (91.6)	33 (97.1)	0.471
Anticoagulant treatment day	10.0 [1.0–45.0]	14.0 [3.0–55.0]	**0.005**
Anticoagulant dosage‡			
0.4 ml. 1/day	1 (0.7)	0 (0.0)	0.261
0.4 ml. 2/day	27 (18.9)	8 (24.2)	
0.6 ml. 1/day	72 (50.3)	10 (30.3)	
0.6 ml. 2/day	17 (11.9)	5 (15.2)	
0.8 ml. 1/day	25 (17.5)	10 (30.3)	
0.8 ml. 2/day	1 (0.7)	0 (0.0)	
Antiaggregant treatment ‡	15 (9.7)	7 (20.6)	0.082
Antiaggregant treatment day	4.0 [2.0–31.0]	7.0 [1.0–11.0]	0.831
Proton pump inhibitor treatment ‡	149 (96.1)	34 (100.0)	0.594
Proton pump inhibitor treatment day	10.0 [1.0–46.0]	16.0 [2.0–62.0]	<0.001
Proton pump inhibitor treatment dosage ‡			
1/day	55 (36.9)	6 (17.6)	0.002
2/day	89 (59.7)	21 (61.8)	
3/day	4 (2.7)	6 (17.6)	
4/day	1 (0.7)	1 (2.9)	
Regular daily use PPI treatment ‡	90 (58.4)	21 (61.8)	0.870
Antiviral ‡	136 (87.7)	33 (97.1)	0.133
Antibiotic ‡	153 (98.7)	34 (100.0)	0.999

‡: n (%). §: median [min-max]

Table 8. Comparison of patients with and without GIB in terms of treatment outcomes				
		GIB (-) (n=155)	GIB (+) (n=34)	p
Need for intubation‡		82 (52.9)	27 (79.4)	**0.008**
Intubation in the presence of GIB‡		0 (0.0)	15 (51.7)	0,999
Total days of hospitalization (day)§		11.0 [0.0 – 51.0]	17.0 [3.0–65.0]	**<0.001**
Intensive care unit length of stay (day)§		6.0 [1.0 – 31.0]	13.5 [2.0–48.0]	**<0.001**
Prognosis‡				
	Survivor	76 (49.0)	9 (26.5)	**0.027**
	Exitus	79 (51.0)	25 (73.5)	

‡: n (%), §: median [min-max]

median duration of use PPI was found to be significantly higher in patients with GIB (16 days vs 10 days, p=0.002). In patients with GIB, the use of PPI drugs three times a day more preferred (17.6% vs 2.7% p=0.002). No significant differences were found between the groups regarding other treatments (Table 7).

Intubation need, and length of stay in the intensive care unit were significantly higher in patients with GIB (Table 8). The mortality rate was 51% in patients without GIB, whereas 73.5 % in patients with GIB. The difference was statistically significant (p=0.027).

DISCUSSION

In our study, we examined the frequency of gastrointestinal bleeding and the relationship between antiaggregant, anticoagulant, corticosteroid, antibiotic, and antiviral therapy and GIB in COVID-19- ICU. In this study, GIB was observed in 34 patients (18%). The duration of corticosteroid and anticoagulant treatment was founded to be significantly longer in patients with GIB. In addition, we observed that there was a significantly longer duration of hospitalization in the intensive care unit and total hospitalization length of stay in those patients. The mortality rate was higher in the GIB group than in those without GIB.

In this study, we observed that the mean age of the patients was 67.6, 57.1% of the patients were male, and the most common comorbidity was hypertension followed by diabetes mellitus and coronary artery disease. These findings were similar to the results of the multicenter COVID-19-ICU study in our country. In this multicenter study, 58.6% of the male patients and 51.3% of them had hypertension, the most common comorbidity, and the other common comorbidities were diabetes mellitus and cardiac disease (12). Similarly, in Italy, the most common comorbidity was hypertension, and was more common in male patients. In addition, hypercholesterolemia was founded as the second most common disease in them. We could not comment on this subject, because we did not examine hypercholesterolemia, but other common comorbidities were similarly heart disease and diabetes mellitus (13).

We also found that 62.4 % of the patients had COVID-19 PCR positivity, and 95.2% had a COVID-19 appearance in thorax CT. According to a study conducted in Turkey, COVID-19 PCR positivity was observed at 65%, which is similar to ours (14). The number of studies that we can compare on this subject is limited since the exclusion criterion is COVID-19 PCR negative in most COVID-19 ICU studies.

In light of current literature, mortality due to COVID-19 has been reported as 55-61% in various studies (15,16). In our study, the mortality rate was observed at similar rates to 55 % in the COVID-19- ICU.

In our study, GIB was observed in 18% of the patients followed in the COVID-19- ICU. When the literature on COVID-19 was examined, it was observed that GIB ranged from 2-13% in patients followed up with COVID-19. The high rate of patients in our study may be due to the inclusion of patients followed in the ICU (6,17-20).

We know from previous studies that GIB is more common in patients with respiratory failure and coagulopathy in critically ill patients, and that stress ulcer bleeding is more common in patients hospitalized in intensive care units (21,22). Our patients are critically ill patients with respiratory distress and predisposition to coagulopathy, as they are treated in the intensive care unit due to COVID-19. For these reasons, an increase in the frequency of gastrointestinal bleeding may have been observed.

Studies have shown that patients receiving therapeutic doses of anticoagulants in COVID-19 patients tend to bleed more than patients receiving prophylactic doses of anticoagulants (23,24). In our study, no significant relationship was found between anticoagulant doses and bleeding, which may be due to the lower size of patients compared to other studies. In this study, it was observed that bleeding was more frequent in patients with a long duration of anticoagulant use.

A meta-analysis of 159 studies and 33253 patients showed that corticosteroid therapy increased the risk of gastrointestinal bleeding (8). In our study, it was observed that steroid use was not significantly associated with bleeding, and the day of steroid use was associated with bleeding. The reason for this can be explained by the use of PPI in 96.8% of our patients.

In addition, in this study, it was observed that the length of stay in the hospital and ICU of patients with GIB was

prolonged, and the mortality of patients with GIB was higher. It is seen that there is no significant relationship between GIB and mortality in the literature (25).

There are several limitations in our study. One of the limitations of our study is that endoscopy and colonoscopy were not performed on patients with a diagnosis of GIB. It is not possible to differentiate the patients as upper and lower GIB. In addition, the initial body weights of the patients were present and the body weight of the patients in the catabolic process was not followed up, and the anticoagulant doses of the patients were not adjusted according to weight. Also, intubated patients were examined in our study, and it was not possible to distinguish between patients who received noninvasive mechanical ventilation and those who did not receive oral intake, since the study was retrospective.

CONCLUSION

There is a risk of gastrointestinal bleeding due to COVID-19 and the drugs used in the treatment of this disease. Due to limitations in our study, this relationship was only shown with the duration of the anticoagulants and corticosteroids used. There is a need for studies conducted in centers with a higher size of patients, gastroenterologists, and endoscopy and colonoscopy to determine the relationship of other parameters associated with GIB.

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MEDICAL RECORDS-International Medical Journal

Research Article

Ten Year Hepatitis A, B, And C Seroprevalence Trend in Children: Results From A Single Center

Çocuklarda On Yıllık Hepatit A, B ve C Seroprevalans Trendi: Tek Merkez Sonuçları

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Abstract

Aim: Hepatitis B vaccination since 1998 and hepatitis A vaccination since 2012 is available in the childhood routine vaccination program in Turkey. There is no vaccine for hepatitis C yet. The seroprevalence of hepatitis A, B, and C differs between regions. For this reason, each region should assemble its own rates. Therefore, this study aimed to determine the seroprevalence of hepatitis A, B, and C in children in Kastamonu province, to evaluate whether there is a change in prevalence according to years and patient age, and to review whether there is a change in hepatitis A virus seroprevalence with hepatitis A vaccination.

Material and Methods: File records of all patients under 18 whose hepatitis serology was studied at Kastamonu Training and Research Hospital between 01.01.2012 and 21.12.2021 were reviewed retrospectively.

Results: A total of 19885 patients and 55738 test results were included in the study. Accordingly, hepatitis A seroprevalence increased year by year. Anti-HAV IgG positivity was higher in the vaccinated group, whereas anti-HAV IgM positivity was higher in the unvaccinated group ($p<0.01$). Anti-HBs gradually decreased until the age of 13 and increased again thereafter. Anti-HCV was positive in 11 patients (0.1%).

Conclusions: Our study shows successful results of hepatitis A and hepatitis B vaccination. Therefore, we recommend that the extended immunization program carried out in Turkey be continued meticulously, and prevention methods should always be applied for hepatitis C.

Keywords: Hepatitis A, hepatitis B, hepatitis C, seroprevalence, children

Öz

Amaç: Türkiye'de çocukluk çağı rutin aşılama programında 1998'den beri Hepatit B aşısı, 2012'den beri hepatit A aşısı bulunmaktadır. Hepatit C için henüz bir aşı yoktur. Hepatit A, B ve C seroprevalansı bölgeler arasında farklılık gösterir. Bu sebeple her bölgenin kendi oranlarını göstermesi önemlidir. Bu çalışmada Kastamonu ilindeki çocuklarda hepatit A, B ve C seroprevalansının belirlenmesi, yıllara ve hasta yaşına göre prevalansında değişiklik olup olmadığının değerlendirilmesi ve hepatit A aşısı ile hepatit A virüsü seroprevalansında değişiklik olup olmadığının gözden geçirilmesi amaçlanmıştır.

Materyal ve Metod: Kastamonu Eğitim ve Araştırma Hastanesi'nde 01.01.2012-21.12.2021 tarihleri arasında hepatit serolojisi çalışılan 18 yaş altı tüm hastaların dosya kayıtları geriye dönük olarak incelendi.

Bulgular: Çalışmaya toplam 19885 hasta ve 55738 test sonucu dahil edildi. Buna göre hepatit A seroprevalansı yıldan yıla artış göstermiştir. Anti-HAV IgG pozitifliği aşılı grupta daha yüksek iken, anti-HAV IgM pozitifliği aşısız grupta daha yüksekti ($p<0.01$). Anti-HBs değerinin 13 yaşına kadar giderek azaldığı, 13 yaşından sonra tekrar artış gösterdiği görüldü. Anti-HCV 11 hastada (%0.1) pozitifti.

Sonuç: Hepatit A ve hepatit B aşılamasının başarılı sonuçları çalışmamızda fark edilmektedir. Ülkemizde yürütülen genişletilmiş bağışıklama programına titizlik ile devam edilmesini, hepatit C için de korunma yöntemlerine her zaman uyulmasını önermekteyiz.

Anahtar Kelimeler: Hepatit A, hepatit B, hepatit C, seroprevalans, çocuk

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INTRODUCTION

Hepatitis A virus (HAV) is a common cause of acute viral hepatitis in childhood. It is transmitted by the fecal-oral route. Although it does not become chronic, its most feared complication is acute liver failure. The severity of the acute infection increases with the patient's age. Although 1.5 million new cases worldwide are still seen annually, developing countries are at higher risk (1,2). For HAV seroprevalence, Turkey is in the moderate endemic group (3). Therefore, vaccination is essential for prevention. At the end of 2012, the HAV vaccine was included in Turkey's routine childhood vaccination calendar (4).

Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are significant public health problems that can cause acute and chronic liver damage, and their clinical spectrum can range from asymptomatic infection to cirrhosis and hepatocellular carcinoma (5). Turkey is a low moderate area for HBV seroprevalence and a low endemic area for HCV seroprevalence (6-7). Hepatitis B vaccination has been in Turkey's routine childhood vaccination calendar since 1998. Unfortunately, there is no current vaccine for hepatitis C. According to the World Health Organization data, HBV and HCV caused 3 million new infections and 1.1 million deaths in 2019 (8).

In Turkey, the seroprevalence of HAV, HBV, and HCV differs between regions. For this reason, each region must monitor its own rates.

This study aimed to determine the seroprevalence of hepatitis A, B, and C in children in Kastamonu province, to assess whether there is a change in seroprevalence according to years and patient age, and to review whether there is a change in HAV seroprevalence with hepatitis A vaccination.

MATERIAL AND METHOD

The file records of all patients under 18 years old, whose hepatitis serologies were studied for any reason between 01.01.2012 and 21.12.2021 in the pediatrics and pediatric surgery outpatient clinics of Kastamonu Training and Research Hospital were retrospectively scanned. The study was not designed as a community-based screening, records of patients admitted to our hospital were used. Anti-HAV IgM, anti-HAV IgG, anti-HBs, HBsAg, and anti-HCV values were determined using the Enzyme-Linked Immunosorbent Assay (ELISA) method according to the procedure prescribed by the manufacturer (Abbott Architect, USA). For the anti-HBs level, more than 10 mIU/liter was considered positive. File records were examined for HAV, patients who were born after March 2011 and were over 24 months old at the time of blood test were considered to be fully vaccinated for HAV. The study group was determined by removing multiple test entries for one person. The study group was determined by accepting only the most recent results if there was multiple test entries for one person. Approval of the study, dated 09.03.2022 and numbered 2022-KAEK-31, was obtained from the Ethics Committee of Kastamonu University Faculty of Medicine.

Data were analyzed in the SPSS 22.0 program. Descriptive statistics were given as numbers, percentages, and ratios. The sample of the study was formed as all patients whose data were accessed using the purposeful sampling method, and the normality of the distributions was determined using the Kolmogorov Smirnov test over the package program. The Chi-square test was used to compare non-parametric variables, and Student's t-test was used to compare parametric variables. In all statistical evaluations, $p<0.05$ was accepted as significant.

RESULTS

A total of 19885 patients and 55738 test results were included in the study. Of the patients, 61.5% were male, and 38.5% were female. The mean age of the participants was 10.0±5.0 (1-17 years). The distribution of tests was 1962 anti-HAV IgM, 1746 anti-HAV IgG, 14365 anti-HBs, 19434 HBsAg, and 18231 anti-HCV. The distribution of positivity and negativity of the tests is given in Table 1.

Table 1. Anti-HAV IgM, anti-HAV IgG, anti-HBs, HBsAg, and anti-HCV seropositivity rates

	Anti-HBs		HBsAg		Anti-HAV IgG		Anti-HAV IgM		Anti-HCV	
	n	%	n	%	n	%	n	%	n	%
Negative	4671	32.5	19401	99.8	1234	70.7	1865	95.1	18220	99.9
Positive	9694	67.5	33	0.2	512	29.3	97	4.9	11	0.1
Total	14365	100.0	19434	100.0	1746	100.0	1962	100.0	18231	100.0

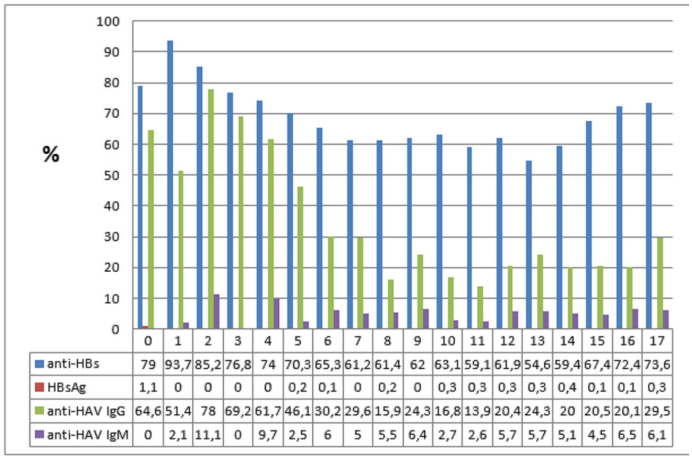
Table 2. Comparison of anti-HAV IgM and anti-HAV IgG values according to hepatitis A vaccination status of patients

	Anti-HAV IgG		Total	p	Anti-HAV IgM		Total	p
	Negative	Positive			Negative	Positive		
Unvaccinated	1225 (77.4%)	356 (22.6%)	1581	<0.01	1673 (94.5%)	97 (5.5%)	1770	<0.01
Vaccinated	2 (1.2%)	163 (98.8%)	165		192 (100%)	0 (0%)	192	
Total	1233	513	1746		1865	97	1962	

Chi Square test; $p<0.05$

Distribution by years and age groups are given in Figure 1 and 2. Accordingly, hepatitis A seroprevalence increased yearly, and the rate of anti-HBs positivity decreased gradually until the age of 13 and increased after 13. Anti-HCV results of 18231 patients aged 0-18 years were evaluated, and it was positive in 11 (0.1%) children.

Anti-HAV IgG positivity was higher in the vaccinated group, and Anti-HAV IgM positivity was higher in the unvaccinated group (p<0.05) (Table 2).



	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
anti-HBs	79	93,7	85,2	76,8	74	70,3	65,3	61,2	61,4	62	63,1	59,1	61,9	54,6	59,4	67,4	72,4	73,6
HBsAg	1,1	0	0	0	0	0,2	0,1	0	0,2	0	0,3	0,3	0,3	0,3	0,4	0,1	0,1	0,3
anti-HAV IgG	64,6	51,4	78	69,2	61,7	46,1	30,2	29,6	15,9	24,3	16,8	13,9	20,4	24,3	20	20,5	20,1	29,5
anti-HAV IgM	0	2,1	11,1	0	9,7	2,5	6	5	5,5	6,4	2,7	2,6	5,7	5,7	5,1	4,5	6,5	6,1

Figure 1. Distribution of anti-HAV IgM, anti-HAV IgG and anti-HBs, HBsAg seropositivity rates by patient age (years)

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
anti-HBs	79,3	79	76,9	76,2	62,2	56,2	63	63,4	60,2	58,9
HBsAg	0,5	0,2	0,1	0,2	0,2	0,1	0,2	0,1	0	0,2
anti-HAV IgG	25,4	23,9	24,3	34,3	20,2	36,3	43,3	37,1	51,6	50,7
anti-HAV IgM	22,3	9	1,1	0	0	0,5	0	0	0,7	0

Figure 2. Distribution of anti-HAV IgM, anti-HAV IgG, anti-HBs and HBsAg seropositivity rates by years

DISCUSSION

Our study is the first to evaluate hepatitis A, B, and C seroprevalences in children in the Kastamonu province. Hepatitis A seroprevalence (percentage of anti-HAV IgG seropositivity) was 29.3% in children aged 0-17. The effect of hepatitis A vaccination, which was included in Turkey's extended immunization program at the end of 2012, was seen in our study. In our study, HAV seroprevalence was 25.4% in 2012, and 50.7% in 2021. In addition, it was observed that anti-HAV IgG seropositivity was significantly higher and anti-HAV IgM positivity was lower in HAV vaccinated children (p<0.01). Anti-HBs positivity was 67%, HBsAg positivity was 0.2%, and anti-HCV positivity was 0.1%, and similar rates were found compared to other studies conducted in Turkey (2,9,10).

A seropositive result of anti-HAV IgG is accepted as an indicator of vaccine-acquired immunity or previous hepatitis A infection and creates permanent immunity to HAV (11,12). In a study conducted with 555 patients in Antalya province in 2022, hepatitis A seroprevalence was 24.7% in children aged 1-15 (13). In another study conducted in Karabük by Doğan et al., in 2017 with 200 patients, HAV seroprevalence was 28% (2). Our seroprevalence percentage is similar to these studies. Tekkanat et al., found that hepatitis A seroprevalence in children aged 0-18 in the Kars province in 2015 was 66.5%, while Okur et al., reported the rate as 69.9% in children in Van province in 2011, and Aslan et al., found the prevalence as 66.5% in children in Şanlıurfa in 2001 (14-16). Our seroprevalence being lower than these studies can be associated with our province's high level of socio-economic development and attention to hygiene conditions.

The Hepatitis A vaccine was included in Turkey's mandatory national immunization program in November 2012, the first dose being at the end of the 18th month, and the second dose at the end of the 24th month (4). The expected seroconversion after the first dose is 90%, and this rate reaches 100% after the second dose (17). In our study, we divided the patients we examined for anti-HAV IgG into two groups regarding whether they were vaccinated against hepatitis A. Anti-HAV IgG was positive in 22.6% in the unvaccinated group, while this rate was 98.8% ,in the vaccinated group. This significant difference reveals the success of the hepatitis A vaccine. In addition, when we evaluated anti-HAV IgG positivity according to age, it was seen that the highest prevalence was at the age of two (24-36 months). This peak can also be attributed to the age group being the first with complete vaccination. Not many studies in the literature evaluate the effect of hepatitis A vaccination on HAV prevalence in children in Turkey. In the study conducted by Kılıçaslan et al., with 762 pediatric patients, seroconversion was 88.4% in the vaccinated group and 34.9% in the unvaccinated group (18). We think that the increase in anti-HAV IgG seropositivity in the presence of a successful vaccination program will be demonstrated by future studies conducted in Turkey.

Anti-HBs and HBsAg are frequently used in screening for hepatitis B infections (19). In clinical practice, HBsAg positivity is the first step in diagnosing HBV-infected individuals (20). The first marker in the serum is HBsAg, which essentially indicates ongoing HBV infection. The serological marker of recovery is anti-HBs, which shows the immunity that develops after an infection or vaccination (17, 21). Therefore, it is essential to detect the patients infected with HBV in the screenings and to identify and vaccinate those who are negative by checking the anti-HBs levels of unvaccinated individuals. In Turkey, hepatitis B vaccination was included in the routine childhood vaccination chart in 1998. Newborns receive three doses, one right after being born, one in the 1st month and one in the 6th month. An anti-HBs level above 10 mIU/liter is considered positive and is an indicator of immunity (22). In the study by Kılıçaslan et al., with 192 patients aged 10-19 years old, anti-HBs

positivity rate was 61.9% (23). In another study by Duran et al., with 208 patients, this rate was 68.3% (9). Similarly, in the study of Sarıgül et al., with 1546 pediatric patients, anti-HBs positivity was 69.9% (10). In our study, this rate was 67.5%, similar to the studies conducted in Turkey.

Another striking point in our study was that the age group with the highest anti-HBs positivity (93.7%) was toddlers (between 12-24 months). This rate decreased gradually towards the age of 13 and increased between 13-17. The reason for this change is the decrease in the protective titer value in the years after vaccination. Accordingly, risk factors can be counted as male gender, smoking, presence of obesity, as well as transferring the vaccine without complying with the cold chain, non-compliance with the vaccine schedule, and failure to apply the vaccine in an appropriate technique (23). The highest percentage of anti-HBs positivity being in the first age group of children whose vaccination program was completed as of the sixth month may be associated with the fact that they are the first age group after a completed vaccination. The percentage of anti-HBs, which was 54.6% at the age of thirteen, increased every year after this and was 73.6% at age 17. We think that the booster vaccination of individuals with low immune response in high school age played a role in the percentage of anti-HBs positivity rising in adolescence. We suggest that this change should be investigated with new studies.

HBsAg seroprevalence in children varies between regions. Studies have shown that HBsAg seroprevalence decreased with hepatitis B vaccination. In the study by Kösecik et al., on children in Şanlıurfa in 1997, HBsAg seroprevalence was 12.5% (24). This study is very valuable because it was done before the hepatitis B vaccine was included in childhood routine practice. In a study by Zeyrek et al., in Şanlıurfa in 2002, HBsAg seroprevalence was 2%, and the effects of the vaccine were observed (25). HBsAg seroprevalence was 0.2% in the study of Kaya et al., in children in the Van region in 2010, 0.2% in the study of Doğan et al., in children in Karabük in 2017, and 0.08% in the study of Altan et al., in children in 2017 (2,26,27). In our study, HBsAg seroprevalence was 0.2%, similar to the studies conducted in the pediatric age group in recent years.

HCV is the most common cause of chronic liver disease, cirrhosis, and hepatocellular carcinoma in adults in developed countries. About 170 million people worldwide are infected with HCV, and almost 3 million new individuals join this group each year. The prevalence under the age of twenty is lower. It is transmitted by the percutaneous or parenteral transmission of infected blood, blood products, or body fluids. Vertical (perinatal) transmission has recently been at the forefront in children. The first test to be used within the scope of HCV infection screening is anti-HCV. In case of anti-HCV positivity or anti-HCV being negative with clinical suspicion, HCV RNA should be checked. There is no vaccine yet to protect against HCV. For this reason, methods of preventing contagion have come to the fore (17). In our study, anti-HCV results of 18231 patients aged 0-18 years were evaluated, and it was positive in 11 (0.1%) children. Two of these patients were positive for HCV RNA and were followed up in pediatric gastroenterology. There are a limited number of studies evaluating HCV seroprevalence in children in Turkey. The results of our study were similar to the anti-HCV seroprevalence; detected as 0.1% in the study by Doğan et al., 0.3% in the study by Deveci et al., 0.09% in the study by Güçlü et al., and 0.1% in the study by Ayvaz et al. (2, 28-30).

CONCLUSION

As a result, our study, in which our 10-year data were evaluated retrospectively, is sample size wise the largest hepatitis seroprevalence study conducted in Turkey. In addition, successful results of hepatitis A and hepatitis B vaccination were noticed in our study. Therefore, we recommend that the extended immunization program carried out in Turkey be continued meticulously, and prevention methods should always be followed for hepatitis C.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *Approval of the study, dated 09.03.2022 and numbered 2022-KAEK-31, was obtained from the Ethics Committee of Kastamonu University Faculty of Medicine.*

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MEDICAL RECORDS-International Medical Journal

Case Report

Fracture of the Elongated Styloid Process by Hanging

Asıya Bağlı Uzun Styloid Proçes Kırığı

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Abstract

It is a routine protocol to examine the soft tissues, cartilage and bone tissues of the neck during post-mortem examinations performed in the cases of hanging-related deaths. Fractures of the hyoid bone and thyroid cartilage, as well as bleeding and ecchymoses around the first fracture are practically of great importance in establishing the case as live hanging. The styloid process is a thin bone at the base of the skull that extends downward, medially, and anteriorly from the temporal bone. Elongated variations of styloid process are encountered in society. In literature, there are no reported cases of elongated styloid process fractures due to hanging. In hanging-related deaths, along with hyoid bone and thyroid cartilage tissues, styloid process should also be evaluated for fractures.

Keywords: Autopsy, styloid proces, hanging

Öz

Asıya bağlı ölümlerin postmortem incelemelerinde boyun yumuşak dokularının, kıkırdak ve kemik dokularının incelenmesi rutin bir protokoldür. Uygulamada hyoid kemik ve tiroid kıkırdak kırıkları ile kırık etrafındaki kanama ve ekimozlar canlı asının belirlenmesinde büyük öneme sahiptir. Stiloid proçes, kafa kaidesinde temporal kemikten aşağı, mediale ve anteriora doğru uzanan ince bir kemiktir. Toplumda uzun styloid proçes varyasyonlarına rastlanılmaktadır. Literatürde asıya bağlı uzun styloid proçes kırığı bulunmamaktadır. Asıya bağlı ölümlerde hyoid kemik ve tiroid kıkırdak dokuların yanısıra styloid proçeste kırık açısından değerlendirilmelidir.

Anahtar Kelimeler: Otopsi, styloid çıkıntı, ası

INTRODUCTION

Hanging is a common method of suicide worldwide. Hanging results in asphyxiation caused by the compression of a material wrapped around the neck due to the gravitational effect of the suspended human body weight (1). It is a routine protocol to examine the soft tissues, cartilage and bone tissues of the neck during post-mortem examinations performed in cases of hanging-related deaths. The incidence of laryngeal and hyoid bone fractures is between 0% and 76% (2,3). The styloid process is a thin bone at the base of the skull that extends downward, medially, and anteriorly from the temporal bone. The styloglossal muscles and the stylohyoid and stylomandibuar ligaments attach to this process (4) . In an adult, a styloid process longer than 25 mm is described as abnormal, which is reported to be present in approximately 4% of the population (5,6) There are no studies in the literature reporting a case of styloid process fracture due to hanging. Our study discusses a case of elongated styloid process fracture in a person who died due to the asphyxiation caused by hanging.

CASE REPORT

A 62-year-old male who had been suffering from psychological problems for about 7 months was also reported to have been hospitalised and given medical treatment at a psychiatric clinic for 1 month and to have been missing for 2 days by his family, who also reported him as missing to judicial units. He was discovered to have committed suicide by hanging himself in an abandoned building, and an autopsy was performed to determine the exact cause of death. According to the external examination, the body is 169 cm tall and weighs 78kg, with hanging traces measuring 1.3cm wide on the front of

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the neck and right over the thyroid cartilage, 1.2cm wide on the right side and the widest area of the neck, 1.3cm wide on the left side with ecchymoses and abrasions inside, and rising towards the back of the neck from both oblique sides of the neck. The cervical vertebrae were intact, but there were fractures and ecchymoses around these fractures on both the cornua of the hyoid bone and the right cornu of the thyroid cartilage, according to the internal examination. Both temporal bones' styloid processes were longer than normal, measuring 4cm on the right and 4.2cm on the left, respectively. The right styloid process had fractured, with bleeding and ecchymoses in the soft tissues around the fractured ends.

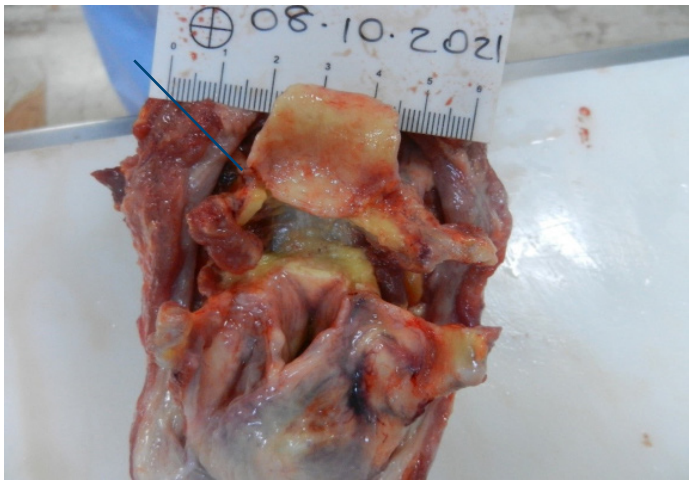

Figure 1. Thyroid cartilage and hyoid bone fractures

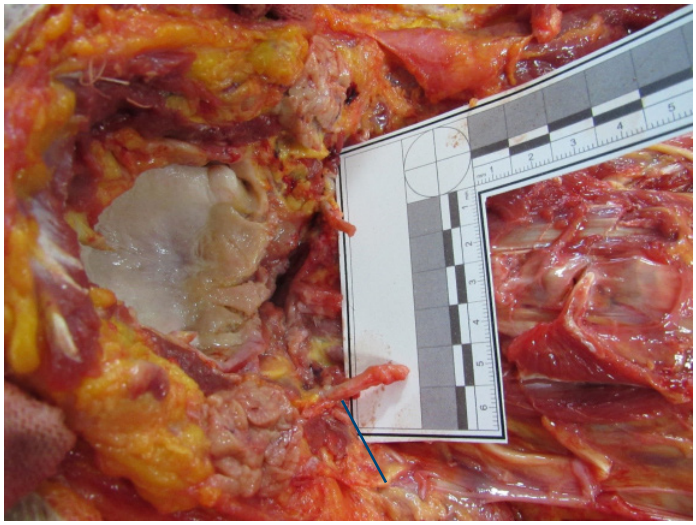

Figure 2. Right styloid process fracture

DISCUSSION

Deaths related to hanging are the most common cause of suicides committed across the globe. In such deaths, the focus is on the tissues in the neck area (7). According to the literature, the fracture of the cervical spine is extremely rare in deaths of hangings (8,9). It is stated that there should be a drop from a distance of at least 2.7m for cervical spinal cord injuries, which does not occur in cases of suicidal hangings in a home setting (10). Despite the varying rates of thyroid cartilage fractures and hyoid bone fractures encountered in deaths of hangings, it is clearly stated that fractures occur in the neck structures (11). In this case, both thyroid cartilage and hyoid bone fractures were detected (Figure 1). Eagle's syndrome is a condition where the elongated styloid process affects neighbouring tissues, causing various clinical symptoms (12). Although it is rarely encountered in society, it is mostly defined in the literature as fractures caused by facial traumas (13,14). The mean length of the styloid process ranges from 20 to 32mm. Styloid process is considered elongated when its length exceeds 30mm from the temporal bone (15). In our study, both styloid processes were found to be longer than normal.

CONCLUSION

In autopsy series, there is no available information in the literature concerning styloid process fracture. In this case, it was observed that the styloid process of the temporal bone extended to the middle line of the cervical vertebrae and the right process was fractured and contained bleeding around this fracture (Figure 2). Therefore, hanging-related deaths, styloid process should also be evaluated for fractures along with hyoid bone and thyroid cartilage tissues.

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MEDICAL RECORDS-International Medical Journal

Case Report

Congenital Insensitivity to Pain with Anhidrosis: A Case Report

Anhidrozisli Konjenital Ağrıya Duyarsızlık Sendromu: Bir Olgu Sunumu

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Abstract

Congenital insensitivity to pain with anhidrosis (CIPA) is a rare autosomal recessive disorder that is characterized by insensitivity to pain, anhidrosis and mental retardation. Mutations in the neurotrophic tyrosine receptor kinase 1 gene are responsible for the disorder. A 3.5-year-old male born to healthy consanguineous Iranian parents presented with such symptoms as insensitivity to pain, anhidrosis, self-mutilation and intellectual disability. At the time of presentation he had multiple scars, especially on his hands, feet and knees resulting from previous trauma. It was ascertained that the wounds, caused by trauma and the self-mutilating behaviors of the patient, did not heal easily. CIPA was diagnosed based on clinical findings and information obtained from the family. Wound care was performed and the patient was started on a support program for cognitive function. In the absence of a cure for the condition, the family was informed about the measures to be taken and provided with genetic counseling, and the patient was followed up. The characteristics of the disorder should be well known to ensure its inclusion in differential diagnosis. As there is as yet no cure for this condition, the family of the patient should be informed about the disease and the measures to be taken, and provided with genetic counseling.

Keywords: Congenital, insensitivity to pain, anhidrosis, pediatric

Öz

Anhidrozisli konjenital ağrıya duyarsızlık sendromu; ağrıya duyarsızlık, anhidrozis ve zeka geriliği ile karakterize otozomal resesif geçişli nadir bir hastalıktır. Nörotropik tirozin reseptör kinaz 1 genindeki mutasyonlar bozukluktan sorumludur. Aralarında birinci dereceden akrabalık olan, sağlıklı, İranlı ebeveynlerden doğan 3.5 yaşındaki erkek hastanın; ağrıya karşı duyarsızlık, terlememe, kendini yaralama ve zihinsel gerilik gibi yakınmaları vardı. Başvuru sırasında özellikle ellerde, ayaklarda ve dizlerinde, önceki travmadan kaynaklanan çok sayıda yara izi vardı. Travma ve kendine zarar verme davranışının neden olduğu yaraların kolay iyileşmediği öğrenildi. Tanı, klinik bulgular ve aileden alınan bilgilere konuldu. Yara bakımı yapıldı ve bilişsel fonksiyonları desteklendi. Hastalığın tedavisi olmadığı için aileye, alınması gereken önlemler hakkında bilgi ve genetik danışmanlık verilerek hasta takibe alındı. Bozukluğun, ayırıcı tanıda yer alabilmesi için özelliklerinin iyi bilinmesi gerekir. Hastalığın henüz bir tedavisi olmadığı için aileler hastalık ve alınması gereken önlemler hakkında bilgilendirilmeli ve genetik danışmanlık verilmelidir.

Anahtar Kelimeler : Konjenital, ağrıya duyarsızlık, anhidroz, pediatrik

INTRODUCTION

Congenital insensitivity to pain with anhidrosis (CIPA), known also as hereditary sensory and autonomic neuropathy type IV, is an extremely rare autosomal recessive disorder (1,2). The clinical features of CIPA include congenital lack of pain and temperature sensation, and absence of sweating, which leads to recurrent episodes of hyperpyrexia or hypothermia. The inability to feel pain results in such secondary complications as repeated injuries and self-mutilation, and delayed developmental milestones and intellectual disability may also be observed. CIPA is caused by mutations in the neurotrophic tyrosine receptor kinase 1 (NTRK1) gene on chromosome 1, which encodes the receptor tyrosine kinase for nerve growth factor (NGF). Although CIPA was defined a long time ago, it is rare and clinical data is limited, therefore unfamiliar to many clinicians (2-5). We present this case report to raise awareness about the disorder.

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CASE REPORT

We present the case of a 3.5-year-old male patient who was the fifth child born to healthy, second-degree consanguineous Iranian parents. The parents reported mild developmental delay in infancy, and insensitivity to pain was noticed when he did not respond to injections or accidental traumas. He had repeated injuries and delayed wound-healing, and a habit of biting the tongue and fingertips emerged upon teething, resulting in malformed fingers. He had a history of recurrent episodes of unexplained fever and two previous febrile convulsions at the age of six months. It was ascertained that there were members of the family who had experienced episodes of unexplained fever that resulted in death.

Figure 1. Skin lesions with slow wound-healing

Figure 2. Ulcerated lesions and deformities to the hand and foot

Figure 3. Auto-amputations to the fingertips

A clinical examination revealed multiple scars on the patient's hands, knee joints and feet due to previous trauma. There were signs of biting on the tips of the fingers and toes, and some fingers were amputated, and eroded and ulcerated wounds were noted on his hands and knees. Sweating was absent in any part of his body and he had dry skin with hyperkeratosis and cracking. An oral examination revealed biting injuries, scarring of the tongue, lips and buccal mucosa due to repeated self-mutilation. He had early tooth loss and a lot of dental caries. The patient responded to tactile stimuli, but there was no response to painful stimuli. Sense of vibration and position were normal. He had no fractures. Intelligence was lower than normal and he had a language delay.

NTRK1 gene could not be analyzed as the family had no health insurance and refused to have genetic testing. Based on the patient's history, family history and clinical findings, CIPA was diagnosed. We treated the injuries, provided mental health support and rehabilitation, counselled the parents on appropriate care for the child. Eight months after the diagnosis, he had a period of resistant fever and long lasting febrile convulsion with respiratory arrest that resulted in death.

DISCUSSION

CIPA is caused by mutations in the NTRK1 gene located on chromosome 1 that encodes the receptor tyrosine kinase for NGF. Mutations in this gene result in the failure of differentiation and migration of neural crest cells, leading to a complete absence of small myelinated and unmyelinated nerve fibers causing a lack of pain and temperature sensation. In addition, the sweat glands are not innervated, leading to anhidrosis (2,6-9). Variable

mutations have been identified in NTRK1 gene from CIPA patients and different phenotypic variations can be attributed to these different identified mutations (4,9-11).

The features of CIPA that are present in most of the patients include insensitivity to pain and self-mutilating behaviors, anhidrosis, mental retardation, and episodes of unexplained fever. Children often have self-inflicted injuries in the form of skin ulcers, burns, bone fractures, and auto-amputations of the fingertips and tongue. Self-mutilating behaviors mostly involve the orofacial region and limbs (2,5).

As physical trauma do not cause normal reaction, it may go unnoticed and lead to multiple scars and bone/joint fractures that are slow to heal. Recurrent trauma may cause deformity and affect functionality of the patient. These manifestations are frequent between 1 and 7 years of age, but other complications have no apparent age relation (2).

Anhidrosis, on the other hand, impairs the homeostasis of the core body temperature, since sweating is essential to normothermia. Depending on the environmental temperature, children with CIPA may develop hyperthermia or hypothermia, and recurrent febrile convulsions may occur in high environmental temperatures (2,5,6). Recurrent febrile episodes due to anhidrosis can begin in early childhood and initially are described as febrile episodes with non-infective origin. The febrile seizures frequently occur during these febrile periods and are causes of death in 20% of cases in first 3 years (2,10). Thermoregulation is imperative in management of CIPA and must include treatment of pyrexia with cooling, paracetamol and non-steroidal anti-inflammatory drugs.

The high incidence of skin and bone infections with antibiotic resistance also affect survival rate. They should be diagnosed in early period for better results.

There is no specific treatment and therapeutic options aim at treating symptoms and preventing self-mutilation, fractures and wound infections that may lead to amputation.

A special multidisciplinary approach is necessary in CIPA patients for better development, to reduce complications and sequelae. Also family members must be trained to avoid all events that cause a risk for the patients.

CONCLUSION

Since the condition is rare, it may be unfamiliar to physicians. The condition must be considered in the differential diagnosis of patients with insensitivity to pain and non-healing wounds. Due to the absence of a cure, the family should be informed about the measures to be taken, and efforts should be made to avoid potential complications from recurrent traumas.

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MEDICAL RECORDS-International Medical Journal

Case Report

Does the Use of Fish Oil Supplements Prolong Benign Pediatric Epistaxis?: A Case Report

Balık Yağı Takviyeleri Kullanımı Benign Pediyatrik Epistaksisi Uzatır Mı?: Bir Olgu

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Abstract

Fish oil is a widely used reinforcer for children by families nowadays due to its many structural and functional benefits. Although its positive effects on children's mental development have been demonstrated widespread in some studies, there is no clear view about the necessity of its use in childhood. Besides the side effects of this promising supplement have not been fully illuminated, its use may cause susceptibility to bleeding, as mentioned in many different literature studies. The present case is a remarkable presentation of a prolonged benign pediatric epistaxis caused by fish oil, often preferred among supplements and used for children today. The patient's condition improved significantly following the discontinuation of the reinforcement (fish oil). We submit our case to emphasize that the use of such products should also be subject to a standard assessment, based on our clinical experience. We suggest that only physicians decide to initiate fish oil in patients who needed it; more importantly, we also consider that they must monitor them closely as it can have side effects.

Keywords: Fish oil, benign pediatric epistaxis, bleeding, omega fatty acids

Öz

Balık yağının yapısal ve fonksiyonel birçok faydasından dolayı günümüzde ailelerce çocuklara yaygın olarak kullandırılmaktadır. Balık yağının çocuklarda zihinsel gelişim üzerinde olumlu etkisi bazı çalışmalarda gösterilmiş olsa da çocukluk çağında kullanımının gerekliliği konusunda net bir görüş yoktur. Yan etkileri yeterince aydınlatılmamış olup bazı çalışmalarda balık yağı kullanımının kanamaya yatkınlığa neden olduğu gösterilmiştir.
Bu olgu, günümüzde takviyeler arasında çocuklar için sıklıkla tercih edilen balık yağının neden olduğu uzamış benign pediatrik epistaksisin dikkat çekici bir sunumudur. Takviyenin (balık yağı) kesilmesinin ardından hastanın durumu önemli ölçüde düzelmiştir. Bu deneyimimizden yola çıkarak bu tür ürünlerin de kullanımının standart bir değerlendirmeye tabi olması gerektiğine, yan etkileri de olabileceğinden dolayı başlanmasına hekimlerce karar verilmesi ve ayrıca yan etkileri olabileceğinden başalanan hastalarda yakından izlem gerektiğini düşünüyoruz.

Anahtar Kelimeler : Balık yağı, bening pediatrik epistaksis, kanama, omega yağ asitleri

INTRODUCTION

Fish oil has become one of the most commonly used food supplements for children in recent years due to its many structural and functional benefits.

Because fatty acids like linoleic acid (LA) and -α-Linolenic acid (ALA) do not exist in the human body, they must be supplemented with a diet. At the same time, LA can be found in sunflower and maize seeds, ALA seafood, and oilseeds like flax and canola. To generate omega fatty acids such as Eicosapentaenoic acid (EPA), Docosapentaenoic acid (DPA), and Docosahexaenoic acid (DHA), -linolenic acid and LA must be provided in the diet. Omega-3 and omega-6 are the most vital polyunsaturated fatty acids for the human body, and they cannot be manufactured in the body. They are the precursors of many critical biological events. Omega-3, which is found in fish oil and is involved in arachidonic acid metabolism, has been demonstrated in multiple studies to have beneficial benefits on the circulatory system, brain and retina, memory, and sperm production. These fatty acids also play a role in the digestive system,

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inflammation, pain, edema, allergic reactions, and blood coagulation by producing prostaglandins, which regulate body temperature and blood pressure, produce certain hormones, and play a role in the digestive system, inflammation, pain, edema, allergic reactions, and blood coagulation (1). Fish oil preparations for children are available under a variety of brand names that are known for their impact on brain development.

Although anticoagulant effects of fish oil have been documented in the literature on occasion, there are few investigations on uncontrollable bleeding. The effects of fish oil use and this reinforcement discontinuance on epistaxis duration in a kid patient we followed up in our institution were investigated in this research.

CASE REPORT

A 7-year-old child was admitted to our outpatient clinic with a history of recurrent benign pediatric epistaxis and uncontrollable nosebleeds at night. There was no medical history and no hereditary familial disease in the patient. The height and weight percentiles were 50 percentiles at 120cm and 23kg, respectively. There was no history of surgery. The mother stated that her son's epistaxis has been going on for three months and that he was not taking any medication other than fish oil supplements with 740mg EPA and 470mg DHA. Except for nasal hyperemia and crusting, there were no abnormal findings on physical examination. Hb 13.7 g/dL, Hct 38.4%, MCV 83.7fL, MCH 29.8 pg, MCHC 35.7g/dL, RBC 4.59x10^6/µL, WBC 7.3x10^3/µL, PLT 377x10^3/µL, MPV 8.2fL, were found in laboratory tests. After getting informed consent from the patient's family, we analyzed the bleeding time at our clinic. The Duke Method was used to calculate the bleeding time. The patient's fingertip was cleaned with alcohol cotton and allowed to dry. The stopwatch was started shortly after the fingertip was punctured. Filter paper was used to gently suck blood every 30 seconds. Finally, when the bleeding ceased, the stopwatch was stopped simultaneously, and the bleeding time was recorded. In the first measurement, the bleeding time was found to be 7 minutes and 35 seconds. As a result, fish oil was removed from the diet. This parameter was discovered to diminish to 3 minutes and 40 seconds when the patient was re-evaluated for the bleeding time at the follow-up appointment one month later. The patient was compliant and stable during and after both applications. In addition, the mother noted that patient had not experienced as much blood during nosebleeds as he had during the first measurement.

DISCUSSION

Idiopathic nosebleeds are the most prevalent cause of nosebleeds in children, with 60% of children experiencing at least one epistaxis before the age of ten. Furthermore, only 10% of children with epistaxis seek medical help; (2); it is more common in males, and the average age of onset is 7.3-8.8 years (3,4).

Fish oil supplements are frequently utilized for health reasons; in fact, multiple studies suggest that they are the most widely used supplemental drug of all (5). While the daily omega-3 requirement is 1g, dosages of 2-4g have been recommended for people who are at risk of cardiovascular disease. Between the ages of 6 months and 2 years, 100mg DHA is advised, and between the ages of 2 and 18 years, 250mg (DHA+EPA) (1-2 fish meals per week) is indicated (6). More research is needed to determine the effects of omega-3 fatty acids on neurodevelopment and the optimal levels to be taken, according to Ryan et al. They reviewed human studies on the subject and concluded that more studies are necessary to determine the effects of omega-3 fatty acids on neurodevelopment and the optimal levels to be taken (7). The Australian National Heart Foundation endorsed omega-3 consumption to prevent heart disease and stroke, based on the findings of the literature evaluation. Nestel et al., on the other hand, found that taking more than the recommended daily dose of 1g provided no additional advantages or negative effects (8). Omega-3 fatty acids have been shown in studies to have physiological benefits on prostaglandins, platelets, lipids, and thrombi (5) as well as several cardiovascular benefits, such as anti-inflammatory effects and blood pressure reduction (9).

Although there are many research on the effect of medications on the incidence of bleeding in the literature, there is little information on the effect of complimentary drugs. Omega-3 fatty acids present in fish oil supplements, such as EPA and DHA, impact the coagulation profile in two ways. In the phospholipid membrane of platelets, EPA and DHA replace arachidonic acid (AA), an omega-6 fatty acid. Because AA is insufficient for activation, thromboxane A2 levels drop and platelet aggregation ensues (10). A decrease in platelet aggregation increases the tendency to bleed. The second and less accepted action mechanism of omega-3 fatty acids in the coagulation profile is reducing vitamin K independent coagulation factor V, vitamin K dependent factor VII, X, IX, and II (Prothrombin), and fibrinogen (11).

We adopted the Duke Method in our circumstance since it was the easiest to use for children and could be utilized if no other bleeding diathesis tests were available (12,13). As in our case, when the bleeding time exceeds 5 minutes, it is considered as coagulopathy (14); it also returned to normal ten days after the fish oil was discontinued. The antiplatelet activity of fish oil has been associated with longer bleeding times in previous studies (15); however this impact of fish oil has been deemed ineffective and physiologically emphasized only in cases of traumatic vascular injury (16). In following investigations, several points of view have been considered. In contrast, no statistically significant effect of fish oil on bleeding time has been identified in literature studies with patients using warfarin. In a review where the findings of the studies conducted between 1980-2017 were evaluated, fish oil has been reported not to be a clinically significant

cause of coagulopathy and to cause clinically significant bleeding in surgical patients using antiplatelet therapies, factor Xa inhibitors, or warfarin (17).

Larson et al. observed that a daily dose of 3 g of fish oil was required to induce coagulopathy, with no increase in effect observed at doses beyond 6 g. (18). Although fish oil supplements are more popular among youngsters, adults prefer them as well, owing to their beneficial benefits on the cardiovascular system (19). Many studies have shown that the omega-3 content of commercial forms of fish oil supplements can vary and deviate from the prescribed quantity, necessitating the discontinuation of these supplements at least 5-7 days before to surgery (20). A sufficiently long time was allowed for this effect of fish oil to wear off, as its mechanism of action is thought to result in a quantitative reduction in platelet aggregation. One week later, the patient in our study was contacted for a check-up, but patient requested a re-examination a month later, and the procedure applied 1st month control.

Because fish oils are considered a nutritional supplement, their substance differs significantly from that of pharmaceutical medications, and little is known about their negative effects. High blood sugar, diarrhea, gastric reflux, bleeding, low blood pressure, and sleeplessness are some of the side effects described (21,22).

CONCLUSION

Primary care clinics are facilities counseling on all health issues, including current health approaches and food supplements. Every family physician may need to provide information about these supplements and their side effects depending on their environment where it is located and the structure of the region they serve. A family physician should manage the use of supplements in a holistic and comprehensive approach.

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MEDICAL RECORDS-International Medical Journal

Case Report

Calcium Deposits of the Metacarpophalangeal Joint on the Fourth and Fifth Finger

Dördüncü ve Beşinci Parmak Metakarpofalangeal Eklemde Kalsiyum Depolanması

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Abstract

Acute calcium deposition disease is characterized by calcium hydroxyapatite crystal deposition within tendons and surrounding tissue of joints. It can manifest acute or chronic. It's most common symptom is pain in affected area. Two patients applied to our outpatient clinic with complaints of hand pain. Calcific masses were detected by radiological imaging. After radiological imaging and laboratory examinations the patients diagnosed acute calcium deposition disease. One of the patients had ongoing symptoms for 2 years, the other one had ongoing symptoms for 3 years. Both of the patients had tried conservative treatment multiple times. These patients were treated surgically because of long-standing symptoms. Although acute calcium deposition disease usually resolves spontaneously with conservative treatment, patients with recurrent or persistent lesions can be treated surgically.

Keywords: Calcium deposition disease, hand surgery, peritendinitis, periarthritis

Öz

Akut kalsiyum birikimi hastalığında hidroksiapatit birikimi meydana gelmektedir. Bu durum, eklemleri çevreleyen tendonlarda ve dokularda oluşmaktadır. Akut veya kronik olarak kendini gösterebilir. En sık görülen semptom etkilenen bölgede ağrıdır. İki hasta polikliniğimize el ağrısı şikayeti ile başvurdu. Radyolojik görüntüleme ile kalsifik kitleler tespit edildi. Radyolojik görüntüleme ve laboratuvar incelemelerinin ardından hastalara akut kalsiyum depo hastalığı tanısı konuldu. Hastalardan birinin semptomları iki yıldır, diğerinin semptomları üç yıldır devam ediyordu. Her iki hasta da konservatif tedaviyi defalarca denemişti. Bu hastalar uzun süredir devam eden semptomlar nedeniyle cerrahi olarak tedavi edildi. Akut kalsiyum birikimi hastalığı genellikle konservatif tedavi ile kendiliğinden düzelse de, tekrarlayan ağrı semptomları ve kalıcı lezyonları olan hastalar cerrahi olarak tedavi edilebilir.

Anahtar Kelimeler: Kalsiyum depo hastalığı, kalsifik peritendinit, kalsifik periartrit, el cerrahisi

INTRODUCTION

Acute calcium deposition disease, most commonly named as calcific tendinitis, is a disease in which calcium phosphate crystals, including hydroxyapatite are deposited around tendons and joint-capsule insertions (1).

Calcium deposition in the hand has been classified as calcific peritendinitis and periarthritis based on the locations of the calcium deposits (2).

Although some cases are asymptomatic, generally it is a painful clinical condition. Symptoms like fever and redness are uncommon. Symptoms can appear sudden onset and generally patients complain of dull pain, tenderness and edema at the joint or around the tendon. A differential diagnosis should be made because gout, pseudogout, tumoral calcinosis and septic arthritis can mimic the same symptoms. Some patients have elevated erythrocyte sedimentation level; however, otherlaboratory findings are usually normal. It is a self-limiting process and showsingresolution within one month (3).

In this case report, we present two cases of calcium

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deposits localized in the hand that have not resolved with non-surgical treatment. Because of long ongoing symptoms the two patients were treated surgically in our clinic.

CASE REPORT

Case 1

A 25 year-old female patient presented to our outpatient clinic with the complaint of pain in the fourth metacarpophalangeal joint of her left hand and an unspecified sensation in the fourth finger. The complaints have been continuing for about three years and elevated periodically. The patient has no history of trauma. In the examination of the patient; there was no redness or warmth in the joint. The fourth finger capillary filling was normal, but there was hyperalgesia on the radial side of the finger. The fourth finger pulp-palm distance measured 1 cm. Plain radiographs of the hand showed an oval-shaped calcific lesion on the radial side of the fourth metacarpophalangeal joint. Magnetic resonance imaging (MRI) revealed this oval-shaped calcific lesion as well as smaller sized calcific deposits around the adjacent flexor tendon with surrounding soft tissue edema and inflammation (Figure 1).

Figure 1. Anteroposterior radiography (a) shows well-defined calcification (open arrow) adjacent to the fourth metacarpophalangeal (MCP) joint. Coronal (b) and axial (e) fat-saturated proton density (PD) MR images show calcific deposit (open arrows) adjacent to the radial aspect of the fourth MCP joint. Also, coronal fat-saturated T1-weighted (c), contrast-enhanced fat-saturated T1-weighted (d) and axial fat-saturated PD (e) MR images show smaller sized calcific deposits just superficial to the flexor tendon with edema and inflammation in the surrounding soft tissues (solid arrows)

Case 2

A 37 year-old female patient was presented to our outpatient clinic with complaints of swelling and pain between her 4th and 5th fingers of the right hand. The complaints have been continuing for two years and have elevated especially with using. The patient has no history of trauma. In the examination of the patient; there was no redness or warmth on the joint. Capillary filling of the fourth and fifth fingers was normal, and the patient's neuro-motor and tendon examinations were normal. The pulp-palm distances of the fourth and fifth fingers measured zero cm. An anteroposterior radiograph of the hand showed an amorphous calcific lesion on the radial side of the fifth metacarpophalangeal joint. MRI demonstrated the calcific lesion and also surrounding soft tissue edema which is extending into the fourth web space (Figure 2).

Both patients were housewives and they had no history of disease. There was no history of regularly used drugs. The rheumatological parameters (C-reactive protein, Anti-Streptolysin O, rheumatoid factor) of the patients were negative. Hemogram and routine biochemical parameters were both normal. The MR images of the patients were reported as calcific deposits (Figure 1,2). With the presented findings, excision was planned.

Figure 2. Anteroposterior radiography (a) shows amorphous calcification (solid arrow) adjacent to the fifth MCP joint. Coronal PD (d), T1-weighted (e) and contrast-enhanced fat-saturated T1-weighted (f) MR images show the calcific deposits with surrounding soft tissue edema and inflammation around the joint (solid arrows). In addition, the extension of the soft tissue edema towards to the fourth finger space on the dorsal side is seen on the axial short-tau inversion recovery (STIR) (b, c) MR images (open arrows)

Axillary anesthesia was applied to both patients before the operation. Both of the patients were operated on in the supine position using the hand table. Dorsal approaches made for both lesions and lesions were excisited carefully. Care was taken not to damage the surrounding anatomical structures (Figure 3a,3b). The obtained materials were sent for pathological examination (Figure 3d). Pathological evaluation for the first patient reported as histiocyte aggregates and fibrosis. For the second patient, pathological evaluation reported as lesion consist of multinuclear giant cells and mononuclear stroma.

The first patient's follow-up showed no symptoms for nine

months and the second patient's follow-up have showed no symptoms for six months.

Figure 3. Intraoperative surgical approach of case 1 (a) Intraoperative surgical approach of case 2 (b) exited mass of case 2 (c) (d)

DISCUSSION

Acute calcium deposition disease is a self-limiting disease process that typically resolves within one month (4). The disease most often occurs in the shoulder; the wrist and hand are affected in only 2% of patients (5). Women are affected more frequently than men. It has been reported in the literature that women are affected two to five times more than men (6). The most commonly affected site in the hand is the insertion of the flexor carpi ulnaris (FCU). Multiple various locations have been reported, including the interphalangeal, metacarpophalangeal joints of all five fingers (6).

Acute calcium deposition disease usually occurs without any other medical problem, it is idiopathic. The pathogenesis of the disease is controversial. Researches on the shoulder suggest that this is a degenerative disease (7). Repetitive tissue stress can cause tissue hypovascularity, which leads to necrotic tissues in which calcium can be deposited. Metabolic disorders and cartilaginous metaplasia are the other theories. The second patient's complaints have elevated with repetitive movement, we can say that using is a kind of irritative tissue stress.

Acute calcium deposition disease consist of three stages; precalcific stage, calcific stage and post calcific stage. The main event of precalcific stage is fibrocartilaginous transformation. In early calcific stage calcium crystals are deposited in matrix vesicles and at the end of calcific stage the deposit is removed by macrophages and multinuclear giant cells. In post calcific stage fibroblasts remodel the remaning space after calcium removal (8).

Calcium deposits in the hand and wrist have a similar symptomatology to commonly encountered conditions. Differential diagnosis is required for infective conditions, fractures, metabolic disorders and rheumatological disease (9). The clinical presentation of the disease, its confinement to a single joint, and radiological imaging of calcium deposits may help differentiate acute calcific tendinitis from other condition (2). The rheumatological parameters (CRP-ASO-RF) of our patients were negative, hemogram and routine biochemical parameters were normal.

Treatment of calcific periarthritis or peritendinitis should first be non-surgical. It is reported that the disease is self-limited. During the acute period, the best treatment is achieved by nonsteroidal anti-inflammatory drugs, with resting or splinting. Local anesthetic or steroid injections are useful to relieve the pain (10). When the patients applied to our outpatient clinic their complaints had been continuing for years. Several times nonsteroidal anti-inflammatory drugs had been given to them. Splinting had been tried for both patients.

Long-term persistence of symptoms and long-term persistence of calcification are not common in acute calcium deposition disease (11). But as in our cases, success can be achieved with surgical treatment in cases with long-term symptoms. Surgical excision provides relieve from pain within a very short time. Surgery is very beneficial in patients who have persistent lesions that do not improve with non-surgical treatment (12).

CONCLUSION

Calcium deposition disease is not rare, the important point in treatment is to evaluate each patient and to make a treatment plan for their own according to the symptoms.

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MEDICAL RECORDS-International Medical Journal

Case Report

Churg Strauss Syndrome after Leech Therapy: A Case Report

Sülük Tedavisi Sonrası Gelişen Churg Strauss Sendromu: Olgu Sunumu

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Abstract

Churg Strauss Syndrome (CSS) is a necrotizing vasculitis affecting small vessels. Although there are many accompanying findings, this syndrome has distinctive clinical findings such as asthma, nasal polyposis, and hypereosinophilia. Here, we describe a case report of a 48-year-old male patient with known asthma and nasal polyposis, who applied to the emergency department with a sudden worsening of consciousness and bullous lesions on the ankle after undergoing leech therapy (hirudotherapy), accompanied by mononeuritis multiplex and other clinical findings. Clinical findings, laboratory, electromyography, lumbar puncture, radiological imaging methods, histopathological examination and transthoracic echocardiography were used to diagnose CSS. In addition, it was desired to draw attention to the fact that leech therapy may trigger hyperosinophilia in vasculitis group diseases and cause serious complications in the individual.

Keywords: Leech therapy, hypereosinophilia, Churg Strauss Syndrome

Öz

Churg Strauss Sendromu (CSS); küçük çaplı damarları tutan nekrotizan bir vaskülittir. Eşlik edebilen pek çok bulgusu olmakla birlikte bu sendrom, astım, nasal polipozis, hipereozinofili gibi belirgin klinik bulgulara sahiptir. Burada bilinen astım ve nasal polipozisi olan 48 yaşında bir erkek hastanın sülük terapisine gittikten sonra ani gelişen bilinçte kötüleşme ve ayak bileğinde yine ani gelişen büllöz lezyonlar ile acil servise başvurduğu ve beraberinde mononöritis multisipleks ve başka klinik bulguların da eşlik ettiği bir CSS olgu sunumu anlatılmaktadır. CSS tanısının konulmasında klinik bulgular, laboratuar, elektromiyografi, lomber ponksiyon, radyolojik görüntüleme yöntemleri, histopatolojik inceleme ve transtorasik ekokardiyografiden yararlanıldı. Ayrıca sülük terapisinin vaskülit grubu hastalıklarda hiperozinofiliyi tetikleyip kişide ciddi komplikasyonlara yol açabileceğine dikkat çekilmek istendi.

Anahtar Kelimeler : Sülük tedavisi, hipereozinofili, Churg Strauss Sendromu

INTRODUCTION

Churg Strauss Syndrome (CSS) is a necrotizing vasculitis affecting small vessels. The prominent clinical features are asthma, eosinophilia, allergic rhinitis, pulmonary infiltrates and extravascular granulomas. It is in the ANCA-associated vasculitis group. Asthma, eosinophilia, paranasal sinusitis, pulmonary infiltration, histological detection of vasculitis and mononeuritis multiplex are the 6 American College of Rheumatology (ACR) criteria used in the diagnosis of CSS. In addition, intestinal bleeding due to gastrointestinal involvement, intestinal perforation, cholecystitis, pancreatitis or unexplained abdominal pain, less commonly glomerulonephritis and interstitial nephritis due to renal involvement, pericarditis due to cardiac involvement, cardiomyopathy and myocardial infarction are also seen in this syndrome (1).

Leech therapy, also known as Hirudotherapy, is a traditional and complementary treatment method applied with leeches. Its therapeutic feature is realized by the enzymes that the leech, which is placed on the problematic area, secretes into the body during blood sucking. This secretion has anticoagulant, blood pressure stabilizer, antidepressant, antibacterial and antioxidant effects.

Here, we present a case report of a patient with a history of asthma and nasal polyposis, who developed bullous

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lesions on his skin after leech therapy and was diagnosed with CSS. The diagnosis of CSS was made by laboratory and clinical findings accompanied by eosinophilia and mononeuritis multiplex.

CASE REPORT

A 48-year-old patient with known asthma and nasal polyposis was admitted to the emergency department with complaints of worsening consciousness and drowsiness. The patient stated that the bullous lesions noticed on his right ankle appeared after the leech treatment he had done 2 days ago. He said that he had numbness and widespread joint pain in the extremities. There was also loss of muscle strength in the extremities, and the muscle strength was evaluated as 3/5 on the right side and 4/5 on the left side, more prominently in the right arm and leg. The patient applied to the emergency department 1 month ago with the complaints of numbness in the extremities and tongue and weakness on the right side. Her complaints were thought to be due to a transischemic attack, but no pathology was observed in cranial CT, and her vertebral and carotid artery Doppler results were also normal. Bile sludge and acalculous cholecystitis were also observed in abdominal USG. In his family history, the patient's mother had angioneurotic edema and patient's siblings had asthma and nasal polyposis. In laboratory tests, leukocytosis (57.700/uL), eosinophilia (75.8-43.770/uL), urea 25mg/dL, creatinine 1.21mg/dL, CRP 171.96mg/L, sodium 120mmol/L, potassium 4.9mmol/L, chloride 83 mmol/L, troponin 220, creatine kinase 3001U/L, brain natriuretic peptide (BNP) 1959ng/L, antinuclear antibody (ANA) and proteinase 3 antineutrophilic cytoplasmic antibody (c-ANCA) negative but myeloperoxidase antineutrophilic cytoplasmic antibody (MPO-ANCA) was positive (76.63RU/ml). Sinus tachycardia was observed in his EKG. Echocardiography of the patient showed 65% EF, normal left ventricular systolic function, and mild mitral valve regurgitation. Since the troponin elevation continued in the follow-ups, the patient was consulted with the cardiology, but myocardial infarction was not considered in the patient. Significant eosinophilia was observed in the peripheral smear (figure 1). With peripheral smear, the patient was consulted to hematology, but hypereosinophilic syndromes or other hematological malignancies were not considered.

Contrast-enhanced lower abdominal MRI revealed 1-2 reactive lymph nodes in both inguinal areas and 1-2 lymph nodes in the paraaortic region in contrast-enhanced upper abdomen MRI. In the thorax CT, bronchovascular prominences in both lungs, interlobular septal thickening, sequela fibrosis in both upper lobes, pleural thickening and irregularities in the right upper lobe were observed. The patient was consulted to dermatology because of bullous lesions on the ankle. The lesions were not evaluated as lesions of a specific pathology.

He was consulted with neurology because he had mononeuritis multiplex-like symptoms describing numbness in his extremities and an arachnoid cyst in his cranial MRI taken in another hospital. EMG was taken. In his EMG, 'polyneuropathy which includes the signs of demyelination, axonal involvement and damaged subacute motor fibers' was observed. Considering Guillain-Barre, the patient underwent lumbar puncture (LP). Cerebrospinal fluid (CSF) examination was normal in LP, there was no growth in the empty fluid culture, viral and bacterial meningitis panel was normal, serum and CSF IgG index were normal.

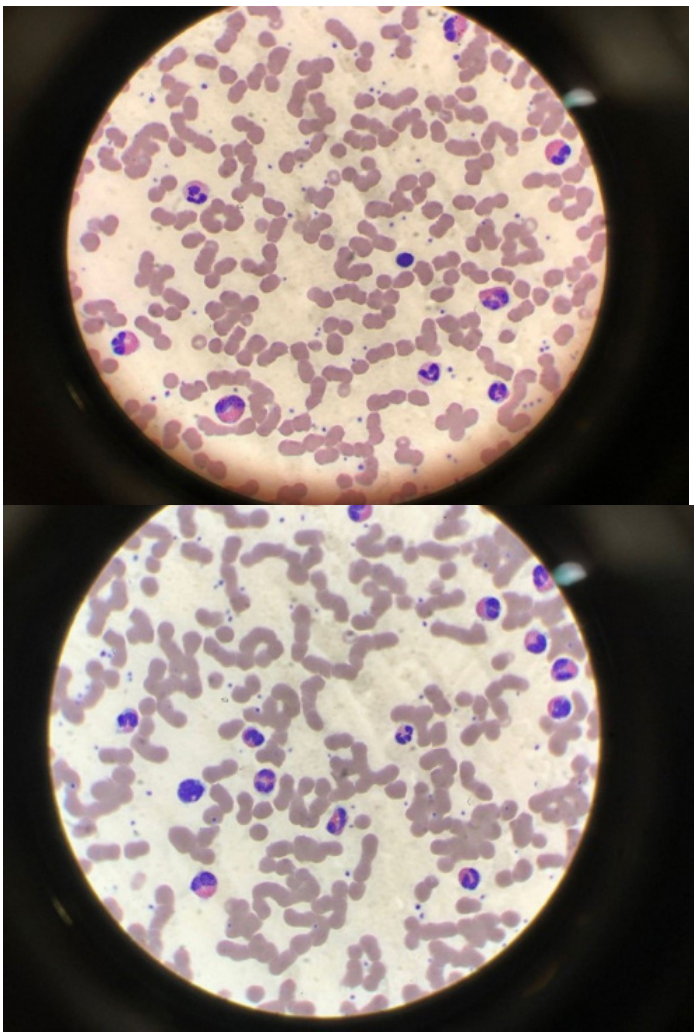

Figure 1. Eosinophilia

The patient's EMG result was re-evaluated by the neurologist and it was decided that he had vasculitic type neuropathy. Fundoscopic examination of the patient was performed, no vasculitic finding was detected. The patient's paranasal sinus CT was taken, multiple polyps were observed (figure 2). Biopsy was taken from the polyps and the pathology result was evaluated as normal. Renal USG showed grade 2 renal parenchymal damage in the right kidney.

There was 1.28g proteinuria in spot urine. In his 24-hour urine, 3.73g proteinuria was detected. The patient was consulted with rheumatology and nephrology because of proteinuria, eosinophilia and pANCA positivity. Renal biopsy was recommended for the histopathological diagnosis of nephropathies and rheumatological diseases.

However, the patient refused.

His hyponatremia resolved with fluid restriction. With the recommendation of neurology and rheumatology, the patient was given pulse steroid (1000mg-5 days) and Ivlg (0.4g/kg/day) for 3 days). Improvement in muscle strength and dramatic decrease in eosinophilia were observed. Afterwards, Prednol (40mg in the morning - 20 mg in the evening) was continued. The patient was discharged after his eosinophil level decreased to 0.02 10^3/uL. He did not have any active complaints and improvement was observed. He started to be followed from rheumatology.

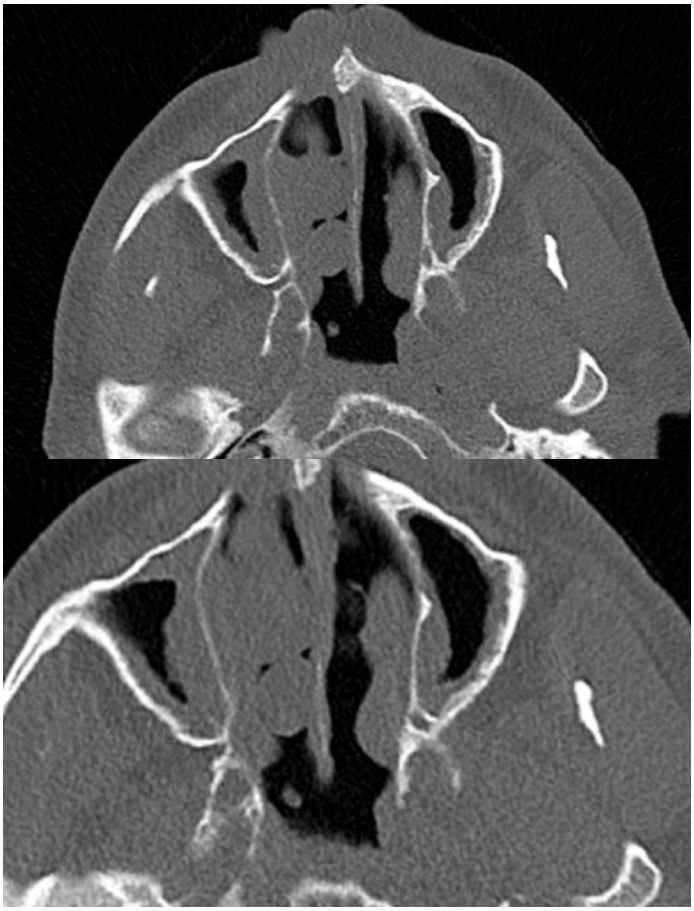

Figure 2. Paranasal sinus CT

DISCUSSION

CSS is a necrotizing vasculitis affecting small vessels. The prominent clinical features are asthma and eosinophilia, and there are many accompanying additional findings. There are 6 criteria determined by the American Society of Rheumatology to diagnose CSS. These are asthma, eosinophilia greater than 10% or 1500/mm³, paranasal sinusitis, pulmonary infiltration, histological vasculitis, and mononeuritis multiplex (2). The presence of 4 of these 6 criteria is sufficient to make a diagnosis. These diagnostic criteria were present in our patient, except for the tissue biopsy sample. The nasal polyp biopsy result was normal in the patient, but the presence of vasculitis could not be detected histologically since he did not accept renal biopsy. In addition to these criteria, the patient also had positivity for pANCA. The elevation of troponin suggested cardiomyopathy and myocardial infarction, which can be seen rarely in Churg Strauss disease, but myocardial infarction was ruled out in the patient. Although the patient had cholecystitis and had no known diagnosis of HT, high blood pressure values during his hospitalization, presence of erythrocyte (30 cells) in the complete urine examination at his admission and 3.73 g proteinuria in his 24-hour urine were also suggestive of glomerulonephritis. This is one of the additional diseases that can be seen in Churgs Strauss disease less commonly.

Corticosteroids are the first choice in the treatment of the disease (3), and in this patient, clinical findings and eosinophilia were improved with the use of steroids (4) (figure 3).

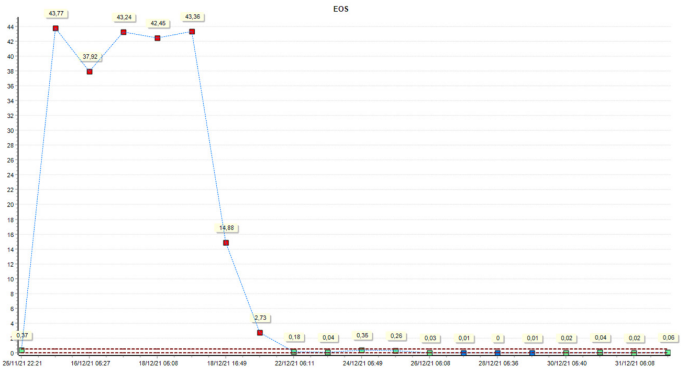

Figure 3. Eosinophil count

CONCLUSION

In relation to this disease, which belongs to the group of vasculitic diseases, it was found remarkable that eosinophilia showing a severe increase and worsening consciousness after leech therapy. Based on this case, it was also desired to draw attention to the fact that such side effects should not be ignored before leech therapy is recommended in vasculitic group diseases.

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Informed Consent: *Informed consent was taken from the patient.*

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MEDICAL RECORDS-International Medical Journal

Erratum

In our article titled “Diffusion MRI Evaluation of Vitreous Humor Changes in Patients with Diabetic Retinopathy” published in Medical Records Journal 2022;4(2):187-90, the word ‘Mizah’ in the Turkish title is misspelled. Corrected Turkish title “Diyabetik Retinopatili Hastalarda Vitreus Humor Değişikliklerinin Difüzyon MRG ile Değerlendirilmesi “

Research Article

Med Records 2022;4(2):187-90

Diffusion MRI Evaluation of Vitreous Humor Changes in Diabetic Retinopathy Patients

Diyabetik Retinopatili Hastalarda Vitreus Humor Değişikliklerinin Difüzyon MRG ile Değerlendirilmesi

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Abstract

Aim: The objective of this study was to use diffusion-weighted imaging (DWI) to determine changes in the vitreous humor in diabetic retinopathy patients.

Materials and Methods: All diabetic retinopathy patients over the age of 18 who had brain diffusion magnetic resonance imaging between May 1, 2019, and May 1, 2021, and whose images were available in the radiological information system were retrospectively scanned on our database. The study included 51 diabetic retinopathy patients and 51 non-diabetic control group patients. The t-test was used to compare the values of the vitreous humor apparent diffusion coefficient (ADC) in diabetic retinopathy patients with control group patients.

Results: Patients with diabetic retinopathy had significantly higher minimum, median, and maximum ADC mean values in the right eye than the control group (p=0.011, p=0.007, p=0.026). Patients with diabetic retinopathy had significantly higher median and maximum ADC averages in the left eye than those in the control group (p=0.020, p=0.012). Although the mean minimum ADC of the left eye was higher in diabetic retinopathy patients than in the control group, the difference was not statistically significant (p=0.387).

Conclusion: Because of the rise in ADC values in diabetic retinopathy patients compared to the normal control group, we detected that DWI could be used to assess if the vitreous humor is affected in this disease.

Keywords: Diabetic Retinopathy, diffusion MRI, vitreous humor, eye

Öz

Amaç: Bu çalışmada, diyabetik retinopatili hastalarda vitreus humor ’de oluşan değişiklikleri difüzyon ağırlıklı görüntüleme (DAG) ile belirlemeyi amaçladık.

Materyal ve Metot: 01 Mayıs 2019 ile 01 Mayıs 2021 tarihleri arasında beyin difüzyon manyetik rezonans görüntüleme yapılmış ve görüntüleri radyoloji bilgi sisteminde bulunan, 18 yaşından büyük olan tüm diyabetik retinopati hastaları veri tabanımızda retrospektif olarak tarandı. Görüntüsü artefaktlı olanlar, vitreus kanaması, glokom, kontrolsüz hipertansiyon olan hastalar çalışma dışında bırakıldı. Sonuçta, 51 diyabetik retinopati hastası ve diyabet hastası olmayan 51 kontrol grubu hastası çalışmaya dahil edildi. Diyabetik retinopatili hastalar ile kontrol grubu hastalarının vitreus humor görünür difüzyon katsayısı (ADC) değerleri t testi ile karşılaştırıldı.

Bulgular: Diyabetik retinopatili hastaların sağ gözde minimum, ortanca ve maksimum ADC ortalamaları kontrol grubu hastalarına göre anlamlı yüksekti (p=0,011, p=0,007, p=0,026). Diabetik retinopatili hastaların sol gözde ortanca ve maksimum ADC ortalamaları kontrol grubu hastalarına göre anlamlı yüksekti (p=0,020, p=0,012). Sol göz minimum ADC ortalaması diyabetik hastalarda kontrol grubuna göre yüksek olmakla birlikte istatistiksel olarak anlamlı değildi (p=0,387).

Sonuç: DAG ile diyabetik retinopatili hastalarda ADC değerlerinde normal kontrol gurubuna göre artış olması nedeniyle vitreus humor ’un bu hastalıkta etkilenip etkilenmediğinin değerlendirilmesinde kullanılabileceğini saptadık.

Anahtar Kelimeler: Diyabetik Retinopati, difüzyon MRG, vitreus humor, göz

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INTRODUCTION

The vitreous makes up about 80% of the volume of the eye and is the transparent part between the lens and the retina. Its structure includes hyaluronic acid, type 2 collagen, and water molecules (1).

Diabetes results in capillary basement membrane thickening, loss of intramural pericytes, and endothelial cell damage. The increase in erythrocyte and thrombocyte aggregation and high fibrinogen levels also contribute to vascular occlusion. Thus, developing capillary and arteriolar occlusion creates retinal hypoxia, which drives the retina to release angiogenic factors, which cause the formation of new vessels in various areas of the eye (retina, optic disk, iris, anterior chamber angle). These veins are abnormal veins that bleed easily. Moreover, microaneurysms and increased permeability result from cell loss in the retinal vessel wall, and retinal macular edema develops due to microaneurysms and deterioration of the internal blood-retinal barrier (2).

Diffusion-weighted imaging (DWI) is a method of magnetic resonance imaging (MRI) based on the random motion of water molecules. The amount of diffusion is influenced by the adjacent environment and the anatomical and physiological structures. Furthermore, the amount of diffusion and the tissue's cellular density have an inverse relationship. When cell density rises, diffusion is limited, and a low signal is acquired in DWI, whereas when cell density lowers, diffusion increases and a high signal is obtained in DWI. The apparent diffusion coefficient (ADC) values and region of interest (ROI) from ADC maps in diffusion MRI are used to obtain quantitative values (3,4). Tight junctions connect the endothelium on the inner surface of retinal vessels to each other. Large and non-carrier molecules are prevented from leaking into the retina and vitreous by these tight junctions, which operate as barriers. In diabetic retinopathy, this barrier, known as the blood-retina barrier, is disrupted, resulting in leakage into the retina and vitreous (5).

The structural content of the vitreous humor changes in patients with diabetic retinopathy (DR); these changes can be assessed with DWI. This study aimed to determine the changes in ADC values due to retinopathy in the vitreous humor.

MATERIAL AND METHOD

51 (29 female, 22 male) patients diagnosed with diabetic retinopathy who underwent diffusion MRI for any reason between May 01, 2019, and May 01, 2021, at Malatya Training and Research Hospital were included in the study. Moreover, 51 (29 female, 22 male) patients from the control group were included in the study, randomly selected at the same dates and matched for age and gender and underwent diffusion MRI for any reason. All patients were evaluated with a standard head-neck coil with a 1.5 T MRI unit. The system generated ADC maps automatically from images with b values of 50 and 1,000. Two radiologists were blinded to the patients' clinical information when evaluating MR images. The minimum, median, and maximum ADC values were measured by placing ROI on the vitreous humor (average 20 mm^2 in all patients) in the right and left orbit (Figure 1).

Statistical analysis

For statistical analysis, the SPSS version 22.0 program was used. For comparisons, the t-test was used. Statistical significance value was accepted as $p<0.05$.

Ethical approval, This retrospective study received ethical approval from the Malatya Turgut Özal University Clinical Research Ethics Committee. Decision no: 2021/90.

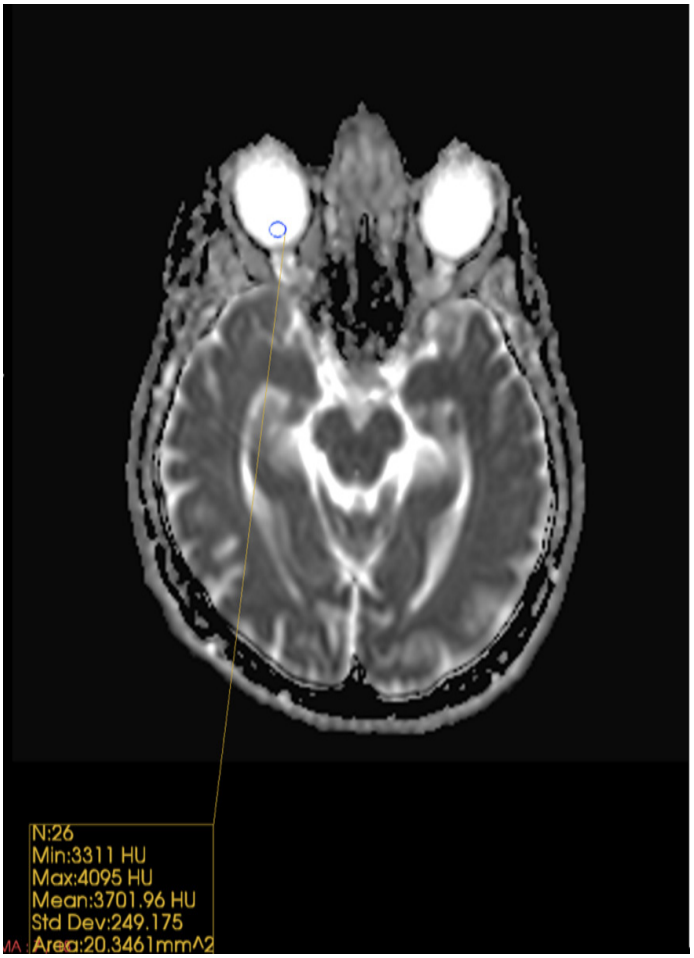

Figure 1. The minimum, median, and maximum ADC values were measured by placing the ROI on the vitreous humor in orbit

RESULTS

58 (56.9%) of the patients were women. The patients' ages ranged from 41 to 88 years old, with a mean of 63.06±9.90. Patients with diabetic retinopathy had significantly higher minimum, median, and maximum ADC mean values in the right eye than the control group ($p=0.011$, $p=0.007$, $p=0.026$).

Table 1. Average ADC values of patients with Diabetic Retinopathy and the control group

VITREOUS HUMOR (VH) ADC	Patients with retinopathy (n=51) Average ADC±SD	Control group (n=51) Average ADC±SD	p
Right VH Min. ADC	2957.6±268.1	2813.9±180.6	0.011
Right VH Avg. ADC	3229.3±281.7	3013.0±193.8	0.007
Right VH Max. ADC	3550.3±319.7	3219.4±234.1	0.026
Left VH Min. ADC	2875.6±214.6	2810.3±189.0	0.387
Left VH Avg. ADC	3167.0±245.5	3006.6±181.9	0.020
Left VH Max. ADC	3477.0±310.4	3199.9±224.5	0.012

SD: Standard deviation; p values were calculated by t-test.
Max.: Maximum, Min.: minimum, Avg.: average

Patients with diabetic retinopathy had significantly higher median and maximum ADC averages in the left eye than those in the control group (p=0.020, p =0.012). Although people with diabetes had a higher mean minimum ADC of the left eye than the control group, this was not statistically significant (p=0.387). Table 1 shows the ADC averages and p-values.

DISCUSSION

Diabetic retinopathy is the leading preventable and/or treatable cause of blindness worldwide in the 20-65 age group. It is one of the most severe complications of diabetes mellitus. The risk of blindness is increased 25 times more compared with the general population (6). Blindness in DR patients is frequently caused by vitreous hemorrhage, tractional retinal detachment, or diabetic macular edema (7).

At DR, pathological changes are observed with increased leukocyte adhesion to vessel walls, death of pericytes, and thickening of the vascular basement membrane. The weakening of endothelial cell connections causes increased vascular permeability. If the fluid leakage is large enough, lipid accumulation in the retina may occur (8). DWI can be used to assess changes in the permeability of cell membranes, changes in water content, such as cell lysis, and morphological and physiological changes in tissues (9). DWI can also be used to assess the microstructural structure of tissues (10). In our study, we assume that DR -related changes in vitreous humor can be detected by DWI.

Our research discovered that patients with DR have high ADC values in vitreous humor in all measurements in the right eye and high maximum and median values in the left eye. Although the minimum ADC value was higher in the left eye than in the normal group, it was not statistically significant. This, we think, is due to the limited number of patients that we have. We think that the increased vascular permeability at DR causes more fluid to enter the vitreous and, accordingly, ADC levels increase.

A low ADC value indicates limited or restricted diffusion and is observed in highly cellular tissues. On the other hand, a high ADC value is observed in structures with relatively free diffusion of tissue fluid, with low cellularity, or in cystic structures (11).

Aldose reductase converts glucose to sorbitol in hyperglycemia. Therefore, sorbitol concentration in the cell may increase to a high level. Sorbitol can lead to an increase in osmolarity (12). We believe that the high ADC values we measured in our study are due to impaired vascular permeability, as more fluid leaks into the extracellular space in DR patients.

DWI is known to be used to diagnose endophthalmitis, optic nerve infarction, orbital cellulitis, pseudotumor, differentiation of lymphoid lesions, diagnosis of orbital abscesses, and characterization of retinoblastoma in pediatric patients, and differentiation of benign and malignant ocular tumors (13). DWI can also be used to assess the microstructural structure of the tissue, so changes due to DR can be detected with DWI. Our research discovered that DWI could be used to evaluate changes in the vitreous humor caused by an increase in ADC values in patients with DR compared to the control group.

Our study's main limitations are the insufficient number of patients and the retrospective character of the study.

CONCLUSION

Using the values from ADC may be essential to understand the structural changes in the vitreous humor due to DR, provide better treatment, and follow up on treatment. More comprehensive studies are still needed on this topic.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *This retrospective study received ethical approval from the Malatya Turgut Ozal University Clinical Research Ethics Committee. Decision no: 2021/90.*

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MEDICAL RECORDS-International Medical Journal

Erratum

In this article titled "Postnatal Outcomes of the Traumatic Childbirth Perception: An Analysis of the Traumatic Childbirth Perception with Pregnancy Avoidance and Mental Health Outcomes" published in Medical Records Journal 2022;4(2):234-41, the institution of the third author, Tuba Ucar, is written incompletely. Corrected Tuba Ucar's institution information "Inonu University, Faculty of Health Sciences, Department of Midwifery, Malatya, Turkey

This article titled "Postnatal Outcomes of the Traumatic Childbirth Perception: An Analysis of the Traumatic Childbirth Perception with Pregnancy Avoidance and Mental Health Outcomes" published in Medical Records Journal 2022;4(2):234-41, "This research was presented as an oral presentation at 5th International Healthy Life Congress, 27-28 April 2021, Online, Turkey"

Research Article

Med Records 2022;4(2):234-41

Postnatal Outcomes of the Traumatic Childbirth Perception: An Analysis of the Traumatic Childbirth Perception with Pregnancy Avoidance and Mental Health Outcomes

Travmatik Doğum Algısının Doğum Sonu Sonuçları: Travmatik Doğum Algısının Gebelikten Kaçınma ve Mental Sağlık Sonuçlarının Analizi

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Abstract

Aim: Several postpartum outcomes of traumatic birth perception have been identified. However, the postpartum results could not be clarified. The study aims were to describe and compare the pregnancy avoidance and mental health outcomes in the women with and without traumatic childbirth perception and to infer which factors may influence the traumatic childbirth perception.

Material and Methods: This cross-sectional and comparative study was conducted with 1109 women who were in the 6-12 months of the postnatal period. The Scale of Traumatic Childbirth Perception (STCP), the Desire to Avoid Pregnancy (DAP) Scale, and the Depression Anxiety Stress Scale-21 were used in the collection of research data. In the study, the women with a moderate or higher level of traumatic childbirth perception (53 points or above) were categorized as 'childbirth perception traumatic'.

Results: In the study, 74.8% of the women obtained 53 points or above from the STCP. It was found that, of the women with traumatic childbirth perception, 46.4% exhibited depressive symptoms, 54.5% experienced anxiety, 41.1% had stress, and the mean of their DAP scores was 2.13±0.96. Women with traumatic birth perception were higher in avoiding depression, anxiety, stress and pregnancy ($p<0.05$). The logistic regression analysis showed that that the variables of being below the age of 30 years (OR=0.543), primiparity (OR=0.459), having depressive symptoms (OR=2.627), having anxiety (OR=1.752), and pregnancy avoidance (OR=1.701) were significant risk factors for traumatic childbirth perception.

Conclusion: It has been found that the perception of traumatic birth can lead to psychological problems and pregnancy avoidance in women.

Keywords: Anxiety, childbirth perception, depression, pregnancy avoidance, stress, trauma

Öz

Amaç: Travmatik doğum algısının çeşitli postnatal sonuçları tanımlanmıştır. Ancak net değildir. Çalışmanın amacı doğum sonu dönemde travmatik doğum algısı olan ve olmayan kadınlarda gebelikten kaçınma ve mental sağlık sonuçlarını tanımlamak ve karşılaştırmak ve travmatik doğum algısını hangi faktörlerin etkileyebileceğini anlamaktır.

Materyal ve Metot: Kesitsel ve karşılaştırmalı tipte tasarlanan araştırma Türkiye'de, 15 Şubat- 15 Mart 2021 tarihleri arasında yürütüldü. Çalışmaya doğum sonu 6-12 ayda olan gönüllü 1109 kadın katıldı. Veriler sosyal medyada (Facebook, Instagram gibi) lohusa kadın grupları aracılığıyla web tabanlı bir çevrimiçi anket kullanılarak toplandı. Veriler toplanırken Kişisel Bilgi Formu, Travmatik Doğum Algısı Ölçeği (TDAÖ), Gebelikten Kaçınma Ölçeği (GKÖ) ve Depresyon Anksiyete Stres Ölçeği (DASÖ-21) kullanıldı. Çalışmada orta düzey ve üzeri travmatik doğum algısı olanlar (53 ve üzeri puan) "travmatik doğum algısı olanlar" olarak sınıflandırıldı.

Bulgular: Kadınların %74.8'i (n=830, travmatik doğum algısı olanlar) TDAÖ'den 53 ve üzeri puan aldı. Travmatik doğum algısı olanların %46.4'ünün depresif semptom, %54.5'inin, anksiyete ve %41.1'inin stres yaşadığı; GKÖ skorunun 2.13±0.96 olduğu belirlendi. Travmatik doğum algısı olan kadınların depresif semptom, anksiyete, stres ve gebelikten kaçınma olasılığının daha fazla olduğu belirlendi ($p<0.05$). Lojistik Regresyon analizine göre kadınlarda 30 yaş altı olma (OR=0.543), primiparite (OR=0.459), depresif semptom varlığı (OR=2.627), anksiyete varlığı (OR=1.752) ve gebelikten kaçınma (OR=1.701) değişkenlerinin travmatik doğum algısı için önemli risk faktörleri olduğu saptandı.

Sonuç: Araştırma bulguları travmatik doğum algısının kadınlarda psikolojik sorunlara ve gebelikten kaçınmaya neden olabileceğini ortaya koymuştur.

Anahtar Kelimeler: Anksiyete, doğum algısı, depresyon, gebelikten kaçınma, stres, travma

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INTRODUCTION

Childbirth serves as a critical role transition in the women's lives and is generally viewed as a positive occasion that changes the women's lives (1). Traumatic childbirth is, on the other hand, the case that the woman perceives the act of childbirth as a threat likely to lead to the injury or death of the infant to be born and herself (2). The women with traumatic childbirth experience define the moment of giving birth as a moment of helplessness, strong fear, and horror (1, 3). In relation to the prevalence of traumatic childbirth perception, various percentages are presented. Around 20-45% of the women state that they had a traumatic childbirth experience (4-6). The traumatic childbirth perception that is described as negative is the entire set of perceptions that come into play as a consequence of blending the childbirth theme created by the woman in her mind and all information acquired by her about childbirth with each circumstance that she is likely to experience during the act of giving birth (7). The traumatic childbirth perception is made up of thoughts, behaviors, information, and attitudes related to that the childbirth is quite bloody, painful, and terrifying incident (8).

The childbirth perception is affected by the woman's viewpoint about childbirth, personal characteristics, previous childbirth experience, and the cultural structure of the society (3). Also, tokophobia plays a quite crucial role in the formation of traumatic childbirth perception (2, 9). Having excessive anxiety and fear can have a negative effect on the woman both physically and emotionally, and thus, even if the woman wants to have a baby, she can avoid becoming pregnant and, accordingly, giving birth (10, 11). To avoid pregnancy, particularly the women with tokophobia can prefer to use the birth-control family planning methods that have high rates of effectiveness (12,13).

If childbirth takes place as a negative experience for the women, the women can develop conflicting feelings (14). It was ascertained that, in the postnatal period, the traumatic experience was associated with anger, guilt, depression, and suicide (6, 15). In a qualitative study conducted with the participation of women experiencing childbirth trauma, it was put forward that the women had negative feelings such as fear, horror, and sadness during the process of childbirth (16).

The perception that childbirth which is a natural component of the female sexuality is a traumatic experience besides the psychological problems likely to be produced by this perception can lead to negative outcomes for the woman herself, her family, and the future generations (7). Having awareness about the variables that are associated with the traumatic childbirth perception in the woman can make it possible to take psychological initiatives at the early stage. Therefore, this study aimed to define and compare the pregnancy avoidance and mental health outcomes of the women with traumatic childbirth perception and the women with no traumatic childbirth perception in the postnatal period and to understand which factors were likely to affect the traumatic childbirth perception.

MATERIAL AND METHOD

Study design and setting

Designed as a cross-sectional and comparative study, the research was carried out in Turkey on 15 February - 15 March in 2021. The research data were collected with a web-based online survey form shared via puerperal women groups in social media (Facebook, Instagram, and so on). The survey form was created by using the application, Google Forms (Google LLC, Mountain View, CA, the USA), and the survey link was shared with the women through social media. The first page of the online survey form presented information on the aim and content of the research besides a form for the women to express consent to participate in the study. The women who consented to participate in the research and satisfied the required inclusion criteria were included in the study. The criteria prescribed for being included in the research were for the woman to be in the 6-12 months of the postnatal period, to be aged 18 years or above, and to have no complications developing in her or her newborn in the postnatal period. A total of 1132 women responded to the online survey. The survey forms with missing data, incomplete parts, or inaccurate coding were identified, and accordingly, 23 respondents were left out of the evaluations as their survey forms were deemed ineligible for evaluations. Thus, the research sample was comprised of 1109 women in total. In the research, upon the collection of research data, the women were categorized into two groups as per having traumatic childbirth perception. In this respect, the women who obtained 52 points or below from the Scale of Traumatic Childbirth Perception were categorized as 'childbirth perception non-traumatic' whereas the women who had 53 points or above were grouped as 'childbirth perception traumatic'. There were 279 women in the group categorized as 'childbirth perception non-traumatic' whilst 830 women were present in the group categorized as 'childbirth perception traumatic', and the data obtained from the two groups were compared.

Measures

The research data were collected by using the Personal Information Form, the Scale of Traumatic Childbirth Perception (STCP), the Desire to Avoid Pregnancy (DAP) Scale, and the Depression Anxiety Stress Scale-21 (DASS-21).

Personal Information Form

This form had questions designed to find out the women's socio-demographic and obstetric characteristics (age, education level, income level, employment status, marriage duration in years, method of childbirth, parity, pregnancy planning, and using contraceptive methods).

STCP

Yalnız H, et al. (2016) developed the scale was to evaluate the traumatic childbirth perception levels of the women in the reproductive age and performed the study to

test its validity and reliability in Turkish (2). The scale is comprised of 13 questions aspiring to uncover the thoughts and feelings such as anxiety, fear, and worry that the woman has when she thinks of the childbirth concept. Each problem is scored from 0 (I am not afraid at all) to 10 points (I am extremely afraid). The minimum and maximum scores to be obtained by a respondent from the scale are respectively 0 and 130 points. The scores ranging from 0 to 26 points, from 27 to 52 points, from 53 to 78 points, from 79 to 104 points, and from 105 to 130 points successively refer to 'very low-level', 'low-level', 'moderate-level', 'high-level', and 'very high-level' traumatic childbirth perception. The Cronbach's alpha coefficient was found as 0.89 for the scale (2). The women with a medium or higher level of traumatic childbirth experience (53 points or above) were categorized as 'childbirth perception traumatic' in this current study. The Cronbach's alpha coefficient was calculated as 0.90 for the scale under the current study.

DAP Scale

The scale was developed by Rocca, Ralph, Wilson, Gould, and Foster (2019) and the study to test its validity and reliability in Turkish was conducted by Karataş Okyay, Güney, and Uçar (2021) (17,18). The scale addresses a woman's future preferences about pregnancy and childbirth. Comprised of 14 items, the scale pertains to the woman's emotions and thoughts about becoming pregnant and childbirth. The items of the five-point Likert-type scale are scored as 0 (I strongly agree), 4 (I strongly disagree). Seven items of the scale are reverse-scored. After the scores calculated from the reverse-scored items are also converted into straight scores, they are added to the scores obtained from the straight-scored items. Subsequently, this sum is divided by 14 and hence, the final score is obtained. The minimum and maximum scores to be obtained from the scale are consecutively 0 and 4 points. A high score obtained from the scale shows that the woman has a high-level desire to avoid pregnancy. As per the analysis of internal consistency conducted to find out the reliability of the scale, the Cronbach's alpha coefficient was found as 0.94 for the scale (18).18 In this current study, the Cronbach's alpha coefficient was calculated as 0.94 for the scale.

DASS-21

The DASS-21 is the measurement tool abridged from the 42-item scale that was developed by Lovibond and Lovibond to evaluate the individual's depression, anxiety, and stress levels (19). The study to test the validity and reliability of the scale in Turkish was performed by Sarıçam (2018). The scale has three sub-scales, that is, depression, anxiety, and stress. Each sub-scale has seven items and thus, the overall scale has 21 items. The items of the four-point Likert-type scale are scored from 0 (Never) to 3 (Always). The scores obtained by a respondent from items under each sub-scale are summed and the sum is evaluated as per a score range specific to each sub-scale. In this regard, the score ranges that are taken into consideration in the evaluations are exhibited in Table 1 (20).

Table 1. DASS-21 Scoring Ranges

Level	Depression	Anxiety	Stress
Normal	0-4	0-3	0-7
Mild	5-6	4-5	8-9
Moderate	7-10	6-7	10-12
Severe	11-13	8-9	13-16
Extremely severe	14+	10+	17+

DASS-21: Depression Anxiety Stress Scale

As the measure of internal consistency, the Cronbach's alpha coefficient was found successively as 0.87, 0.85, and 0.81 for the depression, anxiety, and stress sub-scales (20). Under this current study, the Cronbach's alpha coefficient was calculated consecutively as 0.79, 0.87, and 0.85 for the above DASS-21 sub-scales.

In this current study, the women were divided into two groups as per their depression, anxiety, and stress levels. The women who were deemed to have normal levels of depression, anxiety, and stress as per Table 1 were evaluated as 'having no depression', 'having no anxiety', and 'having no stress'. In this context, firstly, the women who obtained 0-4 points from the depression sub-scale were categorized as 'having no depression' while the women who obtained 5-21 points were categorized as 'having depression', secondly, the women who obtained 0-3 points from the anxiety sub-scale were categorized as 'having no anxiety' whilst the women who obtained 4-21 points were categorized as 'having anxiety', and thirdly, the women who obtained 0-7 points from the stress sub-scale were categorized as 'having no stress' whereas the women who obtained 8-21 points were categorized as 'having stress'.

Statistical analysis

The research data were evaluated with SPSS 25.0 for Windows (SPSS, Chicago, IL, USA). The descriptive statistics were expressed as number, percentage, mean, and standard deviation. While analyzing the research results, the women who obtained 0-52 points from the STCP were categorized as 'childbirth perception non-traumatic' whereas the women who obtained 53-130 points from the STCP were characterized as 'childbirth perception traumatic'. The chi-squared test was used in the comparison of the categorical independent variables. In the evaluation of the continuous data, firstly, whether the variables were normally distributed was checked via the Kolmogorov-Smirnov test. As the data were normally distributed, independent samples t-test was utilized in the comparison of the two groups whilst one-way analysis of variance was employed in the comparison of multiple groups. The variables affecting the traumatic childbirth

perception in the women were evaluated with logistic regression analysis. In the context of identifying the variables to be considered under the regression model, the variables that had a statistically significant relationship ($p<0.05$) with the traumatic childbirth perception were included in the model. In this regard, the regression model covered the age, income level, parity, and the use of contraceptive methods together with the scales that identified the levels of depression, anxiety, stress, and pregnancy avoidance. The statistical significance was identified if the P-value was lower than 0.05.

Ethical aspect of the research

Before collecting the research data, the ethical endorsement was obtained from the Health Sciences Non-Invasive Clinical Trials and Publications Ethics Committee (Endorsement no. 2021/1694). Upon getting information about the research on the first page of the survey form, the respondents were informed that the confidentiality of their personal data would be protected.

RESULTS

In the context of this study, it was found that, of the women, 7.4% had very low-level traumatic childbirth perception (n=82), 17.8% had low-level traumatic childbirth perception (n=197), 30.4% had moderate-level traumatic childbirth perception (n=337), 29.8% had high-level traumatic childbirth perception (n=331), and 14.6% had very high-level traumatic childbirth perception (n=162). In the study, 74.8% of the women obtained 53 points or above from the STCP (n=830, childbirth perception traumatic) whereas 25.2% of them had 52 points or below (Figure 1). On the basis of the STCP scores, Table 2 displayed the comparison of traumatic childbirth perception according to the characteristics of the women. It was discerned that the women who were aged 30 years or below, who had moderate/high-level income, who were primiparous, and who currently used contraceptive methods had higher frequencies of having 'childbirth perception traumatic' and the differences between the groups were statistically significant ($p<0.05$, Table 2).

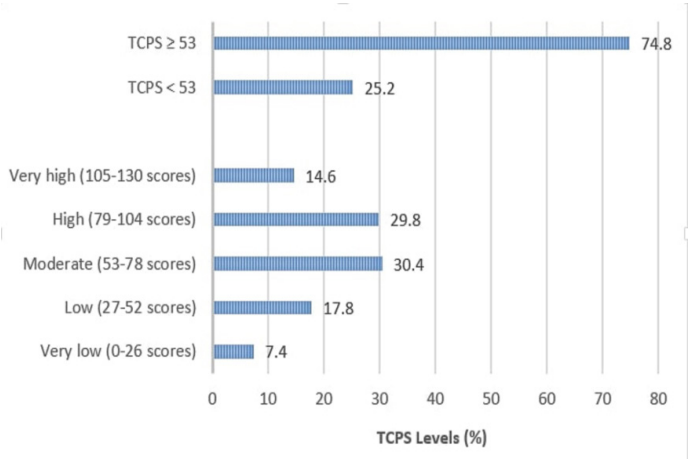


Figure 1. Women's Perception of Traumatic Childbirth Levels

Table 2. Comparison of traumatic childbirth perception (according level of STCP) according to the characteristics of the women (n=1109)

Characteristics	STCP < 53 score (n=279)		STCP ≥ 53 score (n=830)		Total (n=1109)		Test* and p value
	n	%	n	%	n	%	
Age, y							
≤30	112	40.1	422	50.8	534	48.2	χ^2=9.576
>30	167	59.9	408	49.2	575	51.8	p=0.002
Educational level, y							
≤12	170	60.9	535	64.5	705	63.6	χ^2=1.121
>13	109	39.1	295	35.5	404	36.4	p=0.290
Income status							
Low	6	2.2	45	5.4	51	4.6	χ^2=5.093
Moderate/ High	273	97.8	785	94.6	1058	95.4	p=0.024
Employment status							
Employed	79	28.3	204	24.6	283	25.5	χ^2=1.534
Unemployed	200	71.7	626	75.4	826	74.5	p=0.215
Marriage, y							
≤5	100	35.8	330	39.8	430	38.8	χ^2=1.349
≥ 6	179	64.2	500	60.2	679	61.2	p=0.245
Mode of birth							
Vaginal	165	59.1	489	58.9	654	59.0	χ^2=0.004
Caesarean section	114	40.9	341	41.1	455	41.0	p=0.948
Parity							
Primipara	35	12.5	159	19.2	194	17.5	χ^2=6.325
Multipara	244	87.5	671	80.8	915	82.5	p=0.012
Planning to pregnancy							
Yes	95	34.1	242	29.2	337	30.4	χ^2=2.364
No	184	65.9	588	70.8	772	69.6	p=0.124
Current contraceptive use							
Yes	172	61.6	569	68.6	741	66.8	χ^2=4.491
No	107	38.4	261	31.4	368	33.2	p=0.034

TCP: Traumatic Childbirth Perception, STCP: The Scale of Traumatic Childbirth Perception, *chi-square test

On the basis of the STCP scores, Table 3 displayed the pregnancy avoidance and mental health outcomes of the traumatic childbirth perception. It was ascertained that 46.6% of the women with traumatic childbirth perception and 21.1% of the women with no traumatic childbirth perception exhibited depressive symptoms, 54.5% of the women with traumatic childbirth perception and 30.5% of the women with no traumatic childbirth perception had anxiety, 41.1% of the women with traumatic childbirth perception and 25.4% of the women with no traumatic childbirth perception had stress, and the differences between the groups were statistically significant. Besides, it was identified that the women with traumatic childbirth perception had a higher mean of DAP Scale scores than the women with no traumatic childbirth perception (2.13±0.96 points vs. 1.73±0.99 points, p<0.001, Table 3).

Table 3. Comparison of traumatic childbirth perception (according level of STCP) of women according to the DASS-21 and DAP (n=1109)

		STCP<53 score (n=279)		STCP≥53 score (n=830)		Total (n=1109)		Test* and p value
	Scales	n	%	n	%	n	%	
DASS-21	**Depression**							
	Yes (5-21 score)	59	21.1	385	46.4	444	40.0	χ^2=55.404
	No (0-4 score)	220	78.9	445	53.6	665	60.0	p<0.001
	Anxiety							
	Yes (4-21 score)	85	30.5	452	54.5	537	48.4	χ^2=48.125
	No (0-3 score)	194	69.5	378	45.5	572	51.6	p <0.001
	Stress							
	Yes (8-21 score)	71	25.4	341	41.1	412	37.2	χ^2=21.865
	No (0-7 score)	208	74.6	489	58.9	697	62.8	p <0.001
		Mean ± SD		**Mean ± SD**		**Mean ± SD**		**Test** and p value**
	DAP score	1.73±0.99		2.13±0.96		2.03±0.99		t=-5.974 p<0.001

* chi-square test, **Independent Samples t Test, SD: Standard Deviation, STCP: The Scale of Traumatic Childbirth Perception, DASS-21: Depression Anxiety Stress Scale, DAP: Desire to Avoid Pregnancy Scale

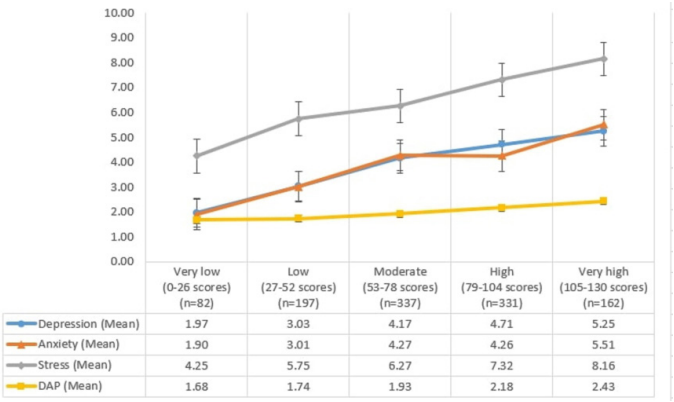
In the context of the model created with the variables that had a statistically significant relationship with traumatic childbirth perception as per the above bivariate analyses, the results of the logistic regression analysis were shown in Table 4. According to the results of the logistic regression analysis, it was identified that the variables of being below the age of 30 years (OR=0.543), primiparity (OR=0.459), exhibiting depressive symptoms (OR=2.627), having anxiety (OR=1.752), and pregnancy avoidance (OR=1.701) were significant risk factors for traumatic childbirth perception.

Table 4. Logistic Regression Analysis of significant variables related to STCP

	B	SE	df	P	OR	95% CI Lower	95% CI Upper
Age, y							
≤30	(Reference)						
>30	-0.610	.165	1	<0.001	.543	.543	.750
Income status							
Moderate/ High	(Reference)						
Low	0.614	.467	1	0.188	1.848	.740	4.614
Parity							
Primipara	(Reference)						
Multipara	-0.780	.235	1	0.001	.459	.289	.727
Current contraceptive use							
Yes	(Reference)						
No	-0.201	.162	1	0.215	.818	.595	1.124
Depression							
Yes(5-21 score)	(Reference)						
No (0-4 score)	0.966	.180	1	<0.001	2.627	1.846	3.738
Anxiety							
Yes(4-21 score)	(Reference)						
No (0-3 score)	0.561	.173	1	<0.001	1.752	1.249	2.457
Stress							
Yes(8-21 score)	(Reference)						
No (0-7 score)	0.026	.184	1	0.886	1.027	.716	1.472
DAP score [a]	0.531	.089	1	<0.001	1.701	1.430	2.023

a Numerical data were used, B: Regression Coefficient; SE: Standard Error; OR: Odds Ratio; CI: Confidence Interval. DAP: Desire to Avoid Pregnancy Scale

Figure 2 indicated the means of the women's depression, anxiety, stress, and DAP Scale scores as per their traumatic childbirth perception levels. The means of depression scores of the women with very low-level, low-level, moderate-level, high-level, and very high-level traumatic childbirth perception were successively 1.97±2.11, 3.03±2.28, 4.17±3.15, 4.71±3.21, and 5.25±3.40 points, the means of anxiety scores of the women with very low-level, low-level, moderate-level, high-level, and very high-level traumatic childbirth perception were respectively 1.90±2.78, 3.01±3.12, 4.27±3.76, 4.26±3.77, and 5.51±3.98 points, the means of stress scores of the women with very low-level, low-level, moderate-level, high-level, and very high-level traumatic childbirth perception were consecutively 4.25±3.74, 5.75±4.19, 6.27±3.78, 7.32±4.16, and 8.16±4.40 points, and the means of the DAP Scale scores of the women with very low-level, low-level, moderate-level, high-level, and very high-level traumatic childbirth perception were successively 1.68±0.97, 1.74±1.00, 1.93±0.91, 2.18±0.99, and 2.43±0.92 points. It was discerned that there were statistically significant differences in the means of the women's depression, anxiety, stress, and DAP Scale scores as per their STCP levels (respectively, F=25.886, F=18.355, F=18.124, F=17.048; p< 0.001, Figure 2).



	Very low (0-26 scores) (n=82)	Low (27-52 scores) (n=197)	Moderate (53-78 scores) (n=337)	High (79-104 scores) (n=331)	Very high (105-130 scores) (n=162)
Depression (Mean)	1.97	3.03	4.17	4.71	5.25
Anxiety (Mean)	1.90	3.01	4.27	4.26	5.51
Stress (Mean)	4.25	5.75	6.27	7.32	8.16
DAP (Mean)	1.68	1.74	1.93	2.18	2.43

Figure 2. Means of the participant women's depression, anxiety, stress, and DAP Scale scores as per their STCP levels

DISCUSSION

In this study in which the women's traumatic childbirth perceptions were analyzed, it was found that approximately three fourth of the women (74.8%) had traumatic childbirth perceptions. In relation to the traumatic childbirth perception prevalence, various percentages are present. Just as the changes in these percentages are affected by a variety of factors, they can also be affected by the use of a different measurement tool. In the study by Alcorn et al. (2010), it was ascertained that 45.5% of the women characterized their childbirth experiences as traumatic according to the criteria outlined in the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Version) (6). The study by Boorman et al. (2014) found that 29.4% of the women satisfied the criteria for traumatic childbirth (11). In these two studies, the Posttraumatic Diagnostic Scale was utilized. In Turkey, until 2016, no scale measured the traumatic childbirth perception. The finding of this current study is closer to the prevalence rate, 69.5%, that was obtained in the study performed by Aktaş (2018) on multigravidas with the STCP (21). The STCP that was used in this current study is a relatively new scale that helps to measure any form of childbirth trauma.

In this current study, it was identified that the women with traumatic childhood perception were more likely to have emotional distress (depression, anxiety, stress) and pregnancy avoidance. Also in the previous studies, it was asserted that the traumatic childbirth experience could be associated with a minimum of one post-natal emotional health problem and the childbirth-related negative emotions could give rise to outcomes such as preferring not to get pregnant again (6,22,23). Grenfield et al. (2019) found that the women with traumatic childbirth perception made research and analysis about pregnancy and childbirth to prevent their previous childbirth experiences from occurring once again (24). James (2015) ascertained that the women exhibited avoidance behaviors to control threats and symptoms emerging in the wake of the traumatic childbirth experience (25). In the study by Boorman et al. (2014), it was put forth that stress, anxiety, and depression were predictors of the traumatic childbirth criteria (11). In the study by Simpson and Catling (2016), it was reported that there was a relationship between traumatic childbirth and mental diseases in women (26). Of course, this study and other similar studies do not indicate that there is causation between a traumatic childbirth experience and emotional problems. The postnatal period is not the sole factor for the traumatic childbirth perception as the perinatal period is characterized by the physical, social, and psychological transitions that are likely to influence a woman's emotional well-being (25).

Under this current study, it was found that being young and being primiparous were significant risk factors for the women to have traumatic childbirth perception. Considering this finding, it is inevitable that the primiparous women at a relatively early age view childbirth as an unknown phenomenon and, as it is an unknown phenomenon for them, they cannot avoid having fears and hence, their childbirth perceptions become negative (11,27). Likewise, Boorman et al. (2014) set forward that the primipara, the women who gave birth for the first time, were more likely to find childbirth as a traumatic experience (11). In this current study, it was identified that the women that used contraceptive methods were more likely to have traumatic childbirth perception. It can be considered that the women with traumatic childbirth experience might have escaped from becoming pregnant to avoid having this experience again and used contraceptives for this purpose. As a matter of fact, in the study by Gipson, Bornstein, Berger and Rocca (2021), it was stated that the women with a high percentage of using contraceptives exhibited pregnancy avoidance attitudes (28). Thus, it is discerned that the result of the study by Gipson et al. supported the finding of this current study.

As per this current study, the women with medium/high-level income were more likely to have traumatic childbirth perception. Güleç et al. (2014) asserted that there was a relationship between childbirth fear and income level (29). On the other hand, Üst and Pasinlioğlu (2015) put forward that the income level had no effect on childbirth and post-natal worries (30). In this sense, it can be considered that the income level is not the sole factor affecting childbirth perception, nevertheless, as it is accompanied by other negative circumstances such as the place of childbirth, setbacks in accessing the necessary information, and the lack of social support, it can have an effect on the traumatic childbirth perception held by the women.

CONCLUSION

This study indicated that pregnancy avoidance and psychological factors (depression, anxiety, and stress) affected the traumatic childbirth perception and were significant risk factors for the traumatic childbirth perception. To ensure that childbirth which is considered as a physiological process does not turn to be a traumatic experience by being estranged from its normal course, the identification of risk factors in the prenatal period and the application of necessary midwifery approaches at an early stage are quite essential. Raising the individuals' awareness about these risk factors, restructuring negative memories if any, and reducing risk factors by referring the women who have depression, anxiety, and stress to the specialists when necessary will also lower the risk of having traumatic childbirth perception. Moreover, it is considered that the psychoeducational interventions will be effective in alleviating the tokophobia and, accordingly, changing the traumatic childbirth perception.

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