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MEDICAL RECORDS-International Medical Journal

Araştırma Makalesi / Research Article

Early Detection of Coronary Heart Disease Based on Machine Learning Methods

Makine Öğrenme Yöntemlerine Dayali Kroner Kalp Hastaliğinin Erken Tespiti

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Abstract

Aim: Heart disease detection using machine learning methods has been an outstanding research topic as heart diseases continue to be a burden on healthcare systems around the world. Therefore, in this study, the performances of machine learning methods for predictive classification of coronary heart disease were compared.

Material and Method: In the study, three different models were created with Random Forest (RF), Logistic Regression (LR), and Support Vector Machine (SVM) algorithms for the classification of coronary heart disease. For hyper parameter optimization, 3-repeats 10-fold repeated cross validation method was used. The performance of the models was evaluated based on Accuracy, F1 Score, Specificity, Sensitivity, Positive Predictive Value, Negative Predictive Value, and Confusion Matrix (Classification matrix).

Results: RF 0.929, SVM 0.897 and LR 0.861 classified coronary heart disease with accuracy. Specificity, Sensitivity, F1-score, Negative predictive and Positive predictive values of the RF model were calculated as 0.929, 0.928, 0.928, 0.929 and 0.928, respectively. The Sensitivity value of the SVM model was higher compared to the RF.

Conclusion: Considering the accurate classification rates of Coronary Heart disease, the RF model outperformed the SVM and LR models. Also, the RF model had the highest sensitivity value. We think that this result, which has a high sensitivity criterion in order to minimize overlooked heart patients, is clinically very important.

Keywords: Heart disease, machine learning, classification, random forest, parameter optimization

Öz

Amaç: Kalp hastalıklarının dünya çapında sağlık sistemleri üzerinde bir yük olmaya devam etmesi nedeniyle, makine öğrenme yöntemlerini kullanarak kalp hastalığı tespiti olağanüstü bir araştırma konusu olmuştur. Bu nedenle, bu çalışmada, koroner kalp hastalığının tahmin edici sınıflandırması için makine öğrenme yöntemlerinin performansları karşılaştırılmıştır.

Materyal ve Metot: Çalışmada koroner kalp hastalığının sınıflandırılması için Rasgele Orman (RF), Lojistik Regresyon (LR) ve Destek Vektör Makinesi (SVM) algoritmaları ile üç farklı model oluşturulmuştur. Hiperparametre optimizasyonu için 3 tekrarlı 10 katlı tekrarlı çapraz doğrulama yöntemi kullanıldı. Modellerin performansı Doğruluk, F1 Skoru, Seçicilik, Duyarlılık, Pozitif Tahmin Değeri, Negatif Tahmin Değeri ve Karışıklık Matrisi (Sınıflandırma matrisi) temel alınarak değerlendirilmiştir.

Bulgular: Koroner kalp hastalığını RF 0.929, SVM 0.897 ve LR 0.861 doğrulukla sınıflandırdı. RF modelinin seçicilik, duyarlılık, F1-skor, negatif tahmin ve pozitif tahmin değerleri sırasıyla 0.929, 0.928, 0.928, 0.929 ve 0.928 olarak hesaplanmıştır. Ek olarak SVM modelinin duyarlılık değeri RF'ye göre daha yüksek çıkmıştır.

Sonuç: Koroner Kalp hastalığının doğru sınıflandırma oranları göz önüne alındığında, RF modeli SVM ve LR modellerinden daha iyi performans göstermiştir. Ayrıca RF modeli en yüksek duyarlılık değerine sahipti. Gözden kaçırılan kalp hastalarını en aza indirmek için yüksek bir duyarlılık kriterine sahip olan bu sonucun klinik açıdan oldukça önemli olduğunu düşünmekteyiz.

Anahtar Kelimeler : Kalp hastalığı, makine öğrenmesi, sınıflandırma, rastgele orman, parametre optimizasyonu

INTRODUCTION

Coronary heart disease (CHD) is the world's leading cause of death. CHD is often referred to as ischemic heart disease or coronary artery disease. Coronary heart disease arises when fatty deposits in the coronary arteries impede or disrupt blood flow to the heart. Over time, the walls of coronary arteries may become furrowed with fatty deposits. Atheroma is the term for fatty deposits, and

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atherosclerosis is the term for the process. Smoking and ingesting excessive amounts of alcohol on a regular basis are two lifestyle factors that induce atherosclerosis. CHD is caused by excessive cholesterol, high blood pressure (hypertension), and diabetes (1, 2).

The most frequent symptoms of coronary heart disease are chest pain (angina) and shortness of breath. Patients' medical/family history and risk factors are requested if a doctor believes you are at risk of coronary. Although coronary heart disease cannot be cured, medicines can help manage the symptoms and extend life by reducing the risk of complications such as heart attacks and heart failure. As a result, early detection and treatment of the disease are critical for lowering the mortality rate (3-5).

Artificial intelligence (AI) are used for the diagnosis of many diseases such as heart, diabetes and cancer, and thus is becoming more and more popular in healthcare. AI is a broad term that encompasses analytical algorithms that iteratively learn from data, allowing computers to discover hidden insights without being explicitly instructed where to seek. These are a group of operations that include terminology like machine learning, cognitive learning, deep learning, and reinforcement learning-based methods for integrating and interpreting complicated biological and healthcare data in situations where traditional statistical methods fail (6).

Machine learning (ML) is an area of AI that involves using mathematical models to assist a computer in learning without being given explicit instructions. Algorithms are used in machine learning to find patterns in data. These patterns are also utilized to build a data model that predicts the future. Machine learning algorithms are used in prospective clinical trials to compare existing standard of care procedures with the goal of introducing precision diagnostics, risk stratification, and personalized medicines.

Cardiovascular diseases are a group of disorders that can benefit tremendously from proactive care, prevention, and prediction, and hence AI approaches. Understanding the intricate individual risk factors, behavioral variables, and treatment pathways predictive of illness outcomes in specific patient cohorts, as well as establishing early therapeutic interventions, will require a variety of AI algorithms (7-14).

The aim of this study is to classify coronary artery disease with machine learning methods and to compare the classification performances of Logistic Regression, Random Forest, and Support Vector Machine methods.

MATERIAL AND METHOD

Dataset

The heart disease dataset used in this study was obtained from the IEEEDataPort database (https://ieee-dataport.org/open-access/heart-disease-dataset-comprehensive#files). The dataset was created by combining Cleveland, Hungarian, Switzerland, Statlog (Heart) Data Set, and Long Beach VA datasets. Combining was performed using 11 covariates from these 5 heart disease datasets. In this way, a rather large data set was obtained compared to the existing heart disease datasets. In the data set, 281 (23.6%) of the patients were female and 909 (76.4%) were male. The mean age of female was 53±10 and the mean age of male was 54±9. Detailed information about the data set is as in Table I and Table II (15).

Logistic Regression (LR)

Logistic Regression Analysis (LR) is a method used to determine the cause-effect relationship between the dependent variable and the independent variables, without being dependent on a certain distribution assumption, when the dependent variable is categorical and the independent variables are mixed-scale. Using the maximum likelihood estimation method, LR estimates the unknown parameter values that maximize the probability obtained from the data set. Thus, the parameter estimates that maximize the likelihood function are selected and the parameter estimates that best match the observed data are obtained (16, 17).

Table 1. Heart disease dataset attribute description

Attribute	Code given	Unit	Data type
Age	age	in years	Numeric
Sex	sex	1,0	Binary
Chest pain type	chest pain type	1, 2, 3, 4	Nominal
Resting blood pressure	resting bp s	in mm Hg	Numeric
Serum cholesterol	cholesterol	in mg/dl	Numeric
Fasting blood sugar	fasting blood sugar	1,0>120 mg/dl	Binary
Resting electrocardiogram results	resting ecg	0, 1, 2	Nominal
Maximum heart rate achieved	max heart rate	71-202	Numeric
Exercise induced angina	angina	0,1	Binary
Oldpeak=ST	oldpeak	depression	Numeric
The slope of the peak exercise ST segment	ST slope	0, 1, 2	Nominal
Class	target	0,1	Binary

Table 2. Description of nominal attributes in dataset	
Attribute	**Description**
Sex	1=male, 0=female
Chest Pain Type	Value1: typical angina Value 2: atypical angina Value 3: non-anginal pain Value 4: asymptomatic
Fasting blood sugar	fasting blood sugar >120 mg/dl (1=true;0=false) Value 0: normal
Resting electrocardiogram results	Value1: having ST-T wawe abnormality (T wawe inversions and/or ST elevation or depression of>0.05 Mv Value 2: showing probable or definite left ventricular hypertrophy by Estes criteria
Exercise induced angina	1=yes,0=no
The slope of the peak exercise ST segment	Value1: unsloping Value2: flat Value3: downsloping
Class	1=heart disease,0=Normal

Support Vector Machine (SVM)

Support Vector Machine (SVM) is a set of supervised learning algorithms that detect patterns. It is a type of classification method that estimates the classification function and analyzes the data used for classification. When compared to other approaches, it often delivers better categorization results. It is a nonlinear classification method that has been reported. SVM's main concept is to use a hyperplane as a decision surface to optimize the margin of separation between positive and negative samples (Figure 1). This method converts non-linear input sample data into a high-dimensional space where the data may be separated linearly, resulting in improved classification (or regression) accuracy. SVMs are unique in that they have a strong theoretical base as well as cutting-edge success in real-world applications, especially in bioinformatics (18).

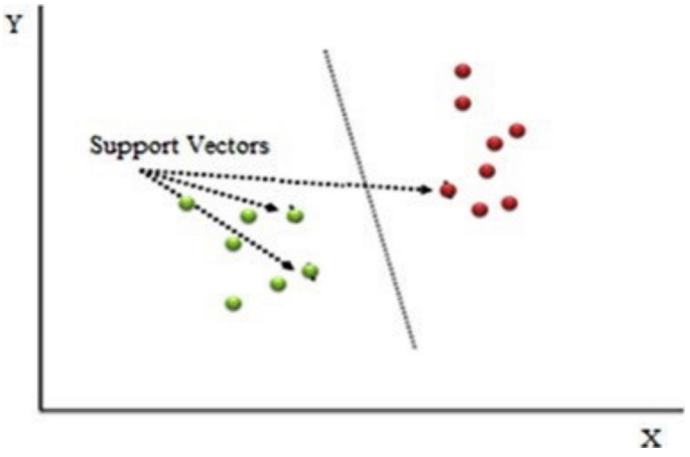

Figure 1. Support Vector distribution

Random Forest (RF)

Random Forest (RF) is community classification used for classification and regression analysis. In this community classifier, it is aimed to increase the classification success by creating more than one decision tree. RFs work by creating various decision trees and labels according to the majority during the training phase. The difference of RFs from decision tree algorithms is that basically finding the root node and splitting the nodes work randomly. The reason why the RF method is also considered in this study is that it is good at detecting noise and outliers and can solve the over-learning problem. It is also one of the most appropriate methods to define the most important feature among the data set features. Thus, feature extraction is applied in the most accurate way and the success rate is achieved to reach the highest rates. The classification logic of the random forest algorithm is as in Figure 2 (19, 20).

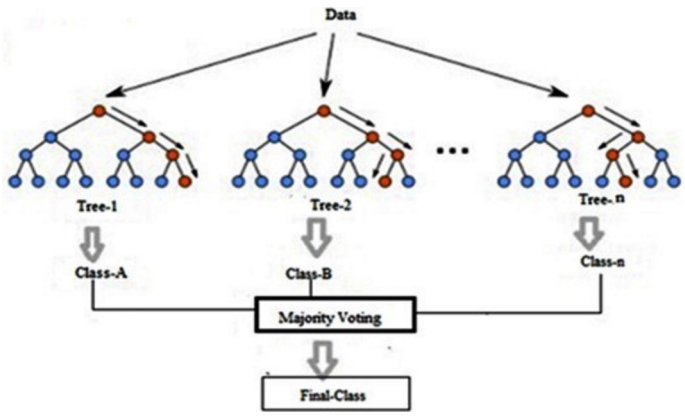

Figure 2. Random Forest algorithm

Data Preprocessing, Modeling and Evaluation of Predictive Models

The SVM-SMOTE method was first applied to the data set. After SVM-SMOTE, a total of 1258 (initially 1190) samples were obtained, 629 in each class. The dataset was then split with 80% for training and 20% for testing. LR, SVM and RF algorithms were used for the classification task. The optimal hyper-parameters of each model were determined by Grid Search with 3 repeats and 10-fold Repeated k-Fold Cross- Validation. The created models were evaluated with Accuracy, Specificity, Sensitivity, F1-score, Negative predictive value, and Positive predictive value.

RESULTS

In Table 3, hyper-parameters and their values determined by grid search for each model are given.

Figure 3, Figure 4, and Figure 5 show the confusion matrices for the LR, RF and SVM algorithms, respectively.

Table 3. Optimal Hyper- Parameters Determined By Grid Search

Algorithm	Parameter	Optimal Hyper- Parameters
RF	criterion	entropy
	max_depth	10
	min_samples_leaf	1
	min_samples_split	2
LR	C	1
	penalty	l2
	solver	newton-cg
SVM	C	10
	Gamma	1

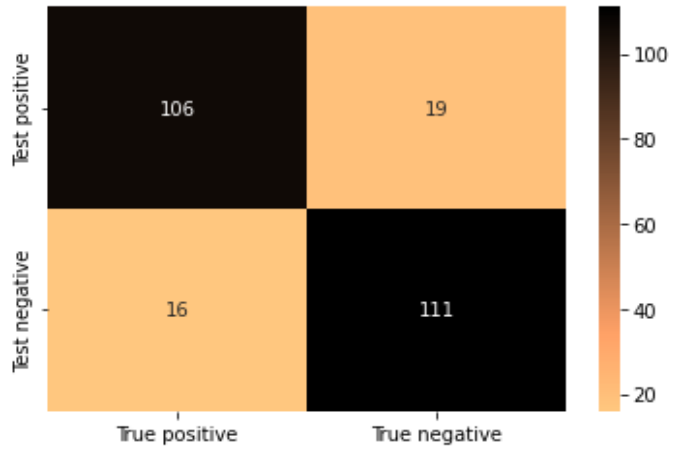

Figure 3. Confusion matrices for LR algorithm

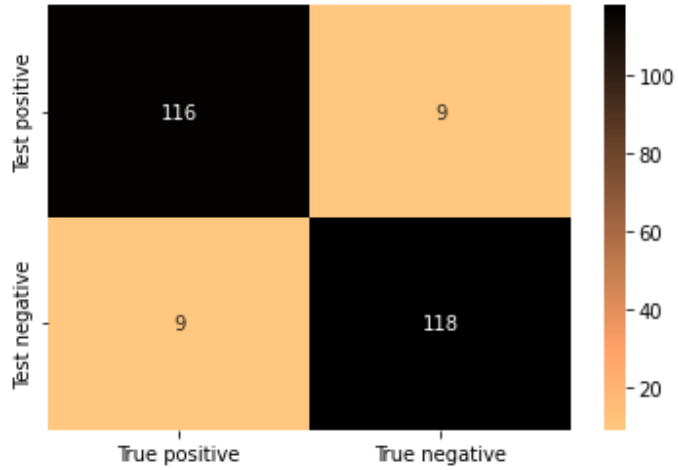

Figure 4. Confusion matrices for RF algorithm

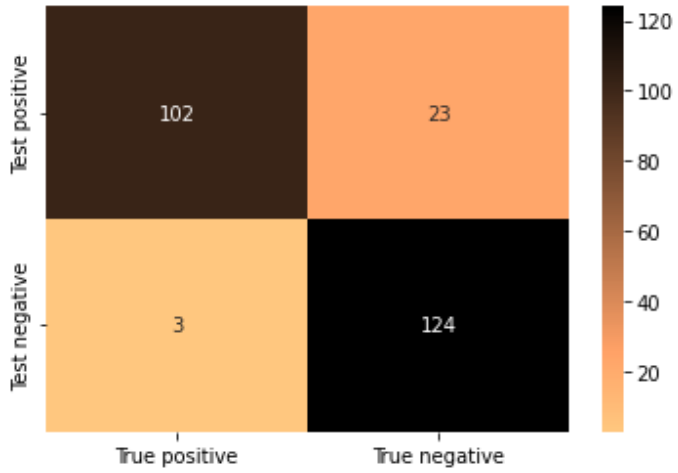

Figure 5. Confusion matrices for SVM algorithm

In Table 4, the performance criteria of the classification algorithms used in the study such as Accuracy, Specificity, Sensitivity, F1-score, Negative predictive value, and Positive predictive value are given.

- The values of Accuracy, Specificity, F1-score, Sensitivity, Negative predictive value, and Positive predictive value criteria obtained from the RF model were calculated as 0.929, 0.929, 0.928, 0.928, 0.929, and 0.928 respectively.
- The values of Accuracy, Specificity, F1-score, Sensitivity, Negative predictive value, and Positive predictive value criteria obtained from the SVM model were calculated as 0.897, 0.844, 0.887, 0.971, 0.976, and 0.816 respectively.
- In addition; the values of Accuracy, Specificity, F1-score, Sensitivity, Negative predictive value, and Positive

predictive value criteria obtained from the LR model were calculated as 0.861, 0.854, 0.858, 0.869, 0.874, and 0.848 respectively.

• As a result; The RF method offers the highest performance compared to SVM and LR.

Table 4. Performance Metrics Results for Classification Models

Score/Model	LR	RF	SVM
Accuracy	0.861	0.929	0.897
Specificity	0.854	0.929	0.844
Sensitivity	0.869	0.928	0.971
F1-score	0.858	0.928	0.887
Negative predictive value	0.874	0.929	0.976
Positive predictive value	0.848	0.928	0.816

DISCUSSION

Early detection of anomalies aids in the long-term saving of human life. The processing of raw healthcare data of heart disease lead to the discovery of this procedure. Machine learning algorithms can be used to process the raw data, resulting in a new and original recommendation for heart disease. Heart disease prognosis is regarded as one of the most difficult and significant issues in medicine. If the condition is detected early on, the mortality rate can be managed, and preventive measures can be implemented as soon as feasible (21, 22).

In this study, a model for heart disease prediction with the help of machine learning is proposed. For this purpose, three machine learning algorithms, RF, SVM and LR, were used. The results were that the RF algorithm performed better in heart disease prediction compared to other methods (LR, SVM).

There are many studies in the literature for the prediction of heart diseases. In a study, algorithms such as J48, K Nearest Neighbors (KNN), Decision Tree and Naive Bayes (NB) were used for heart disease detection and the highest accuracy (83.732%) was obtained with J48 (23). Another article estimated whether a person has heart disease as a percentage using Data Mining classification techniques. In the study, Decision Tree, KNN, and Naive Bayes (NB) algorithms were used and heart diseases were estimated. NB achieved the highest accuracy (73.7%) in classifying heart diseases (24). In 2017, Hend Mansoor et al. looked examined the performance of LR and RF classification algorithms for assessing CVD patients' risk exposure. They demonstrated that the LR Model outperformed the RF classification technique. The LR Model had an accuracy of 89 percent, whereas the RF Model had an accuracy of 88 percent (25). A different paper Random Forest algorithm was used to classify heart disease. They classified new and unknown patients with 84.448% accuracy in the test dataset (26).

The performance measures obtained in most of the studies mentioned above are lower than the current study. In this study, hyperparameter optimization for LR, SVM and RF algorithms used to classify heart disease helped to create models with higher performance by choosing the most optimal model. In other words, hyper parameter optimization is an important step to create the most optimal model in machine learning models. In the study, many of the classical machine learning algorithms were tried and the three algorithms with the highest performance were continued to work. The current study predicted coronary artery heart disease more successfully than the literature. The values of Accuracy, Specificity, F1-score, Sensitivity, Negative predictive value, and Positive predictive value criteria obtained from the RF model were calculated as 0.929, 0.929, 0.928, 0.928, 0.929, and 0.928, respectively.

In conclusion, the present study aimed to find the best ML technique among the ML algorithms that are well accepted and easy to implement, and found that the proposed RF algorithm performs well, at least for this dataset. Therefore, the RF algorithm can be recommended for the development of prediction models for heart and different diseases in the future.

CONCLUSION

In conclusion, the RF model may be useful for early detection of coronary heart disease.

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

Ethical approval: *Ethics committee approval is not required in this study.*

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Araştırma Makalesi / Research Article

The Protective Role of Vitamin E Against Teratogenic Effects of Nicotine on Embryonic Bone Development

Nikotinin Embriyonik Kemik Gelişimi Üzerindeki Teratojenik Etkilerine Karşı E Vitamininin Koruyucu Rolü

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Abstract

Aim: According to World Health Organization data, around 1.5 billion people in the world use tobacco products. Nicotine, the most common use of tobacco, is the main psychoactive substance that causes addiction. Exposure to nicotine during pregnancy increases the risk of low placenta weight, stillbirth, congenital heart disease, musculoskeletal defect. Antioxidants are used to protect against teratogenic substances such as nicotine. The purpose of the study was to determine the skeletal system malformations caused by low (3 mg/kg) and high (6 mg/kg) doses of nicotine during embryonic bone evolution by using the double skeletal staining method and the protector role of vitamin E in preventing these malformations.

Material and Method: The rats were divided into 6 groups: the control, low-dose nicotine, high-dose nicotine, low-dose nicotine+vitamin E, high-dose nicotine+vitamin E and vitamin E. The development of the skeletal system of the fetuses was examined by the skeleton staining method. The anterior and posterior extremity images of the fetuses were examined under the stereomicroscope and then through photographing total bone length, ossification length and ossification rate were calculated in the ImageJ program.

Results: There was an important decline in the total bone length, ossification length and ossification rate ($p<0.05$) in the bone measurements of the front and hind extremities, while it was found that the treatment groups approached the control group and the increases were important ($p<0.05$).

Conclusion: It was concluded that being to nicotine during pregnancy delayed skeletal ossification and that vitamin E, which is an antioxidant, may be protective opposite the teratogenic effect of nicotine on the bone.

Keywords: Bone development, double skeletal staining, nicotine, rat, vitamin E

Öz

Amaç: Dünya Sağlık Örgütü verilerine göre dünyada yaklaşık 1.5 milyar insan tütün ürünleri kullanmaktadır. Tütünün en yaygın kullanımı olan nikotin, bağımlılık yapan başlıca psikoaktif maddedir. Hamilelik sırasında nikotine maruz kalmak, düşük plasenta ağırlığı, ölü doğum, doğuştan kalp hastalığı, kas-iskelet sistemi kusuru riskini artırır. Antioksidanlar, nikotin gibi teratojenik maddelere karşı koruma sağlamak için kullanılır.

Bu çalışmanın amacı, embriyonik kemik gelişimi sırasında düşük (3 mg/kg) ve yüksek (6 mg/kg) doz nikotinin neden olduğu iskelet sistemi malformasyonlarını ikili iskelet boyama yöntemi ile belirleyerek; E vitamininin koruyucu rolünü ortaya koymaktır.

Materyal ve Metot: Çalışmada ratlar; kontrol, düşük doz nikotin, yüksek doz nikotin, düşük doz nikotin+E vitamini, yüksek doz nikotin, yüksek doz nikotin+E vitamini ve E vitamini olmak üzere 6 gruba ayrıldı. Fetüslerin iskelet sistemi ikili boyama yöntemi ile boyandı. Fetüslerin ön ve arka ekstremite görüntüleri stereomikroskop altında incelendikten sonra; ImageJ programında toplam kemik uzunluğu, kemikleşme uzunluğu ve kemikleşme alanları hesaplandı.

Bulgular: Ön ve arka ekstremite kemik ölçümlerinde toplam kemik uzunluğu, kemikleşme uzunluğu ve kemikleşme alanında ($p<0.05$) anlamlı bir düşüş varken, tedavi gruplarının kontrol grubuna yaklaştığı ve artışların anlamlı olduğu saptandı ($p<0.05$).

Sonuç: Gebelikte nikotine maruz kalmanın iskelet kemikleşmesini geciktirdiği ve bir antioksidan olan E vitamininin nikotinin kemik üzerindeki teratojenik etkisine karşı koruyucu olabileceği sonucuna varıldı.

Anahtar Kelimeler : Kemik gelişimi, ikili iskelet boyama, nikotin, sıçan, E vitamini

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INTRODUCTION

Bone is an active tissue that is permanently affected by nutritional, hormonal and metabolic status (1-3). Women throughout pregnancy may be exposed to some chemicals depending on their living experience. These can cause various teratogenic impacts in the embryo (4,5). Smoking is bad habit that has harmful consequences for human health because it includes 7000 toxic chemicals. This habit results in addiction. The main addictive substance in cigarettes is nicotine. The total alkaloid constitutes about 95% of the content and nicotine constitutes about 0.5 to 8.0% of the dry weight of the tobacco. Other alkaloids are cotinine, nornicotine, database and nicotine-N-oxide (6). Only one cigarette generally includes 0.6-2 mg nicotine (7). Nicotine reaches the fetus through the placenta (8). It has been reported that the concentration of nicotine in fetal circulation is 15% higher than the maternal serum and 88% higher than amniotic fluid (9-11).

Passive exposure to smoking or smoking during pregnancy can cause fetal defects (12). Scientific studies have shown that nicotine significantly delays fetal bone development (13). Smoking has a direct effect on bone tissue. Nicotine is an inhibitor of osteogenesis and angiogenesis processes that play a role in bone development (14). It has been shown in the literature that it reduces the storage of vitamin D, which plays a role in bone metabolism, and delays scar tissue (15-17). Several studies have shown that nicotine disrupts the oxidant-antioxidant process. Different studies have reported that antioxidants are beneficial to this deteriorating process (18). Vitamin E refers to tocopherols and tocotrienols which are synthesized by plants and are soluble in fat. It is found in fatty foods with different proportions (19). Studies are showing that vitamin E, a potent antioxidant, has a positive effect on the skeletal system (20). Vitamin E prevents the increase of osteoclast activity by clearing free radicals in the body and keeps the bone remodeling process in balance Vitamin E prevents the increase of osteoclast activity by clearing free radicals in the body and keeps the bone remodeling process in balance. It has been reported in various studies that vitamin E increases bone trabeculae and bone volume, decreases osteoclast activity, and increases osteoblast activity (21).

Skeletal system malformations that may occur due to the use of nicotine during pregnancy can be reduced by taking appropriate doses of vitamin E. The purpose of the study is to define the skeletal system malformations caused by nicotine during embryonic bone development by using the double skeletal staining method and the protective role of vitamin E in preventing these malformations.

MATERIAL AND METHOD

Animal selection

The study was conducted with the decision of the local ethics centre of Erciyes University Experimental and Clinical Research Center dated on 11.11.2015 and decision number 15/143. 18 with grown-up female (5-7 months old) Wistar-Albino rats weighed 180-220g. Female rats and male rats were put in the same lattice. The following morning, samples of vaginal smears received from female rats were examined under the light microscope. Females, whose vaginal smear showed sperm, were accepted as 0.5 days pregnant.

Experimental groups

Ethically, a minimum number of rats and fetuses were used. Six different groups (n=3) were formed from pregnant rats.

Control Group (C): To the rats in this group, 1 ml/kg/day saline was given into the peritoneum (i.p.).

Vitamin E Group (Vit E): To the rats in this group were given 60 mg/kg/day vitamin E administration by i.p.

Low Dose Nicotine Group (LDN): The rats were given 3 mg/kg/day nicotine administration subcutaneous (s.c.)

Low Dose Nicotine+Vitamin E Group (LDN+Vit E): The rats were given 3 mg/kg/day nicotine by s.c. and half an hour after, 60 mg/kg/day vitamin E was administered by i.p.

High Dose Nicotine Group (HDN): Nicotine administration was performed at a rate of 3 mg/kg/day s.c. twice a day, a total of 6 mg/kg/day.

High Dose Nicotine+Vitamin E Group (HDN+Vit E): Nicotine administration was performed at a rate of 3 mg/kg/day s.c. twice a day. Vitamin E was administered 60 mg/kg/day by i.p. half an hour after nicotine administration.

* Every day injection was given to rats in all groups, 1st and 20th day of pregnancy.

* Pregnant rats in all groups were sacrificed on the 20th day of pregnancy.

Preparation of injections

Nicotine with the code N3876 and Vitamin E with the code T3251 as a-tocopherol form were obtained from the Sigma-Aldrich company (Darmstadt, Germany). Saline was used for nicotine solution and olive oil was used for vitamin E solution.

Obtaining fetuses

The fetuses were dissected together with the placentas. The weight of fetuses was weighed with a precision scale. Head and stern lengths were measured with a digital calliper. Obtained data were recorded. Considering the exclusions, in each group, without gender detection, 15 of the fetuses were used for double skeletal staining method. Fetuses used for the double skeletal staining were separately measured on both extremities (15 right front and hind extremity, 15 left front and hind extremity).

Double skeletal staining of fetuses

Fetuses were taken to 70% ethyl alcohol for 4-7 days. After this process, they were kept in acetone for 1-3 days. The internal organs of the fetuses were removed. After acetone, they were taken into a double staining solution prepared with Alizarin Red-S (100 mg) and Alcian Blue (300 mg).

Then they were kept in the oven at 38-40 0C. Afterwards, the tissues of the fetuses were washed with tap water for 2 hours. The transparency phase was started with 1% potassium hydroxide (KOH). Skeletal stained fetuses were preserved in 20%, 50%, 80% and 100% glycerin. For the measurement of fetal extremities, photographs were taken with a Nikon E5700 trademark digital camera under a stereomicroscope. The length and area measurements of the bones were made in ImageJ (http://rsb.info.nih.gov/ij/docs/index.htlm) program. Findings from area measurements were used to determine ossification.

Statistical analysis

Bone and ossification lengths were examined by the ImageJ program. All bone and ossification surface areas were calculated. Data obtained from measurements were analyzed with IBM Statistical Package for the Social Sciences 22 program. The Kolmogorov–Smirnov test was applied to determine the normal distribution of throughputs. A One-Way ANOVA test was done on the data. One-way analysis of variance with the post hoc Tukey honestly significant difference (HSD) test has applied to the differences between the groups. Results of the analysis, it was admitted that there was a meaningful difference between the groups with p values of <0.05.

RESULTS

Effects on growth parameters

Table 1 showed that a statistically meaningful decline in the weights of the fetuses in the experimental groups with low dose (3 mg/kg) and high dose (6 mg/kg) nicotine compared to the control group ($p<0.05$). Table 2 showed that a statistically meaningful decline in head-rump lengths ($p<0.05$). When 60 mg/kg vitamin E was given as a preservative, it was determined that there was a statistically meaningful increase in the growth parameters and the values approached the control group.

Table 1. Weight of fetuses

Fetus No	Weight (g)					
	C	LDN	LDN+Vit E	HDN	HDN+Vit E	Vit E
1	2.15	2.03	2.35	2.06	1.93	2.42
2	2.40	2.15	2.22	1.68	2.05	2.21
3	2.41	2.00	2.58	2.04	1.97	2.23
4	2.20	2.14	2.60	1.56	2.10	2.36
5	2.40	1.89	2.17	2.20	2.21	2.33
6	2.17	2.10	2.25	2.01	2.09	2.35
7	2.24	2.43	2.47	2.05	2.30	2.45
8	2.43	2.05	2.40	1.95	2.38	2.62
9	2.54	2.21	2.07	1.93	2.00	2.20
10	2.27	2.20	2.03	1.98	1.91	2.25
11	2.32	2.26	2.14	1.87	1.86	2.30
12	2.38	2.38	2.23	1.95	2.07	2.43
13	2.65	2.11	2.11	2.01	2.14	2.40
14	2.63	2.18	2.15	2.10	2.20	2.54
15	2.23	2.31	2.27	1.94	2.17	2.24
Mean±SD	2.36±0.15	2.16±0.14a,d	2.26±0.17	1.95±0.15a,b,d,e	2.09±0.14a,d	2.35±0.12

*in the statistical evaluation of all table data; ANOVA test; P<0.05 was considered statistically significant; C: Control, LDN: low-dose nicotine, HDN: high-dose nicotine, Vit E: Vitamin E; (a) It is significant when compared with the control group; (b) It is significant when compared with the LDN+Vit E group; (c) It is significant when compared with the HDN+Vit E group; (d) It is significant when compared with the Vit E group; (e) It is significant when compared with the LDN group

Table 2. Head-rump length of the fetus

Fetus No	Length (mm)					
	C	LDN	LDN+Vit E	HDN	HDN+Vit E	Vit E
1	28.55	25.13	30.15	26.64	25.00	30.32
2	27.74	24.33	28.87	23.56	25.64	29.76
3	29.18	25.17	27.67	23.75	27.17	28.86
4	29.10	27.70	28.51	21.89	27.54	29.27
5	29.52	29.15	27.32	23.47	25.03	31.92
6	28.73	25.17	28.20	23.32	28.67	28.63
7	28.80	26.87	26.76	26.54	27.06	27.69
8	30.32	29.76	27.15	25.44	27.21	28.42
9	31.68	28.04	27.28	22.74	25.45	29.54
10	27.33	25.23	28.11	24.65	26.19	31.01
11	30.78	27.21	27.30	26.58	26.83	29.46
12	31.16	29.18	28.67	22.87	26.05	29.15
13	28.45	27.59	27.92	25.14	28.23	30.35
14	30.12	27.78	30.95	26.02	27.70	27.47
15	29.89	28.54	30.88	25.20	26.43	29.58
Mean±SD	29.42±1.23	27.12±1.73a,b,d	28.38±1.33	24.52±1.55a,c,d,e	26.68±1.12a	29.42±1.17

*in the statistical evaluation of all table data; ANOVA test; P<0.05 was considered statistically significant; C: Control, LDN: low-dose nicotine, HDN: high-dose nicotine, Vit E: Vitamin E; (a) It is significant when compared with the control group; (b) It is significant when compared with the LDN+Vit E group; (c) It is significant when compared with the HDN+Vit E group; (d) It is significant when compared with the Vit E group; (e) It is significant when compared with the LDN group

Findings of front extremity bones

In the study, (humerus, radius, ulna) bones of the anterior extremity were evaluated. The istatistically meaningful decline in ossification length and ossification rate was found in 3 mg/kg nicotine compared to the control group (p<0.05). A statistically meaningful decline in ossification data was detected in the 6 mg/kg nicotine treated group compared to the 3 mg/kg given group (p<0.05). When nicotine, vitamin E were applied with, ossification raised and approached the control group (Table 3), (Figure 1), (p<0.05).

Findings of hind extremity bones

In the study, (femur, tibia, fibula) bones of the posterior extremity were evaluated. A statistically meaningful decline in ossification length and ossification rate was found in 3 mg/kg nicotine compared to the control group (p<0.05). A statistically meaningful decline in ossification data was detected in the 6 mg/kg nicotine treated group compared to the 3 mg/kg given group (p<0.05). When nicotine, vitamin E were applied with, ossification raised and approached the control group (p<0.05), (Table 4), (Figure 2).

Table 3. Ossification rate of the front extremity long bones

		Humerus			Ulna			Radius		
	N	Total bone length	Length of ossified part	Ossification rate (%)	Total bone length	Length of ossified part	Ossification rate (%)	Total bone length	Lengthof ossified part	Ossification rate (%)
Control	30	4.30±0.06	1.86±0.18	44.89±1.69	4.16±0.20	1.92±0.13	45.08±2.75	3.32±0.09	1.58±0.13	43.78±4.53
LDN	30	4.23±0.23	1.55±0.24a,b,d	37.72±6.31a,d	4.07±0.17	1.57±0.32a,b,d	34.45±6.43a,b,d	3.27±0.16	1.30±0.25a,b,d	37.04±4.92a,d
LDN+Vit E	30	4.27±0.21	1.83±0.23	41.55±3.81	4.30±0.29	1.86±0.15	40.17±5.63	3.30±0.13	1.52±0.16	40.40±3.42
HDN	30	3.97±0.23 a,c,d,e	1.17±0.42 a,c,d,e	30.39±13.43 a,c,d,e	3.72±0.20 a,c,d,e	1.12±0.43 a,c,d,e	28.96±14.18 a,c,d	2.98±0.26 a,c,d,e	1.10±0.44 a,c,d,e	32.08±12.11 a,c,d,e
HDN+Vit E	30	4.15±0.16a	1.71±0.20	39.01±2.84a	4.01±0.17	1.75±0.14	38.75±5.89a,d	3.24±0.17	1.41±0.13	39.13±4.05
Vit E	30	4.28±0.17	1.85±0.17	42.70±2.49	4.11±0.13	1.87±0.16	44.97±3.40	3.29±0.07	1.55±0.08	42.43±4.14

*in the statistical evaluation of all table data; ANOVA test; P<0.05 was considered statistically significant; C: Control, LDN: low-dose nicotine, HDN: high-dose nicotine, Vit E: Vitamin E; (a) It is significant when compared with the control group; (b) It is significant when compared with the LDN+Vit E group; (c) It is significant when compared with the HDN+Vit E group; (d) It is significant when compared with the Vit E group; (e) It is significant when compared with the LDN group

Table 4. Ossification rate of the hind extremity long bones

		Femur			Tibia			Fibula		
	N	Total bone length	Length of ossified part	Ossification rate (%)	Total bone length	Length of ossified part	Ossification rate (%)	Total bone length	Length of ossified part	Ossification rate (%)
Control	30	3.71±0.34	1.32±0.17	33.85±4.30	3.75±0.15	1.48±0.25	37.41±5.46	3.55±0.19	1.45±0.13	40.52±5.11
LDN	30	3.52±0.19 a,d	0.96±0.19 a,b,d	25.16±2.51 a,b,d	3.60±0.20d	1.02±0.12 a,b,d	24.46±4.93 a,b,d	3.53±1.77	0.85±0.27	27.86±5.13 a,b,d
LDN+Vit E	30	3.68±0.25	1.31±0.22	32.22±4.83	3.70±0.19	1.38±0.28	33.44±6.91	3.56±0.20	1.20±0.32	36.87±6.57
HDN	30	3.35±0.23 a,c,d	0.70±0.28 a,c,d,e	18.82±8.04 a,c,d,e	3.10±0.40 a,c,d,e	0.75±0.23 a,c,d,e	21.51±11.05 a,c,d,e	3.10±0.17 a,c,d,e	0.60±0.31	22.33±8.90 a,c,d,e
HDN+Vit E	30	3.60±0.18	1.23±0.12	27.31±5.19a,d	3.35±0.20a,d	1.10±0.17a,d	30.38±3.63a,d	3.30±0.18a,d	1.10±0.18	31.70±6.31a,d
Vit E	30	3.72±0.18	1.33±0.09	32.04±4.39	3.80±0.19	1.46±0.18	36.05±2.90	3.62±0.27	1.42±0.20	39.38±4.40

*in the statistical evaluation of all table data; ANOVA test; P<0.05 was considered statistically significant; C: Control, LDN: low-dose nicotine, HDN: high-dose nicotine, Vit E: Vitamin E; (a) It is significant when compared with the control group; (b) It is significant when compared with the LDN+Vit E group; (c) It is significant when compared with the HDN+Vit E group; (d) It is significant when compared with the Vit E group; (e) It is significant when compared with the LDN group

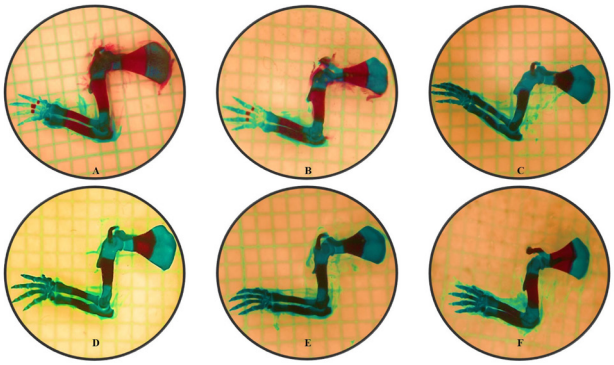

Figure 1. View of the anterior extremity bones. (A) Control group, (B) Low-dose nicotine group, (C) Low-dose nicotine+Vitamin E group, (D) Vitamin E group, (E) High-dose nicotine group, (F) High-dose nicotine+Vitamin E group

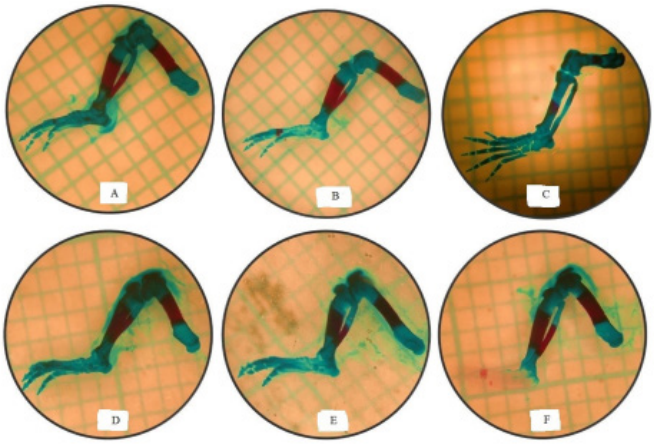

Figure 2. View of the posterior extremity bones. (A) Control group, (B) Low-dose nicotine group, (C) Low-dose nicotine+Vitamin E group, (D) Vitamin E group, (E) High-dose nicotine group, (F) High-dose nicotine+Vitamin E group

DISCUSSION

Nicotine damages both the development and function of the placenta. It was detected that nicotine deteriorates the metabolism and increases oxidative stress in the placenta (22,23). It also increases the destruction of exogenous estrogens by suppressing the activity of osteoblasts. Therefore, it causes low body weight and earlier menopause (24). In this study, in which we aimed to show the protection of vitamin E on the harms of nicotine on fetal development, your most emphatic result is that the ossification of the radius, ulna and femur develops well, close to the control group.

Hakem 2: "Nikotinin fetal gelişim üzerindeki zararlarına karşı E vitamininin koruyuculuğunu göstermeyi amaçladığımız bu çalışmada en önemli sonucumuz radius, ulna ve femur kemikleşmesinin kontrol grubuna yakın bir şekilde iyi geliştiğidir" şeklinde cümle eklendi.

Oruç (25), applied rats to 1.67 mg/kg nicotine by i.p. between 6 and 21 days of pregnancy in 1996. In the study, they weighed 50 offspring in the control group (6.29±0.33 g) and nicotine (4.99±0.32 g) on the 4th day after delivery and they reported that the birth weight of the offspring in the nicotine group was low and this decrease was statistically significant. Also Oruç, reported that in the control group samples, molar teeth showed a normal development while the molar tooth sections of the nicotine group samples showed thinning and demineralization areas in the dentin layer and indicated that nicotine hurt hurmed bone development and thus on tooth development. In our study, there was a statistically meaningful decline in the body weights of fetuses in the control group (2.36±0.15 g) and low-dose nicotine (2.16±0.14 g) and high-dose nicotine (1.95±0.15 g) in the control group (Table 1), ($p<0.05$).

Yazıcı (26) have studied the teratogenic effects of nicotine on growth and development of head and face skeleton with prenatal palate formation in rats; nicotine hydrogen tartrate was started before the pregnancy (14 days before pregnancy and it was left at the zero day of the pregnancy), during pregnancy (nicotine applied until 17th day of pregnancy) nicotine was applied 2.7 mg/kg as i.p. in different groups. When the growth and development of the head and facial skeleton, depending on the nicotine application during pregnancy and before pregnancy, it was reported that the width of the foramen incisive increased, the length was decreased and the length of the corpus mandibulae decreased. As a result of their studies, they reported that nicotine delayed ossification. In our study, we applied low dose (3 mg/kg) and high dose (6 mg/kg) nicotine by s.c. throughout pregnancy. In the rats, we looked at the total length of the front and hind extremity bones, ossification length and ossification surface area. We found a significant decrease in total bone/ossification length and narrowing of ossification surface area ($p<0.05$).

Bastug (27) investigated that the effects of exposure to nicotine on the development of juvenile bone during pregnancy and lactation (until postnatal 21st day). In their study, they administered nicotine 3 mg/kg/day by s.c. In our study, we formed high-dose nicotine and low-dose nicotine groups. Our low-dose nicotine group was given 3 mg/kg/day, as applied by Bastug. As a result of the study of Bastug, it was concluded that the birth weight, epiphyseal and hypertrophic zone thickness of the nicotine group were lower than the other groups. Similarly, in our study, the birth weight was low in the nicotine group. The mean weight of the offspring in our control group was 2.36±0.15 g; the mean weight of the offspring rats in the 3 mg/kg nicotine treated group was 2.16±0.14 g. The difference was statistically significant ($p <0.05$).

Kurtoglu et al. (28) gave 3 mg/kg/day nicotine to rats in the gestational and lactation period. At the end of the study, they looked at the femoral length, bone density with bone content of the fetuses of 21 days. They reported that the birth weight of the offspring of the mothers exposed to nicotine was 5.47±0.39 g, which was lower than the control

group and the values of nicotine groups were meaningful lower in the femoral neck, bone density and content than the control groups. In our study, we found that both the body weight and the femur length of the offspring in the low dose nicotine group (3.52 ±0.19) were significantly shorter than the control group (3.71±0.34), ($p<0.05$).

Farag et al. (29) investigated the effect of chronic nicotine exposure on the bone mineral content of adult and young rats. For 6 months 3-4.5 mg/kg/day nicotine was given to rats as s.c. The weight gain in nicotine-treated rats decreased to the dose compared to the control group. They also reported that the femur weights of rats treated with nicotine were lower than the control group and that the concentration of calcium and phosphorus in femur and lumbar vertebrae decreased significantly. They reported that older rats were more affected by changes. They found that the femoral lengths of the rats treated with nicotine were shorter than the control group. As a result, the negative effect of nicotine on bone was found to be increased with age. In our study, the length of the femur belonging to the low dose group of nicotine was 3.52±0.19 mm and the length of the high dose group of nicotine was 3.35±0.23 mm. Both lengths were shorter than the control group and the difference was statistically significant ($p<0.01$). The total shortening of bone length was found to be increased as the dose exposed to nicotine was increased.

The negative effects of nicotine on bone development have been scientifically introduced and protective antioxidants have been used. One of them is vitamin E. Vitamin E is an antioxidant that can prevent lipid peroxidation (21). It is soluble in oil. There are two forms of it as tocopherol and tocotrienol in nature. Vitamin E prevents the increase of osteoclast activity by clearing free radicals in the body and keeps the bone remodeling process in balance. It also increases bone trabecular density by preventing bone calcium loss (30).

Norazlina et al. (31) investigated the effects of vitamin E supplementation in rats with impaired bone metabolism due to nicotine administration. For 3 months, rats received nicotine as 7 mg/kg by i.p. They gave nicotine to one group of rats with nicotine administered as 60 mg/kg alpha-tocopherol in the last two months and 60 mg/kg in the last two months. They looked at serum interleukin-1 (IL-1) and interleukin-6 (IL-6), osteocalcin and bone calcium levels. They also made evaluations in the left femur and the fourth lumbar vertebra. As a result, they indicated that increased levels of IL-1 and IL-6 due to nicotine was turned back after the addition of vitamin E and there was no change in osteocalcin level. Calcium levels were unchanged in femoral bone, whereas bone calcium levels in lumbar vertebrae were lower than in the control group.

Hermizi et al. (32) studied the beneficial effects of vitamin E forms on bone histo-morphometrically parameters after discontinuation of nicotine. After giving nicotine to one of the groups in which they gave 7 mg/kg nicotine for 2 months, they gave alpha-tocopherol and the other had given gamma-tocotrienol (60 mg/kg). At the end of a total of 4 months, they looked at trabecular bone volume, bone mineral ratios and osteoclast amount. They stated that the negative effects of nicotine were reversed in the groups with vitamin E added. As a result, they concluded that vitamin E could be used therapeutically as bone damage in chronic smokers. In our study, we used 60 mg/kg alpha-tocopherol to be protective against nicotine and we found a statistically significant increase in ossification parameters (bone height, ossification length, ossification surface area) ($p<0.05$).

In the study of Soysal et al. (2), the effects of phenytoin, folic acid and vitamin E on bone development were investigated by dual skeletal staining in rat fetuses. The average head and stern length of the fetuses in the control group were found to be 3.21±0.27 mm and their weight was 3.51±0.35 g. They found that the phenytoin groups had shortened the length of the fetus and found a decrease in their weight. They reported a statistically significant increase in these parameters in vitamin E supplemented experimental groups. These findings showed that the vitamin E which we used against the teratogenic effect of nicotine showed a similar effect.

Yılmaz et al. (3) evaluated the skeletal system by double staining method in the study of the protection of melatonin against the teratogenic effect of nicotine on embryonic bone development. Similar to our study, they applied nicotine as 3 mg-6 mg/kg by s.c. In parallel with the dose of nicotine, they found statistically significant reductions in both bone length and ossification length of the bones in the front and hind extremities. In the study, the fetuses in the control group (sacrificed on the 20th day) were reported with a height of 29.57±1.25 mm and a weight of 2.40±0.13 g. These data were similar to the control group in our study as height (29.42±1.23 mm) and weight (2.36±0.15 g). While the height was 27.71±1.28 mm and the weight was 2.20±0.13 g in a low dose of nicotine, the height was 24.87±1.6 mm, and the weight was 1.99 ±0.15 g in a high dose of nicotine. The length and weight of the nicotine groups were close to the data in our study. Yılmaz et al. (3) have shown that the teratogenic effect of nicotine causes a statistically significant reduction in rat offspring's weight, height and bone development.

As a result of the literature review, several studies have shown that the effects of nicotine on the skeletal system and the effects of vitamin E on these damages are given. However, there were no studies conducted on nicotine and vitamin E related to the double skeletal staining method. In our study, we aimed to investigate the preservation of vitamin E against the negative effects of nicotine on bone and cartilage by double skeletal staining. In parallel with the dose increase, we detected that total bone/ossification increased in length, decreased ossification surface area and negatively affected bone development.

When the bones in the front and hind extremities (humerus, radius, ulna, femur, fibula, tibia) were compared with the nicotine and treatment groups, significant

increases were observed in ossification length, total bone length, ossification surface area in vitamin E groups. As a result, it was observed that nicotine negatively affected ossification in the embryonic period and thus decreased ossification percentages. It was found that vitamin E decreased the damage caused by nicotine and brought it closer to the values of the control groups. We conclude that supplementation of antioxidant vitamin E in women who continue to use nicotine during pregnancy will affect the skeletal development of the fetus positively. We think that this study will serve as an example and contribute to future studies.

CONCLUSION

It was concluded that exposure to nicotine during pregnancy delayed skeletal ossification and that vitamin E, which is an antioxidant, may be protective against the teratogenic effect of nicotine on the skeletal system.

Financial disclosures: *The authors declared that this study hasn't received no financial support.*

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 centre of Erciyes University Experimental and Clinical Research Center dated on 11.11.2015 and decision number 15/143. .*

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MEDICAL RECORDS-International Medical Journal

Araştırma Makalesi / Research Article

Role of Platelet Mass Index in the Differential Diagnosis of Patients with Elevated Prostate-Specific Antigen Levels

Prostat Spesifik Antijen Yüksekliğinde Trombosit Kitle Indeksinin Ayırıcı Tanıdaki Yeri

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Abstract

Aim: To evaluate the role of platelet mass index (PMI) calculated using hemogram parameters obtained from a routine blood test in the differentiation of prostate cancer in patients with prostate-specific antigen (PSA) values of 2.5-10 ng/dl.

Material and Method: Seventy-five patients with prostate cancer and 48 with prostatitis were included in the study and grouped according to their pathology results. The white blood cell (WBC), hemoglobin (HGB), thrombocyte (PLT), neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), mean platelet volume (MPV) and PMI values were compared between the two groups.

Results: The PMI and PLT levels of the prostate cancer group were statistically significantly lower than those of the prostatitis group ($p<0.05$). In predicting prostate cancer, the cut-off value for the PMI level was determined as 1.480, at which the likelihood ratio was calculated as 1.08.

Conclusion: We consider that PMI calculated using hemogram parameters in patients with a PSA value below 10 ng/dl will guide the clinician in differentiating prostate cancer from other prostate pathologies without performing an unnecessary biopsy.

Keywords: Prostate-specific antigen, platelet mass index, prostate cancer

Öz

Amaç: Bu çalışmamızda rutin bakılan bir kan tahlili olan hemogram parametlerinden faydalanılarak hesaplanan Trombosit Kitle İndeksinin 2.5-10 ng/dl arası PSA değerlerinde prostat kanserini ayırt etmedeki rolünü değerlendirmeyi amaçladık.

Bu çalışmanın amacı, embriyonik kemik gelişimi sırasında düşük (3 mg/kg) ve yüksek (6 mg/kg) doz nikotinin neden olduğu iskelet sistemi malformasyonlarını ikili iskelet boyama yöntemi ile belirleyerek; E vitamininin koruyucu rolünü ortaya koymaktır.

Materyal ve Metot: Çalışmaya patoloji sonucuna göre prostat kanseri olan 75 ve prostatit olan 48 hasta dahil edildi. Bu hastalar patoloji sonuçlarına göre gruplandırıldı. White blood cell (WBC) , hemoglobin (HGB), trombosit (PLT) , nötrofil lenfosit oranı (NLR) , trombosit lenfosit oranı (PLR), ortalama trombosit hacmi (MPV), PMI değerleri her iki grup arasında karşılaştırıldı.

Bulgular: Prostat kanserli grubun PMI ve PLT düzeyi prostatit grubundan istatistiksel olarak anlamlı şekilde düşük saptanmıştır ($p<0.05$). Prostat kanserini tahmin etmede PMI düzeyi için cut-off noktası 1480 saptanmış olup, bu noktadaki Likelihood Ratio değeri 1.08 saptanmıştır.

Sonuç: PSA değeri 10 ng/dl altında olan hemogram parametreleri kullanılarak hesaplanan PMI'nın gereksiz biyopsiden kaçınılarak prostat kanseri ayrımını yapmada klinisyene yol gösterici olacağını düşünmekteyiz.

Anahtar Kelimeler : Prostat spesific antijen, trombosit kütle indeksi, prostat kanseri

INTRODUCTION

Prostate-specific antigen (PSA) is a glycoprotein produced by both normal and neoplastic prostate tissues. The main causes of high serum PSA are benign prostatic hyperplasia (BPH), prostate cancer (PCa), prostatitis/prostate infection, and perineal trauma (1). Acute bacterial and/or inflammatory prostatitis is an important cause of increased PSA (1-2). The presence of malignancy should either be confirmed or excluded in patients with elevated PSA. There for prostate biopsy, which is invasive method, should be performed in this patient group. The procedure of transrectal ultrasound (TRUS)-guided prostate biopsy is still accepted as the standard approach in the current

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guidelines in the diagnosis of prostate cancer (3). However, in addition to various complications, a biopsy can be considered as an uncomfortable procedure for patients. For this reason, various non-invasive strategies have been developed to prevent unnecessary biopsies (4). In addition, various combinations of hemogram parameters have been used to facilitate the differentiation between inflammatory process and malignancy (5), which led to the development of several indexes. Platelet mass index (PMI) is a new parameter that shows platelet (PLT) functions; i.e., the inflammatory process (6). PLTs, which are also a hemogram parameter, play various and important roles in the inflammatory process (7) and also act as a modulator in other cells involved in the response to infection (8). PLTs can also interact with leukocytes and alter their functions. In addition to this parameter, the neutrophil-lymphocyte ratio (NLR) is a well-known indicator of the inflammation cascade.

Considering the complications of TRUS-guided prostate biopsy performed due to elevated PSA, unnecessary invasive procedures should be avoided. As the PSA value increases, the cancer detection rate increases, while the unnecessary biopsy rate increases as the PSA value approaches 2.5 ng/dl. Cancer is not detected in the TRUS biopsy in 60-75% of patients with a PSA value of 4-10 ng/ml (9-10).

In this study, we aimed to evaluate the role of PMI calculated using hemogram parameters obtained from a routine blood test in the differentiation of PCa in patients with PSA values of 2.5-10 ng/dl.

MATERIAL AND METHOD

This study was conducted by Health Sciences University Şanlıurfa Mehmet Akif İnan Training And Research Hospital's Urology Clinic. According to the Declaration of Helsinki, approval was obtained from the ethics committee of Harran University Faculty of Medicine before the study (HRU/20.22.08). The files of 278 patients who presented to the urology outpatient clinic of the university between January 2016 and December 2020 due to increased PSA and underwent a prostate biopsy were retrospectively examined. Patients with additional diseases affecting the inflammation cascade, diabetes mellitus, renal failure or hyper/hypothyroidism, those receiving chemotherapy or radiotherapy, those with extraprostatic cancer, those without hemogram tests before the biopsy, and those with a PSA value of above 10 ng/dl were not included in the study. A total of 123 patients who met the inclusion criteria were included in the study. After the patients were divided into the PCa (n = 75) and prostatitis (n = 48) groups according to their pathology results obtained from their files, white blood cell (WBC), hemoglobin (HGB), PLT, NLR, platelet-lymphocyte ratio (PLR), mean platelet volume (MPV) and PMI values were recorded. NLR was obtained by dividing the neutrophil (NEU) count by the lymphocyte (LYM) count, PLR was calculated by dividing the PLT count by the lymphocyte count, and PMI by multiplying the PLT count by MPV. WBC, HGB, PLT, and MPV were calculated using the results of the hemogram analysis performed on the venous blood taken from the cubital vein.

IBM SPSS Statistics v. 22.0 was used for statistical analyses when evaluating the findings obtained in the study. For the evaluation of the study data, the conformance of the parameters to normal distribution was evaluated with the Kolmogorov-Smirnov test. In addition to descriptive statistical methods (mean and standard deviation), Student's t-test was used for the comparison of the two groups in relation to the parameters showing normal distribution, and the Mann-Whitney U test for the comparison of non-normally distributed data. The receiver operating characteristic (ROC) curve and likelihood ratio methods were used to determine the cut-off value. Significance was evaluated at the $p < 0.05$ level.

RESULTS

The study was conducted between January 2016 and December 2020 with a total of 123 cases, of which 75 were in the PCa group and 48 were in the prostatitis group. The ages of the cases ranged from 52 to 87 years, with a mean value of 65.94 ± 8.73 years.

The mean age of the PCa group was statistically significantly higher than that of the prostatitis group ($p < 0.01$). PSA, NLR, PLR, MPV, WBC, NEU, LYM and HGB levels did not statistically significantly differ between the two groups ($p > 0.05$). The PMI level of the PCa group was found to be statistically significantly lower than that of the prostatitis group ($p < 0.05$). The PLT level of the PCa was also statistically significantly lower compared to the prostatitis group ($p < 0.05$) (Table 1).

Table 1. Comparison of age, PSA and hemogram parameters between the prostate cancer and prostatitis groups

	Prostate cancer	Prostatitis	P
	Mean ± SD (Median)	Mean ± SD (Median)	
Age	68.89 ± 9.01	61.18 ± 5.67	10.001**
PSA	8.89 ± 1.5 (9.5)	8.99 ± 5.47 (8.5)	20.085
NLR	3.30 ± 2.04 (2.42)	4.83 ± 6.24 (2.10)	20.707
PLR	139.67 ± 78.01 (108.3)	152.33 ± 100.59 (128)	20.715
MPV	8.33 ± 1.77	8.55 ± 1.99	10.539
PMI	2136.93 ± 581.11	2466.10 ± 930.27	10.017*
WBC	9.09 ± 2.66 (8.42)	11.50 ± 11.54 (8.51)	20.957
NEU	5.63 ± 2.24 (4.95)	8.42 ± 11.63 (4.86)	20.756
LYM	2.23 ± 0.94	2.34 ± 0.94	10.528
HGB	13.51 ± 1.85	13.56 ± 2.53	10.903
PLT	262.90 ± 69.39	291.41 ± 76.91	10.035*

SD: Standart Deviation 1Student's t-test 2Mann-Whitney U test *p < 0.05 **p < 0.01
PSA: prostate specific antigen , NLR: neutrophil-lymphocyte ratio , PLR: platelet-lymphocyte ratio , MPV: mean platelet volume , PMI: platelet mass index , WBC: white blood cell , NEU: neutrophil , LYM: lymphocyte , HGB hemoglobin: , PLT: platelet

In predicting PCa, the cut-off value for the PMI level was determined as 1,480, at which it had a sensitivity of 0.95, specificity of 0.88, and a likelihood ratio of 1.08. The area under the ROC curve value was determined to be 0.375 (Figure 1).

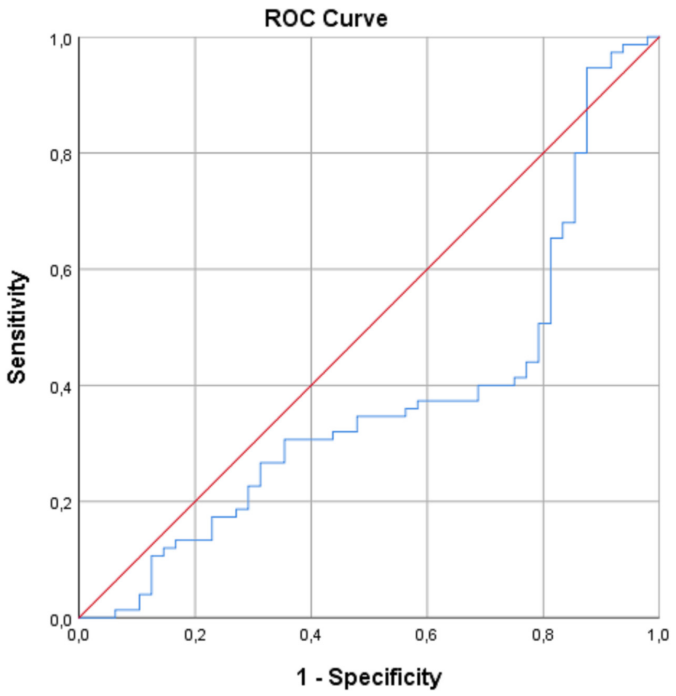

Figure 1. VROC curve and cut-off value calculation for the PMI level in predicting prostate cancer

DISCUSSION

In this study, we determined that PMI calculated using the hemogram parameters obtained before a prostate biopsy could be useful in predicting the biopsy result in patients with a PSA value of 2.5-10 ng/dl. In addition, we found that the number of PLTs was significantly lower in the PCa group compared to the chronic prostatitis group.

Currently, there is no biochemical parameter other than PSA that can predict the prostate biopsy result in PCa (11). The serum PSA level is used for the screening and early diagnosis of PCa. However, as a dilemma, this results in a significant number of unnecessary biopsies, especially when the PSA value is in the range of 4 to 10 ng/ml (12). A transrectal/transperineal prostate biopsy is currently performed to exclude PCa. However, the cost of the biopsy procedure performed due to high PSA values placing a burden on the health system of countries, as well as related complications have led scientists interested in this subject to seek alternative methods. There are publications supporting that PMI, which has recently been introduced, can help differentiate malignant-benign or malignant-inflammatory processes. Many inflammatory biomarkers, such as WBC, NEU, LYM, red blood cell distribution width, and NLR have been used in differential diagnosis studies (13). The ratio of blood cells to each other has been investigated in many cancers (14).

MPV is an early marker of activated PLTs. Lower MPV values suggest increased depletion of large PLTs in inflammatory conditions. Recent studies have confirmed that low MPV levels are associated with high-grade inflammatory diseases and return to their normal range in the anti-inflammatory treatment process (15). When MPV is interpreted together with the PLT count, a more definite result can be reached about PLT function (16). It is known that MPV is associated with PLT function and activation and affected by various inflammatory conditions (17,18). PLTs are circulating cells that play an important role in wound healing, thrombosis, hemostasis, and inflammation (19). Recent studies have found a relationship between PLT activation and the pathophysiology of inflammatory diseases. It is accepted that PLT activity and function are related to PLT size, with larger PLTs being generally younger and more reactive (20-21). It has been reported that the MPV level decreases in high-grade inflammatory conditions due to the predominance of small PLTs in peripheral blood after the increased sequestration and destruction of large and active PLTs in inflammatory areas (22).

MPV is an early marker of activated PLTs. Lower MPV values suggest increased depletion of large PLTs in inflammatory conditions. Recent studies have confirmed that low MPV levels are associated with high-grade inflammatory diseases and return to their normal range in the anti-inflammatory treatment process (15). It is known that MPV is associated with PLT function and activation and affected by various inflammatory conditions (17). Recent studies have shown that MPV is also associated with inflammatory diseases (18). When MPV is interpreted together with the PLT count, it can provide more precise information about PLT function (16). In our study, when comparing the PCa and prostatitis groups were compared in terms of MPV, no significant difference was found, but there was a significant difference in relation to PMI. This shows that assessing the volume and the count together leads to the results being less affected by factors affecting only the volume.

In a study by Fukuokaya et al., MPV was used to predict castration-resistant PCa and it was reported that MPV and PLT count were low in patients with PCa (23). This can be considered to support our findings considering that this situation would result in a decrease in PMI. In addition, since the increase in PLT count in inflammation is proportionally higher than MPV, we indirectly obtained similar results.

Watts et al. found evidence for the relationship of hematological parameters with PCa risk in British men (24). They found that higher red blood cell and PLT counts were associated with a higher risk of PCa while higher mean values of corpuscular volume, corpuscular hemoglobin concentration and spherical cell volume were associated with a lower risk of PCa. In contrast, WBC count was not determined to be associated with a risk of PCa, but higher WBC and NEU counts were related to increased

PCa mortality. Tumors can increase PLT indexes even in the onset period (25). Tumors can also increase the half-life of NEU, which can then promote tumor growth and metastasis (24).

PLTs play an important role in tumor growth and metastasis through tumor cell-derived platelet aggregation. Rudzinki et al. found that increased PLT aggregation in PCa (26), which is in agreement with our results because the number of PLTs in circulation decreases with aggregation, resulting in a lower PMI value.

Fu et al., investigating the role of hemogram parameters in combination with PSA in the differentiation of BPH from PCa, found that MPV was lower and platelet distribution width (PDW) was significantly higher in PCa, and MPV was significantly reduced in patients with PCa compared to those with BPH. In addition, the authors stated that the combination of PSA, MPV and PDW had a significantly increased ability to distinguish PCa from BPH (5). In our study, the difference is that the PSA level was selected from the range considered as the gray zone and we used the mass index including the PLT count in addition to the volume. In our study, there was no significant difference between the PCa and prostatitis groups in terms of NLR and MPV, but a significant difference was observed in PMI.

In another recent study conducted retrospectively, Yüksel et al. also compared the whole blood values of 873 patients who underwent a TRUS biopsy (27). Unlike our study, the authors also included patients with BPH in the sample and found that PLR was the highest in the prostatitis group, followed by the PCa group while the lowest value was obtained from the BPH group (27). In addition, they also examined the PLT level alone and found that it did not significantly differ between the groups but they did not investigate PMI values.

Huang et al. evaluated NLR in 662 patients who underwent a TRUS-guided prostate biopsy (28). When they classified the patients similar to our study, they determined that a high NLR rate, especially in the range of 4-10 ng/dl, was associated with a significant increase in PCa according to the pathology results. Unlike similar publications in which hemogram parameters were evaluated, the authors performed their evaluation according to the PSA ranges. In our study, patients in the same PSA range, which is considered to be the gray zone, was evaluated. The reason for choosing this PSA range in our study is that non-cancerous factors that cause PSA elevation are mostly in this range. In addition, the highest negative biopsy rate is also in this range.

The most important advantage of the platelet mass index is that it is non-invasive and inexpensive, and it can be widely examined wherever a hemogram test can be undertaken. However, the most important disadvantage of the method is that it is not an organ-specific indicator and it is affected by conditions that affect the PLT volume and number. The limitations of the study include the retrospective design, the small number of patients, and the exclusion of patients diagnosed with BPH.

CONCLUSION

We consider that in patients with a PSA value below 10 ng/dl, PMI calculated using hemogram parameters combined with a detailed history and physical examination findings can guide the clinician in the differentiation of PCa from other prostate pathologies and prevent unnecessary biopsies. Further studies with a prospective randomized design and larger series are needed to confirm our findings.

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MEDICAL RECORDS-International Medical Journal

Araştırma Makalesi / Research Article

Gossypin Suppresses Cell Growth by Cytotoxic Effect and Induces Apoptosis in MCF-7 Cells

Gossypin, Sitotoksik Etki ile Hücre Büyümesini Baskılar ve MCF-7 Hücrelerinde Apoptozu İndüklemektedir

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Abstract

Aim: Today, breast cancer is a disease that is encountered commonly in women with limited options for treatment. It is needed to find new agents that can be effective in preventing or managing this disease. It has been demonstrated that gossypin inhibits tumor growth. In our study, it has been targeted to examine the effects of gossypin regarding both anticancer activity and apoptosis in MCF-7 cells.

Material and Method: MCF-7 cells were treated with different doses of gossypin and with 50 μM cisplatin for 24, 48, and 72 hours. The MTT analysis, Caspase-3, Caspase-9, and Nf-KB mRNA expressions of those MCF-7 cells which were treated with gossypin were also conducted in order to evaluate the apoptosis or necroptosis-induced cell death.

Results: In MTT experiments, it has been observed that the administration of 100 μM dose of gossypin had similar effects to the routine cisplatin administration, caused a significant decrease in cell proliferation, and increased apoptosis in the evaluations of Hoechst staining and morphology. It has been put forth that gossypin decreases the expression of CASP-3 and CASP-9 mRNA and increases the expression of NF-kB.

Conclusion: Our results demonstrate that for the breast cancer cells, the 100 μM of gossypin positively affects cell death pathways due to apoptosis.

Keywords: Gossypin, Apoptosis, Caspase-3, Caspase-9, NF-kB

Öz

Amaç: Meme kanseri günümüzde kadınlarda sık görülen ve tedavi seçenekleri kısıtlı olan bir hastalıktır. Bu hastalığı önlemede veya yönetmede etkili olabilecek yeni ajanların bulunması gerekmektedir. Gossypin'in tümör büyümesini engellediği gösterilmiştir. Çalışmamızda MCF-7 hücrelerinde hem antikanser aktivitesi hem de apoptoz üzerine gossypin'in etkilerinin incelenmesi hedeflenmiştir.

Materyal ve Metot: MCF-7 hücreleri, 24, 48 ve 72 saat boyunca farklı dozlarda gossipin ve 50 uM sisplatin ile muamele edildi. Apoptoz veya nekroptoz kaynaklı hücre ölümünü değerlendirmek için, gossipin ile tedavi edilen MCF-7 hücrelerinin MTT analizi, Caspase-3, Caspase-9 ve Nf-KB mRNA ekspresyonları da yapıldı.

Bulgular: MTT deneylerinde 100 μM dozda gossypin uygulamasının rutin sisplatin uygulamasına benzer etkiler gösterdiği, Hoechst boyaması ve morfolojisi değerlendirmelerinde hücre proliferasyonunda anlamlı azalmaya ve apoptoz artışına neden olduğu gözlendi. Gossypin'in CASP-3 ve CASP-9 mRNA ekspresyonunu azalttığı ve NF-kB ekspresyonunu arttırdığı ileri sürülmüştür.

Sonuç: Sonuçlarımız meme kanseri hücreleri için 100 μM gossipinin apoptoza bağlı hücre ölüm yollarını olumlu etkilediğini göstermektedir.

Anahtar Kelimeler: Gossypin, apoptosis, Caspase-3, Caspase-9, NF-kB

INTRODUCTION

Breast cancer is one of the most common malignant diseases in women and its emergence is increasing rapidly due to the stress of modern life (1). Because surgical resection, radiation therapy and chemotherapy are limited options for breast cancer treatment, there is a need to find new chemotherapeutic agents that can be effective in preventing or managing breast cancer pathology (2).

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For the treatment of cancer and some diseases, natural products that have antioxidant, antimutagenic, and anticarcinogenic properties are utilized as an important resource regarding the development of modern drugs (3,4). When these compounds' properties are considered regarding their low toxicity, fewer side effects and high efficiency as chemopreventive and chemotherapeutic agents in cancer, they are widely used in cancer treatment (5). Gossypin has been isolated from plants of the Malvaceae family, in particular Hibiscus vitifolius. It has been reported to suppress the β amyloid-induced toxicity through its strong antioxidant activity, analgesic, and anti-inflammatory activities (6,7). Recently, it has been reported that gossypin is a potential anticarcinogenic agent and inhibits cell proliferation and tumor progression in some tumor cells (8). Nuclear factor KB (NF-kB) is both inducible for genes that are involved in cell viability, inflammation, adhesion, growth and differentiation, and plays a role in the regulation of critical genes in the early and late stages of cancers. Additionally, apoptosis suppressor proteins, genes required for metastasis, and angiogenesis are regulated by NF-kB (9). In a recent study, it was shown that gossypin induces apoptosis of cancer cells through inhibition of Aurora kinase A and p90 ribosomal S6 kinase-2 proteins in HGC27 and AGS cancer cells. Inhibition of these proteins resulted in the induction of cleavage of caspase-3, caspase-9 and PARP and induced cytochrome c expression (10). Even though gossypin has been demonstrated to inhibit various stages of tumor growth in recent studies, its molecular mechanism regarding anticancer activity and apoptosis has not been fully defined. In our study, it has been targeted to examine in MCF-7 cells whether there is an apoptotic, anticarcinogenic, and proliferative difference or not between different doses of cisplatin, which is utilized as a routine chemotherapeutic in cancer, and gossypin, a natural bioflavonoid. This study happens to be the first research report in the literature that examines the anticancer activity of gossypin on MCF-7 cells.

MATERIAL AND METHOD

MCF-7 Breast Cancer Cell Proliferation and Viability Analysis

The MCF-7 cell line was obtained from ATCC (USA). Cell lines stored in Cyrotube at -80°C were thawed by incubating in a 37°C water bath. Dissolved cells were taken into T75 cm2 flasks. Cells were counted after 48 hours at 2 x 105 cells/well in DMEM medium containing 10% FBS. These cells were seeded in a 96-well plate and incubated at 37°C in 5% CO2. After 24 h, cells were exposed to 50 µM cisplatin as a positive control with different concentrations of gossypin (5-100 µg/ml). Then, MTT method was performed to the cells for 24 h, 48 h and 72 h and measurements at 620 nm absorbance value were made with a spectrophotometer (Epoch Microplate Spectrophotometer, BioTek, USA) in 3 repetitions. Cell viability rates were analyzed by comparison with control wells.

Determination of Gene Expressions in MCF-7 Cell Lines

MCF-7 cells were seeded at 200,000/well in 6-well plates and then incubated at 37°C in a 5% CO2 environment. After removing the MCF-7 cells from the plates, they were homogenized by trypsinization using a Tissue Lyser II (Qiagen) device (by adding 350 µl of RLT buffer to 1 x 105 cells). RNA extraction was maintained in the QIAcube RNA isolation device according to the instructions for use.

Performing Reverse Transcriptase Reaction and Obtaining cDNA Synthesis

cDNA was obtained from Total RNA using the High Capacity cDNA Reverse Transcription Kit. All reactions were performed with 10 µl of RNA. Veriti 96 Well Thermal Cycler (Applied Biosystem) device was used for cDNA synthesis. The amount of cDNA was determined by nanodrop spectrophotometry (EPOCH Take3 Plate, Biotek) and stored at -20˚C.

Detection of mRNA Expressions using Real-Time PCR

The CASP-3 (Hs00234387_m1), CASP-9 (Hs00962278_m1), and NF-kB (Hs01042014_m1) mRNA expression was quantified through the utilization of the Taq Man Gene Expression Master Mix kit. The amplification and quantification process was conducted in StepOne Plus Real-Time PCR System (Applied Biosystems) device. As the reference gene, β-actin (Hs01060665_g1) was used. For the 200 ng cDNA, the TaqMan® Gene Expression Assays, which are represented as a table below, were pippetted again as demonstrated below, and 40 cycles were run. Ct values are automatically converted to ΔΔCT. Statistical evaluation of our findings was made in IBM SPSS 20.0 package program.

Fluorescent Staining (Hoechst 33342)

With the help of trypsin, cells were removed from the 75 cm2 flask and were counted. The calculation was made as there would be 5,000 cells in each well. The process of seeding was conducted on 96-well plates as there would be 3 repetitions for 24 hours. After 24 hours, gossypin and cisplatin were administered. Hoechst stain was prepared. Hoechst was prepared for application by calculating as 5 µg/ml from the base stock. 48 hours after the application, the medium was removed from the wells and the wells were washed with PBS and Hoechst (5 µg/ml) dye (Thermo Fisher) was applied. It was incubated in the dark for 30 min. Visualized with a fluorescent microscope (Leica, DMIL LED).

Statistical Analysis

For statistical analysis, the results obtained using SPSS 20.0 software (IBM, USA) for all data were shown as mean±SD. Data analysis was conducted first through the utilization of a one-way analysis of variance (ANOVA), then through Dunnett's test. $p<0.05$ was considered significant.

RESULTS

Anti-proliferative/cytotoxic effect of Gossypin on MCF-7 cells

The ability of Gossypin to inhibit MCF-7 cell proliferation at different concentrations was determined by MTT assay for 24, 48 and 72 hours. As represented in Figure I, it has been observed that gossypin inhibits the cell viability of breast cancer cells according to the time and dose. In addition, it has been observed that 50 µM concentration of cisplatin (CISP), which is utilized as a routine chemotherapeutic, significantly reduces the cell activity in MCF-7 cells at 24, 48, and 72 hours. Excluding the gossypin's group of concentration at 100 µg/ml, it was determined that the other dose groups did not have a significant effect on cell viability in MCF-7 cells (Figure 1). After 48 hours, on the other hand, decreases in cell viability were observed in concentrations at 25 µg/ml, 50 µg/ml, 75 µg/ml, and 100 µg/ml (Figure 1). It has been observed that the optimal effect was in 72 hours of gossypin administration at 10 µg/ml, 25 µg/ml, 50 µg/ml, 75 µg/ml, and 100 µg/ml concentrations (Figure 1). It was observed that after 48 and 72 hours, the gossypin dose group that was at 100 µg/ml concentration demonstrated the same cell viability effect as that of CISP (Figure 1).

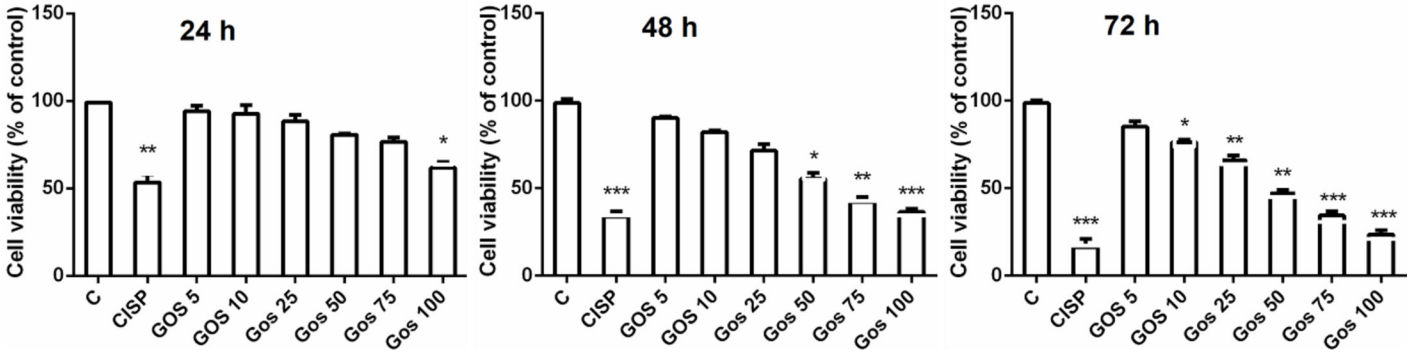

Figure 1. Effects of gossypin and cisplatin on the viability of MCF-7 cells. (a. 24 hours, b. 48 hours c. 72 hours). * MTT shows significant differences between experimental groups compared to control (* P <0.05, ** P <0.01, *** P <0.005).

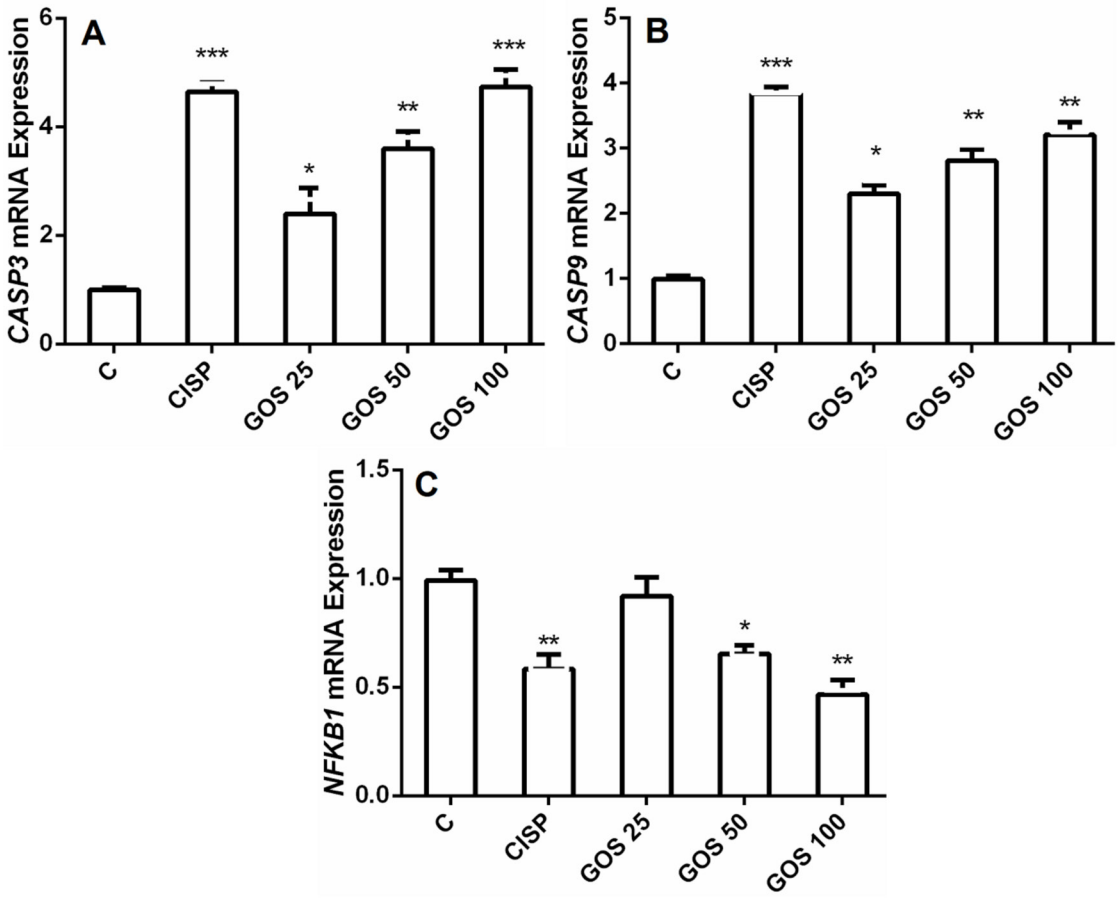

Figure 2. 24-hour CASP-3, CASP -9 and NF-kB mRNA expression levels of all experimental groups. * shows significant differences between caspase-3, caspase-9 and NF-kB mRNA expression levels compared to control (* P <0.05, ** P <0.01, *** P <0.005).

Analyses results of mRNA expression via RT-PCR

It has been observed that in MCF-7 cells, CISP prompted a significant increase in the expression of CASP-3 and CASP-9 mRNA levels, whereas a significant decrease in the expression of NF-kB mRNA level. At the same time, it has been determined that there were a significant increase in NF-kB mRNA expression levels and a decrease in CASP-3 and CASP-9 mRNA expression levels due to the utilization especially at the concentration of 100 µg/ml of gossypin, which is utilized as therapeutic, when compared to the control group ($p < 0.05$) (Figure 2).

Cell death analyzed via the Hoechst (33342) staining

Immunofluorescent Hoechst staining was used in order to determine the apoptotic level (Figure 3). No apoptotic nucleus or commonly stained area was observed in the control cell groups. The presence of apoptotic cell nuclei was observed in the evaluation of a comparison between the cells treated with 50 µg/ml CISP and the control group. In therapeutic gossypin applications, apoptotic cell nuclei characterized by concentrated chromatin, nuclear shrinkage, and irregular fragmentation were determined in gossypin dose groups of 50 and 100 µg/ml. This situation demonstrated that in MCF-7 cells, apoptosis was significantly induced in the 50 and 100 µg/ml of gossypin dose groups (Figure 3).

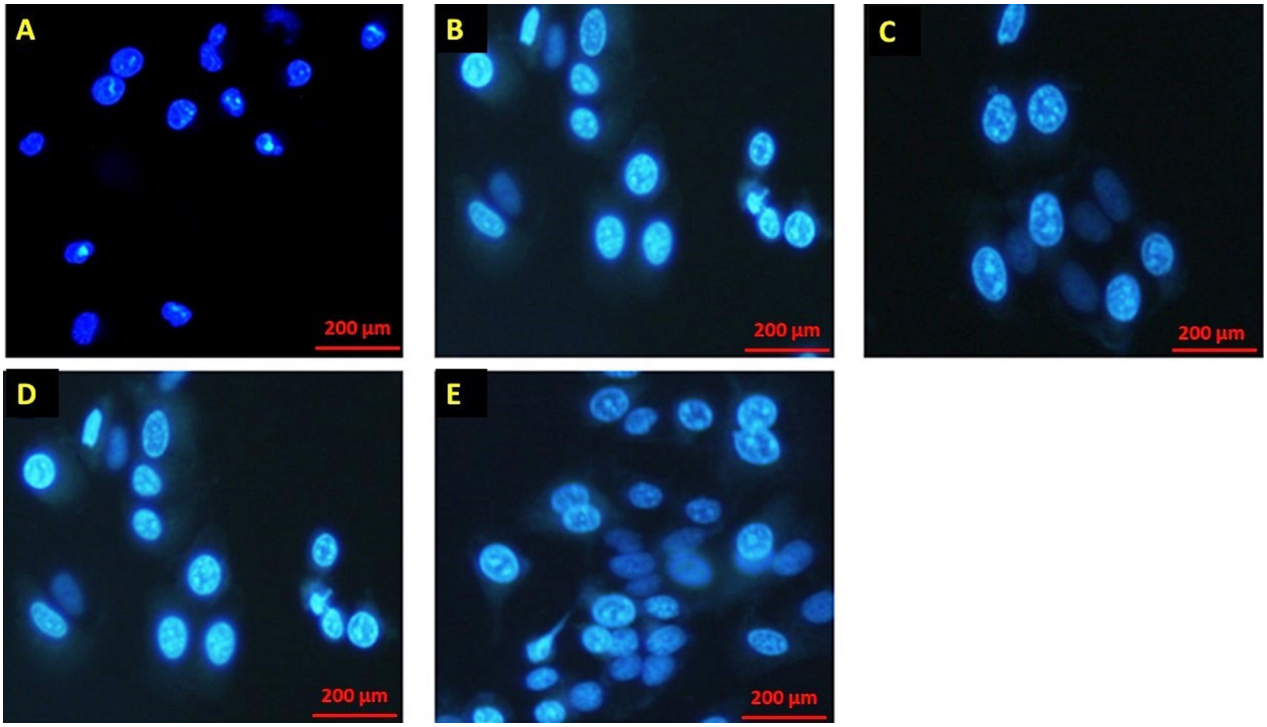

Figure 3. Detection of cell apoptosis and cell morphological changes with Hoechst 33342 staining of MCF-7 cells. Fluorescence photomicrographs of cells stained with Hoechst 33342 at magnification. (A) Control, B) Cisplatin 50 µM C) Gossypin 25 µg / ml D) Gossypin 50 µg/ml, E) Gossypin 100 µg / ml).

DISCUSSION

Breast cancer is cancer that is encountered most commonly in women, and its incidence worldwide is increasing by an average of 0.4% each year. This frequent increase of breast cancer and the economic burden it brings on society augments the search for a new, effective, and fruitful treatment procedure (11). It is known that available chemotherapeutic drugs restrict the growth of cancer and induce the apoptosis of the cancer cell. Yet, these drugs are not sensitive to some patients and cause negative side effects on healthy cells (12). For this reason, it is necessary to find an effective and non-toxic therapeutic agent from natural bioflavonoids in order to treat breast cancer. In our study, it has been aimed to examine the effect of the natural compound gossypin, which is obtained from Hibiscus vitifolius, on MCF-7 breast cancer cells, and it is also the first authentic research article within this scope in the literature. Tumor cell formation is associated with reduced cellular apoptosis and uncontrolled cell proliferation. Therefore, the use of cytotoxic drugs that activate apoptotic pathways and inhibit cell proliferation is one of the most valid methods in cancer treatment (13). After the use of chemotherapeutic drugs, serious side effects such as drug resistance, kidney and liver damage, allergic reactions and gastrointestinal system disorders are encountered (14). Recently, researchers have conducted studies for the utilization of natural compounds due to the serious side effects of chemotherapeutics and determined that these

compounds demonstrate fewer side effects with high efficiency and low toxicity (5). Since natural compounds are known to be the main source of apoptosis-inducing agents, they are utilized in many studies in order to induce apoptosis in human cancer cells (15,16). Gossypin is conventionally used for the treatment of diabetes and is known to have anti-inflammatory, antioxidant, and anticancer activities (10). In a study conducted regarding the cancer cell lines, it was reported that gossypin has an antiproliferative effect (17). In recent cancer research, it was demonstrated that gossypin inhibits cell growth and cell migration (10). In this study, it has been targeted to assess the apoptotic, antiproliferative, and cytotoxic effects and activities of different doses of gossypin, a natural bioflavonoid, on breast cancer cells. In this context, gossypin was administrated to MCF-7 cells on different concentrations, and the MTT viability test was assessed according to the dose and time. Gossypin has demonstrated an antiproliferative effect at concentrations of 25 µg/ml, 50 µg/ml, 75 µg/ml, and 100 µg/ml for 48 and 72 hours periods. When compared to cisplatin, a routinely used chemotherapeutic, the effect of gossypin, especially in the dose groups of 100 µg / ml, was found to be almost the same. Intracellular signaling pathways and secondary messengers that suppress the apoptosis mechanism are selected as targets for treatment in cancerous cells (18). Caspases affect the release of regulatory factors in the cell by participating in immunological functions, cell proliferation and migration. In addition, since the expression of caspases is associated with the frequency of metastasis of cancer cells, their use as a prognostic factor has become widespread (19). In order to prove the anti-cancer activities of natural compounds, the apoptotic properties and mechanisms of these compounds are assessed. It is defined as the form of controlled cell death, adjusted by the organism's own autonomic mechanism, and genetically programmed in the nucleic cells of the organism ever since the fetal development to adult tissue homeostasis (20). In mitochondria-mediated apoptosis, through the release of cytochrome c to the cytosol, the apoptosis complex consisting of cytochrome c/Apaf-1/ATP/procaspase-9 activates first caspase-9, and then caspase-3 (21). For this reason, the induction of apoptosis in cancer cells can easily be demonstrated by evaluating the protein expression of caspase enzymes or mRNA expression levels (22). Compared to the literature, it has been observed that a significant increase in CASP-3 and CASP-9 mRNA expression levels occurred in gossypin treated MCF-7 cells compared to the control group. At the same time, it has been detected that when compared to the cisplatin administration, the gossypin dose group of especially 100 µg/ml had the same effect as the cisplatin dose administration of 50 µg/ml. NF-kB is a protein complex that plays a role in the regulation of DNA transcription, initiates the transcription of cytokines and chemokines, and is known as an apoptosis inhibitor (23). Activation of the NF-κB protein can promote the growth of cancer cells in breast tissue by modulating the expression of proteins associated with the mechanism of tumorigenesis (24). When considered within this scope, the suppression of NF-kB activity can induce apoptosis. In our study, it has been determined that compared to the control group, NF-kB expression was decreased significantly in the MCF-7 cells that were administrated with especially 50 and 100 µg/ml of gossypin. When compared to cisplatin, which is a routine chemotherapeutic, it has been observed that the dose group at 100 µg/ml demonstrated the same effect as cisplatin. In accordance with our research findings, it has been observed that gossypin can suppress the apoptosis inhibitory activity of NF-kB via preventing translocation from the cytoplasm to the nucleus of MCF-7 cells. Our study findings suggest that gossypin can induce apoptosis in cancerous tissue by suppressing the NF-kB-related anti-apoptosis signaling pathway. Since the NF-kB activation is responsible for the transcription of cytokines and chemokines, we think that its effects on both inflammation and cancer cells may be stemming from the inhibition of gene expression that is regulated by NF-kB. On the other hand, in order to analyze the apoptosis, Hoechst staining was performed. In untreated cells, the cell wall remained intact and Hoechst dye could not pass through the cell membrane. Thus, the staining of the cells decreased. On the other hand, the cells treated with Gossypin showed that the cell walls of the cancer cells were damaged, so the Hoechst dye penetrated the cells and apoptosis of MCF-7 cells was observed. The results demonstrate that the high dose (100 µg/ml) of gossypin administration in cells leads to the gradual increase in the morphological change to reach the maximum. Additionally, the cell size and number were significantly reduced, thus it was clearly seen that gossypin caused cell separation and change in morphology.

CONCLUSION

In conclusion, we showed that gossypin inhibited cell growth and induced apoptosis in MCF-7 breast cancer cells. Among the tested doses of gossypine, the dose concentration at 100 µg/ml is the most potent inhibitor of MCF-7 cell growth, and apoptosis stimulant. It has been observed that gossypin's ability to inhibited MCF-7 breast cancer cell growth was in a relationship with the activation of CASP-3 and CASP-9 and inhibition of NF-kB activity. Our immunofluorescent staining results also support this situation. As a result, it has been shown that gossypin can demonstrate proliferation damage, anti-inflammatory, and anti-carcinogenic activity in MCF-7 cells. In this regard, we think that in breast cancer, gossypin can be utilized as an anti-carcinogenic natural compound for cancer patients, or at least it may be of benefit.

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

Ethical approval: *Ethics committee approval is not required as it is a cell study.*

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MEDICAL RECORDS-International Medical Journal

Araştırma Makalesi / Research Article

Relationship Between Adverse Childhood Experiences and Premenstrual Syndrome

Çocukluk Çağı Olumsuz Yaşantılar Ile Premenstruel Sendrom Arasındaki Ilişki

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Abstract

Aim: It is known that adverse experiences in childhood are associated with various mental and physical illnesses. In some studies, it is stated that it also affects women's reproductive health. The aim of this study is to determine the relationship between childhood adverse experiences and the prevalence of premenstrual syndrome.

Material and Method: The research was conducted as a cross-sectional and relationship seeker at a public university on young girls aged between 18 and 25 years. The sample size was calculated to be at least 623 students with 0.05 error level, 80% representation power and 99% confidence interval, and the study was conducted with 754 participants. To collect data; "Personal Introduction Form", "Childhood Adverse Experiences Scale (ACES)" and "Premenstrual Syndrome Scale (PMSÖ)" were used. In statistical evaluation; arithmetic mean, percentage distribution, standard deviation, linear regression analysis were used.

Results: 60.5% of the students had at least one ACE, the average age was 20.68±1.98, 52% studied at the faculty of health sciences, 40.3% studied in the first year, 73.2% had PMS, the average age of menarche was found to be 14.84±28.82. In addition, the mean score of ACES is 1.50±1.75, and the average of PMSÖ is 132.36±36.22. As a result of the linear regression analysis, it has been determined that ACES affects the total and all sub-dimensions of PMSÖ.

Conclusion: In conclusion, it can be said that adverse childhood experiences affect PMS symptoms and PMS symptoms increase as the number of ACES increases.

Keywords: Childhood adverse experiences, premenstrual syndrome, young girls

Öz

Amaç: Çocukluk çağındaki olumsuz yaşantıların çeşitli zihinsel ve fiziksel hastalıklarla ilişkili olduğu bilinmektedir. Bazı çalışmalarda kadın üreme sağlığını da etkilediği belirtilmektedir. Bu araştırmanın amacı, çocukluk çağı olumsuz yaşantılar ile premenstruel sendrom görülme sıklığı ve arasındaki ilişkiyi belirlemektir.

Bu çalışmanın amacı, embriyonik kemik gelişimi sırasında düşük (3 mg/kg) ve yüksek (6 mg/kg) doz nikotinin neden olduğu iskelet sistemi malformasyonlarını ikili iskelet boyama yöntemi ile belirleyerek; E vitamininin koruyucu rolünü ortaya koymaktır.

Materyal ve Metot: Araştırma kesitsel ve ilişki arayıcı olarak bir kamu üniversitesinde yürütülmüştür. Örneklem büyüklüğü 0.05 yanılgı düzeyi, %80 temsil gücü ve %99 güven aralığı ile en az 623 öğrenci olarak hesaplanmış olup çalışma 754 katılımcı ile gerçekleştirilmiştir. Verileri toplanmasında; "Kişisel Tanıtım Formu", "Çocukluk Çağı Olumsuz Yaşantılar Ölçeği (ÇÇOYÖ)" ve "Premenstrüel Sendrom Ölçeği (PMSÖ)" kullanılmıştır. İstatistiksel değerlendirmede; aritmetik ortalama, yüzdelik dağılım, standart sapma, linear regresyon analizi kullanılmıştır.

Bulgular: Öğrencilerin %60.5'inin en az bir tane ÇÇOY yaşadığı, yaş ortalamasının 20.68±1.98 olduğu, %52'sinin sağlık bilimleri fakültesinde okuduğu, %40.3'ünün 1. sınıfta okuduğu, %73.2'sinin PMS yaşadığı, menarş yaş ortalamasının 113.12 ±1.52 olduğu saptanmıştır. Ayrıca ÇÇOYÖ puan ortalaması 1.50±1.75, PMSÖ ortalaması 132.36±36.22'dir. Linear regresyon analizi sonucunda ÇÇOY'ın PMSÖ toplam ve tüm alt boyutlarını etkilediği saptanmıştır.

Sonuç: Sonuç olarak çocukluk çağı olumsuz yaşantılarının PMS semptomlarını etkilediği ve ÇÇOY sayısı arttıkça PMS semptomlarının da arttığı söylenebilir.

Anahtar Kelimeler : Çocukluk çağı olumsuz yaşantılar, premenstrual sendrom, genç kızlar

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INTRODUCTION

The term adverse childhood experiences (ACEs) appeared after the Adverse Childhood Experiences Study was published in 1998. ACEs are grouped in three fields as abuse, neglect, and dysfunction at home and include adverse experience categories (1,2). It has been stated that ACEs are effective on general health and female reproductive health (3). Adverse experiences in childhood are known to be associated with various mental and physical diseases (4). Thus, it is considered that being exposed to traumatic experiences in childhood may distort women's ability to recognize, adjust and comply with physical and emotional changes before menstruation, and may increase the distress and dysfunction before menstrual bleeding (5). A few studies have found its relationship with premenstrual syndrome (4,6). PMS is a common health problem among women of productive age. Many women experience physical and emotional changes in the days before menstruation. The occurrence of these symptoms at the luteal phase of each menstrual cycle, their cessation as the bleeding starts, and their negative impact on the women's lives are defined as premenstrual syndrome (PMS) (7). The worldwide prevalence of PMS has been reported as 47.8% (8). According to the results of the studies on PMS conducted in Turkey, its prevalence changes between 5.9-76% (9). It is stated that 5% of women experience PMS at a serious level that negatively affects their work and home life (4). The known risk factors for PSM are hormonal changes, stress, serotonergic dysfunction while factors like lack of exercising, short sleeping time, or malnutrition are unhealthy behaviors (4,10). Additionally, it is stated that experiencing dysmenorrhea, one of the family members experiencing PMS, and negative thoughts about PMS increases the occurrence of PMS (11).

Considering that ACEs cause negative consequences such as depressive dysfunctions, alcohol use, and suicidal thoughts (1,4), it is inevitable for PMS to be not affected by ACEs. It was reported that the management of the effects of premenstrual symptoms is more unsuccessful in individuals who experience childhood trauma (12,13). Thus, this study was conducted to determine the relationship between ACEs and PMS.

MATERIAL AND METHOD

Type of the Study

The study has a cross-sectional and correlational design.

Place and Time of the Study

This research, which was carried out on students receiving midwifery education in Turkey, was carried out on the social media platform between March-May 2021.

Population and Sample of the Study

The population of the study consisted of almost 10.000 students who were studying in the Department of Midwifery in the spring semester of the 2020-2021 academic year in Turkey (14). Participants were determined using the virtual snowball chain sampling method from purposive sampling methods. The least number of individuals who must be included in the sample of the study was determined as 623 students using the power analysis at 0.05 error level, 80% representative power, and 99% confidence interval, and the study was conducted with 754 participants.

Inclusion Criteria

-Being single,
-Being aged between 18 and 25,

Exclusion Criteria

-Leaving study questions unanswered.

Data Collection Tools

The data of the study were collected using the "Personal Identity Form", "Adverse Childhood Events Turkish Form" and the "Premenstrual Syndrome Scale".

Personal Identity Form

The personal identity form, which was developed after the literature review by researchers (15,16), includes 26 questions about the participants' sociodemographic characteristics and menstrual features.

The Adverse Childhood Events Turkish Form (ACE-TR)

The scale was adapted to Turkish by Ulukal et al. (17) and its validity and reliability tests were carried out by Gündüz et al. in 2018. The ACE-TR is a self-report scale that has 10 items and examines adverse experiences before the age of 18 in the yes-no format. The questions contain only the yes option and if the otherwise applies, the question is left. The lowest score that can be obtained from the scale is 0 while the highest score is 10. The scale has no cut-off value. The Cronbach's alpha value was found as 0.742 in the validity and reliability study conducted by Gündüz (17). It was calculated as 0.672 in this study.

The Premenstrual Syndrome Scale (PMSS)

The validity and reliability study of the scale was conducted by Gençdoğan in 2006. The scale, which is used to determine premenstrual symptoms and severity, is a five-point Likert-type scale with 44 items. The scale has nine subdimensions as depressive sensation, anxiety, fatigue, nervousness, depressive thoughts, pain, appetite changes, sleep pattern changes, and bloating. The lowest score that can be obtained from these nine subdimensions is 44 and the highest score is 220. High scores indicate the high intensity of premenstrual symptoms. The Cronbach's alpha coefficient of the scale was found as 0.75 (18). It was calculated as 0.973 in this study.

Data Collection

The data were collected via Google Forms. The participants provided data with the online self-report method on the Google survey system. The data collection tools were designed in the Google form format and were sent to single young women aged between 18-25 who agreed to participate in the study via WhatsAppIt took approximately 10 minutes to fill the form.

Data Analysis

Considering the conformity of the data to the normal distribution, the data were determined to be between the ±3 standard deviation ranges (19). It was determined that

the data were between the ±3 standard deviation range as a result of the transformation of raw scores into Z scores and no extreme values were distorting the linearity. The data were coded and analyzed using the SPSS 22 package program. Arithmetic means, frequency distribution, standard deviation, and linear regression analysis were used for statistical analyses. The statistical significance level was $p< 0.05$.

Limitations of the Study

This study has some limitations like all studies. The study was only conducted with young women who had internet connection, who were single and in the age range of 18-25; thus, it is a limitation that the results cannot be generalized to married women and older women. In addition, conducting the study online may have negatively affected the answers of young girls with little technical experience.

Ethical Considerations

The Ethical Committee approval (Decision No: 2021/1855) was obtained to conduct the study. The participants were informed about the study and those who volunteered to participate were included in the study after stating this in the Google form survey.

RESULTS

Sociodemographic characteristics and menstrual cycle-related features of the students, who participated in this study, are presented in Table 1. Of the students, 60.5% experienced at least one ACE, 52% studied at the health sciences faculty, 40.3% were 1st grade students, and 93.4% did not work. The mean age of the students was 20.68±1.98. The mothers of 89.1% of the students did not work while the fathers of 72.1% of the students worked. Of them, 82.2% had middle income, 76.1% had nuclear family, 91.8% did not smoke, and 62.1% did not have boyfriends. The mean body mass index (BMI) was 21.94±3.54. Of the students, 74.8% had regular menstruations, 73.2% experienced PMS, and the mean age at menarche was 13.12 ±1.52 and the mean cycle duration was 28.71±7.28 days (Table 1).

Table 1. Sociodemographic and Menstrual Cycle Characteristics of the Participating in the Study

Variable	n	%
Number of ACE		
0	298	39.5
1	154	20.4
2	124	16.4
3	82	10.9
4 and above	96	12.7
Class		
1	304	40.3
2	116	15.4
3	248	32.9
4	86	11.4
Employment status		
Employed	50	6.6
Unemployed	704	93.4
Mother's employment status		
Employed	82	10.9
Unemployed	672	89.1
Father's employment status		
Employed	544	72.1
Unemployed	210	27.9
Perceived income level		
Low	112	14.9
Middle	620	82.2
High	22	2.9
Living place		
City	526	69.8
County	142	18.8
Village	86	11.4
Family structure		
Nuclear family	574	76.1
Extended family	152	20.2
Broken family	28	3.7
Smoking status		
Yes	62	8.2
No	692	91.8
Status of having a boyfriend		
Yes	286	37.9
No	468	62.1
The regularity of menstruation		
Regular	564	74.8
Irregular	190	25.2
Premenstrual syndrome have status		
Yes	552	%73.2
No	202	26.8
Total	754	100
Age (years)		X±SS 20.68±1.98
Age of Menarche (years)		13.12 ±1.52
Cycle duration (days)		28.71±7.28
BMI (average)		21.94±3.54

ACE: Adverse Childhood Experiences, BMI: Body Mass İndex

Table 2 shows the numbers and frequency distribution of the participants who said yes to the items of the ACE-TR. Of the participants, 33.4% 33.4% answered as yes to Item 1 (Has a parent or an adult member of your household often or very often ... abused you, despised you, humiliated you, or belittled you? Or has she/he acted in a way that physically hurt you and scared you?), 25.2% 25.2% answered as yes to Item 2 (Has a parent or an adult member of your household often or very often ... assaulted you, slapped you or thrown something at you? Or has she/he ever hit you hard enough to leave a scar or get injured?), and 12.5% 12.5% answered as yes to Item 3 (Has an adult or someone at least 5 years older than you ever touched you or caressed you or asked you to sexually touch his/her body?) Additionally, 27.1% 27.1% answered as yes to Item 4 (Have you often or very often felt as follows? No one in your family loves you or thinks you are important or special? Or Your family has not taken care of you, you have not felt close to your family or you have not supported each other?) and 11.1% 11.1% answered as yes to Item 7 (Has your mother or step-mother often or very often assaulted you, slapped you or thrown something at you? Or has she often or very often kicked you, beat you, or hit you with a fist or something harder? Or has she hit you continuously at least for a few minutes or has she threatened you with a gun or knife?).

The lowest and highest scores of the students included in the study and their mean scores are presented in Table 3. The mean score on the ACE-TR was 1.50±1.75, and the lowest and highest scores were 0 and 8, respectively. The mean score on the PMSS was 132.36±36.22, and the lowest and highest scores were 44 and 216, respectively (Table 3).

It was determined as a result of the regression analysis performed that adverse childhood experiences significantly predicted premenstrual syndrome and its subdimensions positively and the models formed were statistically significant. Considering the R2 values regarding the models, it was observed that 6% of the variance in the depressive sensation, 5.3% of the variance in the anxiety, 6.6% of the variance in fatigue, 5.1% of the variance in nervousness, 9.6% of the variance in depressive thoughts, 3.3% of the variance in pain, 1.2% of the variance in appetite changes, 3.5% of the variance in sleep pattern changes, 3% of the variance in bloating, and 7.1% of the general variance of PMS were explained by the changes in ACEs (Table 4).

Table 2. Number and Percentage Distribution of Participants Who Say Yes to Their ACE's Items

Items	n	%
1. Did a parent or other adult in the household often. Swear at you, insult you, put you down, or humiliate you? or Act in a way that made you afraid that you might be physically hurt?	126	33.4
2. Did a parent or other adult in the household often. Push, grab, slap, or throw something at you? or Ever hit you so hard that you had marks or were injured?	95	25.2
3. Did a parent or other adult in the household often. Push, grab, slap, or throw something at you? or Ever hit you so hard that you had marks or were injured?	47	12.5
4. Did you often feel that. No one in your family loved you or thought you were important or special? or Your family didn't look out for each other, feel close to each other, or support each other?	102	27.1
5. Did you often feel that. You didn't have enough to eat, had to wear dirty clothes, and had no one to protect you? or Your parents were too drunk or high to take care of you or take you to the doctor if you needed it?	12	3.2
6. Were your parents ever separated or divorced?	26	6.9
7. Was your mother or stepmother: Often pushed, grabbed, slapped, or had something thrown at her? or Sometimes or often kicked, bitten, hit with a fist, or hit with something hard? or Ever repeatedly hit over at least a few minutes or threatened with a gun or knife?	42	11.1
8. Did you live with anyone who was a problem drinker or alcoholic or who used street drugs?	16	4.2
9. Was a household member depressed or mentally ill or did a household member attempt suicide?	32	8.5
10. Did a household member go to prison?	13	3.4
Number of pregnant women not living any Adverse Childhood Experience	149	39.5

ACE: Adverse Childhood Experiences

An increase of 1 unit in the adverse childhood experiences score causes an increase of 1.031 unit (B) in the depressive sensation score, .922 unit (B) in the anxiety score, .813 unit (B) in the fatigue score, .698 unit (B) in the nervousness score, 1.231 unit (B) in the depressive thoughts score, .308 unit (B) in the pain score, .183 unit (B) in the appetite changes score, .333 unit (B) in the sleep pattern changes, .329 unit (B) in the bloating score, and 5.849 unit (B) in the total score of PMSS based on the equations that can be formed in relation to regression models. Regarding the standardized beta coefficients, it was observed that ACEs were more significant predictors for general PMS and Depressive Sensation (β= .248) subdimension. Thus, it can be stated that higher levels of ACES accompany higher levels of PMS among young women.

Table 3. The Lowest and Highest Scores and Average Points of the Students Who Participated in the Study from the Scales

Variable	X ±SS	Min/max points that can be obtained	Min/max points received
ACES	1.50±1.75	0-10	0-8
PMSS	132.36±36.22	44-220	44-216

ACES: Adverse Childhood Experiences Scale, PMSS; Premenstrual Syndrome Scale

Table 4. Linear Regression Analysis Results of the Prediction of the ACES's and its Sub-Dimensions of PMSS

Scales		B	t	β	R^2	F	p
ACES	Depressive Affect	1.031	4.950	.248	.061	24.504	.000
	Anxiety	.922	4.601	.231	.053	21.153	.000
	Fatigue	.813	5.153	.257	.066	26.552	.000
	Irritability	.698	4.77	.225	.051	20.041	.000
	Depressive Thoughts	1.231	6.32	.310	.096	39.957	.000
	Pain	.308	3.554	.181	.033	12.667	.000
	Appetite Changes	.183	2.104	.108	.012	4.428	.036
	Sleep Changes	.333	3.672	.186	.035	13.497	.000
	Swelling	.329	3.382	.172	.030	11.437	.000
	PMS_Total	5.849	5.365	.267	.071	28.782	.000

ACES: Adverse Childhood Experiences Scale, PMSS; Premmesntrual Syndrome Scale, B; Non-standardized Beta Coefficient, β; Standardized Beta Coefficient, R2; Explanatory Coefficient, *p<0.05; t test result for the significance of the regression coefficients and the F test result for the significance of the model

DISCUSSION

Premenstrual syndrome is experienced every month regularly and causes dysfunctions in daily life activities, negatively affects education life and decreases the life quality of those who experience it (16). Most studies in the literature have stated that PMS has caused negative outcomes regarding the quality of life, sleep quality, and anxiety-stress (15,20). However, the factors that cause PMS have mostly been disregarded. There is a limited number of studies on the relationship between the ACEs and PMS (4,6); however, there is no such study conducted in Turkey.

This study found the total mean score on the ACE-TR of participants as 1.50±1.75 (Table 3). This score was found as 1.8±1.55 (21) and 2.8± 2.4 (22) in other studies. The number of ACEs was mostly emphasized in relevant studies using the ACE-TR instead of focusing on the mean score. A relevant study reported that the rate of children's physical abuse in Turkey changes between 15% and 75% and the rate of sexual abuse is almost 20% (23). Of the participants, 60.5% had at least one ACE within the first 18 years of their lives while 12.5% had four or more ACEs (Table 1). Bellis et al. found that 46.5% of the participants had at least one ACE and 8.3% had four or more ACEs (24). Furthermore, Angerud et al. found that 58.6% of the participants had at least one ACE while 8% had five or more ACEs (25). Strine et al. found that 72% of the participants had at least one ACE and 12.6% had four or more ACEs (26) Similarly, Felitti et al. determined that two-third of

adults had at least one ACE while more than 10% had four or more ACEs (1). The results of this study are in line with the literature.

Adults, who were not loved, cared for, sympathized with by their parents in their childhood, have significantly higher scores on depression, somatization, interpersonal sensitivity, and paranoid ideation compared to adults who were not exposed to such actions (17). This study determined that 27.1% of the participants felt such emotions (Item 4: Table 2). In a systematic compilation of many studies conducted in Turkey, 25.7% of the participants stated that they experienced domestic neglect at least once (23). Such problems experienced in childhood may cause a very serious social problem in adulthood (27). Additionally, physical, mental, and psychophysical disorders caused by this may become a life-long health issue for individuals (28).

Many children and teenagers start working at an early age to contribute to the living of their families or to support themselves in Turkey and encounter various types of abuse and neglect (23). The most common types of physical abuse are pulling hair, pulling ear, throwing something, hitting by hand, and slapping (29). The present study found that 38.2% of young women were subjected to physical violence (Item 3-7: Table 2). This rate reaches 90% in African countries (28). Individuals, who were subjected to physical abuse in childhood, have low self-esteem and more emotional and behavioral problems. Physical abuse is considered a way of upbringing instead of violence but many interpersonal, cognitive, emotional, and behavioral problems, low emotional intensity, high temper, and abusive behaviors are more common among individuals, who were subjected to physical abuse (23,28).

The rate of sexual abuse has been found as 20% in Turkey (23). This rate was found as 12.5% (Item 3; Table 2) in this study, and the WHO states that 120 million young women are sexually abused (30). This result is similar to those in the literature. It is stated that physical and sexual abuse in the first 18 years of life may cause mood disorders and PMS (31). It is also stated that being subjected to physical and sexual abuse in the first 18 years of life may cause mood disorders and such abuse might be associated with the sex life and reproductive health of individuals. Abused individuals may have an increased tendency to problems related to sex (vaginismus, etc.). Additionally, the tendency to problems related to the menstrual cycle, pregnancy and postpartum periods as well as sex may increase (32. The presence of PMS symptoms is important in terms of improving the reproductive/sexual health and life quality of young women (16). This study found the total mean score on the PMSS of the participants as 132.36±36.22 (Table 3). The mean scores on PMSS were found as 22.14±32.60 (15), 144.84±27.28, (33), and 148.77±23.26 (16) in studies conducted in Turkey. This mean score indicates that most young women experience PMS. The rate of young women who stated to have experienced PMS was 73.2% in this study (Table 1). The American College of Obstetricians and Gynecologists (ACOG) determined that 85% of women experience PMS while this rate was 57.4% in the study by Kısa et al. and the occurrence rate of PMS was 60.1% in the study by (11,35). Considering the results of the regression analysis performed, 7.1% of the total score on the PMSS, 6% of the depressive sensation score, 5.3% of the anxiety score, 6.6% of the fatigue score, 5.1% of the nervousness score, 9.6% of the depressive thoughts score, 3.3% of the pain score, 1.2% of the appetite changes score, 3.5% of the sleep pattern changes score, and 3% of the bloating score can be explained by the score obtained from the ACE-TR (Table 4). It was observed that ACEs increased depressive thoughts, fatigue, depressive sensation, and anxiety the most. Studies in the literature indicate that ACEs mostly cause anxiety, depression, and mood disorders (6,36) and have a relationship with fatigue/bad sleep quality (36,37). ACEs play an important role in the mental health and hardiness of young people. Thus, PMS might become difficult to handle for young women. As some studies reported that negative mood might cause PMS (38,39), this study found that ACEs cause PMS.

Additionally, an increase of 1 unit in the total score on the ACE-TR causes a positive increase of 0.267 unit (β1) in the total score on the PMSS (Table 4). This result indicates that childhood traumas are effective variables in increasing PMS symptoms in young women. It is believed that this result will contribute to the literature due to the limited number of studies supporting this result (4,6).

CONCLUSION

This study found that ACEs had within the first 18 years of life affect the reproductive health of women. The study also found that ACEs are common in Turkey and they affect the total and subdimension scores of the PMSS. It was determined that ACEs affected the depressive thoughts, fatigue, depressive sensation, and anxiety subdimensions the most. Agreeing that ACEs are an important determinant of PMS will allow health professionals to better communicate with young women and facilitate handling PMS. It is recommended to work on a larger sample to better understand the importance of "ACEs"..

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

Ethical approval: The Ethical Committee approval (Decision No: 2021/1855) was obtained to conduct the study.

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Araştırma Makalesi / Research Article

Reflections of COVID-19 Pandemic on Dermatology Outpatient Clinics

COVID-19 pandemisinin dermatoloji polikliniklerine yansımaları

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Abstract

Aim: We aimed to investigate the effects of stress on dermatological diseases that come into our lives with this new infection, which can have vital effects and limitations in social life during the covid 19 pandemic process.

Material and Method: In this retrospective study, patients who were examined in the dermatology outpatient clinic during the COVID-19 pandemic (April - May 2020) and the same period last year (April - May 2019) were evaluated. The number of patients who applied, application dates, age and sex of patients, and ICD-10 (International Classification of Diseases-10th Revision) diagnosis codes were recorded by scanning the electronic database of the hospital.

Results: The rate of referral to the dermatology outpatient clinic decreased by 6.3 times compared to the previous year. The average age of the patients who applied to the dermatology outpatient clinic during the COVID-19 pandemic period was significantly higher compared to that of the patients who applied during the same period in the previous year. It was observed that during the pandemic period, men applied to the dermatology outpatient clinic significantly more than in the previous year. COVID-19 infection was not detected in patients who applied to the Dermatology outpatient clinic during the early period of the pandemic.

Conclusion: While there was a decrease in outpatient consultations for cosmetic reasons, a significant increase in consultations for stress-induced dermatoses was found. Stria rubra development in the young population for reasons such as a sedentary life and possible nutritional disorders as a result of the restrictions experienced during the pandemic period was one of the interesting findings of this period. We think that patients with the coronavirus infection and associated skin findings apply to other clinics instead of the dermatology clinic due to the presence of other accompanying systemic symptoms.

Keywords: Covid-19, dermatology, outpatient clinic

Öz

Amaç: Çocukluk çağındaki olumsuz yaşantıların çeşitli zihinsel ve fiziksel hastalıklarla ilişkili olduğu bilinmektedir. Bazı çalışmalarda kadın üreme sağlığını da etkilediği belirtilmektedir. Bu araştırmanın amacı, çocukluk çağı olumsuz yaşantılar ile premenstruel sendrom görülme sıklığı ve arasındaki ilişkiyi belirlemektir.

Bu çalışmanın amacı, embriyonik kemik gelişimi sırasında düşük (3 mg/kg) ve yüksek (6 mg/kg) doz nikotinin neden olduğu iskelet sistemi malformasyonlarını ikili iskelet boyama yöntemi ile belirleyerek; E vitamininin koruyucu rolünü ortaya koymaktır.

Materyal ve Metot: Bu retrospektif çalışmada, COVID-19 pandemisi sırasında (Nisan- Mayıs 2020) ve geçen yılın aynı döneminde (Nisan- Mayıs 2019) dermatoloji polikliniğinde muayene edilen hastalar değerlendirildi. Hastanenin elektronik veri tabanı taranarak başvuran hasta sayısı, başvuru tarihleri, hastaların yaşı ve cinsiyeti ile ICD-10 (International Classification of Diseases-10th Revision) tanı kodları kaydedildi.

Bulgular: Dermatoloji polikliniğine başvuru oranı bir önceki yıla göre 6,3 kat azaldı. COVID-19 pandemi döneminde dermatoloji polikliniğine başvuran hastaların yaş ortalaması, bir önceki yıl aynı dönemde başvuran hastalara göre anlamlı derecede yüksekti. Pandemi döneminde erkeklerin dermatoloji polikliniğine bir önceki yıla göre anlamlı derecede daha fazla başvurduğu görüldü. Pandeminin erken döneminde Dermatoloji polikliniğine başvuran hastalarda COVID-19 enfeksiyonu tespit edilmedi.

Sonuç: Kozmetik nedenlerle poliklinik başvurularında azalma olurken, stres kaynaklı dermatozlar için başvurularda anlamlı artış saptandı. Pandemi döneminde yaşanan kısıtlamalar sonucunda hareketsiz yaşam ve olası beslenme bozuklukları gibi nedenlerle genç nüfusta stria rubrae gelişimi bu dönemin ilginç bulgularından biriydi. Koronavirüs enfeksiyonu ve eşlik eden deri bulguları olan hastaların eşlik eden diğer sistemik semptomların varlığı nedeniyle dermatoloji kliniği yerine ilgili diğer kliniklere başvurduklarını düşünüyoruz.

Anahtar Kelimeler : Covid-19, dermatoloji, poliklinik

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INTRODUCTION

Outpatient examinations in dermatology are mostly non-urgent examinations. Considering asymptomatic viral carriage, it is recommended to postpone non-urgent examinations as much as possible due to the risk of COVID-19 transmission (1). The first COVID-19 cases were reported in Turkey on March 11. Afterwards, on March 21, schools were closed and a curfew was imposed on persons aged over 65 years. As of April 4, a curfew had been imposed for individuals aged less than 20 years. The public was informed through various media outlets about taking the necessary protective measures when going out. However, outpatient clinic services continued to be provided, although it was reduced that usual.

Many skin diseases are known to be associated with stress. During the COVID-19 pandemic period, people developed intense mental distress and stress (2). However, dermatological findings due to the coronavirus infection have also been reported in the literature (3). In this study, we aimed to determine the demographic findings of patients who presented to the dermatology outpatient clinic during the COVID-19 pandemic period, their diagnosis, and the presence of other skin lesions that may be associated with COVID-19.

MATERIAL AND METHOD

Study design

In this retrospective study, patients who were examined in the dermatology outpatient clinic during the COVID-19 pandemic (April - May 2020) and the same period last year (April - May 2019) were evaluated. The number of patients who applied, application dates, age and sex of patients, and ICD-10 (International Classification of Diseases-10th Revision) diagnosis codes were recorded by scanning the electronic database of the hospital. Repeated admissions of the same patient for control and follow-up purposes were ignored. The patients' records were screened to determine whether they had COVID-19. The study was conducted in accordance with the Helsinki Declaration principles and was approved by our Corporate Ethics Committee (2020/283).

Statistical analysis

SPSS version 21 (SPSS software, Chicago, IL, USA) was used for data analysis. Descriptive statistics were expressed as percentage, mean, standard deviation, median, and minimum and maximum values. Chi-Square test was used to compare the diagnosis frequency of patients who presented to the dermatology outpatient clinic before and after the COVID-19 pandemic. P-values <0.05 were considered to indicate statistical significance.

RESULTS

While 10207 patients were examined in the dermatology outpatient clinics between April and May 2019, only 1637 patients were examined in during the COVID-19 pandemic period between April and May 2020. The rate of referral to the dermatology outpatient clinic decreased by 6.3 times compared to the previous year. The average age of the patients who applied to the dermatology outpatient clinic during the COVID-19 pandemic period was significantly higher compared to that of the patients who applied during the same period in the previous year. It was observed that during the pandemic period, men applied to the dermatology outpatient clinic significantly more than in the previous year (Table 1). None of the patients who applied to the dermatology outpatient clinic had COVID-19 infection. The prevalence of diseases in 2019 and the COVID-19 pandemic period is shown in table 2.

Table 1. Age and gender distribution of patients who applied to the dermatology outpatient clinic in 2019 and during the COVID-19 pandemic period

	April-May 2019 N = 10207		COVID-19 pandemic period april-may N = 1637		P-value
Age (year)					
Mean	33.75±19.50		38.00±19.24		<0.001[a]
Min-max	0-95		0-92		
Sex	n	%	n	%	<0.001[b]
Male	4345	42.6	790	48.3	
Female	5862	57.4	847	51.7	

[a] Mann-Whitney-U test, [b] Chi-Square test

Table 2. Diagnoses and rates observed in dermatology outpatient clinic during 2019 and COVID-19 pandemic periods

Diagnosis	April-May period of 2019		COVID-19 pandemic April-May period		P-valuea
	n	%	n	%	
Significantly increasing diseases during the pandemic period					
Scabies	155	1.5	113	6.9	<0.001
Herpes Zoster	101	1	36	2.2	<0.001
Alopecia areata	141	1.4	42	2.5	<0.001
Urticaria	303	3	91	5.5	<0.001
Allergiccontact dermatitis	147	1.5	44	2.7	<0.001
Drug eruption	5	0.04	6	0.3	<0.001
Psoriasis	451	4.4	103	6.3	0.002
Vitiligo	136	1.3	38	2.3	0.002
Erythema nodosum	7	0.06	5	0.3	0.005
Striae Distencea	13	0.1	7	0.4	0.006
Erythema annulare centrifigum	2	0.01	2	0.1	0.036
Irritant Contact dermatitis	559	5.5	111	6.8	0.046
Diseases with no significant change in frequency during the pandemic period					
Prurigo-lichen simplex chronicus	174	1.7	25	1.5	0.609
Pruritus	525	5.1	101	6.2	0.103
Atopic dermatitis	151	1.5	28	1.7	0.483
Seborrheic dermatitis	315	3.1	45	2.7	0.473
Dermatitis	468	4.6	78	4.7	0.758
Nail Diseases	62	0.6	15	0.9	0.152
Dermatophytosis	753	7.3	115	7.0	0.636
Telogen effluvium	175	1.7	24	1.5	0.474
Pyoderma	315	3.1	56	3.4	0.484
Parapsoriasis	63	0.6	14	0.8	0.269
Hidradenitis suppurativa	9	0.08	4	0.24	0.077
Lipoma /cyst	36	0.3	11	0.67	0.057
Lichen Planus	42	0.4	9	0.5	0.429
Herpes infection	44	0.4	5	0.3	0.463
Erythema multiforme	9	0.08	1	0.06	0.726
Bullous Disease	11	0.1	4	0.2	0.149
Oral aphthae	42	0.4	10	0.6	0.288
Skin malignancy	10	0.1	4	0.2	0.110
Follicular disorders	57	0.5	4	0.2	0.100
Burn	21	0.2	4	0.2	0.752
Pityriasis rosea	83	0.8	14	0.8	0.958
Callus	115	1.1	14	0.8	0.330
Seborrheic keratosis	43	0.4	2	0.1	0.068
Diseases whose frequency decreased significantly during the pandemic period					
Acne	2516	24.7	275	16.8	<0.001
Androgenetic alopecia	94	0.9	0	0	<0.001
Xerosis cutis	393	3.8	34	2.1	<0.001
Verruca vulgaris	506	5	45	2.7	<0.001
Melanin pigmentation	173	1.7	15	0.9	0.02
Actinic keratosis	57	0.6	3	0.1	0.048
Other reasons	925	9.1	80	4.9	

[a] Chi-Square test

DISCUSSION

During the COVID-19 pandemic period, dermatology outpatient consultations decreased by 6.3 times compared to the previous year. While there was a decrease in outpatient consultations for cosmetic reasons, a significant increase in consultations for stress-induced dermatoses was found. Stria rubra development in the young population for reasons such as a sedentary life and possible nutritional disorders as a result of the restrictions experienced during the pandemic period was one of the interesting findings of this period. We think that patients with the coronavirus infection and associated skin findings apply to other clinics instead of the dermatology clinic due to the presence of other accompanying systemic symptoms.

Psoriasis, atopic dermatitis, urticaria, alopecia areata, chronic pruritus, and acne are known as stress-sensitive skin diseases (4-6). We also found a significant increase in the frequency of the outpatient clinic consultations for diseases such as psoriasis, vitiligo, alopecia areata, and urticaria. Although there was an increase in the frequency of chronic pruritus and atopic dermatitis cases, this difference was not statistically significant. Kutlu et al. (7) in their study comparing second and third level hospital admissions during the COVID-19 period, reported that the frequency of psoriasis, alopecia areata, and urticaria cases increased due to the social stress experienced during the COVID-19 pandemic period. An increase in cortisol response to psychosocial stress has been reported in psoriasis patients (5). This increased neuroendocrine response leads to an increase in psoriasis disease severity following stressful periods. In addition, it has been reported that vitiligo patients have high levels of stress perception and psychological stress can affect the onset and progression of the disease (8).

Acne is one of the most common diseases encountered in the dermatology outpatient clinic. In our study, it was observed that the frequency of acne application during the COVID-19 period decreased from 23% to 15.5% compared to the previous year. It is one of the dermatological diseases that are sensitive to stress, and acne was the only disease whose frequency decreased during the COVID-19 period compared to the previous year. The reason for this may be that acne is perceived as a cosmetic problem by the society and therefore, acne patients do not apply to the dermatology clinic.

During the COVID pandemic process, we found a significant increase in the frequency of scabies from April to May compared to that of the previous year. Kutlu et al. (9) stated that there was an increase in cases of scabies during the COVID-19 pandemic, and they attributed this to the increase in domestic contact with the "stay at home policy". They suggested that the symptoms of parasite infection, which has an incubation period of 2-3 weeks, emerged 4-6 weeks after the start of the stay at home policy (9). We also think that the number of scabies cases has increased due to increased domestic contacts after the pandemic.

In our study, we found significant increases in the frequency of irritant contact dermatitis and allergic contact dermatitis. During the pandemic period, an increase in irritant contact dermatitis cases has been reported due to increased hygiene behaviors, excessive hand washing, and the use of occlusive gloves and alcohol-based disinfectants (10). Skin allergic responses can be triggered by xerosis, damage to the epidermal barrier, and the passage of allergens through the damaged skin (11). Erdem et al. (12) investigated the prevalence of hand eczema in healthcare workers during the COVID-19 period and found that the incidence of hand eczema is 50.4%. They reported that the majority of cases in their study consisted of irritant contact dermatitis (96.3%) (12). In their study, Kutlu et al. found a similar increase in the frequency of irritant contact dermatitis after the COVID-19 pandemic (7).

During the COVID-19 pandemic, we observed a significant decrease in cosmetic applications to dermatology outpatient clinics. The most striking finding was that androgenetic alopecia has a zero referral rate. While there was a significant decrease in applications with cosmetic components such as melanin hyperpigmentation and verruca, the frequency of admission for telogen efflivium remained the same. Turan C et al. 13 found a decrease in the frequency of verruca vulgaris and hyperpigmentation in their study, in which they compared dermatology outpatient clinic admissions before and after the COVID-19 pandemic.

Particulary in the young population, as a result of the introduction of distance education, spending much more time at home, a sedentary life, malnutrition, and sudden weight gain during the COVID pandemic period, an explosion in the frequency of striae rubrae occurred. Although there is a cosmetic problem, most patients applied to the dermatology outpatient clinic during this risky period to get information about these rashes that first developed on their bodies (14).

In our study, a significant increase was found in the frequency of herpes zoster after the pandemic. It has been reported that this increase in the frequency of herpes zoster may be related to the psychological stress experienced during this period, as well as a symptom accompanying subclinical COVID-19 infection (15).

Many dermatological findings have been described in the course of the COVID pandemic, including maculapapular rash, urticaria, vesicular and petechial rash, distal ischemia, and livedo racemosa. In our study, COVID-19 infection was not detected in patients who applied to the dermatology outpatient clinic; therefore, we did not find an increase in the frequency of these findings. In the literature, a 2% mortality rate in COVID-19-associated urticaria cases is mentioned (16). Therefore, we think that COVID-19-related urticaria cases present to the emergency of chest or infectious diseases outpatient

clinics instead of the dermatology outpatient clinic due to the other accompanying COVID-19 findings.

The limitation of this study is that it does not show the long-term effects of the pandemic on dermatological diseases, since it covers only the first two months after the COVID-19 pandemic.

CONCLUSION

As a result, during the COVID pandemic, in dermatology outpatient clinics, there was a period in which the number of patients presenting for concultation decreased, an explosion was observed in stress-related dermatological diseases, and cosmetic diseases were delayed and ignored.

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

Ethical approval: The study was conducted in accordance with the Helsinki Declaration principles and was approved by our Corporate Ethics Committee (2020/283).

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Araştırma Makalesi / Research Article

Relationship Between Foot Muscle Strength with Achilles Tendon Thickness and Plantar Fascia Thickness

Ayak Kas Kuvveti ile Aşil Tendonu Kalınlığı ve Plantar Fasya Kalınlığı Arasındaki İlişki

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Abstract

Aim: There is essential coordination between foot muscle strength, Achilles tendon, and plantar fascia. This study aims to show the mathematical relationship between foot muscle strength and plantar fascia thickness and Achilles tendon thickness.

Material and Method: The study was conducted with 57 volunteering individuals (30 males, 27 females) between the ages of 18 and 40. Plantar fascia thickness and Achilles tendon thickness were measured with the ultrasound. Foot muscle strength was measured with a digital hand dynamometer. The data obtained were statistically evaluated.

Results: A positive, moderately strong correlation was found in men between left side Achilles tendon thickness and plantar fascia thickness ($p<0.05$). A positive, reasonably strong relationship was found in women between left foot muscle strength average and plantar fascia thickness ($p<0.05$). However, in all groups, the right foot muscle strength average had a positive, moderately strong correlation with Achilles tendon thickness and plantar fascia thickness ($p<0.05$). In all groups, it was found that the right-side Achilles tendon thickness had a positive, moderately strong correlation with plantar fascia thickness ($p<0.05$). On the other hand, when the genders were compared, a statistically significant difference was found between right foot muscle strength and plantar fascia thickness and Achilles tendon thickness ($p<0.05$).

Conclusion: We believe that the fact that there are different results between men and women and even on the right and left sides of the same gender will be useful, especially in terms of clinic physicians' approaches towards diagnosis and treatment.

Keywords: Achilles tendon, plantar fascia, muscle strength, foot, plantar flexion

Öz

Amaç: Ayak kas kuvveti, aşil tendonu ve plantar fasya arasında temel bir koordinasyon vardır. Bu çalışma, ayak kas kuvveti ile plantar fasya kalınlığı ve aşil tendonu kalınlığı arasındaki matematiksel ilişkiyi göstermeyi amaçlamaktadır.

Materyal ve Metot: Çalışma; yaşları 18 ile 40 arasında değişen, gönüllü 57 birey (30 erkek, 27 kadın) ile gerçekleştirildi. Ultrason ile plantar fasya kalınlığı ve aşil tendon kalınlığı ölçüldü. Ayak kas kuvveti dijital el dinamometresi ile ölçüldü. Elde edilen veriler istatistiksel olarak değerlendirildi.

Bulgular: Erkeklerde sol aşil tendon kalınlığı ile plantar fasya kalınlığı arasında pozitif, orta derecede güçlü bir korelasyon bulundu ($p<0.05$). Kadınlarda sol ayak kas kuvveti ortalaması ile plantar fasya kalınlığı arasında pozitif, anlamlı güçlü bir ilişki bulundu ($p<0.05$). Ancak tüm gruplarda sağ ayak kas kuvveti ortalaması ile aşil tendon kalınlığı ve plantar fasya kalınlığı arasında pozitif, orta derecede güçlü bir korelasyon vardı ($p<0.05$). Tüm gruplarda sağ Aşil tendonu kalınlığı ile plantar fasya kalınlığı arasında pozitif, orta derecede güçlü bir korelasyon olduğu bulundu ($p<0.05$). Öte yandan cinsiyetler karşılaştırıldığında sağ ayak kas kuvveti ile plantar fasya kalınlığı ve aşil tendonu kalınlığı arasında istatistiksel olarak anlamlı fark bulundu ($p<0.05$).

Sonuç: Kadın ve erkek arasında ve hatta aynı cinsiyetin sağ ve sol taraflarında bile farklı sonuçların bulunmasının özellikle klinik hekimlerinin tanı ve tedaviye yaklaşımları açısından faydalı olacağı kanaatindeyiz.

Anahtar Kelimeler : Aşil tendonu, plantar fasya, kas gücü, ayak, plantar flexion

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INTRODUCTION

Achilles tendon (tendo calcaneus) is the common tendon of gastrocnemius muscle and soleus muscle (sometimes plantaris muscle is also included). It is the most robust, comprehensive and thickest tendon of the human body (1-3). Approximately 70% of its structure consists of collagen fibers (4). It has a significant role in conducting moves, such as walking, running, jumping and in the biomechanics of the lower extremity (5). In addition to being the strongest tendon of our body, Achilles tendon is the most frequently injured tendon due to its anatomic region and being used intensively concerning function (1). Achilles tendon may show various pathological situations. These injuries generally occur in the ankle part. It is of considerable importance to know the functional anatomy of Achilles tendon in detail to reveal the effects of these pathological situations on the functions of Achilles tendon and to be able to plan the period of treatment how we administer the treatment (6).

Plantar fascia or plantar aponeurosis starts from the medial tubercle at the calcaneus and ends by attaching to the plantar part of the metatarsophalangeal joint (7-9). Studies conducted have shown that plantar fascia statically and dynamically supports the longitudinal arch of the foot and that plantar fascia resists to shocks the foot is exposed to (10). While plantar fascia gives active support to the arch of the foot in the advancing phase of walking, at the same time, it prevents the deterioration of the foot shape passively (11). Also, ptosis has been observed in the arch of the foot following plantar fasciotomy. It has been shown that plantar fascia may show severe tension, especially in situations, such as lifting weight and carrying a load (12). A study show a positive correlation between Achilles tendon and plantar fascia tension (13). For the stability of the arch of the foot and for the plantar to show resistance against the load being carried, the correlation of plantar fascia and Achilles tendon is essential.

In the case of weakness of the muscles supporting the longitudinal arch, the amount of stress on non-contractile plantar fascia increases (14). Besides, weakness in gastrocnemius muscle and soleus muscle, Achilles tendon and intrinsic foot muscles are considered as a risk factor for plantar fascia (15-17).

There is critical coordination between foot muscle strength, Achilles tendon and plantar fascia. This study aims to show the mathematical relationship between foot muscle strength, plantar fascia thickness and Achilles tendon thickness.

MATERIAL AND METHOD

Type of the Study

To conduct this study, ethical approval was obtained from Uşak University Faculty of Medicine Non-Interventional Clinical Research Ethical Board with the decision numbered 83-06. This study was conducted with 57 volunteers (30 males, 27 females). The study's aim was explained verbally to all the participants who participated in this study, and they signed an "informed volunteer consent form."

Inclusion criteria were as follows:

- Healthy, volunteering asymptomatic individuals between the ages of 18 and 40

Exclusion criteria were as follows:

- Heel pain
- Plantar fasciitis
- Those with sensory heel pain
- Those with nerve compression
- Those who had diabetes mellitus
- Those with inflammatory joint disease
- Individuals who underwent foot surgery
- Those who did active sports activities or those still doing

After the participants' height and weight measurements were made, body mass index (BMI) was calculated.

Foot muscle strength measurement

One of the first devices that are accepted as reliable for isometric muscle strength measurement is digital hand manometers. In a study that compared measurements made using digital hand dynamometers and isokinetic dynamometer, a strong correlation was found between measurement values (18, 19). A study that compared three different hand dynamometers found that measurements made with MicroFet showed fewer differences with an isokinetic dynamometer (20, 21). In our research, a MicroFet hand dynamometer was used to assess foot muscle strength (MicroFet2TM, Hoggan Health Industries, West 130 Jordan, UT, USA). In addition to the high reliability of MicroFet2TM, its ease of use, portability, cost, and compact size have already been considered in studies.

Muscle force measured in Newton (N) with a 4 cm-wide transducer pad. All muscle strength tests were performed by the same physiatrist. Plantar flexion involves a coordinated effort between several muscles in the ankle, foot, and leg. These include gastrocnemius, soleus, plantaris, flexor hallucis longus, flexor digitorum longus, and tibialis posterior muscles. Strength ability tests for plantar flexors were performed. For evaluation, the volunteers sat on the edge of a chair with the only heel touching the floor and arms crossed in front of the body. The volunteer was asked to keep their buttocks on the chair and make a plantar flexion to the ankle joint without a swing movement. The transducer was placed between the distal part of the foot and floor. No warm-up was performed before testing. A higher score represents better muscle strength ability.

Ultrasound (US) screening technique

After the volunteers lay on the examination table in the prone position, their ankles were brought to flexion, and

Achilles tendon thickness and plantar fascia thickness were measured. Measurements were made on the right and left feet of all individuals. A standard ultrasound gel was used to obtain a clear image. A linear ten megahertz probe (MINDRAY DC-8 EXP Mindray DS USA, Inc.) was used. A physiatrist made measurements and assessments of both sides. The probe was placed vertically to the long axis of the Achilles tendon. After a general evaluation was made on the axial plane, thickness (anteroposterior) measurement was made from the lower side of the medial malleolus (Figure. 1).

Foot soles were kept in the same position, and plantar fascia thickness was measured from the attachment point to the calcaneal tubercle in longitudinal appearance (Figure. 2).

Participants had anomalies, such as calcification, plantar fasciitis, bursitis, tendinopathy, or calcaneal irregularities, were excluded from this study.

Statistical Analysis

IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA) program was used in statistical analysis. The normality distribution of the data was tested using the Kolmogorov-Smirnov test and the findings showed that data were not normally distributed. The data were given as median (min-max). The Mann-Whitney U test was used in the comparison of genders. The data which were not normally distributed were analyzed using Spearman Rho correlation analysis. The limits of the correlation coefficient were assumed to be between -1 and +1. While the correlation coefficient, whose magnitude is between 0.5 and 1.0, indicates variables are considered highly correlated, those between 0.3 and 0.5 are moderately correlated and those between 0 to 0.3 have a low correlation (22).

RESULTS

Median (min-max) values of the participants' age, height, weight and BMI variables are given in Table 1. The median value of all the individuals who participated in this study was 19 years, the median value of height was 175 cm, the median value of weight was 66 kg and the median value of BMI was 22.6. Mann-Whitney U test was conducted on the data to investigate whether there were statistical differences between men and women concerning the variables of age, height, weight and BMI. According to the Mann-Whitney U test conducted, there was a statistically significant difference between men and women concerning age, weight and BMI ($p<0.05$) (Table 1).

Table 1. Median (min-max) values of the groups' age, height, weight and BMI variables

Group	Age	Height (cm)	Weight (kg)	BMI
Male	19 (18-21)	178 (169-195)	76.5 (49-100)	24.2 (16-30.5)
Female	19 (18-27)	163 (153-183)	55 (45-100)	20.2 (16.5-35.4)
p value	0.204	0.000*	0.000*	0.006*

*P<0.05 statistically significant

Median (min-max) values of the participants' right and left muscle strength averages, Achilles tendon thickness and plantar fascia thickness variables are given in Table 2.

Spearman Rho correlation analysis was conducted on the data to find out how participants' variables of muscle strength average, Achilles tendon thickness and plantar fascia thickness taken from their right foot differed with age, height, weight and BMI. The analysis results showed that right side Achilles tendon thickness in men had a moderately strong correlation with weight and BMI ($p<0.05$). As the whole group, the findings showed that the right foot muscle strength average had a strong positive correlation with height and weight and a weak positive correlation with BMI ($p<0.05$). Right side Achilles tendon thickness had a positive moderate correlation with height, weight and BMI ($p<0.05$) and the right side plantar fascia thickness had a positive weak correlation with weight ($p<0.05$) (Table 3).

Table 2. Median (min-max) values of the groups' right and left foot variables

Side	Group	Muscle Strength Average (Newton)	Achilles Tendon Thickness (mm)	Plantar Fascia Thickness (mm)
Male	Male	117.2 (74.6-245.2)	0.47 (0.33-0.62)	0.32 (0.19-0.44)
Female	Female	85.5 (46.9-119)	0.43 (0.32-0.57)	0.29 (0.2-0.36)
p value	All Group	104 (46.9-245.2)	0.46 (0.32-0.62)	0.31 (0.19-0.44)
	Male	119.5 (81.8-223)	0.45 (0.29-0.66)	0.32 (0.2-0.46)
Left	Female	82.8 (44.7-155.6)	0.42 (0.32-0.55)	0.3 (0.18-0.36)
	All Group	107.4 (44.7-223)	0.42 (0.29-0.66)	0.31 (0.18-0.46)

Spearman Rho correlation analysis was conducted on the data to find out how participants' variables of left foot muscle strength average, left side Achilles tendon thickness and plantar fascia thickness differed with age, height, weight and BMI. The findings showed that left foot Achilles tendon thickness in men had a strong positive correlation with weight and BMI ($p<0.05$). As the whole group, the left foot muscle strength average had a strong positive correlation with height and weight, and a weak positive moderately strong correlation with BMI ($p<0.05$). The left Achilles tendon thickness had a positive moderately strong correlation with weight and a strong positive correlation with BMI ($p<0.05$) (Table 4).

Spearman Rho correlation analysis was conducted on the data to find out the correlation between right foot variables of the participants. In all groups, right foot muscle strength average had a positive moderate correlation with Achilles tendon thickness and plantar fascia ($p<0.05$). Achilles tendon thickness had a positive moderately strong correlation with plantar fascia ($p<0.05$) (Table 5).

Table 3. Spearman Rho correlation analysis results between the groups' age, height, weight and BMI variables and right foot variables

Groups	Variables	Statistics	Muscle Strength Average	Achilles Tendon Thickness	Plantar Fascia Thickness
Male	Age	r	-0.035	0.146	0.191
		p	0.854	0.442	0.313
	Height	r	0.206	0.191	0.076
		p	0.274	0.313	0.690
	Weight	r	0.257	0.467	0.272
		p	0.171	0.009*	0.145
	BMI	r	0.140	0.422	0.167
		p	0.459	0.020*	0.377
Female	Age	r	0.269	0.214	-0.009
		p	0.193	0.304	0.968
	Height	r	0.274	0.016	-0.167
		p	0.185	0.940	0.426
	Weight	r	-0.039	0.108	0.005
		p	0.853	0.609	0.982
	BMI	r	-0.119	0.072	0.087
		p	0.571	0.731	0.678
All Groups	Age	r	-0.002	0.121	0.017
		p	0.990	0.381	0.902
	Height	r	0.564	0.307	0.192
		p	0.000*	0.023*	0.160
	Weight	r	0.527	0.482	0.287
		p	0.000*	0.000*	0.033*
	BMI	r	0.296	0.459	0.260
			0.028*	0.000*	0.055

*P<0.05 statistically significant

Table 4. Spearman Rho correlation analysis results between the groups' age, height, weight and BMI variables and left foot variables

Groups	Variables	Statistics	Muscle Strength Average	Achilles Tendon Thickness	Plantar Fascia Thickness
Male	Age	r	0.102	-0.057	0.131
		p	0.591	0.765	0.490
	Height	r	0.316	0.173	0.208
		p	0.089	0.362	0.269
	Weight	r	0.311	0.581	0.289
		p	0.094	0.001*	0.121
	BMI	r	0.136	0.590	0.176
		p	0.472	0.001*	0.353
Female	Age	r	0.141	-0.105	0.019
		p	0.502	0.617	0.927
	Height	r	0.260	-0.275	0.172
		p	0.209	0.183	0.410
	Weight	r	0.002	0.239	0.163
		p	0.993	0.250	0.436
	BMI	r	-0.058	0.264	0.059
		p	0.784	0.201	0.778
All Groups	Age	r	0.035	-0.123	0.029
		p	0.802	0.370	0.832
	Height	r	0.584	0.191	0.209
		p	0.000*	0.162	0.126
	Weight	r	0.574	0.471	0.248
		p	0.000*	0.000*	0.068
	BMI	r	0.324	0.514	0.168
		p	0.016*	0.000*	0.221

*P<0.05 statistically significant

Spearman Rho correlation analysis was conducted on the data to find out the correlation between left foot variables of the participants. A positive moderately strong correlation was found in men between Achilles tendon thickness and plantar fascia thickness ($p<0.05$). A positive moderately strong correlation was found in women between muscle strength average and plantar fascia thickness ($p<0.05$) (Table 6).

Mann-Whitney U test was conducted on the data to find out whether there were statistical differences between men and women in terms of the variables of muscle strength average, Achilles tendon thickness and plantar fascia. According to the Mann-Whitney U test, a statistically significant difference was found between men and women concerning muscle strength averages for the right foot, Achilles tendon thickness and plantar fascia thickness ($p<0.05$). Concerning left foot, a statistically significant difference was found only in muscle strength average ($p<0.05$) (Table 7).

Table 5. Spearman Rho correlation analysis results of the groups' right foot variables

Groups	Right	Statistics	Muscle Strength Average	Achilles Tendon Thickness	Plantar Fascia Thickness
Male	Muscle Strength Average	r	1.000	0.059	0.136
		p	-	0.758	0.475
	Achilles Tendon Thickness	r	0.059	1.000	0.357
		p	0.758	-	0.053
	Plantar Fascia Thickness	r	0.136	0.357	1.000
		p	0.475	0.053	-
Female	Muscle Strength Average	r	1.000	0.335	0.005
		p	-	0.101	0.982
	Achilles Tendon Thickness	r	0.335	1.000	0.099
		p	0.101	-	0.638
	Plantar Fascia Thickness	r	0.005	0.099	1.000
		p	0.982	0.638	-
All Groups	Muscle Strength Average	r	1.000	0.339	0.300
		p	-	0.011*	0.026*
	Achilles Tendon Thickness	r	0.339	1.000	0.374
		p	0.011*	-	0.005*
	Plantar Fascia Thickness	r	0.300	0.374	1.000
		p	0.026*	0.005*	-

*P<0.05 statistically significant

Table 6. Spearman Rho correlation analysis results of the groups' left foot variables

Groups	Right	Statistics	Muscle Strength Average	Achilles Tendon Thickness	Plantar Fascia Thickness
Male	Muscle Strength Average	r	1.000	0.059	0.136
		p	-	0.758	0.475
	Achilles Tendon Thickness	r	0.059	1.000	0.357
		p	0.758	-	0.053
	Plantar Fascia Thickness	r	0.136	0.357	1.000
		p	0.475	0.053	-
Female	Muscle Strength Average	r	1.000	0.335	0.005
		p	-	0.101	0.982
	Achilles Tendon Thickness	r	0.335	1.000	0.099
		p	0.101	-	0.638
	Plantar Fascia Thickness	r	0.005	0.099	1.000
		p	0.982	0.638	-
All Groups	Muscle Strength Average	r	1.000	0.339	0.300
		p	-	0.011*	0.026*
	Achilles Tendon Thickness	r	0.339	1.000	0.374
		p	0.011*	-	0.005*
	Plantar Fascia Thickness	r	0.300	0.374	1.000
		p	0.026*	0.005*	-

*P<0.05 statistically significant

Table 7. Assessment of right and left foot variables in terms of gender			
Side	**Muscle Strength Average**	**Achilles Tendon Thickness**	**Plantar Fascia Thickness**
Right	0.000*	0.013*	0.012*
Left	0.000*	0.069	0.113

*P<0.05 statistically significant

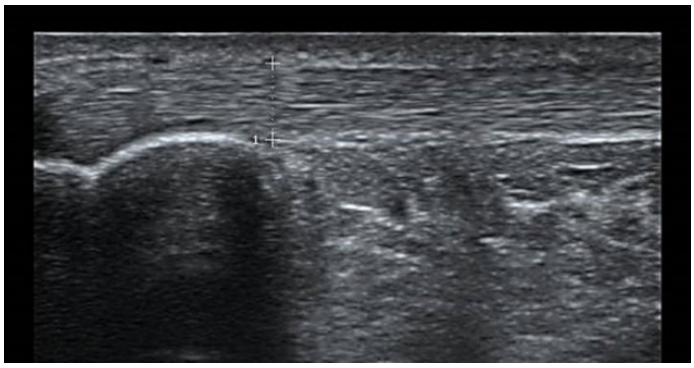

Figure 1. Achilles tendon thickness measurement by US

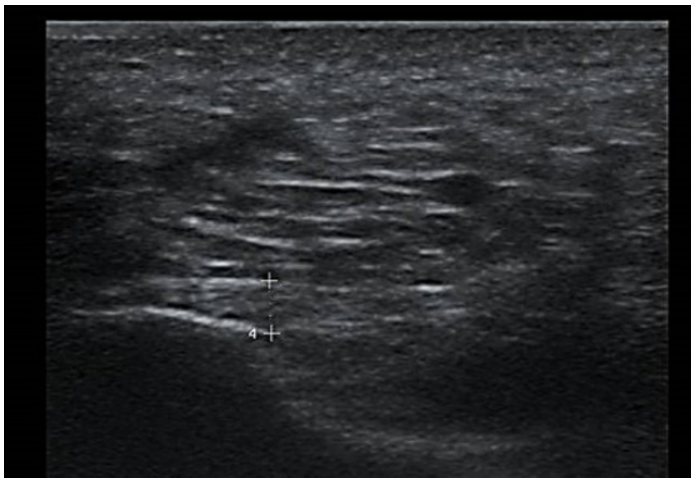

Figure 2. Plantar fascia thickness measurement by US

DISCUSSION

Achilles tendon thickness differs concerning ethnic groups and populations. In a study conducted in Holland, average Achilles tendon thickness was reported as 6.8 mm in asymptomatic individuals, while it was published as 9.2 mm in symptomatic groups (23). In a study conducted in Hong Kong, Achilles tendon thickness of individuals in the second, third, fourth, and fifth decades were examined, and no differences were found between them. Average Achilles tendon thickness was found as 5.1 mm (3.8 mm - 6.9 mm) (24). In another study conducted in Denmark, when pre-exercise and post-exercise Achilles tendon thickness were compared, average Achilles tendon thickness was measured as 5 mm. The tendon was reported to be 0.13 mm thicker after acute exercise. However, this difference was not statistically significant (25). A study conducted between senior athletes in their seventh and eighth decades and sedentary individuals in Finland, while the difference was found in terms of Achilles tendon width, no difference was found between Achilles tendon thickness and average Achilles tendon thickness was measured as 5.7 mm (26). In our study, average Achilles tendon thickness was measured as 4.6 mm (3.2 mm - 6.2 mm) in the right foot and 4.2 mm (2.9 mm - 6.6 mm) in the left foot. In our study, although the statistical difference was found between female and male groups in terms of height, weight and BMI, in the comparison of female and male participants in terms of Achilles tendon thickness, statistically significant difference was found only in the right foot, no statistically significant difference was found between female and male participants in terms of Achilles tendon thickness in the left side (Table 7). While the positive correlation was found in men between weight and BMI and Achilles tendon thickness, when both females and males were assessed as a whole (in both feet), a positive correlation was found between height, weight, and BMI and Achilles tendon thickness.

In one study, the findings showed that the average plantar fascia thickness was about 3.2 mm in the right foot of men, while it was 3.3 mm in the left foot and about 2.8 mm in the right and left foot of women. However, plantar fascia thickness did not have a statistical significance or positive correlation with age, height, weight, and BMI (27). In our study, plantar fascia thickness average was measured as 3.2 mm (1.9 mm - 4.4 mm) in the right foot of women, 2.9 mm (2 mm – 3.6 mm) in the left foot of women; as 3.2 mm (2 mm - 4.6 mm) in the right foot of men and 3 mm (1.8 mm - 3.6 mm) in the left foot of men. When the results were assessed, a statistically significant difference was found in the right foot when plantar fascia thickness was compared between the two genders. Concerning the left foot, no statistically significant difference was found between men's and women's plantar fascia. In a study conducted by Uzel et al. (28), the average thickness of plantar fascia was 3.3 mm and 3.9 mm in women and men, respectively. They showed a mild correlation between plantar fascia thickness and height, weight, and BMI values. However, they did not find a significant difference between athletes and healthy populations concerning plantar fascia thickness. Similarly, no significant difference was found in our study in both male and female groups (in both feet) between plantar fascia thickness and height, weight, and BMI. No correlation was found between Achilles tendon

thickness and height. However, a significant positive relationship was found in men between weight and BMI and Achilles tendon thickness. When all groups (women and men) were assessed (in both feet), a significant positive correlation was found between plantar fascia thickness and weight (Tables 3-4).

When the correlation between Achilles tendon and plantar fascia thickness was analyzed, while a positive correlation was found in the left foot of men, the right foot correlation was not statistically significant. In women, no correlation was found between Achilles tendon and plantar fascia thicknesses in both feet. When all the groups were analyzed, a meaningful positive relationship was found only on the right side (Tables 3-4).

In the studies related to ankle muscle strength measurement in old and young groups with digital hand dynamometer, weakening between 24% and 37% was found in muscle strength (29). In our study, no correlation was found between muscle strength average values and participants' ages. The reason for this is that the age distribution range of the volunteers in the study was less than ten years. This provides more reliable information us in assessing the correlation of plantar fascia thickness and Achilles tendon thickness with muscle strength.

When both genders were compared concerning muscle strength, a significant difference was found in both right and left feet (Table 7). While no significant correlation was found between plantar fascia thickness and Achilles tendon thickness in both feet of women, a strong correlation was found between muscle strength average and plantar fascia in the left foot (Tables 5-6). According to this result, on the side where the plantar fascia is not thick, foot flexion and plantar fascia load are supported by the Achilles tendon.

In our study, no correlation was found between muscle strength average, plantar fascia thickness and Achilles tendon thickness in both feet of men. When all the groups were assessed together, no correlation was found between left foot muscle strength and plantar fascia and Achilles tendon thicknesses. On the other hand, a moderately strong relationship was found between right foot muscle strength and both plantar fascia thickness and Achilles tendon thickness (Tables 5-6).

In the literature review we conducted, we found mostly plantar fascia assessment in plantar fasciitis etiology. Besides, differences in ankle movement angles and lower extremity dorsal muscle groups were examined in individuals doing sport (30). To our knowledge, there are any studies in the literature on the correlation between muscle strength and plantar fascia thickness and Achilles tendon thickness to compare with this study.

CONCLUSION

In this study, we set out to present the correlation between muscle strength and plantar fascia thickness and Achilles tendon thickness, which is anatomically and clinically (especially in terms of doctors of orthopedics and physiotherapy) important. We believe that our results can guide both physicians in diagnosis and treatment and anatomists in terms of the literature. Given that there are different results between men and women and even on the right and left sides of the same gender, this can be useful, especially concerning the approaches of clinic physicians towards diagnosis and treatment. For instance, we believe that our study's findings are of the same importance as the importance of knowing the average values of Achilles tendon thickness in the society in cases when tendinitis diagnosis should be made. Also, the present study will be a source for more detailed and practical studies.

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

Ethical approval: To conduct this study, ethical approval was obtained from Uşak University Faculty of Medicine Non-Interventional Clinical Research Ethical Board with the decision numbered 83-06.

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Araştırma Makalesi / Research Article

The Incidence of the Zygomatico-orbital Foramen and the Importance of Its Location in Surgical Approaches

Foramen Zygomaticoorbitale'nin Görülme Sıklığı ve Lokasyonunun Cerrahi Yaklaşımlardaki Önemi

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Abstract

Aim: The present study aimed to reveal the frequency of the zygomatico-orbital foramen (ZOF) in the zygomatic bone, its location, and its connection with the zygomatico-orbital foramen (ZFF) and zygomaticotemporal foramen (ZTF).

Material and Method: Ethics committe eapproval of our study was received by the Istanbul Medical Faculty Clinical Research Ethics Committee. Fifty (27 right; 23 left) hemicraniums of Istanbul University, Department of Anatomy of unknown gender were included in the study. Connections with ZOF were determined by passing fine wire through ZTF and ZFF. The closest point of the ZOF to the orbital rim was measured. The distance from the area used for retrobulbar injections (defined as the point where the 1/3 inferolateral edge and 2/3 inferomedial edge of the aditus orbitalis intersect.) to the ZOF was measured. All measurements were measured with a digital caliper and the data were evaluated with SPPS v.21.

Results: The number of ZOF was found 46 (51.68%) on the right and 43 (48.32%) on the left side. ZOF, was found to be single in 18 (36%) orbits, double in 16 (32%) orbits, 3 (18%) in 9 orbits, and 4 (6%) in 3 orbits. ZOF was absent in 4 (8%) orbits. Of 89 ZOFs, 37 (20 right; 17 left) were found to be associated with (via a channel) ZFF and 16 (8 right; 8 left) with ZTF. It was noted that 36 (18 right; 18 left) ZOF had no connection with any foramina. The closest distance of ZOF to the orbital rim was 4.54±2.33 mm and the distance to the retrorobulbar injection area was 7.89±2.98 mm.

Conclusion: The location and variations of FZO may be helpful in preventing complications during retrobulbar injection, lateral orbitotomy approach for intraorbital tumors, and during surgical interventions such as repair of zygomatic fractures.

Keywords: Zygomatico-orbital foramen, zygomaticofacial foramen, zygomaticotemporal foramen, zygomatic bone, retrobulbar injection

Öz

Amaç: Os zygomaticum'un facies orbitalis'inde bulunan foramen zygomaticoorbitale (FZO)'nin görülme sıklığının ortaya konulması, konumunun belirlenmesi, foramen zygomaticofaciale (FZF) ve foramen zygomaticotemporale (FZT) ile bağlantılarının tespit edilmesi amaçlanmıştır.

Materyal ve Metot: Çalışmamızın Etik kurul onayı İstanbul Tıp Fakültesi Klinik Araştırmalar Etik Kurulu tarafından alındı. İstanbul Üniversitesi, İstanbul Tıp Fakültesi Anatomi Anabilim Dalı laboratuvarında bulunan, cinsiyeti bilinmeyen 50 adet (27 sağ; 23 sol) hemicranium çalışmaya dahil edildi. FZT ve FZF'den ince tel geçirilerek FZO ile olan bağlantılar tespit edildi. FZO'nin aditus orbitalis'in inferior kenarına olan en yakın mesafe ölçüldü. Son olarak, retrobulbar enjeksiyon için kullanılan noktadan (aditus orbitalis'in 1/3 inferolateral kenarı ile 2/3 inferomedial kenarının kesiştiği nokta) FZO'ye olan mesafe ölçüldü. Tüm ölçümler için dijital kaliper kullanıldı ve verilerin değerlendirilmesi SPPS v.21 ile gerçekleştirildi.

Bulgular: FZO'nin sayısı sağ tarafta 46 (%51,68) sol tarafta ise 43 (%48,32) olarak bulundu. FZO; 18 (%36) orbitada tek, 16 (%32) orbitada çift, 9 (%18) orbitada 3 ve 3 (%6) orbitada 4 foramenli olarak bulundu. 4 (%8) orbitada ise FZO hiç görülmedi. 89 FZO'den 37'si (20 sağ; 17 sol) FZF ile 16'sı (8 sağ; 8sol) FZT ile bağlantılı (bir kanal aracılığı ile) olduğu bulundu. 36 (18 sağ; 18 sol) FZO'nin ise herhangi bir foramen ile bağlantısı olmadığı kaydedildi. FZO'nin aditus orbitalis'in inferior kenarına olan en yakın mesafe 4,54±2,33 mm ve retrorobulbar enjeksiyon noktasına olan mesafe 7,89±2,98 mm olarak ölçüldü.

Sonuç: FZO'nin lokasyonu ve varyasyonları retrobulbar enjeksiyon sırasında, intraorbital tümörler için uygulanan lateral orbitotomi yaklaşımında ve zigomatik fraktürlerin onarımı gibi cerrahi girişimler esnasında komplikasyonlarının önlenmesinde yardımcı olabilecektir.

Anahtar Kelimeler: Foramen zygomaticoorbitale, foramen zygomaticofaciale, foramen zygomaticotemporale, os zygomaticum, retrobulbar enjeksiyon

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INTRODUCTION

The zygomatic bone (ZB) is one of the important viscerocranium bones in the facial region due to its anatomical location. Three important surfaces, namely lateral surface, temporal surface, orbital surface, and zygomaticofacial foramen (ZFF), zygomaticotemporal foramen (ZTF), and zymatico-orbital foramen (ZOF) are located on these surfaces, respectively (1). The number, location, and interconnection (via canal) of these foramina may differ between individuals.

The zygomatic nerve, which emerges as a branch of the maxillary nerve in the pterygopalatine fossa, reaches the orbit by passing through the inferior orbital fissure. After advancing on the outer wall of the orbit, it passes through the ZOF and reaches the ZB, where it divides into two branches called the zygomaticotemporal and the zygomaticofacial branch (1). The zygomaticotemporal branch reaches the temporal fossa after passing through the ZTF. Here, it penetrates the temporal fascia 2.5 cm above the zygomatic arch, reaches the skin, and performs the sensory innervation of the region. After the zygomaticofacial branch passes through the ZFF, it pierces the orbicularis oculi muscle and distributes in the skin of the region, and provides sensory innervation (2-5).

The zygomatico-orbital artery, which is usually a branch of the superficial temporal artery, courses near the zygomatic arch and between the two layers of the temporal fascia. This artery supplies the orbicularis oculi muscle by anastomoses with the lacrimal and palpebral branches of the ophthalmic artery (1). Moreover, the lacrimal artery, which is a branch of the ophthalmic artery gives two branches, the zygomaticofacial and the zygomaticotemporal branch. These arteries are very important for surgeons, especially during facial surgery. However, the intraorbital course of this artery has rarely been described in the literature, but it is an important structure that ophthalmologists should consider when approaching the orbit. Therefore, the zygomaticoorbital foramen is the junction of neurovascular structures on the orbital surface of the ZB, where occurs between the ZOF, ZFF, and the ZTF. The ZOF is the common opening on the orbital surface of the ZB that transmits neurovascular structures through other foramina. Although the opening of ZFF on the lateral surface of the ZB has been found in many studies in the literature, there are not enough studies on ZOF and its connections, although it has clinical importance (6-8).

The ZB is an important guide point for surgical dissections of the facial, maxillofacial, and periorbital interventions, due to it contains (nerves and vessels) and its anatomical position. The variability of the number and location of the foramina makes the area far from being completely safe (6,8). Neurovascular structures in the region should be protected, especially in transmaxillary surgical interventions to the orbit. In case of damage to these structures, paresthesia, dysesthesia, or neuralgia-type pain may occur in half of the face of the patient. In addition, damage to vascular structures can cause intraoperative hemorrhage or postoperative hematomas. Therefore, a good knowledge of the anatomy and variations of the region is important in surgical planning or the prevention of iatrogenic injuries and subsequent morbidity (8-10). In the literature review, cadaver studies show that the foramina on the zygomatic bones perform multiple variations (11). This study aimed to describe the morphological and morphometric features of the ZOF on its orbital surface. Additionally, it is also aimed to determine a safe intervention area during the surgical approach to the lateral orbital wall and during retrobulbar injections.

MATERIAL AND METHOD

Fifty (27 right; 23 left) hemicrania of unknown gender and age in the laboratory of Istanbul University, Istanbul Faculty of Medicine, Department of Anatomy were included in the study. Ethics committee approval of our study was received by the Istanbul Medical Faculty Clinical Research Ethics Committee (date: 30.07.2021, number: 358356). The non-metric and metric measurements described in Figure 1, Figure 2, Figure 3 and Figure 4 were made:

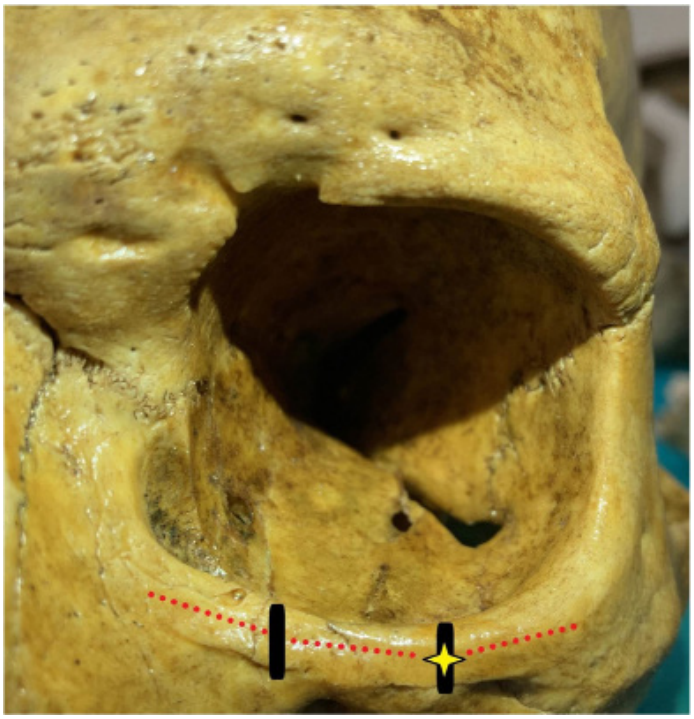

Figure 1. The point of the retrobulbar injection (yellow asterisk): The transverse distance to the ZOF from the point used for retrobulbar injection. First, the inferior part of the orbital rim (red points) is divided into three parts then the lateral 1/3 edge (yellow asterisk) is marked

Non-metric analysis

1. The numbers of ZOF

2. The connections of ZOF with ZFF and ZOF: These connections were determined by passing a thin wire

through the ZTF on the temporal surface of the ZB and the ZFF on the lateral surface of the zygomatic bone.

Metric analysis

3. The position of ZOF: The closest distance to the orbital rim of the ZOF was measured to determine the position. When more than one foramen was detected, the closest to the orbital rim was included in the measurement.

4. The point of the retrobulbar injection: The transverse distance to the ZOF from the point used for retrobulbar injection (the point where the 1/3 inferolateral edge of the orbital rim and the 2/3 inferomedial edge) (Figure 1).

By 0.01 mm precision digital caliper (Mitutoyo Company, Kawasaki-shi, Kanagawa, Japan) was used for all measurements.

Statistical analysis

All data were expressed as mean, standard deviation, minimum and maximum. IBM SPSS V21(IBM corporation, Armonk, NY) was used for all data analyses. Since the hemicrania are not bilateral, no correlation was made between left and right.

Figure 2. Different types and frequency of zygomtico-orbital foramen (black arrows)

Figure 3. The closest distance to the orbital rim (red points) of the zygomtico-orbital foramen

Figure 4. The position of needle during the retrobulbar injection (left orbit).

RESULTS

The incidence of ZOF in a total of 50 hemicrania (54% right; 46% left) included in our study was recorded as 92%. The number of ZOF was 46 (51.68%) on the right and 43 (48.32%) on the left side. ZOF was single in eighteen (36%) orbits, double in 16 (32%) orbits, three in 9 (18%) orbits, and four in 3 (6%) orbits. In addition, ZOF was not found at all in four (8%) orbits (Table 1). Of 89 ZOF, 37 (20 right; 17 left) were found to be associated (via a channel) with ZFF and 16 (8 right; 8 left) with ZTF. It was noted that 34 (16 right; 18 left) ZOF had no connection with any foramina (Figure 2 and Figure 5).

The metric analyzes of the two parameters determined for ZOF are as follows:

The closest distance of the ZOF to the inferior border of the orbital rim was 4.54 ± 2.33 mm, and the values of this distance varied between 1.50 mm and 8.90 mm on the left side and between 2.68 mm and 10.50 mm on the right side. The distance to the retrobulbar injection point was measured as 7.89 ± 2.98 mm and ranged from 5.70 mm to 13.60 mm on the left side, and between 4.60 mm and 12.80 mm on the right side. Since the hemicrania included in the study did not belong to the same side, correlations

Table 1. Incidence of ZOF

Number of Foramen (%)		0 (%)	1 (%)	2 (%)	3 (%)	4 (%)
ZOF	LEFT	1(4.35%)	8 (34.78%)	8 (34.78%)	5 (21.73%)	1 (4.35%)
	RIGHT	3 (11.11%)	10 (37.03%)	8 (29.63%)	4 (14.81%)	2 (7.40%)
	TOTAL	4 (8%)	18 (36%)	16 (32%)	9 (18%)	3 (6%)

ZOF: zygomatico-orbital foramen

Table 2. Location of ZOF

mm	ZOF-OR		ZOF-RIP	
	LEFT	RIGHT	LEFT	RIGHT
Mean	4.45	4.62	8.08	7.73
Minimum	1.50	2.68	5.70	4.60
Maximum	8.90	10.50	13.6	12.8
SD	2.01	2.61	2.62	3.30

ZOF-OR: The closest distance to the orbital rim of the ZOF. ZOF-RIP: The point of the retrobulbar injection. SD: Standard Deviation

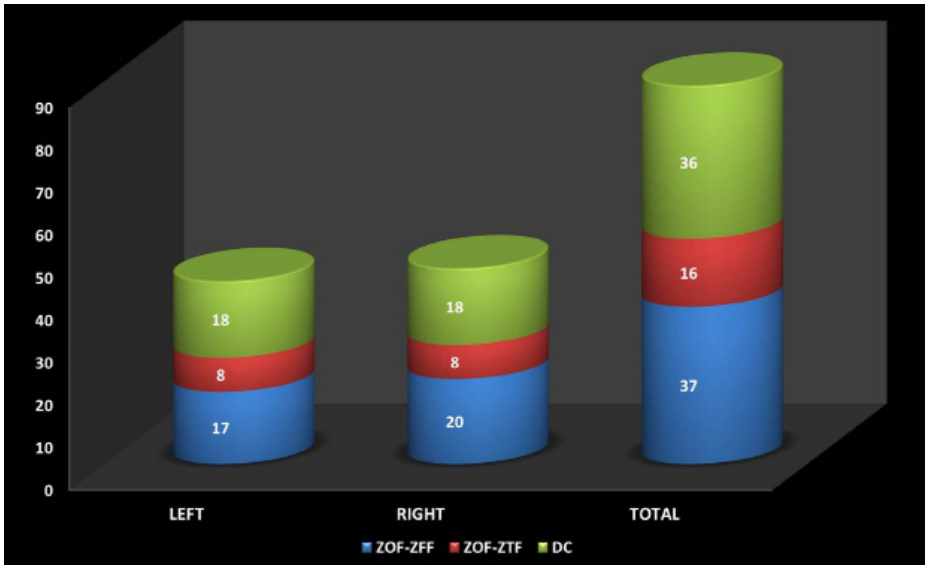

Figure 5. Number of connections of zygomatico-orbital foramen with zygomaticotemporal and zygomaticofacial foramen. ZOF-ZFF: The connection between the zygomatico-orbital foramen and zygomaticofacial foramen. ZOF-ZTF: The connection between the zygomatico-orbital foramen and zygomaticotemporal foramen. DC: Disconnected

between the right and the left sides were not evaluated (Table 2).

DISCUSSION

The ZB is a hard bone that plays an important role in shaping the face in terms of aesthetics. In therapeutic or cosmetic surgical procedures, ZB osteotomies are frequently used to access the skull base and orbit. Foramina such as ZFF, ZTF, and ZOF, which provide the passage of the terminal ends of the maxillary nerve on the ZB and allow the branches of the ophthalmic artery and superficial temporal artery to pass, constitute important landmarks for neurosurgery, plastic surgery, maxillofacial surgery and oculoplastic surgery (6,12). Embryological studies have shown that the branching of the maxillary nerve begins before it enters the zygomatic bone, and these branches contribute to the emergence of foramina such as ZFF, ZTF, and ZOF (6, 13). The variation in the number of ZFF, ZTF, and ZOF in the embryological development process is also stated that the ZB is associated with the number of ossification centers that begin to emerge at the 8th week and begin to fuse at approximately 22nd week (7). Knowing the location of these foramina, which varies in terms of location and number, is very important for surgeons and anesthesiologists (10). ZOF contains vascular structures that carry a risk of bleeding in interventions associated with the lateral orbital wall and may complicate operations such as oculoplastic surgery, which requires deep dissection to reach the orbital apex (14). In terms of peribulbar and retrobulbar blocking and orbital surgery, it is important to know the location of the ZOF on the inferolateral wall of the orbit and its connections with the ZFF and ZTF (15). Loukas et al. (6) examined 400 orbits in 200 skulls, and the rates of cases where ZOF was not seen at all, single foramen, two foramina, three foramina, and four foramina were found to be 17%, 50%, 20%, 10%, and 3%, respectively. Kim et al. (12) have detected on 14 zygomatic bone, 1 orbit with single foramen, 2 with double foramina, 5 with triple foramina, 5 with 4 foramina, and 1 orbit with five foramina, but it was not found the ZB in which the ZOF is absent. Likewise, Babcan et al. (16) have not reported absent ZOF in 28 orbits while the most common was seen as a single foramen. Similar to the results of Lukas et al. (6), our study have supported that in 4 (8%) of 50 orbits the ZOF was absent agrees with the well-documented finding that foramen number can also vary, with larger case studies showing a range from none to many (Table 1 and Figure 2). Examining the connection of ZFF with the ZOF, Jibu et al. (17) observed that ZFF was associated with ZOF by a canal at a rate of 62%. On the other hand, Kim et al. (12), using micro-computed tomography, three-dimensionally demonstrated the foramina and canals in the zygomatic bone. According to their results, ZTF and ZFF can be opened to ZOF independently, through a single canal, as well as ZTF can also be opened into the intraosseous canal formed between ZFF and ZOF (12). This may mean that there are structures that pass through these foramina and may be interconnected, or these foramina are interconnected (18). Since the exits ossified over time, a few of the skulls used did not have an exit (19). However, it should be taken into account that the skulls and their morphology may differ slightly with the change in the population, the place, or the area of their occurrence (20). However, the main foramen of exit from the Anatolian population considered in our study is the zygomatico-orbital foramina. The results of studies with different populations and people with different demographic characteristics may differ. On the other hand, the location of the ZOF within the orbital surface of the ZB is highly variable. Patel et al. (15) have examined 28 orbits in which the closest distance between the ZOF and the orbital rim was calculated as 4.70 mm. Also, Coutinho et al. (21) have measured this distance as 5.00 mm on the right side and 4.50 mm on the left side in 69 orbits. We observed that our results are consistent with previous studies measuring the position of the ZOF relative to the orbital rim. However, only one study was found in the literature measuring the proximity of the ZOF to the retrobulbar injection point, and this distance was recorded as 6.00 mm by Patel et al. (15). ZOF includes vascular structures that carry a risk of bleeding in interventions related to the lateral orbital wall and may complicate operations that require deep dissection to reach the orbital apex (14). It is important to know the location of the ZOF on the inferolateral wall of the orbit in terms of peribulbar blocking and orbital surgery (15). The generally accepted approach to administering retrobulbar anesthesia is to direct the needle under the lateral third of the lower lid just above the orbital rim. Here, the ZOF and its critical neurovascular structures are found, the zygomaticofacial and zygomaticotemporal arteries and nerves. Therefore, it is an important structure that ophthalmologists should consider when applying retrobulbar block or oculoplastic surgery. So that; in the study reported by Mootha et al. (22), has been presented a case of subperiosteal orbital hemorrhage resulting in blindness during the retrobulbar injection. The authors speculate that this complication is likely a rupture of the zygomaticofacial artery. Other clinical situations where recognition of these structures is important to include elevation of the periorbita from the lateral wall, lateral orbitotomy approach to intraorbital tumors, and zygomatic fracture repairs. As a result, our study is presented with the conclusion that in addition to the surgical procedures to be performed on the facial region, knowing the variations of the foramina in access to the cranium and providing the passage of neurovascular structures in this region will contribute to the anatomy literature and will also be beneficial for anesthesiologists and surgeons.

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

Ethical approval: This study was approved by the ethics committee (approval date and number: 2021/358356).

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Araştırma Makalesi / Research Article

Opinions of Medical Faculty Students about Anatomy Practical Education: A Survey Study

Tıp Fakültesi Öğrencilerinin Anatomi Pratik Eğitimi Hakkındaki Görüşleri: Bir Anket Çalışması

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Abstract

Aim: In our study, it was aimed to evaluate the opinions of students studying at Kahramanmaras Sutcu Imam University Faculty of Medicine about the current state of anatomy practical education.

Material and Method: A total of 64 students, 36 men and 28 women, were included in the study. In this cross-sectional, descriptive type study, students' views on anatomy education were determined using a voluntary survey method. In the content of the survey, there were questions that questioned the demographic characteristics of the students, their thoughts about the practical education of anatomy they received, and questions that determined their ideas about the provision of models. In the answer to other questions, a likert-type scale of 5 was used consisting of the options “always”, “mostly”, “often”, “occasionally”, “never”. The data was analyzed with IBM SPSS Statistics 25.0 package program.

Results: The average age of 64 students participating in the study was 20.98± 1.10. Of these students, 33(51.6%) were in semester II and 31(48.4%) were in semester III. Students reported that the practical training in anatomy they received was moderate, that the model and cadaver should be used together in lessons, that training on the model was very effective in learning anatomy. In the results, it was observed that the variety of models available in our laboratory was sufficient, but due to the presence of classes, the number of models was not sufficient, it would be better to drop one model for every 1-5 people on the average.

Conclusion: Students were moderately satisfied with the learning practices within the scope of the anatomy practical course. With the support of Kahramanmaraş Sütçü İmam University Research Projects Coordination Unit (Project no:2020/3-28A), thanks to the newly provided models, the reinforce laboratory allows students to better understand the lesson and learn the subjects they are having difficulty with.

Keywords: Anatomy, model, laboratory, survey

Öz

Amaç: Çalışmamızda Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi'nde eğitim gören öğrencilerin anatomi pratik eğitiminin mevcut durumu hakkındaki görüşlerinin değerlendirilmesi amaçlanmıştır.

Materyal ve Metot: Çalışmaya 36 erkek ve 28 kadın toplam 64 öğrenci dahil edilmiştir. Kesitsel, tanımlayıcı tipteki bu çalışmada öğrencilerin almış oldukları anatomi eğitimi hakkındaki görüşleri gönüllülük esasına dayalı bir anket yöntemi kullanılarak belirlenmiştir. Anket içeriğinde öğrencilerin; demografik özellikleri, aldıkları anatomi pratik eğitimiyle ilgili düşüncelerini sorgulayan sorular ve maket teminine ait fikirlerini belirleyen sorular bulunmaktaydı. Diğer soruların cevabında ise “her zaman” , “çoğunlukla” , “sık sık” , “ara sıra”, “hiçbir zaman” seçeneklerinden oluşan 5'li likert tipi ölçek kullanıldı. Elde edilen veriler IBM SPSS Statistics 25.0 paket programı ile analiz edilmiştir.

Bulgular: Çalışmaya katılan 64 öğrencinin yaş ortalaması 20.98± 1.10 olarak tespit edildi. Bu öğrencilerin 33(%51.6)'ünün dönem II'de, 31(%48.4)'inin dönem III'de olduğu belirlendi. Öğrenciler aldıkları anatomi pratik eğitiminin orta seviyede olduğunu, derslerde maket ve kadavranın birlikte kullanılması gerektiğini, maket üzerinde eğitim almanın anatomiyi öğrenmede çok fazla etkili olduğunu bildirmişlerdir. Sonuçlarda laboratuvarımızda bulunan maket çeşitliliğinin yeterli olduğu ancak sınıf mevcudunun fazla olması nedeniyle maket sayılarının yeterli olmadığını, ortalama her 1-5 kişiye bir maket düşmesinin daha iyi olacağı görülmüştür.

Sonuç: Öğrencilerin anatomi pratik dersi kapsamındaki öğrenim uygulamalarından orta düzeyde memnun oldukları ortaya çıkmıştır. Kahramanmaraş Sütçü İmam Üniversitesi Bilimsel Araştırma Projeleri Koordinasyon Birimi'nin (Proje no:2020/3-28A) destekleri ile yeni temin edilen maketlerle güçlendirilmiş laboratuvar sayesinde öğrencilerin dersi anlamada ve zorlandıkları konuları da daha iyi öğrenmelerine olanak sağlanmıştır.

Anahtar Kelimeler: Anatomi, maket, laboratuvar, anket

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INTRODUCTION

With the medical education given before graduation, it is aimed that students gain basic knowledge and skills, comprehend social ethical elements, and acquire medical skills in general (1). Human anatomy, which is the oldest known medical science, constitutes one of the most important components of medical education (2,3). In addition to contributing to the teaching of other basic medical sciences, it provides functional structural integrity in order to make medical practice and other health applications more successful. Along with technological developments, devices such as ultrasonography and computerized tomography, which are offered to the service of humanity and medicine, while providing speed and reliability that will revolutionize diagnosis, have also shown that knowledge of anatomy is very important (4).

The anatomic training in medical faculties is given in the form of theoretical and practical courses (5). The basis of anatomy education consists of practical lessons with cadavers that provide the opportunity to recognize the three-dimensional structure of the body (4). Today, three-dimensional imaging techniques, virtual reality applications, models showing the smallest anatomical details make the instructors' work quite easier. However, the gold standard for anatomy education is still cadaver. None of the existing technological innovations can replace the cadaver. Although the cadaver is the most important resource in anatomy education, there are difficulties in accessing it. For an efficient anatomy education, the number of students per cadaver should not exceed six. However, it is a known fact that we are far from this figure for our country (6). In this cadaver shortage, models are mostly preferred as they help to do the practical lessons in the best way. Anatomy practice lessons using models and cadavers allow students to identify and examine the anatomical structures in the theoretical lessons by seeing them personally (7).

Receiving regular feedback from students, analyzing them and sharing the obtained reports with the trainers in a timely and appropriate way can be effective in improving the quality of education programs (8). The application, which is called student appreciation, satisfaction or feedback, is the most frequently used method in evaluating education (9,10).

Feedback in medical education is a complementary and important component of the teaching process and increases students' knowledge-skill levels and professional success (11). The opinions of the medical faculty students about the theoretical and practical anatomy courses are important in updating the content of the education and the presentation methods (12).

This study was carried out in order to evaluate the practical lessons in Anatomy education taken by Kahramanmaraş Sütçü İmam University Faculty of Medicine students in the 2020-2021 academic year. In addition, the situation will be evaluated by obtaining feedback from the students about our anatomy application laboratory, which is strengthened with the models provided within the scope of the infrastructure project from the Scientific Research Projects Coordination Unit.

MATERIAL AND METHOD

The study was carried out with the approval of Kahramanmaraş Sütçü İmam University non-invasive clinical research ethics committee with project number 229. A total of 64 students (36 male, 28 female) who received practical anatomy training at Kahramanmaraş Sütçü İmam University Faculty of Medicine were included in the study. In this cross-sectional, descriptive study, the opinions of the students about the anatomy education they received were determined by using a questionnaire method based on volunteering. Students were asked to fill in a voluntary consent form stating that they wanted to be included in the study. The data were obtained through the feedback method consisting of 17 closed-ended questions. The questionnaire included questions about the demographic characteristics of the students, their thoughts on the practical anatomy education they received, and questions about the supply of models. Students were asked to write down their gender, semester and age. A 5-point Likert-type scale consisting of “always,” “mostly,” “often,” “sometimes,” and “never” options was used to answer the other questions. The names, surnames and student numbers of the students were not included in the questionnaire in order to ensure the reliability of the feedback.

Statistical Analysis

For statistical analysis of the data, IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA) package program was used. Mean and standard deviation were used for numerical data, number and percentage values were used for categorical data, and chi-square test was used for group comparisons. In evaluating the level of significance in the analysis, a p-value equal to and less than 0.05 was considered statistically significant.

RESULTS

The mean age of 64 students participating in the study was detected as 20.98±1.10 (min=19-max=24). It was determined that 28 (43.1%) of these students were female, 36 (56.3%) were male, and 33 (51.6%) were semester II, and 31 (48.4%) were semester III.

It was determined that 22 (34.4%) of the participants spent 0-1 hour, 34 (53.1%) 1-3 hours, 8 (12.5%) 3-5 hours for anatomy lessons. “Does it make it easier for you to comprehend when the model is explained by the teacher beforehand in practice lessons?” 22 (34.4%) of the students answered that question as very much, 20 (31.3%) more, 19 (29.7%) moderate and 3 (4.7%) less. The questions and answers regarding the anatomy practice lessons given in our faculty are given in Table 1 (Table 1).

“Is working on the model effective in learning anatomy?”

19 (57.6%) of the semester II students answered this question as very much, 13 (39.4%) more, 3 (3%) moderate and 20 (64.5%) of the semester III students said very much, 5 (16.1%) more, 4 (12.9%)moderate and 2 (6.5%) less (p=0.06).

"How many students should work on a model?" While 22 (66.7%) of the semester II students stated that 1-5 people were suitable, the semester III students stated that they agreed with them with a number of 27 (87.1%). While only 1 (3%) student in semester II thinks that the number of people per model should be between 15-20, no one thinks that this number is appropriate in semester III (100%) (p=0.05).

"Do you find the number of models used in anatomy practical lessons sufficient?" In semester II, 3 (9.1%) students said always, 8 (24.2%) said mostly, 7 (21.2%) said often, 9 (27.3%) said sometimes, and 6 (18.2%) said never. In semester III, 2 (6.5%) people answered always, 4 (12.9%) said mostly, 10 (32.3%) said often, 7 (22.6%) said sometimes and 8 (25.8%) said never (p= 0.63).

"Is the types of models in your laboratory sufficient for your course content?" To this question, 1 (3.0%) person in semester II said very few, 7 (21.2%) people said less, 19 (57.6%) people said moderate, 6 (18.2%) people stated much, 1 (3.2%) people in semester III, answered very few, 5 (16.1%) less, 19 (61.3%) moderate, 6 (19.4%) much (p=0.96).

"Which system did using models help you comprehend the most?" Semester II students asked the question as bones with 15 (45.5%), nervous system with 10 (30.3%), joints with 6 (18.2%), muscles with 1 (3%) and circulatory system with 1 (3%) people. In semester III, 10 (32.3%) people chose bones, 4 (12.9%) joints, 10 (32.3%) muscles, 4 (12.9%) circulatory system, 1 (3.2%) digestive system, 1(3.2%) urogenital system and 1 (3.2%) chose the nervous system.

"When compared, which one would you prefer as a tool for aiding the lesson; models or cadavers?" While 2 (6.1%) people from semester II thought that a cadaver, 3 (9.1%) a model, 28 (84.8%) a model and a cadaver should be together, no one preferred only cadaver from semester III, 5 (16.1%) one person selected a model, 25 (80.6%) people chose a cadaver and a model together (p=0.30). Some questions and answers about the anatomy practice lessons given by distance education and the importance of anatomy in the professional life of the participants are given in Table 2 (Table 2).

Table 1. Opinions of students about anatomy practice lessons

Survey questions	Always Number (%)	Mostly Number (%)	Often Number (%)	Sometimes Number (%)	Never Number (%)
Do you think that the practical anatomy education in your faculty is at a sufficient level?	4 (6.3)	Mostly	17 (26,6)	17 (26,6)	2 (3.1)
Can you easily ask questions to the instructor in practical lessons?	17 (26,6)	Often	12 (18.8)	11 (17.2)	0 (0.0)
Do you think that the anatomy practice exams held in your faculty adequately evaluate your anatomy knowledge?	12 (18.8)	Sometimes	14 (21.9)	10 (15.6)	2 (3.1)

Table 2. Opinions of the participants on the conduct of distance education and anatomy practice courses

Survey questions	Very few Number (%)	Less Number (%)	Moderate Number (%)	Much Number (%)	Too much Number (%)
How much did the Anatomy practical course you took with distance education this year contribute to your education?	12 (18.8)	21 (32.8)	22 (34.4)	6 (9.4)	3 (4.7)
Do you think that the practical anatomy training you have received will make a significant contribution to your professional life?	1 (1.6)	6 (9.4)	25 (39.1)	26 (40.6)	6 (9.4)
Is it a deficiency to not be able to work on one-to-one models due to distance education?	1 (1.6)	1 (1.6)	16 (25)	14 (21.9)	32 (50.0)

DISCUSSION

A good anatomy education is needed in order to train qualified physicians, to determine the correct diagnosis for the symptoms as soon as possible, to determine the most appropriate surgical intervention and to apply it in the most accurate way (13). The regular evaluation of the education provided done by the students will be of great benefit in increasing the quality of education offered, eliminating the identified deficiencies and developing new education methods that will contribute to them (14).

"Do you think that the practical anatomy education is sufficient?" This question was answered as 37.5% mostly, 26.6% frequently and 26.6% occasionally. It was stated that 72.2% of Gazi University Faculty of Medicine semester II students were satisfied with the anatomy practical courses (8). In another study, it was determined that the satisfaction of the students from the theoretical and practical education of anatomy was moderate (out of 5, respectively; 3.32 and 3.33) (15). In the study of Gaziantep University, satisfaction levels were determined as 55% (16). In a study conducted at Adıyaman University Faculty of Dentistry, a satisfaction level of 85% was determined for the practical part of anatomy (13). Most of the participants in our study answered this question positively and stated that they were largely satisfied with the training they received.

In our study, the number of students who stated that the lecturer's explanation beforehand of the model made it easier to understand was quite high (34.4% very much, 31.3% more and 29.7% moderate). In the study conducted by Uygur et al., similar to our results, it is seen that they reached a very high result with 89.9% (17). It is clearly seen that the teaching of anatomy practical lessons by the instructor is a correct method for students.

"Is working on the model effective in learning anatomy?" While 57.6% of semester II students stated that it was very much effective, 39.4% stated that it was very effective. In semester III students, with 64.5% very much, 16.1% much and 12.9% moderate options were found to agree with term II students. In a study, similar to our results, it was determined that 98.7% of the students stated that working on a model in practice lessons was quite effective in learning anatomy (17).

"Do you find the number of models used in anatomy practical lessons sufficient?" Among semester III students, 6.5% said always, 25.8% never, and in semester II, 9.1% said always, and 18.2% when asked this question. In the results, it is seen that the people who never found the number of models to be sufficient decrease in semester II. We see that the models obtained with the infrastructure project partially meet the needs of the students. In a study, similar to our results, it was shown that 59.5% of the students did not find the number of models used in practice lessons sufficient (17). The fact that laboratories in our country have limited cadavers in the practical education of anatomy pushes us to establish laboratories powered by models. Thus, we think that the satisfaction level of students in education will be brought to higher levels.

"How many students should work on a model?" While 66.7% of semester II students stated that 1-5 students were suitable for the question, semester III students stated that they agreed with them with 87.1%. The results we found are in line with other studies (17). In a study, it was determined that 86% of the students agreed with the opinion that the crowded classroom affects education negatively. In another study, 95.7% of the students reported that the presence of too many students in the classroom negatively affects learning in the teaching-learning process (18). Although our laboratory has been further strengthened with the new models we have added to our laboratory, we can say that due to the crowded classrooms, we do not have enough models to meet the demands of the students yet, and new studies are needed for this.

When we ask the students whether the model types are sufficient according to the course content, we see that the semester II students give more positive answers than the semester III students. The students stated that the types of models were sufficient, but the number of models was less compared to the large number of students in class. Even if there is no statistically significant difference between the results, it is a positive result that the variety of models increases and the students express this.

Which system did using models help you comprehend the most? In this question, it is seen that the semester II students mostly refer to the bones, followed by the nervous system, and then the joints, while the semester III students said primarily bones, followed by the muscles, joints and circulatory system. In a study, 94.9% of the students agreed with the statement "I learned bones well with the anatomy education given," while 83.5% were agreed for joints, 92.4% for muscles, 63.3% for nervous system (17). In another study, 58% of the students stated that the central nervous system was the subject they learned the worst among the anatomy lessons, which is consistent with the results of our study and shows that the subjects of the nervous system are difficult for students to understand (19). Considering that the models taken to the laboratory are predominantly nervous system according to their content, we see that the nervous system, which is the most difficult for students to understand, rises to the second rank in semester II, even if it does not even enter the first three rankings in their semester III preferences.

When we look at which model and cadaver students prefer in applied education, it is seen that the majority of semester II and III are in agreement that model and cadaver should be used together. In a study similar to the results of our study, the rate of students who believe that the use of auxiliary course tools other than cadavers in anatomy applications is 92.1%; when asked to compare models and cadavers, it was seen that 13.1% chose models, 15.7% chose cadavers, and 68.1% chose both

(19). In another study, similar to our study, in practice, most models were preferred (20). A limitation of our study is that we could not reach all of the students who received anatomy practical training due to the remote training due to the Covid-19 pandemic.

CONCLUSION

It was revealed that the students were moderately satisfied with the education they received in the anatomy practical courses. In order to increase the level of satisfaction, the deficiencies identified should be completed as soon as possible and the developments should be followed by the feedback method. Students mostly prefer interactive, applied Anatomy courses including cadavers. Thanks to the laboratory reinforced with new models, students were given the opportunity to understand the lesson and learn the subjects they had difficulty in a better way. We predict that the data obtained as a result of this study will guide the anatomy education that will be presented to the students in the following years and that the interactive education will contribute more to the students' learning of the lesson.

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Araştırma Makalesi / Research Article

The Effect of Tracheal Diverticulum and Chronic Ostructive Lung Disease on Chest Anthropometry

Trakeal Divertikül Ve Kronik Obstrüktif Akciğer Hastalığının Göğüs Antropometrisi Üzerine Etkisi

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Abstract

Aim: In this study, we aimed to evaluate the effect of tracheal diverticula (TD) on chest anthropometry and its relationship with chronic obstructive pulmonary disease (COPD).

Material and Method: Between January 2019 and March 2020, 995 patients who underwent chest CT were retrospectively analyzed and TD was detected in 62 cases. Group 1 is only TD, Group 2 is TD + COPD, Group 3 is only COPD, Group 4 is defined as control group. We measured the localization, size, the distance to carina and vocal cord of TDs. In all groups chest diameters at T4 and T9 levels were measured as transverse and vertical plans.

Results: TDs detected mostly at the T2 and T3 levels. In Group 1 and Group 2, there was a statistically significant difference the distance to TD of vocal chords. A statistically significant difference was found between Group 1 and Group 3 only in the anteroposterior diameter at the T4 and T9 levels.

Conclusion: The fact that TDs, which we do not know clearly whether they are acquired or congenital, have different TD levels in COPD patients made us think that TDs may be acquired. We also observed that COPD affects TD localization and TD has the opposite effect in increasing anteroposterior chest parameters in COPD. Precence of TD is essential on COPD patients about thorax anthropometry.

Keywords: Tracheal diverticulum, anthropometry, radiology, COPD, chest diameter

Öz

Amaç: Bu çalışmada trakeal divertikülün (TD) göğüs antropometrisine etkisi ve kronik obstrüktif akciğer hastalığı (KOAH) ile ilişkisi değerlendirmeyi amaçladık.

Materyal ve Metot: Ocak 2019 ile Mart 2020 tarihleri arasında göğüs BT yapılan 995 hasta retrospektif olarak incelendi ve 62 vakada TD tespit edildi. Grup 1 sadece TD, Grup 2 TD + KOAH, Grup 3 sadece KOAH, Grup 4 kontrol grubu olarak tanımlandı. TD'lerin lokalizasyonu, boyutu, karina ve vokal korda uzaklığı ölçüldü. Tüm gruplarda T4 ve T9 seviyelerinde transvers ve vertikal planda göğüs çapları ölçüldü.

Bulgular: TD'ler çoğunlukla T2 ve T3 seviyelerinde tespit edildi. Grup 1 ve Grup 2'de vokal kordun TD'ye uzaklığında istatistiksel olarak anlamlı bir fark vardı. Grup 1 ve Grup 3 arasında sadece anteroposterior çapta T4 ve T9 seviyelerinde istatistiksel olarak anlamlı fark bulundu.

Sonuç: Edinsel mi konjenital mi olduğunu net bilmediğimiz TD'lerin, KOAH hastalarında TD seviyelerinin farklı olması bize TD'lerin edinsel olabileceğini düşündürdü. Ayrıca, KOAH'ta anteroposterior artan göğüs parametrelerinde, KOAH'ın TD yerleşimini etkilediğini ve TD'nin ters etki yaptığını gözlemledik. KOAH hastalarında toraks antropometrisi konusunda TD'nin varlığı önemlidir.

Anahtar Kelimeler: Trakeal divertikül, antropometri, radyoloji, KOAH, göğüs çapı

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INTRODUCTION

Tracheal diverticulum (TD) is a benign condition of the tracheal wall. The longest axes of TDs can extend up to 3 cm and they can be single or multiple as oval peduncular cysts or sessile formations that can communicate with the trachea through channels (1). TD can occur as a result of congenital anomalies of the tracheobronchial tree or cavitation in a weak tracheal wall. TD is divided into two with regard to the implantation site and the histological features of the wall. These are congenital and acquired TD (2). Congenital TD is usually smaller than acquired TD and is more closely related to the trachea. Congenital ones usually occur on the right side, 4-5 cm below the vocal cords or a few centimeters above the carina (3). On the other hand acquired TD occur along the right posterolateral wall near the thoracic inlet. This one occurs with chronic cough or chronic obstructive pulmonary disease (COPD) as a result of prolonged increased intraluminal pressure - weakening of the tracheal wall (3, 4).

TD is usually asymptomatic and therefore their frequency can be underestimated (5). Diagnosis is made on X-rays, CT scans, bronchoscopy, and sometimes autopsies. However, CT also provides information about the location, origin and size of the lesion. Therefore, CT should be performed for differential diagnosis (6, 7).

Although rare and nonspecific, tracheal diverticulum may present with symptoms such as chronic cough, dyspnea, dysphagia, dysphonia, recurrent nerve palsy, cervical neck swelling, hematemesis, and hemoptysis (7).

TD may be associated with COPD (8). COPD is a chronic disease with progressive airflow limitation which against harmful gases and particles emerging airlines. This restriction is usually progressive. Lung parenchyma and pulmonary in COPD various inflammatory cells are collected. As a result of this inflammatory factors, interalveolar connective tissue and elastic elastic back gravitational force is a deterioration. COPD causes damage to the small airways and emphysema occurs as a parenchymal destruction. Emphysema, usually defined anatomically, abnormal permanent enlargement of air spaces distal to the terminal bronchioles (9, 10). Emphysema is seen as low density areas surrounded by normal lung tissue on CT (computed tomography) (11). Depending on this condition, there may be a decrease in lung height and width in patients with COPD (12), that's why chest diameter can change.

In this article, our aim is to investigate how the presence of TD, which is a limited study in the literature, affects chest anthropometry in patients with COPD.

MATERIAL AND METHOD

This study was planned in accordance with the Declaration of Helsinki and approved by the Malatya Clinical Research Ethics Committee (Protocol code 2020-1260). 995 patients between the ages of 40-80 who underwent thorax CT between January 2019 and March 2020 were retrospectively screened by a radiologist and 62 TDs were detected. These images were divided into four groups. Group 1 was only TD, Group 2 was TD + COPD, Group 3 was only COPD, Group 4 was the control group. The control group consisted of healthy individuals of the same age and gender who had thoracic CTs on the same dates. The number of people in the group was 19, 12, 12, 19, respectively. The relationship of chest diameters with TD and COPD was evaluated in all groups.

CT scans were examinations taken on a spiral CT scanner and 1 mm slice thickness. The window width was 1200 Hounsfield Units (HU) for the parenchymal window and 350 HU for the mediastinal window. Axial, coronal and sagittal plans were used for measurements.

Patients whose identity and demographic information were missing on CT images and whose investigated parameters were not evident were excluded from the study. Patients between the ages of 40-80 years without mediastinal injury or operation were included in the study. The localization, size, vocal cord and carina distance and level of all detected TDs were noted (Figure 1). In addition, the widest transverse chest diameter at the T4 vertebra and T9 vertebra levels and the widest anteroposterior chest diameters in both hemithoraces were measured and the mean was calculated (Figure 2).

Figure 1. CT image of tracheal diverticulum in the axial (A) and saggital (B) planes, located in the right osterolateral part of the trachea

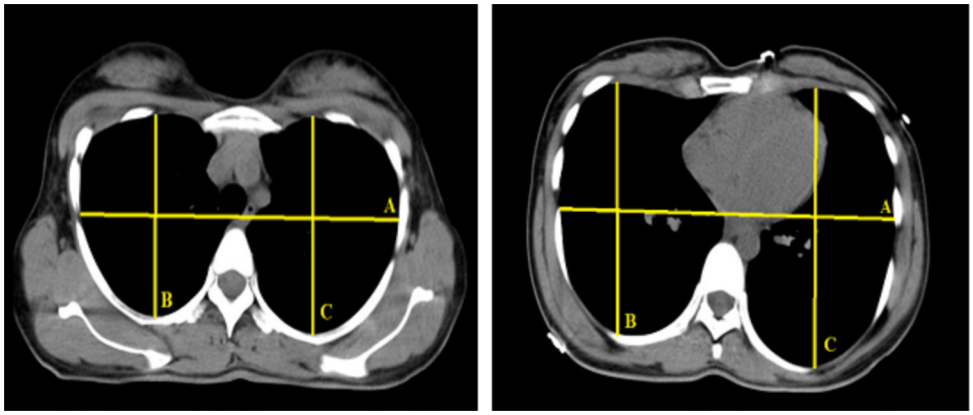

Figure 2. The widest transverse chest diameter measurement (A) and widest anteroposterior chest diameter measurement in both hemithoraces (B, C) an the axial CT T4 and T9 levels

Statistical analysis

Statistical analysis of this study was performed using IBM SPSS Statistics 22.0 package program. The normal distribution fit of the variables was examined with the One sample Kolmogorov-Smirnov test. Normally distributed variables are expressed as mean and standard error mean (× ± SD). Student's-T test was used for statistical analysis. Intergroup nanparametric data were analyzed using the Mann Witney U test. Pearson Correlation Coefficient was used to determine the direction and strength of the relationship between two quantitative variables. For statistical significance, a value of p <0.05 was accepted.

RESULTS

In the statistical analysis made, Group 1 and Group 4, Group 2 and Group 3 show a homogeneous distribution in terms of age and gender distribution. It was found that the groups were not similar in the distribution between Group 1 and Group 2, Group 3 and Group 4 (P = 0.001) (Table 1).

Table 1. Age and gender distribution of patients

		Group 1	Group 2	Group 3	Group 4
Gender (N)	Woman	14	8	8	14
	Man	5	4	4	5
Age (year)		47.31±14.88	61.66±7.49	61.66±7.49	47.05±15.05

While there was a statistically significant difference in the vocal chorda distance of TD in the individuals in Group 1 and Group 2, no significant difference was found in the distance to the carina. While the average distance of TD of all individuals in both groups to the vocal chord is 5.75 ± 1.57, the average distance to the carina is 7.02 ± 2.36 (Table 2).

No statistically significant difference was found in the transverse and anteroposterior magnitude of TD in individuals in Group 1 and Group 2. While the mean transverse size of the TDs of all individuals in both groups is 6.63 ± 3.04, the average anteroposterior size is 19.10 ± 7.24 (Table 3).

Table 2. Opinions of the participants on the conduct of distance education and anatomy practice courses

	Distance to vocal chord		Distance to Carina	
Group	(X±SD) Cm	P*	(X±SD) Cm	P*
1	6.26±1.56	0.015	6.94±2.56	0.82
2	4.95±1.25		7.14±2.09	
Total Average	5.75±1.57		7.02±2.36	

* Independent student's t-test

Table 3. Transverse and anteroposterior sizes of TDs of individuals in Group 1 and Group 2

	Transverse size of TD		Anteroposterior size of	
Group	(X±SD) mm	P*	(X±SD) mm	P*
1	6.60±2.66	0.95	19.93±6.71	0.46
2	6.68±3.69		17.81±8.14	
Total Average	6.63±3.04		19.10±7.24	

* Independent student's t-test

It was observed that the vertebra levels of TDs in Group 1 and Group 2 were mostly at the T2 and T3 levels (Table 4).

Table 4. Percentage of vertebra level of TDs in Group 1 and Group 2

	T1	T2	T3	T4	T5
Group 1	**1(%5)**	6(%32)	**10(%53)**	1(%5)	1(%5)
Group 2	2(%17)	6(%50)	4(%33)	-	-

The average of transverse and anteroposterior diameter lengths at T4 and T9 levels of all groups are shown in Table 5. In this evaluation, a statistically significant difference was found between Group 1 and Group 3 (p = 0.016) (p = 0.017) only in the anteroposterior diameter at T4 and T9 levels.

Table 5. Transverse and anteroposterior diameters of all groups at T4 and T9 level

Group	T4 transvers diameter (mm)	T4 anteroposterior diameter (mm)	T9 transvers diameter (mm)	T9 anteroposterior diameter (mm)
1	215.76±19.36	130.06±18.13	251.74±22.14	181.85±22.32
2	209.21±24.94	132.39±26.04	253.01±21.51	190.63±15.60
3	219.33±16.53	146.83±17.13	258.16±30.94	200.91±18.98
4	211.63±20.50	137.94±21.36	255.57±21.65	192.42±19.43

DISCUSSION

The number of studies investigating the effects of TD and COPD on chest anthropometry and their relationship with each other is limited in the literature.

Kurt et al. (13) Polat et al. (14) and Marina et al. (15) reported that the age of onset of TD was between the 5th and 6th decades. These mean ages are 58, 55 and 59.8, respectively. In our study, the mean age was 47.31±14.88 years only in the TD patient group, and 61.66±7.49 years in the TD+COPD patient group, and the incidence of TD was between the 4th and 6th decades. We think that the younger age of TD patients in our study is due to the larger sample of patients screened.

There are different opinions regarding the incidence of TD according to gender. While TD is more common in males than females in some studies (13, 16, 17), it is more common in females than males in other studies with opposite views (18, 19, 20). In our study, the incidence of TD was higher in women than men by a rate of 70.9%.

Studies in the literature report that TD is mostly seen on the right posterolateral side of the trachea, similar to our study (7, 13, 17, 21, 22). As the reason for this situation, Goo et al. (22) stated that the esophagus supports the left side, Gayer et al. (17) stated that the right side of the trachea is weaker than the increased intratracheal pressure, and the left side is more resistant due to the support of the esophagus and arcus aorta. Amaral et al. (7) reported that tracheal diverticula acquired due to weakening of the structures and vulnerability of the mucous membrane after increased intraluminal pressure or surgical procedures can typically be seen along the right posterolateral wall near the thoracic inlet, but can also be seen at any level. In addition to these comments, we think that the reason why TDs are more common at T2 and T3 levels in our study is because the structures supporting the trachea are weaker at these levels.

The relationship between the TD and the tracheal lumen is shown with axial, coronal and sagittal multiplan images (3). According to Linn et al. (23), multidetector CT is the best method for imaging TD, and stated that it is an important method for evaluating localization, size, contour and wall thickness in TD. Rahalkar et al. (24) reported that the best method for the diagnosis of TD is CT scanning of the trachea at various angles in the coronal plane. In our study, tracheal diverticula were demonstrated with axial, coronal and sagittal multiplan images by CT. Even if the TD is very small, it can be diagnosed noninvasively with CT. In addition, the borders of the diverticulum, its content and its connection with the tracheal lumen can be shown without the need for fiberoptic bronchoscopy.

According to Amaral et al.'s (7) study examining the relationship between COPD and TD, since the diverticulum usually serves as a reservoir for respiratory secretions, it is sometimes associated with chronic cough and can become infected. Flores et al. (8) stated that COPD and other inflammatory conditions may result in tracheomegaly or acquired TD in relation to changes in the elastic properties of the airways. Kurt et al. (13) detected bronchial DV and COPD in 84 out of 412 TDs by performing chest CT retrospective scanning, and the incidence of association between localization of TD and bronchial COPD was shown as 2.38%. Similarly, Goo et al. (22) and Polat et al. (14) found a significant correlation between COPD and TD. Contrary to these studies, Buterbough et al. (18) reported that there was no relationship between emphysema and paratracheal air cysts, and Marina et al. (15) reported that TD was not associated with respiratory symptoms and COPD.

In our study, we thought that TDs in which we did not know clearly whether they were acquired or congenital, may be acquired, since TDs in COPD patients have different TD levels. We found that COPD affects the TD level, and the diverticula is localized closer to the vocal cord. This shows that there is a relationship between COPD and TD. Although TD levels changed in COPD patients, we did not detect a significant difference in TD dimensions. In terms of this result, our study is similar to the studies of Kurt, Goo and Polat.

Griscom et al. (25) investigated the effect of COPD on chest diameters and stated that the anteroposterior tracheal diameter can increase for many reasons, but COPD is the most dominant among chronic inflammatory diseases. Similarly, we think that factors such as TD and COPD may

affect this diameter in our study. As a matter of fact, the mean anteroposterior diameter values were higher in the group with only COPD than in the other groups, and this difference was statistically greater than in the group with only TD. However, there is a need for studies investigating the effect of COPD on the anteroposterior diameter of the chest with studies with a larger number of cases.

In our study, T4 and T9 levels were evaluated in the evaluation of thorax anteroposterior diameter, it was observed that there was a significant difference between only TD and only COPD group, but no significant difference with the control group. Based on this result, we determined that COPD did not have a significant effect on the change of chest anteroposterior distance compared to healthy people, and the effect of COPD was greater than in patients with only TD. In addition, the fact that the COPD+TD group took a value between only TD and only COPD groups indicates that TD has an opposite effect on the anteroposterior distance of the chest in COPD patients, reducing this diameter.

CONCLUSION

In this study, we concluded that by affecting the level of TD of COPD, diverticulum is formed in the upper levels of the trachea, and TDs are more common at T2 and T3 levels. Since there was no significant difference in the transverse and anteroposterior sizes of TDs, we found that COPD had no effect on diverticulum dimensions, but COPD only affected the level of diverticulum. In addition, we concluded that TD reduces the anteroposterior chest diameter in patients with COPD. With all these results we found, we thought that TD had an effect on chest parameters in patients with COPD.

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Araştırma Makalesi / Research Article

The Role of MR Enterography in Crohn's Disease

Crohn Hastalığında MR Enterografisinin Rolü

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Abstract

Aim: The aim of this study was to investigate the efficacy of magnetic resonance enterography (MRE) in the diagnosis and follow-up of Crohn's Disease.

Material and Methot: Between November 2013 and April 2014, patients who were MRE examinations for a preliminary or definitive diagnosis of Crohn's Disease were reviewed retrospectively. MRE imaging of the patients was performed on an 8-channel 1.5 Tesla MRI device. Primary and secondary MRE results and contrast enhancement patterns of active and chronic inflammation of Crohn's disease in jejunum, ileum, terminal ileum, and colon segments were evaluated by two radiologists.

Results: The results consistent with Crohn's Disease were detected in 19 (10 male, 9 female) of 42 patients (24 male, 18 female, mean age was 40.64 years, min-max: 20-69, SD±14.27). Signs of active inflammation which were intestinal wall thickening, T2 signal reduction, and pathological mucosal contrast enhancement were observed in 19 patients (26 intestinal segments). Active inflammation findings were most common in the terminal ileum, with 16 (61.5%), followed by 5 (19.2%) in the ascending colon, 2 (7.6%) in the jejunum, 2 (7.6%) in the nonterminal ileum, and 1 (3.8%) in the sigmoid colon. Chronic inflammation findings such as intestinal stenosis (18 intestinal segments), submucosal fat deposition (16 intestinal segments), and prestenotic dilatation (13 intestinal segments) were observed in 13 patients. There was an ileosigmoid fistula in 1 patient, enterovesical fistula in 1 patient, and enterocutaneous fistula in 1 patient.

Conclusion: MRE is an appropriate diagnostic method without ionizing radiation, which can be used to detect the stage of inflammation (active or chronic) in the diseased intestinal segments in the diagnosis and follow-up of Crohn's disease.

Keywords: Crohn's disease, MR enterography, inflammatory bowel disease

Öz

Amaç: Bu çalışmanın amacı, Crohn hastalığı tanı ve takibinde manyetik rezonans enterografisinin (MRE) etkinliğini araştırmaktır.

Materyal ve Metot: Kasım 2013 ile Nisan 2014 tarihleri arasında Crohn hastalığı ön veya kesin tanısı için MRE incelemesi yapılan hastalar geriye dönük olarak tarandı. Hastaların MRE görüntülemesi 8 kanallı 1.5 Tesla MRI cihazında yapıldı. Crohn hastalığının jejunum, ileum, terminal ileum ve kolon segmentlerindeki aktif ve kronik inflamasyonunun primer ve sekonder MRE sonuçları ve kontrast artış paternleri iki radyolog tarafından değerlendirildi.

Bulgular: 42 hastanın (24 erkek, 18 kadın, ortalama yaş 40.64, min-maks: 20-69, SD±14.27) 19'unda (10 erkek, 9 kadın) Crohn Hastalığı ile uyumlu sonuçlar saptandı. 19 hastada (26 bağırsak segmenti) bağırsak duvarı kalınlaşması, T2 sinyal azalması ve patolojik mukozal kontrast artışı gibi aktif inflamasyon belirtileri gözlendi. Aktif inflamasyon bulguları en sık terminal ileumda 16 (%61,5) ile ardından 5 (%19,2) çıkan kolonda, 2 (%7,6) jejunum, 2 (%7,6) nonterminal ileum ve 1 (%3,8) sigmoid kolonda. 13 hastada barsak darlığı (18 barsak segmenti), submukozal yağlanma (16 barsak segmenti) ve prestenotik dilatasyon (13 barsak segmenti) gibi kronik inflamasyon bulguları gözlendi. 1 hastada ileosigmoid fistül, 1 hastada enterovezikal fistül ve 1 hastada enterokutan fistül mevcuttu.

Sonuç: MRE, Crohn hastalığının tanı ve takibinde hastalıklı bağırsak segmentlerindeki inflamasyonun (aktif veya kronik) evresini saptamak için kullanılabilecek iyonize radyasyon içermeyen uygun bir tanı yöntemidir.

Anahtar Kelimeler: Crohn hastalığı, MR enterografi, inflamatuar bağırsak hastalığı

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INTRODUCTION

Conventional radiological methods such as enteroclysis and small bowel passage graph which have been used for years in the radiological diagnosis of small bowel pathologies, provide direct information about the lumen width and function of the small bowel as well as indirect information about the intestinal wall and surrounding tissues (1). Therefore, the use of conventional modalities in combination with cross-sectional imaging methods (computed tomography, CT, magnetic resonance imaging, MRI) for the evaluation of the small bowel is considered to be a complementary step and creates a chance to investigate intra-abdominal complications that may accompany the intestinal disease. However, the success of cross-sectional imaging methods in demonstrating mucosal pathologies is limited (2). Small bowel passage X-rays have minimal success in demonstrating all small bowel pathologies, including mucosal lesions (3).

As a result of the advances in CT and MRI technology, the small bowel can be imaged in a very short time and with good quality, and reconstructed images may be obtained after the examination (2). The prerequisite for a good small bowel examination with CT and MRI is to ensure adequate intestinal distension (2). In recent years, CT and MR enteroclysis-enterography (MRE), which are used for small bowel imaging, have emerged as methods that combine the advantages of conventional enteroclysis and cross-sectional imaging in a single examination (4).

We aimed to evaluate the contribution of the MRE method to the radiological diagnosis and follow-up of Crohn's Disease (CD), investigate its advantages and disadvantages, and enable it to be widely used.

MATERIAL AND METHOD

Our study was carried out upon permission no. 24.02.2014/75 dated 24.02.2014 of the Medical Ethics Committee of Gaziantep University, Faculty of Medicine.

MRE examination was performed in 42 patients who had a preliminary diagnosis of CD or were followed up with the diagnosis of CD and presented to the Department of Gastroenterology between November 2013 and April 2014 in the Department of Radiology of Gaziantep University Faculty of Medicine.

Patients with a known allergy to the drugs to be used, pregnant women, patients with hemodynamic instability, and those who did not accept MRI were not included in the study. All patients were subjected to examination after 12 hours of fasting. Water and Osmolac were used to provide intestinal distension and reduce the absorption of intraluminal fluid through the small bowel lumen. Two hours before the shooting, the patients were given 1500 ml of drinking water, 250 ml every 10 minutes for one hour. Then, the patients were given a solution prepared by adding 100 ml of Osmolac (667 mg/250 ml lactulose solution) syrup to 1400 ml of drinking water, 250 ml every 10 minutes, 1500 ml in total, for the remaining hour until the shooting time. The patients were administered two ampules of hyoscine-n-butyl bromide (Buscopan, Boehringer Ingelheim) intravenously, 40 mg in total, in 2 doses 20 minutes before and at the beginning of the procedure. Buscopan was given manually by slow infusion over 2 minutes.

The examination was carried out using an 8-channel phased-array body coil on an MRI device with 1.5 Tesla magnet power (Gyroscan Intera, Philips, Holland). The patients were placed in the supine position on the MRI device. Firstly, coronal T2 SSh-TSE (Single Shot Turbo Spin Echo), coronal T1 SPIR (Spectral Presaturation Inversion Recovery), coronal T1 IP (In Phase), axial T1 IP, and axial T1 SPIR sequences were obtained, and 10 mg of IV contrast medium was administered as a bolus. Coronal T1 SPIR, coronal T1 IP, axial T1 IP, and axial T1 SPIR sequences were obtained 40 seconds after contrast medium administration. Adverse effects such as nausea, vomiting, allergic reaction, and abdominal pain that may develop against antispasmodic drugs and IVCM administered before and during the examination were assessed. MRE images were evaluated retrospectively by two radiologists in two stages. Small bowel distension results in the first stage were divided into four groups of no distension, poor distension, moderate distension, and optimal distension. In the second stage, during the analysis of MRE images, evaluations were made primarily in terms of focal or diffuse intestinal wall thickening and contrast-enhancement pattern in these foci, the hypervascular appearance of the intestinal mesentery, presence of mesenteric lymphadenopathy, presence of stenosis, and prestenotic dilatation in the intestinal segment, mesenteric adipose tissue proliferation, intraperitoneal fluid, fistula, and abscess. The intestinal wall thickness of more than 3 mm in distended intestinal segments and a short axis of mesenteric lymph nodes greater than 5 mm were considered pathological. Linear tracts extending between two epithelial surfaces were considered to be fistulas, and collections with peripheral contrast enhancement were considered to be abscesses.

It was attempted to interpret the activation of the disease based on the form and extent of contrast enhancement of the thickened intestinal wall. While the contrast enhancement pattern where mucosal contrast enhancement was prominent was interpreted in favor of active disease, the presence of stenosis in the intestinal lumen and the hypervascular appearance of adipose tissue adjacent to the involved intestinal segment was interpreted in favor of chronic disease.

RESULTS

A total of 42 patients, 24 men (57.14%), 18 women (42.85%), aged between 20 and 69 years (mean ± SD: 40.64 ± 14.27), who had a preliminary diagnosis of CD or were followed up with the diagnosis of CD, were included in our study.

Collapsed jejunal loops were observed in 5 (11.9%) of our cases, 14 (33.3%) had poor distension, 18 (42.8%)

moderate distension, and 5 (11.9%) optimal distension. 5 (11.9%) of our cases had poor distension in the ileal loops, 16 (38.1%) moderate distension, and 21 (50%) optimal distension.

Pathological wall thickening assessed in favor of CD was found in a total of 26 intestinal segments in 19 (45.2%) of 42 cases, and all of them had active stage findings. In 13 (68.4%) of these patients, chronic stage findings were observed in a total of 18 (69.2%) intestinal segments, and there were findings consistent with activation. Of the 26 involved intestinal segments, 2 (7.6%) was jejunum involvement, 2 (7.6%) nonterminal ileum involvement, 16 (61.5%) terminal ileum involvement, 5 (19,2%) the ascending colon involvement, and 1 (3.8%) sigmoid colon involvement.

All 26 involved intestinal segments had T2 signal reduction and thickening of 3 mm or more in the wall as well as stratified contrast enhancement consistent with activation Enlargement of lymph nodes, one of the secondary signs of activation, in the region adjacent to 14 intestinal segments, and the comb sign, the hypervascular appearance in mesenteric adipose tissue in 12 intestinal segments were observed. In our 13 patients with chronic stage findings, there was stenosis in the intestinal lumen associated with the chronic stage in a total of 18 bowel segments, and prestenotic dilatation was observed in 13 of them. An increase in adipose tissue adjacent to the involved intestinal segment, which has a chronic stage finding, was observed in 16 intestinal segments. Extraintestinal pathologies were also detected in our patients. There was an ileosigmoid fistula in 1 case, enterovesical fistula in 1 case, and enterocutaneous fistula in 1 case. In addition, abdominal pathologies not related to CD were found in our patients. Hepatomegaly was found in 1 case, uterine myoma in 1 case, accessory spleen in 1 case, and renal cysts in 2 cases. Examples of MR enterography images of our cases are shown in Figures 1-3.

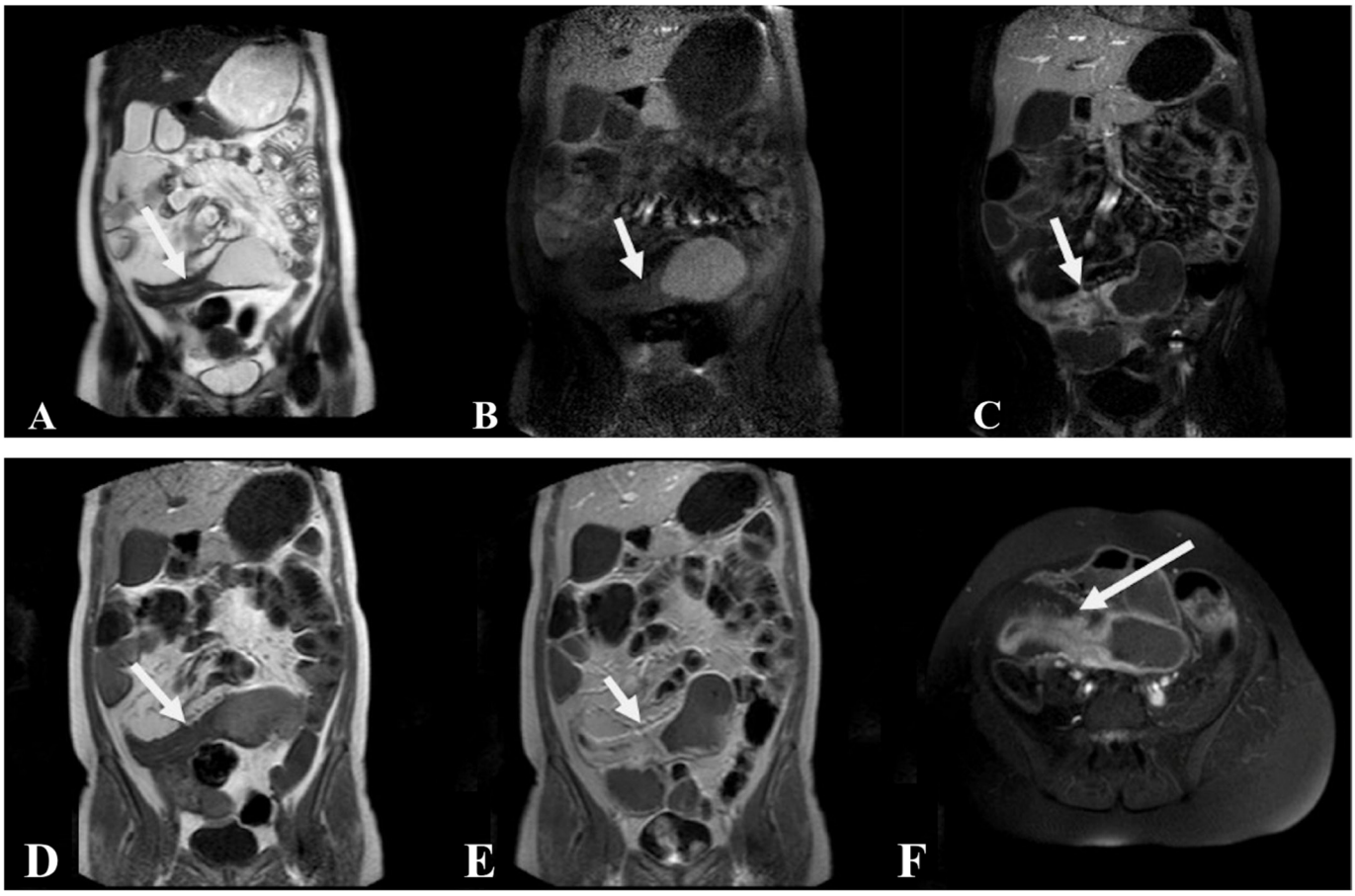

Figure 1. 48-year-old female patient; (A) view of wall thickening, mesenteric adipose tissue increase, stenosis and prestenotic dilatation in the terminal ileum in T2 SSh-TSE sequence, (B-C) coronal view in T1 SPIR pre-/post-contrast sequence of the same region, (D-E) coronal view in T1 IP pre-/post-contrast sequence of the same region, (F) axial view in T1 SPIR post-contrast sequence of the same region.

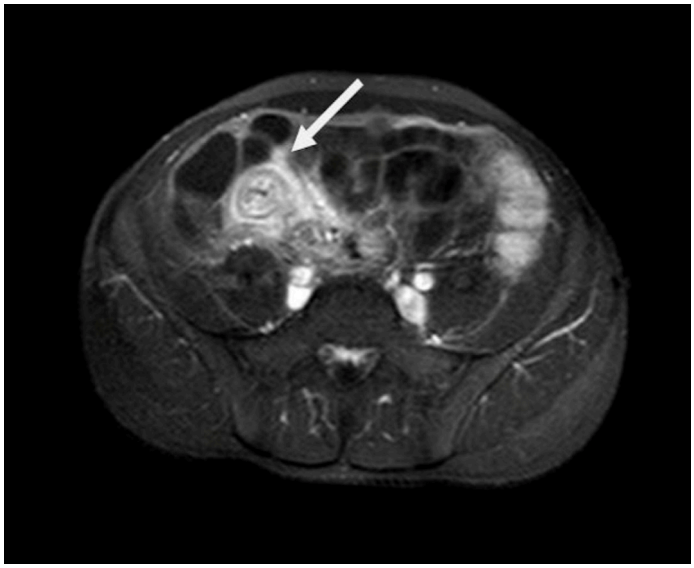

Figure 2. 26-year-old male patient; target sign appearance on the axial view in the T1 SPIR post-contrast sequence

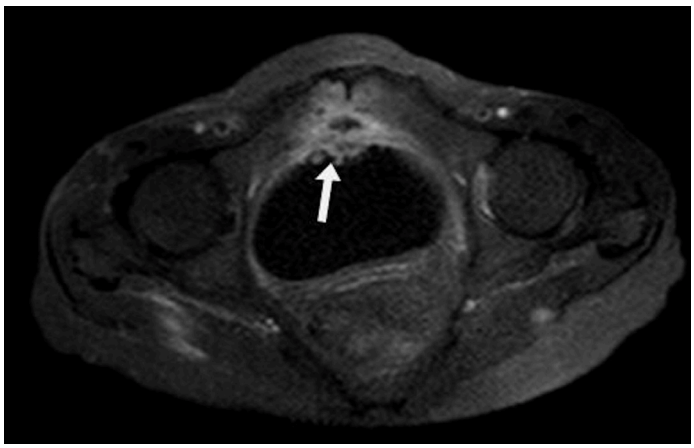

Figure 3. 66-year-old female patient; enterovesical fistula appearance on the axial view in the T1 SPIR post-contrast sequence

DISCUSSION

CD, one of the inflammatory bowel diseases, is characterized by inflammation of the gastrointestinal tract, with granulomatous, non-caseating, transmural, and segmental involvement (5). It usually starts in adulthood and progresses with remissions and relapses (6). Currently, there is no standard method to evaluate CD activity. MRI has been used for diagnostic purposes for CD since many studies have demonstrated its high sensitivity in assessing both disease activity and severity at the terminal ileum level (7, 8).

The Vienna Classification, established by an international working group in 1998, enabled CD to be evaluated under three important clinical entities (9). They were age, GIS localization, and disease type. The disease type was also divided into three as non-penetrating–non-stricturing, stricturing, and penetrating (10). Perianal penetration was added to the Vienna Classification as a distinct disease type, as it was thought to have a different prognosis, being modified by the 2005 Montreal Classification (11). Schill et al. (11) found non-penetrating-non-stricturing type in 5% of the patients, stricturing type in 21%, and penetrating type in 74% in their study of 76 patients. Our research found non-penetrating-non-stricturing type in 31%, stricturing type in 53%, and penetrating type in 16% of patients.

Another radiological method used in the evaluation of the small bowel is CT enterography. However, the most crucial problem in CT enterography is ionizing radiation exposure. It is emphasized that radiation and agents used for treatment, especially in young patients, may increase cancer risk with a synergistic effect (12). However, in comparison with MRE, the advantages of CT enterography include the ability to maintain intestinal distension throughout the examination due to its shorter duration, its good spatial resolution, and the ability to obtain high-quality multiplanar imaging (13).

As many small bowel diseases are pathologies that appear in the first years of life and should be followed up for years, in recent years, the MRE method has been developed to reduce radiation exposure in the diagnosis and follow-up of CD, especially in pediatric patients (14, 15). MRE may also provide information about benign or malignant lesions, polyposis, inflammatory processes such as vasculitis, other diseases of the small bowel such as celiac disease, infectious conditions, systemic sclerosis, intestinal duplications, and mesenteric tumors (16). MRE and MR enteroclysis are very important techniques in the imaging of the small bowel, as they do not contain ionizing radiation. They have high soft-tissue contrast, show extraintestinal pathologies, and obtain reproducible results data in terms of bowel function. In addition, gadolinium, a contrast medium, is preferred because of its safety profile and the ability for real-time imaging (17).

To date, there are no generally accepted techniques in terms of examination parameters and evaluation methods in the preparation of patients who will undergo MRE. Although there is no consensus on the necessity of bowel cleansing before the examination, we recommended 12-hour fasting with a liquid and pulp-free food diet. However, we did not use the methods of cleaning the intestines with laxatives.

Optimal distension in the small bowel with oral contrast medium administration in MRE is very important for the efficiency of the examination (18). Adequate intestinal distension for MRE is of great importance for demonstrating pathological wall thickness and pathological contrast enhancement. Many oral contrast media may be used for this purpose. The contrast media are classified according to their T1 and T2 characters. As biphasic oral contrast media appear hypointense in the intestinal lumen on T1-weighted images, they reveal the contrast-enhancement between the contrast-enhanced wall and the lumen on T1-weighted images obtained after IV contrast medium (19). Hidalgo et al. (20) used 1.5-2 liters of polyethylene

glycol solution as an oral contrast medium before the procedure. In our study, water and Osmolac syrup were utilized as a biphasic oral contrast medium in all cases. Osmolac is a readily available and inexpensive agent in our country. Other biphasic agents (methylcellulose, sorbitol) are not easily available and difficult to find in our country. Osmolac increases intestinal secretions and motility by increasing the intra-intestinal osmotic pressure.

One of the important limitations of the MRE is the insufficient intestinal distension, especially in the jejunal loops. Therefore, an oral contrast medium should be administered at an appropriate dose and rate for optimal intestinal distension. However, there may be cases where optimal distension cannot be achieved because gastric emptying time and passage transit time differs in each patient. In our study, drinking water and Osmolac (667 mg/250 ml lactulose solution) syrup were given orally to all cases. The patients were given 1500 ml of water two hours before the shooting, 250 ml every 10 minutes for one hour. Then, the patients were given a solution prepared by adding 100 ml of Osmolac syrup to 1400 ml of drinking water, 250 ml every 10 minutes, 1500 ml in total, for the remaining hour until the shooting time.

As the patient is taken to the MRI unit with a full stomach, the fluid for sustaining the intestinal distension continues to pass from the stomach to the small bowel, and especially jejunum distension can be achieved. In our study, collapsed jejunal loops were observed in 5 (11.9%) of the cases, 14 (33.3%) had poor distension, 18 (42.8%) moderate distension, and 5 (11.9%) optimal distension. 5 (11.9%) of our cases had poor distension in the ileal loops,16 (38.1%) moderate, and 21 (50%) optimal distension.

In MRE, IVCM is recommended in addition to a biphasic intraluminal contrast medium. Thus, the contrast-enhancement difference between the lumen and the intestinal wall becomes more evident, and the morphology and pathologies of the intestinal segments may be revealed more clearly. In addition, MRE has an important place in the follow-up of patients since pathological contrast enhancement in the intestinal wall is an indicator of mural inflammation. IVCM injection helps reveal active inflammation and detectable masses, especially in IBD (21). In our study, 10 mg of contrast medium was given intravenously as a bolus to all patients. Post-contrast images were taken 40 seconds after IVCM was administered. In this way, pathological intestinal wall thickening and pathological wall contrast enhancement have been optimally imaged. There are also similar studies in the literature.

Another important limitation of MRI in evaluating the small bowel is artifacts due to small bowel movements. It is recommended to administer glucagon or Buscopan to patients to minimize small bowel movements and prevent artifacts that may occur during MRI (13, 22). The use of Buscopan is more common in the literature. In our study, we also administered a total of 40 mg of IV Buscopan in two equal doses, 20 minutes before the procedure and at the beginning of the procedure in all cases. Studies in the literature that Buscopan may be used in doses between 10 mg and 40 mg (20, 23). Besides being inexpensive and readily available, Buscopan, unlike glucagon, is an antispasmodic that does not affect sugar metabolism (24). However, it is inconvenient to use in benign prostatic hyperplasia, glaucoma, myasthenia gravis, congestive heart failure, or Buscopan allergy (24). Glucagon can be used in these cases. Another thing to consider when giving Buscopan is the injection time. When the injection is performed quickly, it may lead to hypotension, dizziness, dry mouth, and accommodation disorders in the eye due to its anticholinergic effect (25). No adverse effects related to Buscopan were observed in our patients.

Non-contrast T2-weighted images and contrast-enhanced fat-suppressed T1-weighted images are critical for MRE in revealing small bowel wall thickening and its cause (13). The upper limit of normal intestinal wall thickness is considered to be 3 mm (26). Onay et al. (27) observed that the most frequent MRE change in CD was mural thickening in the intestinal wall. The reason for the increase in wall thickness may be inflammatory events as well as malignant diseases. Stratified contrast enhancement in the segment with increased wall thickness is significant for the classical target sign appearance and excludes malignant wall thickening (26). In addition, having the thickening in the long segment (except lymphoma) suggests benign conditions (28). While the striations in the perienteric adipose tissue observed adjacent to the wall thickening point an acute inflammatory event, the normal presence of the adipose tissue in the presence of thickening reduces the suspicion of an acute inflammatory event (13). Wall thickening in IBD may be seen in the acute phase as well as in the chronic phase (29). On contrast-enhanced images, intestinal wall contrast enhancement varies in chronic and acute stages. In the chronic stage compared to the acute stage, the thickening of the intestinal wall continues while the contrast enhancement gradually decreases and becomes almost equal to the normal intestinal loops (29). In MRE, it was determined that there was an increase in the intestinal wall thickness in the active stage. Target sign appearance, which is an indicator of active inflammation caused by stratified contrast-enhancement with wall thickening, is also seen considerably more common in the case of fibrostenosis, which is also an indicator of the chronic phase (10). Macarini et al. (30) found that 9% of the cases were in the inactive phase, 57% in the chronic phase, and 34% in the active phase in their study of 100 patients followed up with CD diagnosis. In our study on 42 patients, a total of 26 intestinal segments consistent with CD were found in 19 patients, and all patients were observed to have a target sign, which is the sign of active inflammation. In addition, 13 (68.4%) of the patients had chronic stage findings in a total of 18 (69.2%) intestinal segments, and there were findings consistent with activation. However, no case in remission was found which was attributed to

the low number of cases and the fact that the cases in remission did not present to the outpatient clinic, and this was considered to be the limitation of our study. In the active inflammation phase, the appearance of the target sign is caused by the low signal of the submucosa due to pathological contrast enhancement in the mucosa and serosa; however, the appearance of the target sign in the remission phase is caused by fat accumulation in the submucosa (31). In the light of these findings, the active-remission distinction can be made. One of the limitations of our study is the inability to investigate the significance of the appearance of the target sign in the differentiation of active inflammation and remission due to the absence of intestinal involvement in the remission phase. In our study, in addition to intestinal wall thickening in patients in the active phase, stratified contrast enhancement of the intestinal wall was also detected.

Increased adjacent mesenteric adipose tissue, lymphadenopathy, and the comb sign, which is the hypervascular appearance of the mesenteric adipose tissue, in CD are considered an indicator of transmural inflammation (19). In our study, of 26 involved intestinal segments, increased mesenteric adipose tissue was observed in 16, adjacent mesenteric lymphadenopathy in 14, and comb sign in 12.

Active and non-active strictures may be differentiated by evaluating the motility of the intestinal wall on the "cine" coronal image (32). Fibrotic strictures are observed aperistaltically (33). In our study, there was stenosis in the intestinal lumen associated with the chronic stage in a total of 18 intestinal segments in 13 of our patients, and no peristalsis was observed in these segments on coronal "cine" images.

One of the most important advantages of cross-sectional imaging methods is that it can show the extraluminal complications of the disease and pathologies in the mesentery, other intra-abdominal organs, and vascular structures (8). The extraluminal complications observed in our patients include enterovesical fistula, ileosigmoid fistula, and enterocutaneous fistula in one case each. Abdominal pathologies detected in our patients but not associated with CD were hepatomegaly in 1 case, uterine myoma in 1 case, accessory spleen in 1 case, and renal cysts in 2 cases.

The main limitations of our study were the small number of cases and the absence of lesions at different stages. The limitations of the MRE include the consummation of a large amount of liquid in a short time before the procedure, the difficulty of implementation of the technique, the long duration of the procedure, and its expensiveness.

CONCLUSION

In conclusion, MRE has an important role in the diagnosis and especially in the follow-up of CD due to not containing ionizing radiation, its high tissue contrast, its ability to acquire a real-time and functional image, its ability to reveal intestinal and extraintestinal pathologies in addition to anatomical information in a single examination as it is a cross-sectional imaging method, and the high safety profile of gadolinium administered as an IV contrast medium during the procedure. We believe that MRE is an imaging modality that should be preferred primarily in the diagnosis and follow-up of treatment success of CD, which manifests with terminal-nonterminal ileum and/or jejunal involvement..

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Ethical approval: *Our study was carried out upon permission no. 24.02.2014/75 dated 24.02.2014 of the Medical Ethics Committee of Gaziantep University, Faculty of Medicine.*

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MEDICAL RECORDS-International Medical Journal

Araştırma Makalesi / Research Article

Sociodemographic Characteristics of Persons Treated in the High Security Forensic Psychiatry Service: A Retrospective Study

Makale Başlığı: Yüksek Güvenlikli Bir Adli Psikiyatri Servisinde Tedavi Gören Kişilerin Sosyodemografik Özellikleri: Retrospektif Bir Çalışma

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Abstract

Aim: In the study, it is aimed to analyze the sociodemographic characteristics of the convicted patients, who were treated in the High-Security Forensic Psychiatry Services (HSFPS) of Elazig Fethi Sekin City Hospital within a period of one year.

Material and Methods: 409 convicted psychiatric patients, who applied to Elazig Fethi Sekin City Hospital High-Security Forensic Psychiatry Service were included in this study between March 2020 and March 2021. Personal data pertaining to these patients were obtained from hospital archive records. A general information questionnaire including sociodemographic data prepared by the authors, was used in the study. The sociodemography data form consists of 20 questions in total.

Results: The analysis of the collected data revealed that the convicted psychiatric patients were mostly single or divorced, that they lived mostly in the city, that 51.1% of them have not worked at any job, that 40.7% of them had a psychiatric disorder with psychotic features, that 84.4% of them committed a crime for the first time and that these crimes were mostly directed at other individuals.

Conclusion: In our study, it was observed that the diagnosis of schizophrenia or other psychotic disorders was more common in the convicted group. The high unemployment rate shows the importance of vocational rehabilitation, and the high number of untreated patients shows that closer follow-up will be beneficial. This study shows that applications to high-security forensic psychiatry services are high and it may be beneficial to increase their number throughout the country.

Keywords: High-security forensic psychiatry service, prophylactic treatment, medical observation, sociodemographic characteristics

Öz

Amaç: Bir yıl içerisinde Fethi Sekin Şehir Hastanesi Yüksek Güvenlikli Adli Psikiyatri (YGAP) servisinde tedavi gören kişilerin sosyodemografik özelliklerini incelemeyi amaçladık.

Materyal Metot: Çalışmaya Elazığ Fethi Sekin Şehir Hastanesi Yüksek Güvenlikli Adli Psikiyatri Servisine Mart 2020 ve Mart 2021 tarihleri arasında başvuran 409 hüküm giymiş psikiyatri hastası dahil edildi. Kişilere ait bilgiler hastane arşiv kayıtlarından elde edildi. Veri toplanmasında sosyodemografi verileri de kapsayan tarafımızca hazırlanan genel bilgi formu kullanıldı. Form toplamda 20 adet sorudan oluşturuldu.

Bulgular: Suç işleyen psikiyatri hastalarının daha çok bekâr ya da boşanmış olduğu, şehir merkezlerinde yaşadığı, %51,1'inin hiçbir işte çalışmadığı, %40,7'sinin psikotik özellikli psikiyatrik bozukluğu olduğu, %84,4'ünün ilk kez suç işlediği, bu suçların daha çok kişiye yönelik olduğu bulunmuştur.

Sonuç: Çalışmamızda suç işleyen grupta şizofreni veya diğer psikotik bozukluklar tanısının daha sık olduğu görülmüştür. İşsizlik oranının yüksek olması mesleki rehabilitasyonun önemini, tedavisiz hastaların yüksek olması daha yakın takibin faydalı olacağını göstermektedir. Bu çalışma yüksek güvenlikli adli psikiyatri servislerine müracaatların çok olduğunu ve sayılarının ülke genelinde arttılmasının faydalı olabileceğini göstermektedir.

Anahtar Kelimeler: Yüksek güvenlikli adli psikiyatri servisi, koruyucu tedavi, tıbbi gözlem, sosyodemografik özellikler

INTRODUCTION

Forensic psychiatry is the field of study that provides expertise in the the medical arrangements and procedures pertaining to the diagnosis, treatment and rehabilitation of psychiatric patients who have committed crimes (1, 2). The convicted patients, whose criminal capacities for the respective offenses are concluded to be fully or partially non-existent within the scope of Article 32 of the Turkish

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Penal Code (TPC), are restricted by being placed under protection and treatment (3). In this way, it is aimed to prevent them from committing crimes and to eliminate their "dangerousness" by ensuring that they are under the control of the health team and not in prison conditions (4).

The care and treatment of forensic patients should be carried out in specialized treatment centers (high, medium or low security hospitals) that are safe for both such patients and the society (5). The convicted patients, whose criminal capacities for the respective offenses are concluded to be fully or partially non-existent due to a mental disorder, are referred to secured hospitals pursuant to a court decision in order to receive treatment compulsorily and ensure community safety (6). The previous practice in Turkey in respect of such patients was that they were being kept under observation, evaluated and assessed in specific departments located within the Mental Health and Diseases Hospitals under the Ministry of Health. However, as of 2005, the treatment and care of forensic patients began to be carried out in high-security hospitals within the scope of the 1st paragraph of Article 57 of TPC. The first HSFPS Hospital was established within the body of Adana City Hospital in 2018 to accommodate mentally ill convicts. As of 2020, there are five HSFPS hospitals established under City Hospitals across Turkey (7). One of these five HSFPS hospitals, the HSFPS in Elazig Fethi Sekin City Hospital became operational in 2018.

There are studies available in the literature which retrospectively analyzed the forensic psychiatry data. The general characteristics of the forensic patients admitted to the psychiatry outpatient clinics analyzed within the scope of these studies seem to be affected by different variables such as the specific location and the geographical region of the psychiatry outpatient clinic, demographic, social and cultural structure of the population that inhabit the region where the psychiatry outpatient clinic is located, and the distance of the psychiatry outpatient clinic to the nearest institution it is affiliated with (8, 9). A comprehensive review of the literature in respect thereof did not reveal any study that addressed the sociodemographic characteristics of the convicted patients admitted to the Elazig Fethi Sekin City Hospital High-Security Forensic Psychiatry Service (HSFPS), an HSFPS that admits convicted patients from many provinces in the Eastern Anatolia region. In view of the foregoing, it is aimed in this study to determine the sociodemographic and clinical characteristics and the psychiatric diagnoses of, and the actual crimes committed by, the convicted patients, whose criminal capacities for the respective offenses were concluded to be fully or partially non-existent due to their psychiatric disorders.

MATERIAL AND METHOD

Prior to the start of the study, the related ethics committee approval was obtained from the Fırat University Non-Interventional Ethics Committee with the approval number E-97132852-050.01.04-40884 dated 03.05.2021 and the related hospital permission was obtained from the Elazig Fethi Sekin City Hospital. 409 forensic patients, who were referred to the Elazig Fethi Sekin City Hospital High Security Forensic Psychiatry Service (HSFPS) between March 2020 and March 2021 by judicial authorities and were kept under observation or protection and treatment in accordance with the crimes they committed, were included in this retrospective study. Of the said 409 forensic patients, it was determined that 217 patients have been admitted to the Elazig Fethi Sekin City Hospital HSFPS to be kept under observation, whereas that the remaining 192 patients have been admitted to the Elazig Fethi Sekin City Hospital HSFPS to be placed under protection and treatment. All the patients included in this study were male, as the women's section of the HSFPS service was not active at that time. Elazig Fethi Sekin City Hospital HSFPS serves to many provinces in the Eastern Anatolia region and is responsible for the protection and treatment of all convicts with psychiatric disorders that have committed crimes in these provinces. In addition, Elazig Fethi Sekin City Hospital HSFPS provides expertise on whether the judicial cases, which are generally referred by the courts of the Eastern Anatolia region and by the courts from all over Turkey from time to time, have criminal liability or not. The information specific to each forensic case included in this study, such as age, educational status, economical status, clinical diagnosis, substance use status, an additional organic disease, psychiatric drug use, psychiatric diagnosis, psychiatric diagnosis time, history of previous psychiatric treatment, suicide attempt, alcohol/substance use, reason for being in YGAP, the crime that caused it to be found in YGAP, how many times were treated in YGAP, inpatient treatment in non-YGAP psychiatry, childhood trauma were obtained from the hospital database and analyzed retrospectively.

Statistical Analysis

Windows SPSS 22.0 (IBM Statistical Package for Social Sciences version 22.0) software package was used for the statistical analyses of the research data. Continuous variables such as descriptive statistics and age were expressed as mean ± standard deviation, whereas categorical variables such as sex and diagnosis were expressed as frequency (n) and percentage (%).

RESULTS

409 forensic patients treated in the Elazig Fethi Sekin City Hospital High-Security Forensic Psychiatry Service between 01.03.2020 and 01.03.2021 were included in the study. The mean age of these patients was calculated as 36.4±11.7 years (min.18 years and max. 83 years). Of these 409 forensic patients, 243 (59.4%) were single, 142 (34.7%) were married, and 24 (5.9%) were widowed/divorced.

In terms of educational status of the forensic patients included in this study, it was determined that 72 (17.6%) of the forensic patients were illiterate, 33 (8.1%) were literate,

126 (30.8%) were elementary school graduates, 82 (20%) were middle school graduates, 68 (16.6%) were high school graduates, and 28 (6.8%) had an associate's/undergraduate degree. In terms of residential address, it was determined that 79 (19.3%), 140 (34.2%) and 190 (46.5%) patients were living in a village, town and a city, respectively. On the other hand, in terms of economic status, it was determined that 205 (50.1%), 172 (42.1%) and 32 (7.8%) of the forensic patients defined their economic status as low, medium and high, respectively.

Furthermore, of the forensic patients that were admitted, it was determined that 8 (2%) were students, 24 (5.9%) were civil servants, 70 (17.1%) were laborer, 92 (22.5%) were specialty occupation workers, 209 (51.1%) were unemployed and 6 (1.5%) were retired (Table 1).

In terms of clinical characteristics, it was determined that 74 (18.1%) forensic patients had an additional organic disease (diabetes, hypertension, cardiovascular disease, asthma, benign prostatic hyperplasia, musculoskeletal diseases, epilepsy), 200 (48.9%) patients have been on some sort of psychiatric medication, and 395 (96.6%) patients had a psychiatric disease. From among those with a psychiatric disease, it was determined that 120 (30.4%) forensic patients had a psychiatric disorder for less than 5 years, 77 (19.5%) patients had a psychiatric disorder for a period between 5 and 10 years, and 198 (50.1%) patients had a psychiatric disorder for more than 10 years. Additionally, it was determined that 336 (82.2%) the forensic patients included in this study had previously received psychiatric treatment. Furthermore, it was determined that 83 (20.3%) of the forensic patients had a history of self-mutilation, 61 (14.9%) patients had a history of suicide attempts, 242 (59.2%) patients had a smoking history, and 94 (23%) patients had a history of alcohol/substance abuse (Table 2).

Of the forensic patients with a psychiatric disorder, it was determined that 80 (20.3%) patients had mental retardation, 74 (18.7%) patients had bipolar disorder, 70 (17.7%) patients had schizophrenia, 71 (18%) patients had NOS-psychosis, 23 (5.8%) patients had NOS-emotional disorder, 17 (4.3%) patients had substance-induced mood disorder, 14 (3.5%) patients had delusional disorder, 6 (1.5%) patients had substance-induced psychosis, 24 (6.1%) patients had other types of psychiatric disorders and 16 (4.1%) patients had multiple psychiatric disorders (Figure 1).

Table 1. The sociodemographic characteristics of the patients

		Number	%
Age, Average ± SD(min-max)		36.4±11.7 (18-83)	
Marital Status	Single	243	59.4
	Married	142	34.7
	Widow / Divorced	24	5.9
Educational Status	Illiterate	72	17.6
	Literate	33	8.1
	Primary School	126	30.8
	Secondary School	82	20.0
	High school	68	16.6
	University	28	6.8
Settlement	Village	79	19.3
	Subprovince	140	34.2
	City	190	46.5
Economic Condition	Low	205	50.1
	Medium	172	42.1
	High	32	7.8
Occupation	Student	8	2.0
	Officer	24	5.9
	Employee	70	17.1
	Special Proffession	92	22.5
	Unemployed	209	51.1
	Retired	6	1.5

SD:Standart Deviation

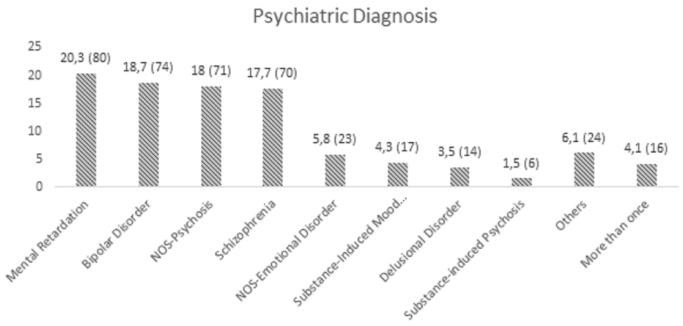

Figure 1. Psychiatric diagnoses of the participants

Of the 409 forensic patients, it was determined that 217 (53.1%) patients have been admitted to the Elazig Fethi Sekin City Hospital HSFPS to be kept under observation, whereas that the remaining 192 (46.9%) patients have been admitted to the Elazig Fethi Sekin City Hospital HSFPS to be placed under protection and treatment (Figure 2).

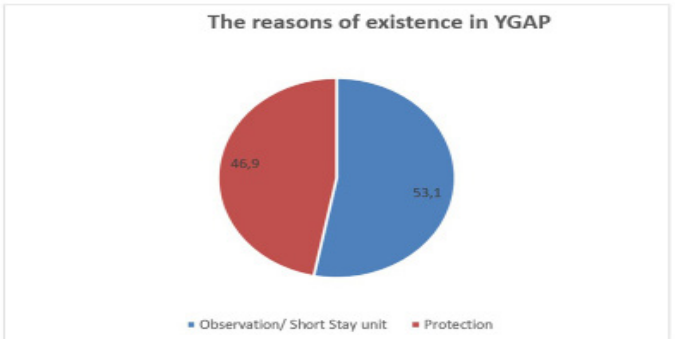

Figure 2. Participants' reasons of existence in HSFP

In terms of the crimes committed by the forensic patients analyzed within the scope of this study, it was determined that 113 (27.6%), 28 (6.8%), 23 (5.6%), 18 (4.4%), 17 (4.2%), 108 (26.4%) and 102 (24.9%) patients were convicted of the offenses of simple injury, sex crime, threat, murder, insult, others types of crimesand multiple crimes respectively (Figure 3).

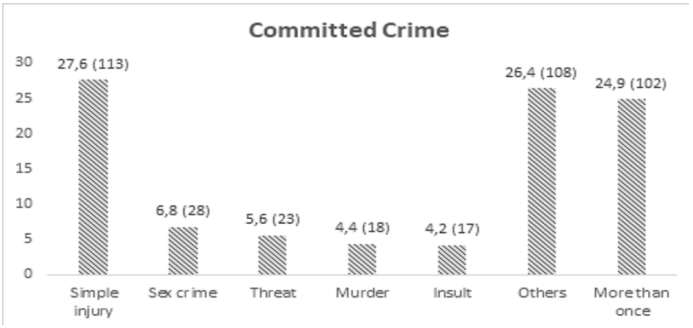

Figure 3. Reasons for forensic patients to be in HSFP

Lastly, it was determined that 345 (84.4%), 54 (13.2%) and 10 (2.4%) of the forensic patients included in this study received treatment at the Elazig Fethi Sekin City Hospital HSFPS, once, twice, and thrice or more, respectively. 201 (49.1%) of the forensic patients were determined to have received inpatient treatment not just at Elazig Fethi Sekin City Hospital HSFPS but also at other institutions. Of these patients, 44 (21.9%) and 157 (78.1%) patients were determined to have received treatment at institutions other than Elazig Fethi Sekin City Hospital HSFPS, once and more than once, respectively (Table 3).

Table 2. The addictions and diseases of patients included in the study

		Sayı	%
Additional organic disease	Yes	74	18.1
	No	335	81.9
Psychiatric drug use	Yes	200	48.9
	No	209	51.1
Psychiatric disease status	Yes	395	96.6
	No	14	3.4
Period of disease	Less than 5 years	120	30.4
	5-10 years	77	19.5
	More than 10 years	198	50.1
Previous Psychiatric Treatment Status	Yes	336	82.2
	No	73	17.8
Self-mutilation	Yes	83	20.3
	No	326	79.7
Suicide Attempt	Yes	61	14.9
	No	348	85.1
Smoking	Yes	242	59.2
	No	167	40.8
Alcohol / Drug Use	Yes	94	23.0
	No	315	77.0

Table 3. The HSFP characteristics of patients included in the study

		Number	%
The reason of existence in HSFP	Observation / Short Stay Unit	217	53.1
	Prevention Therapy	192	46.9
Committed Crimes	Simple injury	113	27.6
	Sex crime	28	6.8
	Threat	23	5.6
	Murder	18	4.4
	Insult	17	4.2
	Others	108	26.4
	More than one	102	24.9
Number of treatment in HSFP	Once	345	84.4
	Twice	54	13.2
	Three times and more	10	2.4
The state of inpatient psyciatric treatment except for HSFP	Yes	201	49.1
	No	208	50.9
The number of inpatient psychiatric treatment except for HSPF	Once	44	21.9
	More than once	157	78.1

HSFP: High Security Forensic Psychiatry

DISCUSSION

In this study, sociodemographic, clinical and criminal characteristics of the forensic patients who were treated in the Elazig Fethi Sekin City Hospital High-Security Forensic Psychiatry Service between 01.03.2020 and 01.03.2021 were analyzed. Consequentially, it was found that 59.4% and 5.9% of the forensic patients included in this study were single and widowed/divorced, respectively. This finding is compatible with the findings of the relevant studies available in the literature in that they also reported high rates of single patients in their study groups (10, 11). Another study with a large sample reported that 83.6% of convicted psychiatric patients without criminal responsibility were single (12). In addition, it was determined that 76.6% of the patients of the forensic patients included in this study had an elementary school degree or less, which is a finding supporting the view that there is a low and certain level of relationship between violent behavior and education level (13). As an example, in a study conducted on homocidal criminal cases, it was found that the subjects had a low level of education (56.2% and 57.2%), and the authors emphasized the relationship between education level and violence (14).

In terms of residential addresses, it was determined that the rate (46.5%) of forensic patients who were living in a city was lower than the rate of patients living in other types of residential areas (15). There are widespread opinions that geographical factors and residential can have an impact on criminal behavior (16). This data in our study has been interpreted as that the rate of forensic patients who have difficulty in accessing treatment may be high, and as a result, they may have been involved in crime due to overlooked disease recurrences. In terms of employment status, it was determined that more than half (51.1%) of the forensic patients included in this study were unemployed. Turkcan et al. reported that 50% of all cases evaluated by forensic psychiatry were not employed in any job (17). In another follow-up study, 61 non-criminal cases were followed for 5 years and it was found that 86% of them did not work at all during this period (18). It is known that psychiatric disorders, including but not limited to the inability to cope with the stresses of the job, poor social skills and decreased cognitive abilities, may render individuals with a psychiatric disorder unsuccessful in business life (19, 20). It has been reported that unemployment increases the probability of being involved in a crime in individuals with a psychiatric disorder (21). 205 (50.1%) of the forensic patients included in this study defined their economic status as low, which is a finding similar to the respective findings of the relevant studies available in the literature (22). It has been reported that low economic status, as unemployment, increases the probability of being involved in a crime in individuals with a psychiatric disorder (23). Factors such as sex, unemployment and divorce have been shown to be related to violence. It has been reported that divorce and unemployment can increase the risk of crime even without having any mental illness, yet unemployment and divorce are more common in individuals with mental illness (24).

Additionally, it was found that the diagnosis of 20.3% of

the forensic patients included in this study was mental retardation. It has been reported that individuals with a diagnosis of mental retardation are more likely to be both a victim of a crime (25) and the perpetrator of a crime (26). It has been also reported that individuals diagnosed with mood disorders and psychotic disorders are more likely to be involved in crime (27, 28). The analysis of the types of psychiatric disorders of the forensic patients included in this study revealed that 40.7% of the patients had schizophrenia and other psychotic disorders. This finding is compatible with the respective findings of the relevant studies available in the literature (29, 30). On the other hand, the finding that 18.7% of the forensic patients included in this study had bipolar disorder was different from the respective finding reported in İnan et al.'s study (31). Furthermore, it was determined that the number of forensic patients with a chronic psychiatric disorder, that is, a psychiatric disorder sustained for long periods, were more than the number of other patients, that is, the patients with an acute psychiatric disorder. This is an important finding since it is known that predisposition to committing crime increases as the psychiatric disorder becomes chronic (32). In addition, it was determined that 51.5% of the patients have not been using psychiatric medication. This is also an important finding, since it was demonstrated in the literature that patients with psychiatric disorders are more prone to violence if they do not receive adequate treatment (33, 34). A study examined homocidal crime before and after treatment in patients with psychosis and showed that the risk of crime was 15.5 times higher before treatment than after treatment (35). This finding emphasizes the importance of regular use of psychiatric medication and close follow-up in respect of the forensic patients in Turkey.

59.2% and 23% of the forensic patients included in this study had a history of smoking and alcohol/substance use, respectively. It is known that the rate of smokers among forensic patients is very high (36). The risk of committing a crime or resorting to violence increases fourfold in patients with a serious psychiatric illness and co-diagnosis of substance use disorder. Studies have shown that the increase in violent crimes committed by individuals with mental disorder can be explained by a history of alcohol and/or substance use (37).

The analysis of the forensic patients included in this study in terms of the offenses they were convicted of revealed that they were mostly convicted of offense of actual bodily harm (27.6%). This finding supports the respective finding of the study conducted in the Psychiatric Hospital Forensic Psychiatry Service of Bakırköy Psychiatric Hospital in Istanbul (31). It is known that forensic patients can exhibit both self-mutilative and suicidal behaviors (38). In parallel with the said finding reported in the literature, it was found that 20.3% and 14.9% of the forensic patients included in this study had a history of self-mutilation and suicide attempt, respectively. Additionally, it was determined that 25.6% of the forensic patients treated at Elazig Fethi Sekin City Hospital HSFPS were treated in more than one forensic psychiatry service, which was interpreted as a finding indicating that forensic patients may be prone to repeat their crimes (39). This finding indicates the importance of providing treatment to forensic patients at an HSFPS in that they can be prevented from harming both themselves and their environments.

The mean age of the forensic patients included in this study was calculated as 36.4±11.7 years as compared to 32 and 41.7 years, which were reported as the mean ages of the patient groups investigated in the studies of Coid et al. (2007) and Özbay (2010), respectively (39, 40).

It is noteworthy that the forensic patients who repeat their crimes were mostly patients with substance use disorder and low educational levels. Nevertheless, the retrospective structure of this study emerges as a limitation, thus the results of this study, such as the result mentioned above, should be supported by prospective follow-up studies using structured scales.

CONCLUSION

Our study presents the sociodemographic data of the cases in the high-security forensic psychiatry service of a city hospital over a one-year period. The relationship between crime and mental illness depends on multiple factors. The reasons that push individuals to commit crimes include individual, psychological and sociological characteristics, which is why it is important to consider sociodemographic concepts in this group. In addition, these data are guiding and informative about possible risk factors of crime.

HSFPSs are needed in order to closely monitor and supervise the control and follow-up of the cases in the forensic psychiatry service. As a result of the cooperation between the judicial system and health systems, HSFPSs enable coordinated work for forensic cases and are important for reintegrating these cases into society. We think that crime rates will decrease with well-functioning HSFPS systems.

It was concluded based on the results of this study that high-security forensic psychiatry services (HSFPSs) are crucial institutions in terms of community mental health, as they play an important role in preventing forensic patients from harming themselves and their environments, and that the number and capacity of these HSFPSs should be increased throughout the country.

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

Ethical approval: *U*the related ethics committee approval was obtained from the Fırat University Non-Interventional Ethics Committee with the approval number E-97132852-050.01.04-40884 dated 03.05.2021

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Araştırma Makalesi / Research Article

The Relationship Between Menopausal Attitudes and Menopausal Symptoms in Women Aged 40-55

40-55 Yaş Arası Kadınlarda Menopoz Tutumları Ile Menopoz Semptomları Arasındaki Ilişki

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Abstract

Aim: In this study, we aimed to reveal the menopausal status of women between the ages of 40-55 and to investigate the effects of their attitudes towards menopause on possible menopausal symptoms.
Material and Methods: 230 participants aged between 40-55 who applied to Ümraniye EAH Education Family Health Center were included in the study. All participants were asked to answer 47 questions including socio-demographic data, the menopausal attitude assesment scale (MAAS), and the menopause rating scale (MRS).
Results: The mean age of 230 women who participated in our study was 47.47±4.37 years, the mean MRS score was 12.78±8.96, and the mean MAAS score was 30.91±5.13. Their attitudes towards menopause and menapusal symptoms were above average and positive. It was found that MRS scores of non-menstrual women were higher than women who have irregular and regular periods (p<0.001). It was found that women who quit smoking got higher MRS scores than those who smoke and never smoked (p = 0.006. Women with primary education education level got lower MAAS scores than women with higher education level (p=0.026). In our study, it was found that non-menstruating women, those who talked to their partner about their menopause, those who quit smoking and those who quit alcohol consumption had milder menopausal symptoms.
Conclusion: Postmenopausal symptoms may vary according to personal, cultural and socio-economic variables. Women should be encouraged to increase their level of knowledge and avoid consuming alcohol and smoking in order to reduce possible symptoms related to menopause and improve their quality of life. Family physicians can play a primary role in this regard.

Keywords: Woman, menopause, menopausal symptoms, menopausal attitudes

Öz

Amaç: Bu çalışmada 40-55 yaş arası kadınların menopozal durumlarını ortaya koymayı ve menopoza yönelik tutumlarının, muhtemel menopoz semptomları üzerine etkilerini araştırmayı amaçladık.
Materyal Metot: Çalışmaya Ümraniye EAH Eğitim Aile Sağlığı Merkezine başvuran 40-55 yaş arası 230 katılımcı dahil edilmiştir. Her katılımcıdan sosyodemografik veriler, menopoz tutum değerlendirme ölçeği (MTDÖ) ve menopoz semptomlarını değerlendirme ölçeğinin (MSDÖ) ait soruları cevaplaması istendi.
Bulgular: Çalışmamıza katılanların yaş ortalaması 47,47±4,37 olup, MSDÖ puanı ortalaması 12.78±8.96, MTDÖ puanı ortalaması ise 30.91±5.13 idi. Menopoza yönelik tutumları ve semptomları orta seviyenin üzerinde ve olumluydu. Adet görmeyen kadınların MSDÖ puanları, düzenli veya düzensiz adet gören kadınlara göre daha yüksekti(p<0,001). Sigara kullanıp bırakmış olanlar, kullanan ve hiç kullanmamışlara göre daha yüksek MSDÖ puanına sahipti (p=0,006). İlköğretim mezunu olanların MTDÖ puanları, daha yüksek öğrenim durumu olanlara göre daha düşüktü (p=0.026). Çalışmamızda adet görmeyenlerin, eşi ile menopoz hakkında konuşanların, sigara kullanıp bırakmış olanların, alkol kullanıp bırakmış olanların daha hafif menopoz semptomlarına sahip olduğu saptandı.
Sonuç: Postmenopozal semptomlar kişisel, kültürel ve sosyo ekonomik farklılıklara göre değişebilmektedir. Kadınlar menopoza bağlı muhtemel semptomları azaltmak ve yaşam kalitelerinin iyileşmesi için, bilgi düzeylerini arttırmaları, alkol ve sigaradan uzak durmaları konusunda teşvik edilmeliler. Bu konuda aile hekimleri birincil rol oynayabilir.

Anahtar Kelimeler: Kadın, menopoz, menopoz semptomları, menopozal tutumlar

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INTRODUCTION

Menopause is a natural and ultimate situation in which estrogen and progesterone production decreases and the reproductive period ends due to the termination of the function of the ovaries in women (1). It is defined as "permanent cessation of menstruation due to loss of ovarian follicular activity" accompanied by vasomotor, psychological and sexual changes. The climacterium, on the other hand, is an intermediate period in a woman's life between the ages of 45 and 65, in which productivity decreases physiologically and functionally as aging continues.

Different approaches are applied for the relief of complaints that occur in the menopausal period. Diet/nutrition, lifestyle changes and exercise recommendations are among the preferred methods in this period in addition to Hormone Replacement Therapy, (2,3).

Guidance services and education that start from the premenopausal period may help identifying the factors that have an impact on the symptoms of the menopausal period and detecting them in the early period. Thus, patients' awareness of health will increase and it will be easier for them to struggle and cope with the social, psychological and physiological problems they experienced. With the increase in life expectancy, the population aged 65 and over is rapidly increasing all over the world, and the postmenopausal period has started to constitute one-third of a woman's life with the extended life expectancy (4).

Primary health care institutions are important in terms of evaluating the attitudes and perceptions of women towards menopause and raising their awareness level, as they are the facilities that women in the peri-menopausal period frequently refer and are followed up. In this study, we aimed to determine the menopausal symptoms of the participants and their attitudes towards menopause and examine the relationship between the symptoms and the attitudes using Menopause Rating Scale (MRS) and Menopause Attitude Assesment Scale (MAAS) (5,6).

MATERIAL AND METHOD

Our study constitutes a sample of women aged 40-55 who applied to Umraniye Training and Research Hospital Education Family Health Center for any reason in November, December and January. The total female population between the ages of 40-55 years registered in the family health center is 458. In the power analysis, it was aimed to reach 220 people with a probability of error of 0.05 in order to find a 1% difference with 95% power. Our study is a descriptive and cross-sectional clinical study and was conducted by using the face-to-face questionnaire method.

Inclusion criteria

Being a woman between 40-55 years old and registered with the family health center and agreeing to participate to the study.

Exclusion criteria

Not agreeing to participate in the study, not being within above mentioned age limits

Menopause Attitude Assesment Scale (MAAS): This scale is developed by Koyuncu et al. in order to evaluate the menopause attitudes of women in the climacteric period. It's a Likert type of scale that consists of 13 items and 4 sub-dimensions. The items are scored between strongly disagree=0 and strongly agree=4. 1, 2, 3, 4, 5, 10, 12 and 13 in the scale are negative items. The score that can be obtained from the scale is between 0-52. An increase in the score indicates a positive attitude towards menopause.

Menopause Rating Scale (MRS): MRS was developed by Schneider to evaluate menopausal symptoms. Turkish validity and reliability study was conducted by Gürkan. It is a 4-point Likert-type scale consisting of 11 items and scoring between "0=None at all" and "4= Very severe". The score of the scale range between 0-44. The higher the score, the complaints about menopause are more severe.

Statistical analysis: Statistical numerical data were evaluated with normality test, skewness, and kurtosis and histogram and it was found that they did not fit the normal distribution. Kruskal Wallis, Mann Whitney-U, Chi-square test and Spearman correlation tests were for used for statistical analysis between groups. Arithmetic mean, standard deviation, median and percentages will be used as descriptive statistics. The significance value in the 95% confidence interval was accepted as $p<0.05$. In addition, the necessary ethics committee approval was obtained for the study.

RESULTS

Our study was conducted with 230 women with a mean age of 47.47±4.37 years (minimum 40.0-maximum 55.0). It was determined that 205 (89.13%) of the participating women were married, 146 (63.48%) were university graduates, 145 (63.04%) were employed (Table 1).

The mean age of menarche of the women participating in our study was 12.90±1.45 years (minimum 9.0-maximum 13.0). It was determined that 84 of the participants (36.52%) had not had a period for 12 months, and 68 (29.57%) had regular periods. Mean menopausal age was found to be 45.85±1.25 years (Table 2).

The mean MRS total score was found to be 12.78±8.96 while the mean MAAS total score was 30.91±5.13. The score distributions of the MRS and the MAAS are given in Table 3.

A statistically significant correlation was found between the participants' menstrual patterns and the total score of the MRS ($p<0.001$). A statistically significant correlation was found between the participants' talking about the menopause period with their spouses and the total score of the MRS ($p=0.004$). A statistically significant correlation was found between the MRS total score of the participants and their status of smoking ($p=0.006$).

A statistically significant correlation was found between the MRS total score of the participants and their status of alcohol use (p=0.029) (Table 4).

A statistically significant relationship was found between the educational status of the participants and the total score of the MAAS (p=0.026) (Table 5).

A good positive correlation was found between the MRS somatic sub-factor and the psychogenic sub-factor (r=0.726). In the MRS moderately positive correlation was found between the somatic sub-factor and the urogenital

Table 1. Demographic characteristics of the participants

		n (number of people)	% (percent)
Your marital status	Married	205	89.13
	Single	8	3.48
	Divorced/Widowed	17	7.39
Your education level	Primary education	60	26.09
	High School	24	10.43
	University	146	63.48
Occupation	Housewife	64	27.83
	Worker	7	3.04
	Private sector	20	8.70
	Retired	21	9.13
	white collar	21	9.13
	Public Officer	97	42.17
Family type	Nuclear	200	86.96
	Large family	20 8.70	
	Lives alone	10	4.35
Monthly income	2300 TL	32	13.91
	2301-7000 TL	114	49.57
	7001 TL and above	84	36.52
Education level of your spouse	Primary education	26	12.62
	High School	38	18.45
	University	142	68.93
Your spouse's occupation	Not working	6	2.91
	Worker	5	2.43
	Private sector	82	39.81
	Retired	22	10.68
	white collar	17	8.25
	Public officer	74	35.92
Number of pregnancies	None	11	4.82
	One	27	11.84
	two	77	33.77
	three	69	30.26
	four	30	13.16
	five	10	4.39
	Six	4	1.75
Number of living children	None	6	5.65
	One	5	22.17
	two	82	53.48
	three	22	17.39
	four	17	1.30
	five	74	4.82

Chronic disease	None	134	58.26
	Yes	96	41.74
Disease	Hypertension	34	35.41
	Diabetes	31	32.29
	Thyroid diseases	17	17.70
	Malignancy	8	8.33
	Asthma/COPD	8	8.33
	Rheumatological diseases	7	7.29
	Hyperlipidemia	7	7.29
	Cardiovascular	5	5.20
	Neurological	3	3.12
	Other	3	3.12
Smoking	Never smoked	127	55.22
	I used, quit	39	16.96
	I am still smoking	64	27.83
Alcohol	Never used	158	68.70
	I used, I quit	23	10.00
	I am using	49	21.30

Table 2. Information about menstruation and menopause

	n(number of people)	%(percent)
Age of first menstrual period	9 years	2 0.87
	10 years	3 1.30
	11 years	34 14.78
	12 years	50 21.74
	13 years	71 30.87
	14 years	40 17.39
	15 years	21 9.13
	16 years	7 3.04
	17 years	1 0.43
	19 years	1 0.43
Talking to the spouse about the menopause process	None	140 66.67
	Yes	70 33.33
Receiving information about the menopause process	I did not receive any information	45 19.57
	From health Health personnel	60 26.09
	Other	60 26.09
	Health personnel and other	65 28.26
Menstrual irregularity	I have regular periods.	68 29.57
	The time between my 2 menstrual periods was shortened or extended for more than 7 days	44 19.13
	I have not had a period for at least 60 days	11 4.78
	I missed 2 or more periods in a row	23 10.00
	I have not had a period for more than 12 months	84 36.52

Table 3. Distribution of participants' scale scores

		Mean	Median (min-max)
Menopause attitude evaluation scale	MRS total	12.78±8.96	12.00(0-36)
	MRS somatic	4.46±3.54	4.00(0-14)
	MRS psychological	5.31±3.93	4.00(0-16)
	MRS urogenital	3.02±2.88	2.00(0-11)
	MAAS total	30.91±5.14	31.5(15-48)
Menopause attitude evaluation scale	Family relations	8.39±3.18	9.00(0-12)
	Positive emotional	6.70±4.2	7.00(0-20)
	Negative emotional	7.34±3.18	7.00(0-12)
	Behavioral	4.88±2.08	5.00(0-8)

Table 4. Comparison of MSAS total score and study variables

		Median	Minimum	Maximum	Test statistics	p
Marital status	Married	12.00	.00	36.00	-0.546	0.585
	Not married	10.00	.00	29.00		
Education status	Primary education	13.50	1.00	36.00	4.081	.130
	High school	7.50	.00	29.00		
	University	12.00	.00	36.00		
Education status of the spouse	Primary education	10.00	1.00	29.00	0.402	0.818
	High school	11.00	.00	29.00		
	University	12.00	.00	36.00		
Family type	Nuclear	12.00	.00	36.00	4.363	0.113
	Extended family	7.00	.00	27.00		
	Living alone	11.00	.00	29.00		
Working ststus	Working	1.00	0,00	36,00	0.024	0.998
	Not working	12.00	0.00	36,00		
Monthly income	2300 TL	9.50	1.00	29.00	0.149	0.928
	2301-7000 TL	12.00	.00	36.00		
	7001 TL and above	12.00	.00	32.00		
Chronic disease	No	11.50	.00	36.00	-0.240	0.810
	Yes	12.00	.00	36.00		
Menstrual irregularity	I have regular periods.	.50	.00	28.00	37.487	<0.001
	The time between my 2 menstrual periods was shortened or extended for more than 7 days	12.00	.00	29.00		
	I have not had a period for at least 60 days	16.00	.00	36.00		
Talking with the spouse	No	11.00	.00	36.00	-2.871	0.004
	Yes	15.00	.00	35.00		
Smoking	Never smoked	12.00	.00	36.00	10.179	0.006
	I used, quit	11.00	.00	35.00		
	I am still smoking	12.00	.00	29.00		
Alcohol	Never used	13.00	.00	36.00	4.738	0.029
	I used, I quit	7.00	.00	26.00		
	I am still using	12.00	.00	32.00		

*Mann Whitney-U, **Kruskal Wallis

Table 5. Comparison of MAAS total score and study variables

		Median	Minimum	Maximum	Test statistics	p
Marital status	Married	32.00	15.00	48.00	-1.573	0.116
	Not married	31.00	26.00	44.00		
Education status	Primary education	30.00	17.00	39.00	7.262	0.026
	High school	32.00	20.00	37.00		
	University	32.00	15.00	48.00		
Education status of the spouse	Primary education	31.00	27.00	36.00	0.441	0.802
	High school	32.00	20.00	37.00		
	University	32.00	15.00	48.00		
Family type	Nuclear	32.00	15.00	48.00	0.441	0.802
	Extended family	30.00	25.00	36.00		
	Living alone	34.50	27.00	44.00		
Working status	Working	32.00	17.00	40.00	-0.276	0.783
	Not working	31.00	15.00	48.00		
Monthly income	2300 TL	30.00	23.00	39.00	3.007	0.222
	2301-7000 TL	32.00	15.00	44.00		
	7001 TL and above	31.00	21.00	48.00		
Chronic disease	No	31.50	15.00	44.00	-0.331	0.741
	Yes	31.50	17.00	48.00		
Menstrual irregularity	I have regular periods	32.00	15.00	48.00	0.948	0.330
	The time between my 2 menstrual periods was shortened or extended for more than 7 days	32.00	21.00	41.00		
	I have not had a period for at least 60 days	30.50	17.00	44.00		
Talking with the spouse	No	32.00	15.00	48.00	-0.311	0.756
	Yes	30.00	22.00	44.00		
Smoking	Never smoked	31.00	17.00	44.00	0.478	0.489
	I used, quit	31.00	20.00	48.00		
	I am still smoking	32.00	15.00	44.00		
Alcohol	Never used	31.00	15.00	44.00	0.124	0.725
	I used, I quit	32.00	21.00	48.00		
	I am still using	32.00	19.00	44.00		

*Mann Whitney-U, **Kruskal Wallis

Table 6 Correlation distribution between scales

	MSAS	MSAS somatic	MSAS psychologic	MSAS urogenital	MAAS	MAAS family relations	MAAS positive emotinal	MAAS Negatie emotinal	MAAS behavioral
MSAS	1.000	.881**	.901**	.799**	-.251**	-.190**	-.033	-.290**	-.174**
MSAS somatic	.881**	1.000	.726**	.581**	-.207**	-.124	-.079	-.174**	-.151*
MSAS psychologic	.901**	.726**	1.000	.582**	-.284**	-.167*	-.045	-.339**	-.146*
MSAS urogenital	.799**	.581**	.582**	1.000	-.136*	-.238**	.055	-.235**	-.176**
MAAS	-.251**	-.207**	-.284**	-.136*	1.000	.094	.471**	.608**	.472**
family relations	-.190**	-.124	-.167*	-.238**	.094	1.000	-.507**	.555**	.316**
positive emotinal	-.033	-.079	-.045	.055	.471**	-.507**	1.000	-.265**	-.302**
Negatie emotinal	-.290**	-.174**	-.339**	-.235**	.608**	.555**	-.265**	1.000	.506**
behavioral	-.174**	-.151*	-.146*	-.176**	.472**	.316**	-.302**	.506**	1.000

*pearson correlation test

sub-factor (r=0.581. In the MRS moderately positive correlation was found between psychogenic sub-factor and urogenital sub-factor (r=0.582) (Table 6).

DISCUSSION

The present study which included the women of age between 40-55 years revealed that the menopausal symptoms of the participants were below average and their attitudes towards menopause were positive in general.

The mean menopausal age was 45.85±1.25 years in our study. In similar studies in the literature, it was 52.90±3.82 years in Tunçarslan's (7) study, 51.08±5.21 years in Koyuncu's (8) study, 54.03±10 years in Alparslan's (9) study, and 57.12±5.6 years Cirban's study (10).

In the literature, studies about attitudes towards menopause have revealed conflicting results that are positive or negative. The MAAS total score, which was found to be 27.86±8.06 in the study of Cirban (10) and 34.50±3.18 in the study of Yağmur (11) and 30.91±13.85 in our study and our result was consistent with the literature.

While we found the mean positive emotional sub-factor score of the MTRS as 6.70±4.20, it was found as 14.11±4.04 in Yağmur's (11) study and 8.61±4.51 in Cirban's (10) study. As the score has increased, the positive attitude towards menopause increased as well.

In our study, the mean negative emotional sub-factor score of the MTRS was determined as 7.34±3.18. Our results were below the average in this sub-factor, where the positive attitude towards menopause increased as the score increased. The score was found to be 8.29±2.73 in Yağmur's (11) study and 5.20±3.44 in Cirban's (10) study.

The mean score of family relations sub-factor in the MAAS was determined as 8.39±3,18 in our study. Our results were below the average in this sub-factor, where the positive attitude towards menopause increased as the score increased.It was determined as 10.05±2.76 in Yağmur's (11) study and 6.44±2.36 in Cirban's (10) study.

The mean behavioral sub-factor score of the MAAS was found to be 4.88±2.08. Our behavioral sub-factor results were below the average. In this scale the higher scores are interpreted as positive attitude towards menopause. The score was determined as 5.66±2.17 in Yağmur's (11) study and 3.98±3.66 in Cirban's (10) study.

The MRS total score was 12.79±8.96 (median 12) in our study. On the other hand, in the study of Yağmur (11), Cirban (10), Sis Çelik and Pasinlioğlu (8), Tunçarslan (7) and Alparslan (9) MRS total scores were 17.11±9.43, 17.56±7.95, 22.67±8.06, 18.84±7.19, and 16.11±1034 respectively. The scores being lower in our study compared to the literature was thought to be linked with the fact that 84 of the participants (36.52%) had been in menopause for a long time and that 68 (29.57%) of them had regular menstruation and thus felt menopausal symptoms less or may not have experienced them yet.

In our study the rate of high school and higher education was determined as 73.91%, which is above the country average. Similarly, the rate was 75.1% in Yağmur's (5) study, 51.4% in Alparslan's (6) study, 26.2% in Tunçlarsan's (7) study, and 31.6% in Pasinlioğlu's (8) study.. According to the findings in the literature, it has been reported that lower education level negatively affects menopausal symptoms (12–13). It can be suggested that women with higher education levels will be less affected by menopausal symptoms due to their higher health literacy. The fact that we could not find a significant difference between education status and menopausal symptoms in our study can be explained by the fact that 63.5% of the participants were university graduates.

In our study, there was no statistically significant difference between the educational status of the spouses of the participants and the MRS total score. Similarly, there are studies in the literature in which no statistically significant difference was found between spouse educational level and MRS total score (12-13). However, in the study of Tunçarslan (7), the MRS total score of the participants whose spouse educational level is literate/ primary school was found to be higher than the other education levels. Similarly, in the study of Kökkaya (14), it was determined that the mean of the MRS total score decreased as spouse education level increased (14).

In our study, no statistically significant difference was found between the working status of the participants and the MRS total score. There are studies with similar results in the literature (12-15). In the study of Tunçarslan (7), the total MRS score of working women was found to be lower than that of non-working women. Alquaiz et al. (16) and Kalahroidi et al. (17) also found lower scores (symptoms) in working women. There are also studies in the literature showing that actively working women have less menopausal problems than non-working women (16-18-19).

Unlike our study, it was found in the literature that the MRS total score of women with good economic status was lower than those of women with poor financial status. (7-15) Kaulagekar (18) found in his study that the frequency of menopausal symptoms was lower in low-income women. High-income women are more likely to benefit from healthcare, which may explain why they have fewer symptoms. However, it should be remembered that families with low income levels may not care about menopause symptoms in their daily life problems and struggles.

The rate of nuclear family structure, which we found to be 86.9% in our study, was 81.6% in Koyuncu's (8) study, 80.7% in Güler's (20) study, and 70.2% in Çelik and Pasinlioğlu's (12) study No statistically significant difference was found between the family type of the participants and the MRS total score. In the studies of Çelik and Pasinlioğlu (8), no relationship was found between menopausal symptoms and family type. In the study of Kaulagekar (18) it was determined that the

menopausal symptoms of women living in a nuclear type family were more severe. In families with nuclear family type, the fact that the woman is someone to share her social role and lack of support from family elders can be a problem, on the other hand the difficulties of life in extended families and the lack of personal space can affect menopause symptoms negatively.

In our study, it was determined that the participants who to quit smoking got lower scores than those who still smoke and never smoked. Chee et al. (15) reported that symptoms were seen more frequently in women who had quit smoking compared to women who had never smoked. In the study of Tunçarslan (7), it was determined that the MRS total scores of non-smokers were higher than those of smokers. In Essa's (21) study it was found that the risk of menopausal symptoms is approximately twice as high in women who smoke compared to women who do not smoke. In another study conducted with women in the climacteric period, no relationship was found between smoking status and menopausal symptoms (22). Smoking is known to lower estrogen levels. Considering that menopausal symptoms are related to estrogen withdrawal, it can be suggested that smoking may increase symptoms. Those who were smoking before the menopause will be less affected, since their estrogen levels are already low, and in those who were smoking before the menopause but quit smoking the relative increase in estrogen levels due to cessation of smoking may reduce symptoms.

In our study, an inverse and weak correlation was found between MAAS and MRS scales (r=-251). In the literature, it has been found that women with negative attitudes towards menopause have more severe menopausal symptoms (23-24).

CONCLUSION

In general, it is seen that women have a positive attitude towards menopause. Negative attitudes towards menopause may cause severe symptoms, and conversely severe menopausal symptoms may negatively affect the attitude towards menopause.

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Araştırma Makalesi / Research Article

Assessment of Thyroid Function Tests in Patients with COVID-19 Infection and Their Relationship with Euthyroid Sick Syndrome

COVID-19 Enfeksiyonlu Hastalarda Tiroid Fonksiyon Testlerinin Değerlendirilmesi ve Hasta Ötiroid Sendromu ile İlişkisi

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Abstract

Aim: Thyroid functions are affected by many factors functions such as some infections and drugs. This study aimed to investigate how the thyroid function tests were affected after COVID-19 infection and their relationship with euthyroid sick syndrome.
Material and Method: Our study was designed as a retrospective and case-control study. The participants consisted of two groups as the control and patient groups. Thyroid function tests (TFT), hemogram and routine biochemistry of the groups were assessed. In addition, the tests of the patient group within the last 6 months before the infection were assessed. The patients' symptoms, presence of a chronic disease, smoking history, and clinical status during COVID-19 infection were recorded.
Results: A total of 473 people were included in the study. Of the participants, 54.5% were female. The white blood count (WBC), hemoglobin (HGB), platelet (PLT), and neutrophil (NEU) counts were higher in the patient group. Lymphocyte (LY) and mean platelet volume (MPV) counts were similar. Tyroid stimulating hormone (TSH) and triiodothyronine (T3) values of the patients were higher compared with the control group. The thyroxine (T4) level was similar in the two groups.TSH, T3 and T4 levels of the patient group before COVID-19 were higher than the results just after the quarantine process after COVID-19 infection.
Conclusion: Thyroid dysfunction develops in COVID-19 patients within the course of the disease. This condition can be partially explained with the euthyroid sick syndrome. It is also possible with the thyroid gland being the direct or indirect target of the virus.

Keywords: COVID-19, thyroid dysfunction, euthyroid sick syndrome

Öz

Amaç: Tiroid fonksiyon testleri bazı enfeksiyonlar ve ilaçlar gibi birçok faktörden etkilenir. Bu çalışma, COVID-19 enfeksiyonu sonrası tiroid fonksiyon testlerinin nasıl etkilendiğini ve hasta ötiroid sendromu ile ilişkisini araştırmayı amaçlamıştır.
Materyal ve Metot: Çalışmamız retrospektif ve vaka kontrol çalışması olarak planlandı. Katılımcılar kontrol ve hasta grubu olarak iki gruptan oluşmuştur. Grupların tiroid fonksiyon testleri (TFT), hemogram ve rutin biyokimyası değerlendirildi. Ayrıca hasta grubunun enfeksiyondan önceki son 6 ay içindeki testleri değerlendirildi. Hastaların semptomları, kronik hastalık varlığı, sigara içme öyküsü ve COVID-19 enfeksiyonu sırasındaki klinik durumları kaydedildi.
Bulgular: Çalışmaya toplam 473 kişi dahil edildi. Katılımcıların %54.5'i kadınd. Hasta grubunda beyaz kan sayımı (WBC), hemoglobin (HGB), trombosit (PLT) ve nötrofil (NEU) sayıları daha yüksekti. Lenfosit (LY) ve ortalama trombosit hacmi (MPV) sayıları benzerdi. Hastaların tiroid uyarıcı hormon (TSH) ve triiyodotironin (T3) değerleri kontrol grubuna göre daha yüksekti. Tiroksin (T4) düzeyi iki grupta benzerdi. Hasta grubunun COVID-19 öncesi TSH, T3 ve T4 düzeyleri, COVID-19 enfeksiyonu sonrası karantina sürecinin hemen sonrasındaki sonuçlara göre daha yüksekti.
Sonuç: COVID-19 hastalarında hastalığın seyri içerisinde tiroid disfonksiyonu gelişir. Bu durum kısmen hasta ötiroid sendromu ile açıklanabilir. Tiroid bezinin virüsün doğrudan veya dolaylı hedefi olması da mümkündür.

Anahtar Kelimeler: COVID-19, tiroid disfonksiyonu, hasta ötiroid sendromu

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INTRODUCTION

Thyroid functions are affected by several functions such as some infections and drugs (1). Some viruses such as mumps, influenza, coxsackie, ebstein barr virus, adenovirus, and human immunodeficiency virus cause thyroiditis and change the production of thyroid hormones (2). Various thyroid diseases can develop in the early and late periods after the virus infections. The inflammation of thyroid gland, which is known as subacute thyroiditis, can develop in the early period, in other words, a few weeks after the virus infection. They can also cause the dysfunction of the immune system in the late period after months and favor the development of autoimmune thyroid diseases (3). Euthyroid sick syndrome is defined as the abnormal findings in the thyroid hormones without a thyroid disease (4). It is known that the thyroid dysfunction is associated with the severity of the underlying disease and that low thyroid hormone levels are associated with poor prognosis in several diseases (5,6,7).

The coronavirus disease-19 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a pandemic disease that rapidly spreads all over the world and affects millions of people (8). It was declared a pandemic by the World Health Organization on the 11th of March 2020 and caused millions of people to be infected and die (9,10,11). COVID-19 has serious and complicated effects of the various human organs and systems (12). After entering the body, COVID-19 can cause damage by binding to the receptors in several tissues and organs including the thyroid gland and thyroid dysfunctions can develop (13). The patients who have had COVID-19 infection can have low TSH and T4 compared with the normal people (14) and hyperthyroidism (15) and subacute thyroiditis (16) due to thyroid gland damage can be seen in blood as well. This study aimed to reveal how the thyroid function tests were affected after COVID-19 infection and investigate the relationship with the euthyroid sick syndrome.

MATERIAL AND METHOD

This study was performed in the Family Medicine Outpatient Clinic of Incesu State Hospital. A total of 885 participants between the 25th of October, 2020 and 25th of November, 2020 were included in the study. Our study was designed as a retrospective and case-control study. The participants consisted of two groups as the control and patient groups. The control group consisted of the participants who were admitted to the outpatient clinic within the date of study, who were not infected with COVID-19, who had no chronic diseases, and who got the tests stated below. The patient group consisted of the participants who were diagnosed with COVID-19 and admitted to the outpatient clinic after the quarantine process. The patient group's tests within the last six months before the infection and within 14 days after the end of the quarantine process were assessed. The tests performed were the TFTs, CBC and routine biochemistry. The patients' symptoms, presence of a chronic disease, smoking history, and clinical conditions during COVID-19 infection were recorded.

Inclusion Criteria for the Study

The inclusion criteria for the control group were not having been infected with COVID-19, not having a chronic disease and having gotten the TFT, hemogram and routine biochemistry. For the patient group, the criteria were having been infected with COVID-19, having gotten the mentioned tests within the last six months before the infection at the latest, and having gotten the mentioned tests again within the 14 days after the infection at the latest.

Exclusion Criteria for the Study

The exclusion criteria were being under the age of 18, having had hypothyroidism and/or hyperthyroidism before, using a medication that could affect the thyroid functions, and having an autoimmune disease.

Statistical Analysis

For the continuous variables that were among the features focused on, descriptive statistics-mean, standard deviation, and minimum and maximum values- were calculated and categorical variables were expressed in counts and percentiles. Whether the numerical data of the variables were normally distributed or not was determined with one sample Kolmogorov-Smirnov test. Chi-square test was used to determine the relationship between the groups and categorical variables. Student-t test was used in comparison of normally distributed numerical data for independent two groups and Mann Whitney U test was used in non-normally distributed two groups. The Wilcoxon test was used in paired groups that were not normally distributed. SPSS 21.0 software program was used for calculations. Statistical significance level in the calculations was accepted as 5%.

Ethics Approval

The institutional approval for the study was obtained from Kayseri Local Health Authority and the ethics approval was obtained from the Non-Interventional Research Ethics Committee of Nuh Naci Yazgan University (Committee Number: 2020/24, Date: 07.12.2020).

RESULTS

A total of 473 individuals were included in the study. While the study group consisted of 259 individuals there were 214 individuals in the control group. Of the participants, 54.5% were female, 40.8% were housewives and 75.5% were married. The rate of the participants with at least one chronic disease was 18.4%. Of the participants, 12.3% had diabetes mellitus, 12.9% had hypertension, 7.4% had cardiovascular disease, 8% had chronic pulmonary disease, and 0.4% had malignancy. While 3.8% of the patient group was hospitalized 3% had pneumonia. Of the participants, 9.9% were smoking. The patient and control groups were similar in terms of age and gender (p: 0.125, p: 0.52). There was no difference between the groups in terms of marital status and occupation (p: 0.158, p: 0.102) (Table

1). WBC, hemoglobin, platelet count, and neutrophil count were higher in the patient group (p: 0.047, p:0.005, p<0.001, p:0.50). Lymphocyte and MPV counts were similar (p: 0.217, p:0.975).

In the patient group, T4 value of 8 patients (3.1%) (1 had low and 7 had high values), T3 value of 12 patients (4.7%) (10 had low and 2 had high values) and TSH value of 12 patients (4.7%) (5 had low and 7 had high values) were not in the reference rage.

TSH and T3 values of the patients were higher compared with the control group (p:0.011, p<0.001). T4 level was similar in the patient and control groups (p: 0.107) (Table 2). TSH, T3 and T4 levels of the patient group before COVID-19 were higher than the results just after the quarantine process after COVID-19 infection (p<0.001, p<0.001, p<0.001) (Table 3).

Table 1. Demographic Data of the Patient and Control Groups

		Patient n(%)	Control n(%)	P
Gender	Male	127(49)	86(40.2)	0.054
	Female	132(51)	149(59.8)	
Age		44(18-87)	51(18-91)	0.125
Occupation	Officer	26(10)	36(16.8)	0.102
	Housewife	106(40.9)	87(40.7)	
	Employee	48(18.5)	46(21.5)	
	Retired	39(15.1)	20(9.3)	
	Student	28(10.8)	19(8.9)	
	Self-employed	12(4.6)	6(2.8)	
Marital Status	Married	203(78.4)	154(72)	0.158
	Single	56(21.2)	60(28)	
Smoking	Yes	26(10)	21(9.8)	0.531
	No	233(90)	193(90.2)	

Table 2. Comparison of CBC and TFTs of the Patient and Control Groups

	Patient Median(min-max)	Control Median(min-max)	p
WBC	7.23(1.03-19.03)	6.9(4.03-17)	0.047
HGB	14.3(7.3-19.9)	14(9.8-19.9)	0.007
PLT	258(88-979)	227(130-351)	<0.001
NEUTROHIL	3.58(1.18-7.98)	3.97(1.07-10.76)	0.05
LYMPHOCYTE	2.5(1.29-4.26)	2.68(1.05-5.86)	0.217
MPV	9.4(0.26-11.1)	9.4(1.1-12.6)	0.975
TSH	1.64(0.06-9.1)	1.88(0.35-4.93)	0.011
T3	2.97(0.67-4.94)	3.18(1.72-4.78)	<0.001
T4	1.06(0.70-4.15)	0.88(0.7-1.47)	0.077

Table 3. Comparison of the Pre-Quarantine and Post-Quarantine TFT Values of the Patient Group

	Pre-Quarantine	Post-Quarantine	P
TSH	1.87(0.28-10.7)	1.52(0.06-6.2)	<0.001
T3	3.32(1.01-4.52)	3.01(1.01-4.32)	<0.001
T4	1.13(0.65-3.24)	1.05(0.74-3.19)	<0.001

DISCUSSION

COVID-19 is an infectious disease that has caused a pandemic worldwide. The pathophysiology of COVID-19, a new type of disease with high contagiousness and mortality, is not fully known. A series of studies have reported that COVID-19 has severe and complex effects on respiratory, digestive, circulatory, and urogenital system (12). Although it has been revealed in some studies that COVID-19 causes thyroid diseases such as subacute thyroiditis and hyperthyroidism its pathophysiology is not clearly known (17).

We found that the participants who had COVID-19 before had lower T3 and TSH levels compared with the control group. T4 levels were not significantly different. In the patient group, T4 of 0.4%, T3 of 3.9% and TSH level of 1.9% were under the reference range. In the study by Chen et al., low TSH and T3 levels were detected in the patient group. There was no difference between the two groups in terms of T4 level. In addition, the degree of the decreases in the TSH and T3 levels revealed a positive correlation with the severity of the disease (18). Lania et al. revealed that TSH value was under the reference value in 20% of the patients who had COVID-19 and that more than half of them experienced apparent thyrotoxicosis (15). Similarly, Müller et al. proved in their study on the patients hospitalized at intensive care unit that the patients had findings compatible with thyrotoxicosis (19). In the study on patients developing pneumonia in China, severe patients had lower TSH and T3 levels compared with mild patients and the dead patients had also lower TSH and T3 levels compared with those surviving (20). Although the effect of COVID-19 seems different in terms of thyroid function tests it is obvious that the disease affects the thyroid hormone release.

COVID-19 is associated with the increased inflammation. SARS-CoV-2 nucleic acid has been seen in respiratory tract, salivary, stool, and breast milk and it has been determined that it reveals a wide distribution. This may be because of the cytokine effect triggered by the virus. This condition is revealed as the cause in inflammatory conditions (21). The increased cytokine profile such as IL-2, IL-6, IL-7, INF-, and TNF-α have been associated with the severity of disease and mortality rate (22, 23). In addition, the increased leukocyte, neutrophil and platelet level and reduced lymphocyte level are the other inflammatory changes that have been detected in the group with thyroid dysfunction. It has been reported that thyroid dysfunction is related to the altered inflammatory process (13). We found that leukocyte, neutrophil and platelet level of the patients increased while lymphocyte level was stable, which is consistent with the findings in literature.

The thyroid sick syndrome is one of the conditions developing after the infection. Its common causes are mainly severe infections, liver and renal failure, severe diabetic complications, malignancy and malnutrition, and burn and trauma (24). It generally occurs as reduced plasma T3 level or low/normal T4 and TSH levels (25).

The thyroid function tests can differ before and after the COVID-19 infection. In a patient who had no thyroid disease history, low TSH level and increased T3 level were detected after the disease (26). Moreover, low TSH and T4 level was detected in a Chinese patient (27). In their study, Khoo et al. reported that most of the COVID-19 patients were euthyroidic, but they observed mild decreases in TSH and T4 compared with the pre-infection values (14). In our study, post-disease TSH, T4 and T3 values of the patients were low compared with the pre-disease values in parallel with the euthyroid sick syndrome.

Limitations of the Study

Our study has various limitations. It is a single center study and has a sample size with a limited number. In addition, the study was retrospectively performed and the severity of the disease could not be assessed. Therefore, the correlation between the severity of the disease and thyroid function tests could not be assessed.

CONCLUSION

In conclusion, the present study has revealed that euthyroid sick syndrome, hypothyroidism and hyperthyroidism can occur in COVID-19 patients. Thyroid dysfunction develops within the course of the disease. While this can partiallybe explained by the non-thyroid disease syndrome it is also possible that thyroid gland can be the direct target of SARS-CoV-2 virus.

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Araştırma Makalesi / Research Article

The Compliance of Intern Nursing Students With Isolation Precautions; During COVID-19 Pandemic Process

COVİD-19 Pandemi Sürecinde İntörn Hemşirelik Öğrencilerinin İzolasyon Önlemlerine Uyumu

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Abstract

Aim: The present study was conducted to determine the level of compliance of intern nursing students with isolation precautions and the factors affecting them.

Material and Method: The research was carried out with fourth-year nursing students in the internship program in a university hospital between December 2020 and April 2021. The data were collected using the "Participant Information Form" and the "Isolation Precautions Compliance Scale".

Results: It was determined that the students received a total of 76.11±9.86 points from the Isolation Precautions Compliance Scale. The statistical analysis indicated that there was no significant difference between the compliance with isolation precautions and the variables of age, gender, the type of the clinic, the training received about isolation precautions and providing care to the isolated patient ($p>0.05$). However, it was found that the difference between the compliance with isolation precautions and the variables of the pandemic process and knowing the infection rate of the institution was significant ($p<0.05$).

Conclusion: It was concluded that the compliance of the intern nurses with isolation precautions was quite high.

Keywords: Isolation, standard precaution, hospital infection, nurse

Öz

Amaç: Bu araştırma, intörn hemşirelik öğrencilerinin izolasyon önlemlerine uyum düzeyi ve etkileyen faktörleri belirlemek amacıyla yapılmıştır.

Materyal ve Metot: Bu araştırma bir üniversite hastanesinde intörnlük uygulamasına çıkan hemşirelik dördüncü sınıf öğrencileri ile Aralık 2020-Nisan 2021 tarihleri arasında yürütülmüştür. Veriler, "Katılımcı Tanıtım Formu" ve "İzolasyon Önlemlerine Uyum Ölçeği" kullanılarak toplanmıştır.

Bulgular: Öğrencilerin İzolasyon Önlemlerine Uyum Ölçeğinden toplam 76.11±9.86 puan aldığı saptanmıştır. Yaş, cinsiyet, çalışılan klinik, izolasyon önlemleri ile ilgili eğitim alma ve izole edilen hastaya bakım verme değişkenleri ile izolasyon önlemlerine uyum arasındaki farkın istatistiksel olarak anlamlı olmadığı saptanmıştır ($p>0.05$). Ancak, çalışılan kurumun enfeksiyon hızını bilme durumu ve pandemi sürecinin izolasyon önlemlerine uyumu etkilediği belirlenmiştir ($p<0.05$).

Sonuç: İntörn hemşirelerin izolasyon önlemlerine uyumlarının oldukça yüksek olduğu sonucuna varılmıştır.

Anahtar kelimeler: İzolasyon, standart önlem, hastane enfeksiyonu, hemşire

INTRODUCTION

Healthcare-associated infections are important factors that negatively affect the quality and output of healthcare services. Infections that develop within 48 hours or longer after hospitalization or develop within 30 days of discharge are stated to be nosocomial (1). The term "nosocomial" refers to any infection that a patient acquires from the hospital during receiving healthcare services (2). Healthcare-associated infections cause prolonged hospital stay of patients, a serious economic burden on patients and their families, and increased morbidity, mortality, and treatment costs (3, 4). Policies and guidelines at the national and international level on infection control provide recommendations on standard principles towards the control and prevention of healthcare-associated infections.

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Policies on infection control are evidence-based and aim to inform best practices and thereby optimize patient care and safety (5).

Infection control precautions should be implemented within the scope of combating healthcare-associated infections. Those standard and elementary precautions aiming to prevent or minimize the risks of cross-infection include many applications such as ensuring hand hygiene, wearing gloves, using personal protective equipment, complying with aseptic technique, management of medical wastes including piercing-cutting tools, hospital/environmental cleaning, and appropriate antibiotic use. The secondary precautions are those applied together with the standard practices to prevent transmission from infected patients. These precautions are contact, droplet and respiratory isolation precautions and training of medical personnel. The tertiary precautions that are not routinely applied include applications such as disinfecting the environment or taking cultures from the environment when necessary (5-7).

All healthcare professionals are expected to have a high level of compliance with these control precautions to reduce the incidence of nosocomial infections, improve patient safety, and decrease the risk of infection (8). Healthcare workers should protect themselves and the patients they care for against infectious agents and take the necessary precautions. The most important factor in the development of infection is the attitudes and behaviors of health personnel. Nurses and nursing students, who are with the patient 24 hours a day, have important responsibilities in this regard. Nurses should have the most up-to-date information on the prevention and control of nosocomial infections, and provide effective care to patients by using this information in their practices (9). One of the infection control precautions is compliance with isolation precautions. Despite all the precautions taken in the world and in our country, the COVID-19 epidemic continues and the number of morbidity and mortality is increasing. The issue of compliance with isolation precautions in keeping the epidemic under control is particularly noteworthy (10). In the literature, there are studies assessing the level of compliance of health workers with isolation precautions and their compliance level is seen to be high (11, 12). However, in the literature review on compliance with isolation precautions during COVID-19 pandemic, a limited number of studies were found with the participation of intern nursing students (10). The infection control and the compliance with isolation precautions is a critical issue for all health workers including intern nursing students. Due to the scarcity of the studies conducted with intern nurses, the present study was decided to be carried out. It is important to evaluate the knowledge and attitudes of future health workers about isolation precautions and to complete their missing knowledge at this stage. The present study was carried out to determine the level of compliance of intern nursing students with isolation precautions and the factors affecting them.

MATERIAL AND METHOD

Research Type: The study is descriptive type.

Place and date of the research

The study was carried out with intern nursing students in a university hospital located east of Turkey between December 2020 and April 2021.

Population and Sample

The population of the study consisted of intern nursing students of the Faculty of Nursing at Inonu University who were in an internship program (N=248). Sample selection was not made, it was target to reach the whole population. The research was completed with 152 students who agreed to participate in the study and were accessible online. 61% of the population has been reached.

Data Collection

Two different data collection forms were used to collect the data. These are the "Participant Information Form" and the "Isolation Precautions Compliance Scale (IPCS)". The scale forms were prepared online by the researchers using Google Forms and distributed to the participants via WhatsApp. Necessary explanations about the research and written consent were attached to the first page of the form. The students who agreed to participate in the research were able to answer the survey questions. The scales took about 5-10 minutes to complete.

Data Collection Tools

Participant Information Form

In this form, besides the demographic characteristics of the students such as age and gender, there are also questions about isolation measures.

Isolation Precautions Compliance Scale (IPCS)

The IPCS was developed by Tayran and Ulupınar in 2011 and its validity and reliability were verified. The scale, consisting of 18 positive and negative statements, aims to measure the compliance of nurses and physicians with isolation precautions, is of 5-point Likert type. Each item on the scale is rated from 1 = strongly disagree to 5 =strongly agree. Negative statements on the scale (5, 7, 12 and 17) are scored backwards. The lowest score to be obtained from the scale is 18, while the highest score to be obtained is 90. It is regarded that as the score received increases, the level of compliance with isolation precautions rises. Although the developers of the scale suggested using the single-factor version of the scale, scores from four sub-dimensions were also taken in consideration in this study. While Tayran and Ulupınar determined the Cronbach's alpha value of the scale to be 0.85 (13), it was calculated to be 0.88 in the present study.

Data Analysis

In the analysis of data; The distribution of socio-

demographic characteristics of the students was given by descriptive tests. The Kolmogorov-Smirnov test was used to evaluate the conformity of the data to the normal distribution. Non-parametric tests were applied in the statistical analysis because the data were not normally distributed ($p<0.05$). The difference between socio-demographic characteristics of students and the total IPCS scores was determined using the Mann Whitney U and the Kruskal-Wallis H tests.

Ethical Approval

Ethical approval from the Health Sciences Scientific Research and Publication Ethics Committee of Inonu University (2021/1554), and institutional permission from the Deanship of the Faculty of Nursing were obtained before conducting the research. In addition, a written consent form was taken from the students who participated in the study.

RESULTS

The mean age of the students was 22.13±1.05. Of the students 65.8% were female, 53.9% were interns in the internal medicine clinic, 73.7% stated that they received training for isolation precautions, 57.9% perceived their level of knowledge about isolation precautions as moderate, 67.1% did not know the infection rate of the institution they worked, 68.4% provided care to isolated patients during their time working, and 67.1% expressed that the pandemic process greatly affected the importance they attach to isolation precautions (Table 1).

Table 1. The distribution of socio-demographic characteristics of the students

	Number (152)	Percentage (%)
Age (X ± SD) 22.13 ± 1.05		
Gender		
Female	100	65.8
Male	52	34.2
Type of the clinic		
Internal medicine	82	53.9
Surgery	52	34.2
Pediatric	18	11.9
Have you received training on isolation precautions?		
Yes	112	73.7
No	40	26.3
What do you think is your level of knowledge about isolation precautions and nosocomial infections?		
Good	46	30.3
Moderate	88	57.9
Low	18	11.8
Do you know the infection rate of the institution you work?		
Yes	50	32.9
No	102	67.1
Have you provided care for the isolated patient during your internship?		
Yes	104	68.4
No	48	31.6
To what extent has the pandemic process affected the importance you attach to isolation precautions?		
Greatly affected	102	67.2
Little affected	44	28.9
Not affected	6	3.9

X: Mean, SD: Standard Deviation

Table 2. Mean scores of Isolation Precautions Compliance Scale and its sub-dimensions

Scale	Min-Max	X ± SD
Transmission Route	5.0–25.0	21.23±3.45
Work and Patient Safety	16.0–30.0	25.38±3.27
Environmental Control	4.0–20.0	16.73±2.61
Hand Hygiene and Glove Use	6.0–15.0	12.76±1.96
IPCS Total	34.0–89.0	76.11±9.86

X: Mean, SD: Standard Deviation

Table 2 shows the IPCS total and sub-dimension scores of the students. It was observed that the mean total IPCS score of the students was 76.11±9.86, while transmission route sub-dimension mean score was 21.23±3.45, work and patient safety was 25.38±3.27, environmental control was 16.73±2.61 and hand hygiene and glove use was 12.76±1.96. Considering the fact that the maximum score that can be obtained from the IPCS is 90, it was observed that the compliance level of the intern students with isolation precautions was high.

Table 3. The comparison of socio-demographic characteristics of students and the mean IPCS scores

	IPCS X ± SD	Test and p-value
Age		r: 0.075
		p = 0.361
Gender		
Female	76.10±10.9	MWU: 2288.0
Male	76.15±7.46	p=0.225
Type of the clinic		
Internal Medicine	76.12±9.39	KW:1.540
Surgery	76.26±11.5	p=0.463
Pediatric	75.66±6.66	
The status of receiving training on isolation precautions		
Yes	76.70±10.6	MWU: 2018.0
No	75.91±9.59	p=0.352
Level of knowledge about isolation precautions and nosocomial infections		
Good	76.61±10.9	KW: 3.224
Moderate	75.91±8.18	p=0.200
Low	74.22±8.25	
The status of knowing the infection rate of the clinic		
Yes	78.05±6.99	MWU:1950.0
No	72.16±13.2	p=0.018*
The status of providing care to isolated patients during internship		
Yes	76.70±10.4	MWU:2204.0
No	75.84±9.62	p=0.247
The effect of the pandemic process on the importance attached to isolation precautions F		
Greatly affected	78.17±9.28	
Little affected	73.04±9.88	KW:23.888
Not affected	63.66±2.25	p=0.000**

*p<0.05, **p<0.001, MWU: Mann-Whitney U Test, KW: Kruskal-Wallis Test, F: Bonferroni Test

It was determined that there was a very weak positive correlation between the students age and the IPCS score (r:0.075), but this relationship was not statistically significant (p>0.05). There was no statistically significant difference between the mean IPCS score and the variables of gender, the type of the clinic, the training received about isolation precautions and the care provided to the isolated patient (p>0.05). On the other hand, the difference between the mean IPCS score and the variables of knowing the infection rate of the clinic and the effects of the pandemic process was statistically significant (p<0.05). It was detected that the compliance with isolation precautions was higher among the students who knew the infection rate. The post-hoc statistical analysis to evaluate the effect of the pandemic process on isolation precautions revealed that the group stating that the pandemic process greatly affected the compliance with isolation precautions created a significant difference (Table 3).

DISCUSSION

Healthcare-associated infections are serious problems that threaten patient safety within the healthcare industry. All health professionals are expected to have appropriate knowledge about these infections and to provide healthcare in accordance with the standard precautions (8, 14). It is extremely important for particularly nurses and nurse candidates, who are personally responsible for the care of patients, to know in which situations the standard and isolation precautions will be applied, and what the precautions include. In addition, their compliance with such precautions in the care and treatment processes is essential for the provision of safe and high-quality health services (15). In this study, intern nurses received 76.11 ±9.86 points from the IPCS. The results obtained in the present study shows similarity with the results of the study (75.45±9.98) by Sakanuz conducted with 2nd, 3rd, and 4th-year nursing students (16). It is thought that completing the theoretical education and having more clinical experience may be effective in the slightly higher IPCS scores of the intern nurses. Many studies in the literature reported that the level of compliance with isolation precautions of the nurses and other health workers are good in Turkey (6, 9, 12, 17, 18, 19). However, the international literature revealed that the knowledge and practices regarding standard precautions among health professionals and students are not sufficient (20-23). Tufail et al. (2017) determined that nurses have a good level of knowledge regarding standard isolation precautions, but their attitudes and practices are not at a sufficient level (14). Yazie et al. also found that health workers' knowledge, attitude and practice scores on infection prevention were low (24). Contrary to these results, in a study conducted with nursing students in the Philippines, it was found that students' awareness of infection control was very high, and the implementation of standard precautions for infection control such as hand washing, proper handling and disposal of contaminated materials was excellent (25). It is considered that socio-cultural factors such as the health and education policies of the countries, personnel insufficiency, the differences in the nursing curriculum, the development level of the countries are the reasons for the difference between the countries. The examination of scores received by intern nurses from the sub-dimensions of the Isolation Precautions Compliance Scale revealed that the students received 21.23±3.45 (min:5-max:25) from the "Transmission Route", 25.38±3.27 (min: 16 - max: 30) from the "Work and Patient Safety", 16.73±2.61 (min: 4 - max:20) from the "Environmental Control" and 12.76±1.96 (min:6 - max:15) points from the "Hand Hygiene and Glove Use". The interns have been observed to have a good level of compliance toward transmission route, work and patient safety, environmental control and hand hygiene and glove use. In the study in which Arli and Bakan evaluated the level of compliance of nurses with isolation measures, it was determined that the nurses received 21.65±3.05 from "Transmission Route" sub-dimensions of the IPCS, 25.05±3.48 from "Work and Patient Safety", 17.08±2.19 from "Environmental Control" and 12.77±1.93 from "Hand Hygiene and Glove Use" (9). The scores of IPCS sub-dimensions, Transmission Route, Work and Patient Safety, Environmental Control, and Hand Hygiene and Glove Use, were detected to be 21.67±5.13, 24.77±4.58, 16.72±4.49 and 12.86±2.47, respectively for the nurses in Tanyeri's study (26) and 21.31±3.27, 25.08±3.08, 16.74±2.52 and 12.31±2.36, respectively for the nursing students in Sakanuz's study (16). According to the results mentioned above, it could be concluded that the positive attitudes of nurses and nursing students towards infection control in Turkey are similar, and their compliance with precautions such as transmission route, patient safety, hand hygiene and glove use is at a good level.

In the present study, there was no statistically significant difference between the mean scores of IPCS and the variables of age, gender, the type of the clinic, the training received about isolation precautions and the care provided for isolated patients. In a study conducted with nurses and physicians, Gecit and Ozbayir found that there was no significant difference between the IPCS scores and the variables of age, gender, occupational group, the clinic in which they work, being satisfied with the working conditions and finding professional development sufficient (18). It was reported by Zencir et al. that there was no statistically significant difference between the mean IPCS score of the nurses and the clinics they worked in, marital status, their willingness to do their job, the training they received on infection and the status of having a blood-borne infection before (12). Another study, investigating the compliance with isolation precautions of intensive care physicians and nurses, indicated that there was no statistically significant difference between the IPCS score and the variables of age, gender, occupation, isolation training status, and the unit they worked in (6). The significant difference between compliance with isolation precautions in terms of demographic variables shows that the students comply with isolation precautions at a similar level.

It was detected that the compliance with isolation precautions differed positively in the intern nurses who

knew the infection rate of the unit where they worked. One-third of the intern nurses were determined to know the infection rate of the unit they worked in. The infection rate is one of the healthcare service quality indicators in the unit. The infection control committee in a hospital monitors the surveillance rate of the units and regularly reports the results obtained to the relevant units. It needs to be pointed out that jointly discussing active surveillance results, problems and solutions by the hospital infection control committee team and unit employees is important in terms of increasing compliance with infection control precautions (27). There was no significant difference between the IPCS scores and knowing the infection rate in the study by Tayran et al. conducted with the nurses. However, there was a significant difference between knowing the infection rate and the IPCS scores, transmission route and environmental control precautions in the physicians. The compliance with isolation precautions was higher in the physicians who knew the infection rate of the unit in which they worked than those who did not (27). It is of the opinion that knowing the infection rate in the unit will contribute to considering the precautions to be taken by reviewing the current situation and increasing the compliance with isolation.

The present study was carried out during the COVID-19 pandemic and it was determined that the pandemic process positively increased the compliance with isolation precautions. The usage rate of protective equipment (gloves, masks, aprons or overalls) in all clinics has increased with the pandemic process. It is an expected result that intern nurses pay more attention to these precautions to protect themselves, their families and patients they provide care during this difficult time.

CONCLUSION

In conclusion, the present study carried out with the intern nurses showed that the participants' compliance with isolation precautions was at a good level. It was determined the difference between the compliance level of isolation precautions and the variables of age, gender, the type of the clinic, the training received regarding isolation precautions and the care provided to the isolated patient was not statistically significant. However, the difference between the compliance with isolation precautions and the variables of the pandemic process and knowing the infection rate of the institution was detected to be significant.

It is recommended to update the knowledge and performance of intern nurses by providing in-service training programs for specific groups found to be at risk for reducing nosocomial infections, emphasize the importance of the use of the latest and evidence-based practices of infection control in current education/training programs, and to conduct researches with larger sample groups and share the results with hospital managements.

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Araştırma Makalesi / Research Article

The Effect of Neuro-Linguistic Programming on Depression, Anxiety and Stress in Liver Transplant Patients

Karaciğer Nakli Hastalarında Nörolinguistik Programlamanın Depresyon, Anksiyete, Stres Üzerine Etkisi

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Abstract

Aim: This study was conducted using a prospective randomized single-blind clinical trial model to examine the effect of neuro-linguistic programming (NLP) on depression, anxiety, and stress in liver transplant patients.

Materials and Methods: This study was conducted with liver transplant patients at a university's Liver Transplant Institute between June 2021 and December 2021. The sample size of the study was determined as 84 (Experimental group: 42, control group: 42). Personal information form and Depression, Anxiety, and Stress Scale (DASS-21) were used to collect data. The data obtained from the research were evaluated with SPSS 25.

Results: In the experimental group, the mean score of DASS-21 was found to be 38.95 ± 11.96 before the NLP application and 25.21 ± 5.43 after the NLP application. It was found statistically significant that the value obtained in the second measurement was lower than the value obtained in the first measurement ($p<0.05$). It was determined that NLP application significantly decreased all parameters of depression, anxiety, and stress ($p<0.05$). In the control group, the mean score of DASS-21 was determined as 51.05 ± 7.53 in the first measurement and 52.57 ± 7.92 in the second measurement. It was found statistically significant that the value obtained in the second measurement was higher than the value obtained in the first measurement ($p<0.05$).

Conclusion: This study found that NLP reduced depression, anxiety, and stress in liver transplant patients. In line with this result, it can be suggested that nurse's benefit from NLP practice and receive training on NLP in managing the depression, anxiety, and stress experienced by liver transplant patients.

Keywords: Anxiety, depression, liver transplantation, neuro-linguistic programming, stress

Öz

Amaç: Bu araştırma karaciğer nakli olmuş hastalarda nörolinguistik programlamanın (NLP) depresyon, anksiyete ve stres üzerine etkisini incelemek amacı ile prospektif randomize tek kör klinik araştırma modeli kullanılarak gerçekleştirildi.

Materyal ve Metot: Araştırma; Bir üniversiteye ait Karaciğer Nakli Enstitüsünde karaciğer nakli olan hastalarla, Haziran 2021–Aralık 2021 tarihleri arasında gerçekleştirildi. Araştırmanın örneklem büyüklüğü 84 (Deney grubu:42, kontrol grubu:42) olarak belirlendi. Verilerin toplanmasında Kişisel Bilgi Formu ve Depresyon Anksiyete Stres Ölçeği (DASS- 21) kullanıldı. Araştırmadan elde edilen veriler SPSS 25. ile değerlendirildi.

Bulgular: Deney grubunda DASS-21 puan ortalaması NLP uygulamasından önce 38.95 ± 11.96, NLP uygulamasından sonra 25.21 ± 5.43 olarak bulundu. İkinci ölçümde elde edilen değerin birinci ölçümde elde edilen değerden düşük olması istatistiksel olarak önemli bulundu ($p<0.05$). NLP'nin depresyon, anksiyete ve stres parametrelerinin tamamını önemli düzeyde düşürdüğü saptandı ($p<0.05$). Kontrol grubunda DASS-21 puan ortalaması ilk ölçüm 51.05 ± 7.53, ikinci ölçüm 52.57 ± 7.92 olarak belirlendi. İkinci ölçümde elde edilen değerin birinci ölçümde elde edilen değerden yüksek olması istatistiksel olarak önemli bulundu ($p<0.05$).

Sonuç ve Öneriler: Araştırmada NLP'nin karaciğer nakli olmuş hastalarda depresyon, anksiyete ve stresi azalttığı bulundu. Bu sonuç doğrultusunda hemşirelerin karaciğer nakli hastalarının yaşadığı depresyon, anksiyete ve stresi yönetmede NLP uygulamasından faydalanması ve bu konuda eğitimler alması önerilebilir.

Anahtar kelimeler: Anksiyete, depresyon, karaciğer nakli, nörolinguistik programlama, stres

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INTRODUCTION

Liver transplantation is accepted as the most effective method in the treatment of end-stage liver disease (1). Improvements in immunosuppressive therapy and surgical methods have led to the increasing preference of liver transplantation (2,3). Although liver transplantation increases the chance of survival of individuals with end-stage liver disease, transplant patients face many psychological problems such as anxiety, depression, stress (1,2). In a study conducted by Yıldız, it was determined that 57.6% of patients with liver transplantation experienced moderate trait anxiety (2). In addition, it has been reported that 3% to 58% of liver transplant patients experience depressive symptoms and psychological problems are at higher levels in the first few years following organ transplantation (4,5). It is stated that changes in life and roles, potential complications such as infection, organ rejection, social isolation, and steroid and/or immunosuppressive drugs used in the post-transplant period have a significant effect on emerging psychological symptoms (2). It is emphasized that this prevalence of psychological symptoms may cause problems such as insomnia and deterioration in quality of life, and therefore, transplant outcomes are negatively affected (3,4).

Although there are various medical and psychiatric methods in the solution of psychological problems, non-drug methods such as Neuro Linguistic Programming (NLP) have also started to attract attention in recent years (6–8). NLP is a method that allows the individual to change the neural programming of any situation or emotional perception with various techniques and is similar to body-mind therapies in this respect. The term neurological means that all behavior results from the neurological processing of information provided by the five senses. The linguistic part of the title refers to the fact that language is the basis for the organization of thoughts and communication. The term programming expresses that, ideas and behaviors can be changed and managed to create desired results (3,4). NLP allows one to decipher the origin of individual words and speech. In this way, people can feel, think, speak, and thus manage themselves (6,9). When the usage areas of NLP are examined, there are studies examining the effects of many factors such as pain, stress, anxiety, depression, alcohol use, and it is seen that it has positive effects (6,10–14).

Since nurses are health professionals who spend the longest time with patients, they should monitor patients both physiologically and psychologically, develop and implement strategies to solve the problems they detect, as well as before and during the organ transplant process (15,16). When the literature was examined, no study was found that examined the effects of NLP on depression, anxiety, and stress levels in liver transplant patients. In the light of this information, this study was conducted to determine the effect of NLP on the depression, anxiety, and stress levels of patients who had liver transplantation in the last two years.

Hypotheses of the Study

H_0: In patients who have had a liver transplant; NLP application does not affect patients' anxiety, depression, and stress levels.

H1: In patients with liver transplant; NLP application affects the anxiety, depression and stress levels.

MATERIAL AND METHOD

Objective and Type of the Study

This study was carried out using a prospective randomized single-blind clinical trial model to examine the effects of NLP applications on depression, anxiety, and stress in liver transplant patients.

Time and Place

This study was conducted with liver transplant patients at a university's Liver Transplant Institute between June 2021 and December 2021.

Population and Sample

The population of the study consisted of patients who had liver transplant at the mentioned liver transplant institute. The sample size was determined by power analysis. According to the calculation made using G*power 3.1 software, the sample size was determined as 84 (Experimental group: 42, control group: 42) with 0.40 effect size, 0.05 margin of error, 0.95 confidence level, and 0.90 population representation power. The adequacy of the number of participants was tested by power analysis. Simple random sampling method, one of the probability sampling methods, was used to determine the participants. Participants were selected on a voluntary basis. Random.org program was used to assign participants to groups and assignments were made to groups. Considering possible losses, data collection was started with 103 people.

Inclusion Criteria

Patients who had moderate and severe depression, anxiety, and stress levels, who were verbally communicative, had no hearing problem, had not practiced NLP before, had no psychiatric disease other than anxiety, depression, and stress, and have passed max 2 years since the transplant were included in the study.

Exclusion Criteria

Patients who could not communicate verbally, who wanted to leave at any stage of the study, and who had organ rejection were excluded from the sample.

Data Collection Instruments

Personal Information Form and Depression Anxiety Stress Scale (DASS-21) were used to collect data.

Personal Information Form

This form, which was prepared by the researchers using the literature, consists of 12 questions (age, gender, education

level, marital status, economic status, occupation, presence of another disease, time passed after transplant, place of residence, previous diagnosis of depression or anxiety disorder the number of years of liver disease in the preoperative period, the existence of a method used to cope with depression, anxiety and stress in daily life) (1,2,5,7).

Depression Anxiety Stress Scale – 21 Items (DASS-21): The Depression Anxiety Stress Scale -DASS, developed by Lovibond & Lovibond in 1995, consists of 42 questions. The original DASS contains 42 self-report items that reveal three components of negative emotional states: Depression (DASS-Depression), Anxiety (DASS-Anxiety), and Stress (DASS-Stress). The validity and reliability of a short version of the measurement has been validated by Antony et al. (1998). The short form DASS-21 consists of 21 self-report questions graded on a four-point scale to indicate severity and severity. It consists of questions about symptoms experienced in the past week. In this scale (DASS-21), there are 7 questions each to measure the dimensions of depression, stress and anxiety. The first 7 items of the scale include questions about anxiety, the second 7 items about depression, and the third 7 items about stress. Three subscales, each consisting of seven items, and the scores of each dimension contain related questions. The scale is a 4-point Likert Type Scale and was coded as: 0 "Did not apply to me at all", 1 "Applied to me to some degree, or some of the time", 2 "Applied to me to a considerable degree or a good part of the time", and 3 "Applied to me very much or most of the time". The Turkish validity and reliability study was conducted by Yıldırım et al. DASS-21 subscales were found to be DASS-Depression α = 0.89, DASS-Anxiety α = 0.87, and DASS Stress α = 0.90 (17,18). In this study, the Cronbach's alpha value obtained for the DASS-21 scale was found to be 0.866 for the experimental group and 0.784 for the control group. The Cronbach's alpha value for the depression subscale was 0.773 for the experimental group and 0.808 for the control group. The Cronbach's alpha value for the anxiety sub-dimension was 0.726 for the experimental group and 0.458 for the control group. The Cronbach's alpha value for the stress sub-dimension was 0.753 for the experimental group and 0.587 for the control group.

Data Collection

Data were collected between 1 July and 30 October. Telephone numbers of patients who had liver transplantation in the last 2 years were obtained from hospital records. The patients were randomly called by the researcher by telephone. After they were informed about the study by telephone and their verbal consent was obtained, the DASS-21 scale was applied. After applying the Personal Information Form and DASS-21 to the patients in the experimental group, the sub-modality technique of NLP was applied once (19). Afterwards, NLP was applied 4 times in total, with one-week intervals. After 28 days, the last NLP application was made, and DASS-21 has applied again. The patients in the control group were informed about the study in the first phone call, the Personal Information Form and DASS-21 were applied after their consent was obtained, the patients were called again 28 days later, and DASS-21 was applied for the second time. No intervention was made in the control group. The application of the Personal Information Form and DASS-21 took an average of 10-15 minutes for each patient, and each NLP application took approximately 30 minutes.

Evaluation of the Data

Data analysis was performed with SPSS (Statistical Program in Social Sciences) 25 software. Whether the data fit the normal distribution was checked with the Sahapiro Wilk Test. The significance level (p) for the comparison tests was taken as 0.05. Since normal distribution was achieved in the variables ($p>0.05$), the analysis was continued with parametric test methods. Since the assumption of normality was ensured in the comparisons in dependent pairs, the significance test of the difference between the two pairs (two paired samples t test) was performed. In repeated measurements, analysis of variance (repeated measure of ANOVA) was used to test whether there was a difference between groups. Multiple normal distribution and homogeneity of variance were controlled in the analyses. Analysis of variance on repeated measures is a generalized form of the test of significance between two peers for more than two groups. This method differs from one-way analysis of variance in independent groups, as it provides the opportunity to examine changes over time. In repeated measures, two-way ANOVA analysis is used in cases where there are repetitions on one of the factors. In these trials, for example, while groups are the first factor, the second factor is time. There are repeated measurements on time, which is one of the factors. The aim here is to test whether the change in the dependent variable according to time differs between the experimental and control groups (20). As a result of the analysis, both within-group and between-group changes according to time can be compared, and at the same time, while the H0 hypothesis is true, the probability of rejection (Type I error) will decrease, and consistent results will be obtained (21).

Ethical Aspect of the Study

Institutional permission and ethics committee permission were obtained from the relevant university in order to conduct the research (Decision Number: 2021/2063). Verbal consent was obtained from the patients participating in the study.

RESULTS

It was tested whether there was a difference between the groups according to the demographic variables of the participants included in the study and the results are given in Table 1 below.

No statistically significant difference was found between

the experimental and control groups according to the variables of gender, marital status, economic status, occupation, additional disease status, and place of residence (p>0.05, Table 1). A statistically significant difference was found between the experimental and control groups according to the educational status of the participants and a method used to cope with depression, anxiety, and stress (p<0.05, Table 1).

It was tested whether there was a difference between the groups according to the demographic variables of the patients included in the study and the results are given in Table 2 below.

There was no statistically significant difference between the experimental and control groups according to the variables of age and time elapsed after transplantation in the patients included in the study (p>0.05, Table 2). A statistically significant difference was found between the experimental and control groups according to the duration of the disease in the patients included in the study (p<0.05, Table 1).

Table 1. Comparison of the groups by distribution of demographic variables

Variable	Group	Experiment		Control		Test value	p value
		Number	Percent	Number	Percent		
Gender	Female	15	35.7	19	45.2	0.792	0.373
	Male	27	64.3	23	54.8		
Education	None			2	4.8	17.481	0.001*
	Primary-Secondary	6	14.3	25	59.5		
	High School	19	45.2	8	19		
	University and above	17	40.5	7	16.7		
Marital Status	Married	39	92.9	32	76.2	4.668	0.074
	Single	3	7.1	10	23.8		
Occupation	Housewife	13	31	15	35.7	0.069	0.793
	Worker	1	2.4	2	4.8		
	Civil Servant	2	4.8	1	2.4		
	Self-employed	8	19	4	9.5		
	Retired	12	28.6	4	9.5		
	Unemployed	6	14.3	16	38.1		
Place of Residence	Province Center	29	69	22	52.4	0.574	0.449
	District	4	9.5	11	26.2		
	Town	2	4.8	1	2.4		
	Village	7	16.7	8	19		
	High	2	4.8	1	2.4		
Income Level	Middle	29	69	20	47.6	5.181	0.075
	Low	11	26.2	21	50		
Additional Disease	Yes	13	31	21	50	3.186	0.074
	No	29	69	21	50		
Method used to cope with depression, anxiety and stress	Nothing	23	54.8	14	33.3	15.373	0.001*
	Finding a Hobby	15	35.7	3	7.1		
	Prayer	2	4.8	13	31		
	Social Media	2	4.8				
	Conversation-Chat			4	9.5		
	Physical Activity			8	19		

Test value; Chi-square Test value ($\chi 2$), p value; statistical significance

Table 2. Comparison of the groups by distribution of demographic variables

Variable	Group	Mn ± sd	Test value	p value
Age	Experiment Control	50.1 ± 12.14 47.43 ± 14.79	**0.903**	**0.369**
Duration of the Disease	Experiment Control	4.76 ± 4.84 9.93 ± 9.54	-3.129	0.002*
Time after transplant (Month)	Experiment	15.38 ± 6.56 14.4 ± 7.66	0.627	0.532

p value; statistical significance

It was tested whether the depression, anxiety, stress, and DASS-21 scores of the participants included in the study changed according to time both within and between groups (experimental and control), and the results are given in Table 3.

In the measurement made, it was observed that while there was a decrease in the depression score in the experimental group, there was an increase in the control group.

For Depression; Depression in the experimental group was statistically significant as the value obtained in the second measurement was lower than the value obtained in the first measurement ($p<0.05$, Table 3). In the control group, the value obtained in the second measurement for depression was found to be higher than the value obtained in the first measurement, which was statistically significant ($p<0.05$, Table 3). It was found statistically significant that the changes in depression scores between the first measurement and the second measurement according to time in the patients included in the study differed between the experimental and control groups ($p<0.05$, Table 3). Changes in time difference explain 50.7% (η= 0.507) of the variation between measurements with groups. The interaction graph of depression measurements is given below;

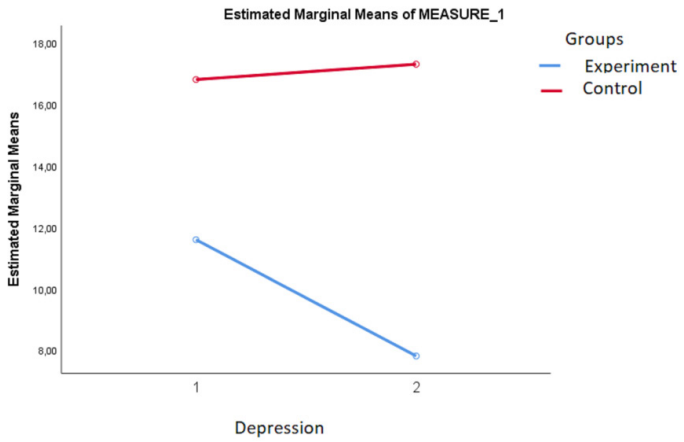


Figure 1. Distribution of depression measurements over time in groups

For Anxiety; In the experimental group, the value obtained in the second measurement of anxiety was found to be lower than the value obtained in the first measurement, which was statistically significant ($p<0.05$, Table 3). In the control group, it was statistically significant that the value obtained in the second measurement of anxiety was higher than the value obtained in the first measurement ($p<0.05$, Table 3). It was found statistically significant that the changes in anxiety scores between the first measurement and the second measurement according to time in the patients included in the study differed between the experimental and control groups ($p<0.05$, Table 3). Changes in time difference explain 50.7% (η= 0.507) of the variation between measurements with groups. The interaction graph of anxiety measurements is given below;

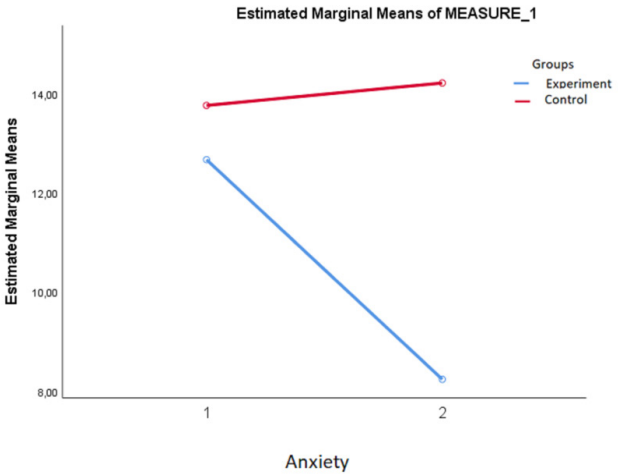


Figure 2. Distribution of anxiety measurements over time in groups

In the measurement made, it was observed that while there was a decrease in the anxiety score in the experimental group, there was an increase in the control group.

For Stress; The fact that the value obtained in the second measurement of stress in the experimental group was lower than the value obtained in the first measurement was found to be statistically significant ($p<0.05$, Table 3). It was found statistically significant that the value obtained in the second measurement of stress in the control group was higher than the value obtained in the first measurement ($p<0.05$, Table 3). It was found statistically significant that the changes in the stress score between the first and second measurements over time in the patients included in the study differed between the experimental and control groups ($p<0.05$, Table 3). Changes in time difference explain 50.7% (η= 0.507) of the variation between measurements with groups. The interaction graph of stress measurements is given below;

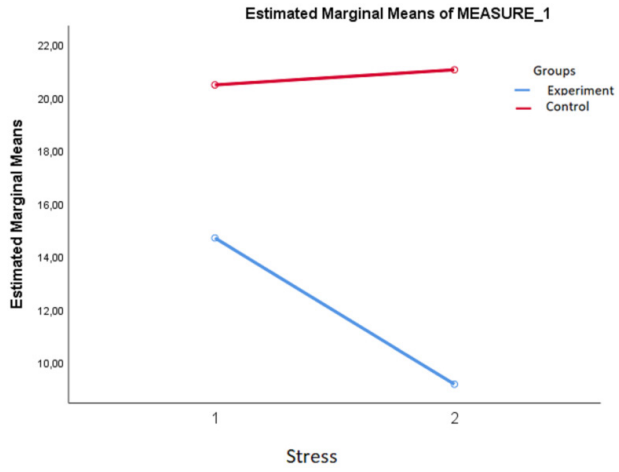


Figure 3. Distribution of stress measurements over time in groups

In the measurement made, it was observed that while there was a decrease in the stress score in the experimental group, there was an increase in the control group.

For DASS-21; The fact that the value obtained in the second measurement of DASS in the experimental group was lower than the value obtained in the first measurement was found to be statistically significant (p<0.05, Table 3). It was found statistically significant that the value obtained in the second measurement of DASS in the control group was higher than the value obtained in the first measurement (p<0.05, Table 3). It was found statistically significant that the changes in the DASS score between the first and second measurements in terms of time in the patients included in the study differed between the experimental and control groups (p<0.05, Table 3). Changes in time difference explain 50.7% (**η**= 0.507) of the variation between measurements with groups. The interaction graph of DASS-21 measurements is given below;

In the measurement made, it was observed that while there was a decrease in the DASS score in the experimental group, there was an increase in the control group.

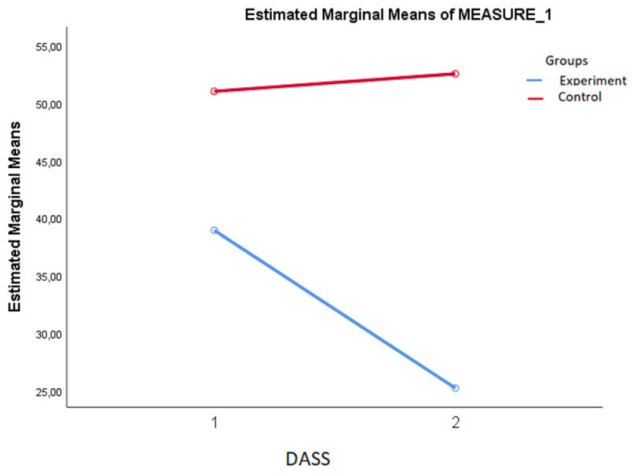


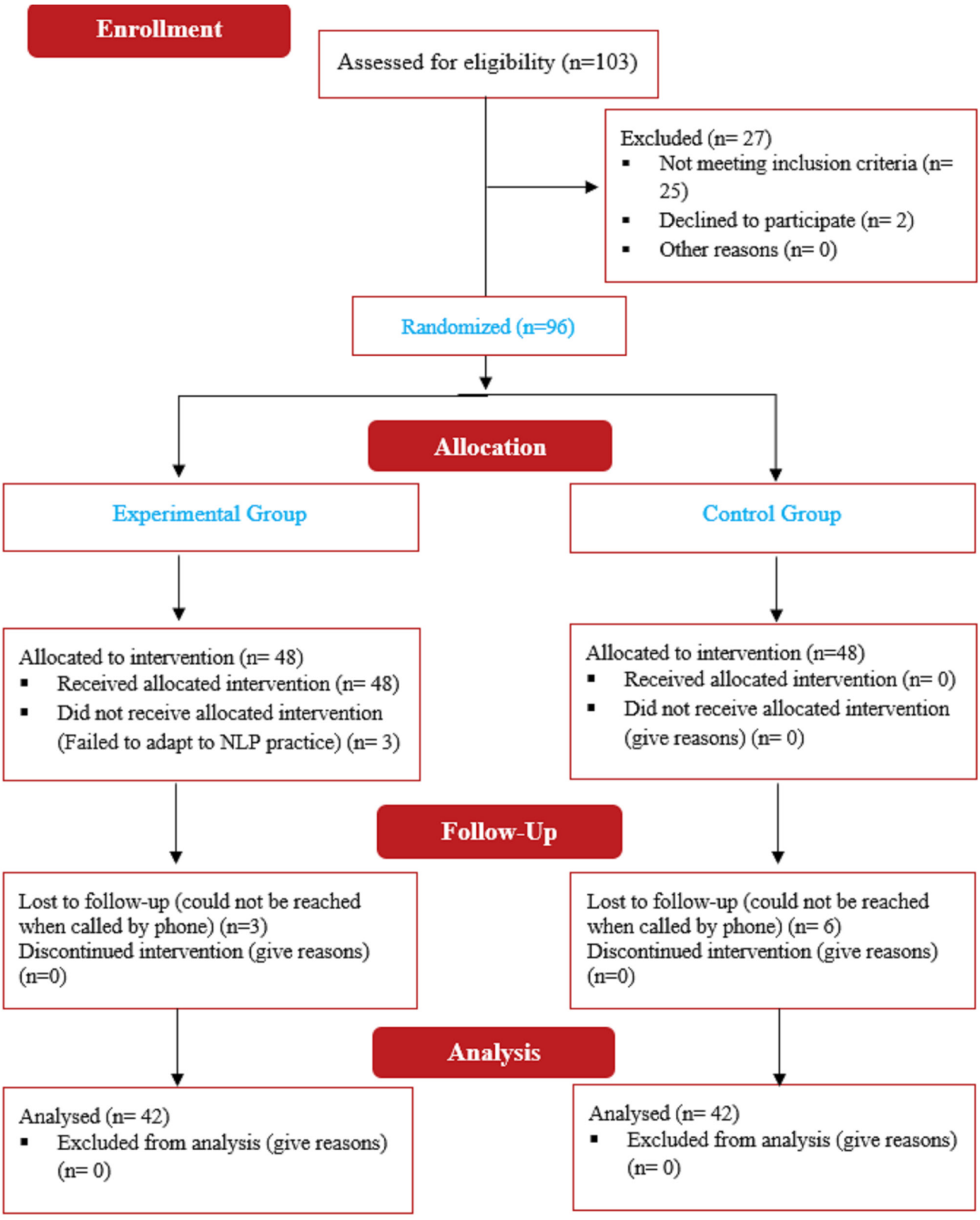
Figure 4. Distribution of DASS measurements over time in groups

Table 3. Intra-group and inter-group comparison of measurement scores

Variable	Group	Measurement	Mn ± sd	Intra-Group		Inter-Group		
				t value	p_1 value	F value	p2 value	η(Eta)
Depression	Experiment	Before	**11.6 ± 4.21**	**7.924**	**0.001****	84.341	0.001*	0.507
		After	7.81 ± 1.69					
	Control	Before	16.81 ± 4.41	-3.344	0.002**			
		After	17.31 ± 4.37					
Anxiety	Experiment	Before	12.67 ± 4.32	9.736	0.001**	26.704	0.001*	0.246
		After	8.24 ± 2.02					
	Control	Before	13.76 ± 3.31	-2.756	0.009**			
		After	14.21 ± 3.24					
Stress	Experiment	Before	14.69 ± 4.73	12.804	0.003**	168.627	0.001*	0.673
		After	9.17 ± 2.74					
	Control	Before	20.48 ± 2.57	-2.496	0.017**			
		After	20.50 ± 2.71					
DAS	Experiment	Before	38.95 ± 11.96	11.928	0.001**	125.096	0.001*	0.604
		After	25.21 ± 5.43					
	Control	Before	51.05 ± 7.53	-4.078	0.001**			
			52.57 ± 7.92					

Mn; mean. sd; standard deviation, p1 Value; intra-group comparison significance test result, p2 Value; ANOVA significance test result in repeated measures between groups, ; Eta value *p<0.05 There is a statistically significant difference between intra-group measurements. **p<0.05, there is a statistically significant difference between the groups

CONSORT 2010 Flow Diagram



DISCUSSION

Many psychological symptoms are seen after liver transplantation (1,2,4,5). These symptoms lead to many important problems such as treatment and drug non-compliance, insomnia, deterioration in the quality of life, and increase morbidity and mortality rates (3,4). In this study, it was determined that 54.8% of the experimental group patients and 33.3% of the control group patients have given the answer "nothing" to the question of "Is there a method you use to deal with depression, anxiety,

and stress in your daily life?" However, the management of psychological symptoms after liver transplantation is extremely important in terms of causing the above-mentioned problems (3–5). Nurses and other health professionals should monitor patients both physiologically and psychologically and develop and implement strategies to solve the problems they detect, as well as before and during liver transplantation (15,16). When the literature is examined, NLP draws attention among the strategies that can be developed for psychological symptoms (6–8,10,11).

Although patients with moderate and severe levels of depression, anxiety, and stress were included in the experimental and control groups in this study, when other studies are examined, it is seen that liver transplant patients experience significant depression, anxiety, and stress (2,5,22). In a study by Mendes et al., it was determined that more than half of the liver transplant patients experienced moderate anxiety, and close to 10 percent had high-level anxiety. It was found that nearly 40% of the same patient group experienced high levels of stress (5). In the study conducted by Yıldız, it was determined that more than half of the patients experienced state anxiety (2). In another study, it was determined that 57.8% of the patients who had a liver transplant one month ago and 75.0% of the patients who had one year passed were depressed (22).

The findings of this study show that NLP statistically significantly reduced the depression, anxiety, and stress scores of liver transplant patients and the total DASS-21 score ($p<0.05$). In the control group, it was determined that the mean DASS-21 score increased in the second measurement ($p<0.05$). When the literature was examined, no study was found that examined the effect of NLP on depression, anxiety, or stress levels in liver transplant patients, but it was seen that there were many studies conducted in different groups (23–25). In two studies conducted with individuals and students with posttraumatic stress disorder, it was found that NLP reduced both depression, anxiety, and stress levels; In another study conducted with athletes, it was seen that the DASS-21 scale was used and NLP reduced the stress level (23–25). In another study, it was determined that NLP application reduced social anxiety in individuals who applied to a counseling center (26). In this study, the sub-modality technique was used in the interviews made using NLP techniques. In this study, based on the principle that nurses use the patient's potential at the highest level while giving care, the principle of "people have the resources they need", one of the NLP assumptions, was used. NLP practices and goal-setting studies focused on the resources to be used to reach the desired state from the current situation, and awareness of their resources was created in patients (27–29). Thanks to NLP studies, patients found the courage and ability to cope with negative emotions, felt strong to reach the goals they set and decreased depression, anxiety, and stress. The fact that the DASS-21 average score of the control group increased as a result of the research is quite remarkable and shows the importance of developing strategies for depression, anxiety, and stress.

CONCLUSION

In this study, NLP intervention was found to reduce depression, anxiety, and stress in liver transplant patients. In line with these results, it can be recommended that nurses closely monitor their patients' symptoms such as depression, anxiety, and stress both during their hospitalization and after discharge. It may also be recommended to create an individualized care plan specific to each patient, to benefit from non-pharmacological strategies such as NLP in the management of some psychological symptoms, and/or to receive training on this subject. In addition, it may be recommended to conduct studies in different patient groups.

Contributions of the Study to Nursing

In this study, it was observed that the NLP sub-modality technique applied to patients who underwent liver transplantation and had moderate to high anxiety, depression, and stress levels contributed to reducing anxiety, depression, and stress levels to a tolerable level. The nurse aims to provide individualized care in the nursing process. In NLP techniques, the individual is evaluated with his own values and his view of the problem is made positive. NLP techniques are compatible with the nursing process with this aspect. Nurses learning NLP techniques and guiding patients on this issue will strengthen individualized care.

Strengths and limitations of the study

The study was carried out with patients who had liver transplantation in the same center living in many different cities of Turkey. Its strength is that it was carried out online with individuals with high anxiety during the pandemic process. Since it cannot be done face-to-face, the compliance of the patients is limited to the patient statement. This is the limitation of the research.

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

Ethical approval: *Institutional permission and ethics committee permission were obtained from the relevant university in order to conduct the research (Decision Number: 2021/2063). Verbal consent was obtained from the patients participating in the study.*

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Araştırma Makalesi / Research Article

Information, Attitudes and Behaviors of the Hospitalized Patients About Organ Donation

Hastanede Yatmakta olan Hastaların Organ Bağışına İlişkin Bilgi, Tutum ve Davranışları

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Abstract

Aim: The research was carried out to determine the knowledge, attitudes and behaviors of the patients who were hospitalized due to their chronic disease.
Material and Method: The descriptive study was completed with 47 patients hospitalized. The data were collected with a questionnaire and chi-square test was used.
Results: It was found that one fifth of the patients donated organs by applying to a health institution and four of them thought to donate organs. Three-fifths of patients who do not want to donate organs are determined to be contrary to their religious beliefs, half of them do not want to donate organs to a person whose religious belief is not the same. It was observed that married patients wanted to donate organs higher than singles.
Conclusion: It is thought that information about media support is needed in this regard, and information on family, aid and survival can be effective in changing the attitude towards organ donation.

Keywords: Organ donation, knowledge, attitude, behavior, chronic disease

Öz

Amaç: Araştırma, kronik hastalığı nedeniyle hastanede yatmakta olan hastaların organ bağışına ilişkin bilgi, tutum ve davranışlarını belirlemek amacıyla yapıldı.
Materyal ve Metot: Tanımlayıcı nitelikte olan araştırma, hastanede yatan 47 hasta ile tamamlandı. Veriler soru formu ile toplandı ve değerlendirmede ki-kare testi kullanıldı.
Bulgular: Hastaların beşte birinin bir sağlık kuruluşuna başvurarak organ bağışında bulunduğu, onda dördünün organ bağışlamayı düşündükleri bulundu. Organ bağışında bulunmayı istemeyen hastaların ise, beşte üçünün dini inançlarına ters olması, yarısının dini inancı kendisiyle aynı olmayan kişiye organ bağışlamak istememesi olarak belirlendi. Evli olan hastaların bekarlara göre daha yüksek oranda organ bağışında bulunmayı istedikleri görüldü.
Sonuç: Bu konuda medya desteği ile yapılacak bilgilendirmelere ihtiyaç duyulduğu, aile, yardım ve bir insanı hayatta tutma temalı bilgilendirmelerin organ bağış konusundaki tutumun değiştirilmesinde etkili olabileceği düşünülmektedir.

Anahtar Kelimeler : Organ bağışı, Bilgi, Tutum, Davranış, Kronik hastalık

INTRODUCTION

Organ transplantation; it is defined as the treatment of damaged organs that are not medically possible by replacing them with a healthy organ (1). Organ transplantation includes operations made from a cadaver or living creature. Its aim is to increase the quality of life and survival of patients with end-stage organ failure, and to reduce the rate of mortality and morbidity by treating the disease (2-8). On the other hand, organ donation includes giving and documenting the tissues and organs for the treatment of other patients, after the person's medical life ends with their free will while alive (3).

The fact that there is not enough organ donation for people in need around the world forms the basis of organ

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transplantation problems (3,9). While approximately 75% of organ transplants in Turkey are performed with organs taken from healthy people, more than 80% of transplants in European countries are performed with organs taken from cadavers (10,11). According to international organ and tissue transplant records, organ donation from cadavers in 2007 was 34.3 per million in Spain, 28.1 in Belgium, 25.3 in France, 20.9 in Italy, and 3.0 in Turkey. Live donor rates are 24.5 per million in Spain, 29.7 in Belgium, 9.7 in France, 6.0 in Italy and 6.9 in Turkey (12). According to the data of the Ministry of Health, the organ donation rate of patients with brain death was 1,703 in 2013, and 20,561 living donors donated organs in the same year (13). As a result, tissue and organ transplantation cannot be performed in many patients with chronic insufficiency in Turkey (14). When the obstacles to organ donation are examined, it is seen that the primary reasons are legal, religious, socioeconomic level, cultural and educational factors (14-16).

Studies on organ donation have been carried out in Turkey with different sample groups that determine knowledge, attitudes and behaviors (11-12,14-19). No study has been found that determines the knowledge, attitude and behavior of organ donation in the hospital treatment process due to chronic disease. The research was carried out to determine the knowledge, attitudes and behaviors of individuals with a chronic disease regarding organ donation during treatment in the hospital.

MATERIAL AND METHOD

Participants and Data Samples

The sample of the descriptive study consisted of 47 patients who were hospitalized under the Ministry of Health in a province of the Eastern Black Sea Region. This patient group was preferred in order to evaluate the perspective of individuals with a chronic disease on organ donation. At the time of collecting the research data from the hospital records, the information of 74 patients who were hospitalized was obtained. After giving information about the research, an appointment was made for the application of the questionnaire from the patients. In the study, it was tried to reach all of the patients who were hospitalized due to chronic diseases without making a sample selection. In the calculation for the number of samples made in the Openepi program, it was found to be 80 with a confidence interval of 90%.

The sample of the study; patient who is older than 18 years of age, conscious, with a history of chronic disease for at least one year and a hospital stay of more than three days were included. The study was completed with 47 patients by excluding 3 patients who could not be contacted and 24 patients who did not volunteer.

Data collection

The information about the patients was collected by face-to-face interview method using a questionnaire created by the researchers (3-5). This form was arranged by the researchers in a way to consist of three parts. In the first part; 17 questions including the introductory characteristics of the patients, their status of organ donation and the definition of organ donation, 25 questions questioning the information of the patients about their attitudes towards organ donation in the second part, and in the third part, 21 questioning the information about their organ donation status and the reasons for not wanting to donate organs.

Data analysis

The data obtained from the research were analyzed using the SPSS (Statistical Package for Social Sciences) 21.0 program. In the analysis of the tests, the significance level was taken as $p<0.05$, and number, percentage, mean and chi-square tests were used in the analysis of the data.

Ethical issues

Verbal consent was obtained from the face-to-face interviews with the patients in the study. While obtaining written permission from the relevant hospital, data collection forms and the names of the researchers were sent to the hospital.

RESULTS

In this study, information on the knowledge, attitudes and behaviors of patients hospitalized for chronic illness regarding organ donation, and the reasons for wanting or not wanting to donate were presented. 63.8% of the patients participating in the study were female and the mean age was 46.3±16.5 (min:18, max:84). The education level of 49% of the patients is primary school or lower, 70.2% of them are married and 72.3% of them have a medium income. 49% of the patients had hypertension, 25.5% had asthma, 19.2% had Chronic Obstructive Pulmonary Disease (COPD), and 6.3% had chronic kidney failure (CKD). It was determined that 2.1% of the patients applied to a health institution to donate their organs, and 40.4% of them were considering donating their organs. Reasons of patients who want to donate organs; It was found that they explained that being a relative of a patient waiting for an organ (94.7%), donating is a beneficial behavior (47.3%) and thinking that there may be a need for organs in the future (36.8%). It was observed that the rate of those who did not want to donate organs was 34%. The reasons of patients who do not want to donate organs are; It was observed that organ donation was contrary to his/her religious belief (56.2%), thinking his family would be upset if he donated his organs (43.7%), and not wanting to be touched after death (37.5%) (Table 1).

72.3% of the patients stated that the blood groups of the recipient and the donor should be the same, 53.2% of the patients stated that organs should not be taken from people who use alcohol, and 48.9% of them stated that verbal expression of organ donation was sufficient. 57.4% of the patients stated that they did not find the information about organ donation sufficient. 95.7% of the patients stated that they would like to donate organs to a family member, 72.3% stated that organs should be donated

while the person was alive, and 70.2% stated that they would not donate organs to a person who used alcohol (Table 2).

It was found that the state of considering organ donation of the patients did not show a significant difference according to age and gender (p>0.005). Educational status, income level and marital status were found to be statistically significant in terms of considering organ donation (p<0.005). It was determined that as the education level increased, the thought of organ donation increased and the married people were more likely to think about organ donation than the single ones (Table 3). It was found that patients who expressed their income level as 'moderate' thought about organ donation more than others (p<0.0001). It was determined that patients with chronic renal failure were more positive in considering organ donation compared to other diseases and the difference was significant (p<0.0001).

Table 1. Reasons of patients for wanting or not wanting to donate organs, N=47

	Number	%*
Requesting	**19**	**40.4**
"There are many patients waiting for organ donation"	18	94.7
"It is better to donate my organs than to rot"	9	47.3
"I may need an organ in the future"	7	36.8
"Helping patients gives me peace"	5	26.3
"Donating organs is a reward"	4	21.0
Not requesting	16	34.0
"Contrary to my religious belief"	9	56.2
"I think my family will be upset"	7	43.7
"I don't want your body to be touched after my death"	6	37.5
"I don't want the integrity of my body to be broken"	4	25.0
"My organs can be taken before my death"	3	18.7
"I don't know about the application centers for organ donation"	3	18.7
"I am afraid that I may feel pain during organ donation"	1	6.2
"I think I am not suitable for organ donation"	1	6.2**
Unstable	12	25.5

*One person gave more than one answer
**Hepatitis B patient

Table 2. Patients' knowledge, attitudes and behaviors regarding organ donation, N=47)

Knowledge	**Patients' thoughts**					
	Yes		**No**		**Not opinion**	
	n	**%***	**N**	**%***	**N**	**%***
Donor and recipient blood groups must be the same	34	72.3	4	8.5	9	19.1
Organs should not be taken from a person who uses alcohol.	25	53.2	16	34.0	6	12.8
Oral expression of organ donation is sufficient.	23	48.9	17	36.2	7	14.9
Organ taken from cadaver gives pain to cadaver	15	31.9	30	63.8	2	4.3
Anyone can receive organs from anyone	13	27.7	29	61.7	5	10.6
Organs can be given to someone else for money	9	19.1	33	70.2	5	10.6
Patients receiving chemotherapy can donate organs	8	17.0	32	68.1	7	14.9
Attitudes and Behaviors	**Yes**		**No**		**Unstable**	
	n	**%***	**N**	**%***	**N**	**%***
"I do not donate organs to a person who uses alcohol"	33	70.2	12	25.5	2	4.3
"I do not donate organs to a person whose religious belief is not the same as mine"	22	46.8	24	51.1	1	2.1
"I do not take an organ from a person whose religious belief is not the same as mine"	20	42.6	26	55.3	1	2.1
"I am against organ donation because of my religious belief"	13	27.7	33	70.2	1	2.1

*One person gave more than one answer

Table 3. Distribution of patients considering organ donation according to introductory characteristics, N=47

Sociodemographic Characteristics	Consideration of Organ Donation								p
	Thinking		Not thinking		Unstable		Total		
	n	%	n	%	n	%	n	%	
Age									
18-41	9	47.4	2	12.5	3	25.0	14	29.8	
42-58	7	36.8	6	37.5	6	50.0	19	40.4	0.58
59-84	3	15.8	8	50.0	3	25.0	14	29.8	
Sex									
Female	8	57.9	14	87.5	8	33.3	30	63.8	0.05
Male	11	42.1	2	12.5	4	66.7	17	36.2	
Education level									
Illiterate	-	-	8	50.0	-	-	**8**	**17.0**	
Primary school	10	52.6	1	6.3	5	41.7	15	34.1	**0.02**
Middle school and above	9	47.4	7	43.8	7	58.3	23	48.9	
Income Level (own statements)									
Good	5	26.3	-	-	2	16.7	7	14.9	
Middle	11	57.9	14	87.5	9	75.0	34	72.3	**<0.0001**
Bad	3	15.8	2	12.5	1	8.3	6	12.8	
Marital status									
Married	11	57.9	12	75.0	10	83.3	33	70.2	**0.006**
Single	8	42.1	4	25.0	2	16.7	14	29.8	
Chronic Disease									
Hypertension	1	5.2	4	25.0	2	16.7	7	14.9	
Asthma	3	15.8	-	-	-	-	3	6.4	**<0.0001**
COPD*	4	21.1	9	56.2	3	25.0	16	34.0	
CRF**	11	57.9	3	18.8	7	58.3	21	44.7	

* Chronic obstructive pulmonary disease, ** Chronic renal failure

DISCUSSION

It is seen that there is not enough organ donation in Turkey and cadaveric transplants are not at the desired level compared to European countries. It is seen that information meetings on organ donation are held and events are organized throughout the country during the organ donation week. Despite all these practices, it is known that not enough donations can be made and the level of knowledge about organ donation in the society is not desired. In this context, the research determines the knowledge, attitudes and behaviors of patients who are hospitalized with chronic diseases regarding organ donation.

In the study, it was determined that one fifth of the patients applied to a health institution and donated organs. In the study Topbas et al., conducted with a sample of health professionals in Trabzon, the rate of having an organ donation card was 2.2% (16), while in the study conducted by Okka and Demireli in Konya it was 3.6% (16), Göz et al. it was found to be 3.1% in the study (11). In a study Efil et al., conducted in Afyon, 3.3% of the people who had an organ donation card (5), in Baykan et al. study, it was found to be 2.9% (6). All studies conducted in different sample groups and regions of our country, it is seen that the rates of organ donation are similar.

In the study, it was determined that four out of ten patients were considering organ donation. In the study Topbas et al., with health professionals, 62.8% (17), Özer et al. study, 64.2% (16) of the students, it was determined that 60.9% of the nurses were found by Göz et al. study, wanted to donate organs (11). In the study Özmen et al, found that 36.1% of the students wanted to donate organs (15). In Baykan et al. study, conducted in Kayseri (6), 34.0% of the students preferred to donate their organs, Yaşar et al. (10) found that 34.9% of the students wanted to donate their organs. When the results of the research were evaluated, it was determined that the rate of considering

organ donation was low in studies conducted with young samples, but in studies conducted with other sample groups, they thought of organ donation at a similar rate as our study.

In the study, it was determined that nine out of ten patients considering organ donation were effective because there were many patients waiting for organ donation. Ozer et al. were found that 43.4% of the students' reasons for wanting to donate organs were to restore health to sick individuals and save the lives of others (16). In the study Göz et al., it was determined that 46.1% of nurses wanted to help patients, 28.2% of them had a large number of patients who needed organ donation, and 23.1% of them wanted to donate organs because they thought they might need an organ (11). In the study Özmen et al., it was determined that 82.2% of the students wanted organ donation for 'service to humanity' and 57.9% for the reasons of 'making the organs that will decay and work' (15). Efil et al. found that 85.2% of the participants had the idea of "saving and improving life" (5). When the results of the research are evaluated, it is seen that there is a desire to donate on the grounds of helping individuals and restoring their health.

It was determined that three-fifths of the patients who did not want to donate organs did not want to donate on the grounds that they were against their religious beliefs, half of them would not donate organs to a person whose religious belief was not the same as theirs, two-fifths would not receive organs from a person whose religious belief was not the same as theirs, and one-fourth of them did not want to have their body integrity deteriorated. In study with health professionals, 21.6% of them were due to their religious beliefs (17), Özer et al. 16.1% of the students did not want to donate organs because they did not want their body to be destroyed, were afraid, and did not feel ready (16). In the study Eye et al., it was found that 71.5% of the nurses did not want to upset their families, 21.4% were afraid that their organs would be removed before they died, and 7.1% did not want to donate their organs due to their religious beliefs (11). In the study Ozmen et al., it was found that 41.2% of the students who did not want to donate organs were 'not comfortable with their conscience' and 38.2% did not think of donating because they did not want their body integrity to be impaired. In the same study, 51.7% of the students thought that organ donation was religiously appropriate (15). In the study Efil et al., it was determined that 20.9% of the participants thought that their religious belief prevented organ donation, and 36.1% of them did not want to donate organs because they did not want to have their bodies intervened after their death (5). In the study Baykan et al., the primary reservations of the students who do not want to donate organs are that they do not want their body integrity to be damaged (5.8%), fear of having their organs removed before they die completely (5.8%), and thinking that it is not appropriate in terms of religion (5.8%). In the study Yasar et al., it was found that 30.2% of the students did not want their body integrity to be damaged, and 16.3% did not want to donate organs for fear of having their organs removed before they died (10). In the study conducted by Aktaş and Karabulut in Giresun, it was found that 4.7% of the students stated that their religious belief was against organ donation (19). When the results of the research are evaluated, it is seen that religious belief is the most decisive reason affecting the attitude towards organ donation, and the lack of knowledge on this subject affects the behavior.

In order for organ donation to take place, the organ donor must have given prior written consent. In some European countries (Austria, Belgium, Portugal, France) laws accept as a donor candidate anyone who has not documented otherwise while alive, except for judicial cases. In this system, permission is not required from the family or relatives of the donor candidate (20). How to obtain permission in the Law No. 2238 in Turkey 'In order to obtain organs and tissues from a person who is over 18 years of age, the donor's written and signed pre-given in the presence of at least two witnesses, consciously and without influence, or verbally given before at least two witnesses. written and signed or verbally declared and signed in front of at least two witnesses must be approved by a physician. According to the law, even if the person has donated organs (although they do not have the legal right to object), organs and tissues can be obtained with the permission of one of their first-degree relatives who are with them at the time of death (21). Even if the deceased did not donate organs while alive, a positive opinion on this matter may facilitate the family's permission for organ donation (8). It was determined that four-fifths of the patients in the study stated that "the person should donate their organs while alive", and two-fifths of them said "verbal expression of organ donation is sufficient". Kara et al. in his study, this rate was found to be 45.1% (8).

More than four-fifths of the patients in the study could donate an organ to a family member if necessary. In the study Ozer et al., it was found that 96.2% of the students stated that they could donate an organ to a family member if necessary (14). In the study conducted by Baykan et al., it was determined that 81.2% of the students would donate to one of their families or close relatives if organ-tissue transplantation was necessary (6). When the results of the research are evaluated, it is seen that the rates are similar and it is an effective variable in considering organ donation if the family needs it.

CONCLUSION

As a result, it is seen that the knowledge levels of the group with chronic disease participating in other studies conducted in Turkey are similar to those of organ donation, and the rate of willingness to donate organs is low. The lack of information on organ donation makes us think that it is necessary to inform especially about religious issues. It can be said that there is a need for information to be made with the support of the media on this subject, and that information on family, aid and keeping people alive can be effective in attitudes and behaviors about donation. Since it has been determined that the greatest resistance

to organ donation is experienced in religious belief, it is anticipated that information on this subject may cause desired changes in donation. It can be recommended to carry out studies based on accurate information on religious issues related to organ donation.

Limitation

This research is limited to chronic patients who were hospitalized in a state hospital in a province during the study period. More general information on organ donation of chronic patients in Turkey can be obtained by conducting similar studies in different provinces. It is thought that awareness of organ donation can be increased by conducting similar studies on this subject.

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MEDICAL RECORDS-International Medical Journal

Olgu Sunumu/ Case Report

Progressive Supranuclear Palsy Following as Major Depressive Disorder: A Case Report

Majör Depresif Bozukluk Olarak Takip Edilen Progresif Supranükleer Palsi: Bir Olgu Sunumu

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Abstract

Progressive Supranuclear Palsy (PSP) is a rare neurodegenerative disease that is classified among Parkinson plus syndromes, manifesting itself with behavioral, cognitive and emotional symptoms as well as parkinsonian symptoms such as postural instability, ophthalmoplegia, bradykinesia, rigidity affecting the brain stem, basal ganglia and cerebellum. Although there is sufficient information about the pathological process and clinical presentation of PSP, there is no valid biomarker for diagnosis, clinical findings and neuroimaging are very important in diagnosis, patients often get misdiagnosis at their first application. It has been reported that psychiatric symptoms are common in these individuals due to the involvement of the frontal-subcortical circuits, and therefore patients can get psychiatric diagnoses in the early period. We aimed to present a 72-year-old female patient who was followed up with the diagnosis of major depressive disorder in various centers for about 4 years, who did not benefit from psychiatric treatment, and diagnosed with PSP eventually. We also aimed to emphasize that importance of considering neurodegenerative diseases in differential diagnosis in patients whose depressive symptoms begin at an advanced age, are resistant to treatment and have atypical symptoms such as the presence of accompanying neurological findings, and psychiatric symptoms may be the first symptom of neurodegenerative diseases.

Keywords: Depression, neurodegenerative diseases, Progressive supranuclear palsy

Öz

Progresif Supranükleer Palsi (PSP), Parkinson plus sendromları arasında sınıflandırılan, davranışsal, bilişsel ve duygusal semptomların yanı sıra postural instabilite, oftalmopleji, bradikinezi,rijidite gibi parkinsonyen semptomlarla kendini gösteren beyin sapını, bazal ganglionları ve serebellumu etkileyen nadir bir nörodejeneratif hastalıktır. PSP'nin patolojik süreci ve klinik görünümü hakkında yeterli bilgi olmasına rağmen, tanı için geçerli bir biyobelirteç bulunmamakta, klinik bulgular ve nörogörüntüleme tanıda çok önemli yer edinmekte, hastalar ilk başvurularında sıklıkla yanlış tanı almaktadır. Bu kişilerde frontal subkortikal devrelerin etkilenmesi nedeniyle psikiyatrik belirtilerin yaygın olduğu ve bu nedenle hastaların erken dönemde psikiyatrik tanı alabileceği bildirilmiştir. Burada yaklaşık 4 yıldır çeşitli merkezlerde major depresif bozukluk tanısıyla takipli, psikiyatrik tedaviden yarar görmeyen , değerlendirmeler sonucunda PSP tanısı alan 72 yaşında kadın olgunun sunulması amaçlanmış olup, depresif semptomları ileri yaşta başlayan, tedaviye dirençli ve eşlik eden nörolojik bulguların varlığı gibi atipik belirtileri olan hastalarda ayırıcı tanıda nörodejeneratif hastalıkların düşünülmesinin önemi, psikiyatrik belirtilerin nörodejeneratif hastalıklarda ilk belirti olabileceği vurgulanmak istenmiştir.

Anahtar Kelimeler: Depresyon, nörodejeneratif hastalıklar, progresif supranükleer palsi

INTRODUCTION

Progressive supranuclear palsy (PSP) is a rare neurodegenerative disease affecting the brainstem, basal ganglia, and cerebellum. The age of onset of the disease is often between 60 and 65 years, and its frequency does not differ between genders (1). PSP is a disorder manifested by postural instability, ophthalmoplegia, bradykinesia, rigidity as well as behavioral, cognitive and emotional symptoms. Postural instability and falls are the most common complaints. Patients' gait is slow and unsteady. Bradykinesia and rigidity are symmetrical. Dysarthria and dysphagia can be seen due to pseudobulbar paralysis. Frontal lobe symptoms occur at the early stages (2). It has been reported that psychiatric symptoms are common in these individuals due to the involvement of the frontal-subcortical circuits, and therefore patients can get psychiatric diagnoses in the

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early period (3). Among the neuropsychiatric symptoms of PSP; apathy, depression, sleep disorders, personality changes, disinhibition, and cognitive disorders can be listed (4). In this study, we aimed to share the clinical features of a patient who had been followed up with depression for a long time and was diagnosed with PSP.

CASE REPORT

72-year-old female, unemployed and primary school graduate patient applied to the psychiatry clinic with complaints of unwillingness, despair, inability to enjoy life, not wanting to leave the house, occasional crying attacks, inability to fall asleep and inability to continue to sleep, which started about four years ago and continued increasingly. The patient applied to various outpatient psychiatry clinics and was diagnosed with depression and Fluoxetine and Trazodone were started. The patient used these medications regularly for 1 year but did not get any response. The patient applied to other clinics due to depression and she was started on Escitalopram, Venlafaxine and Quetiapine due to depression diagnosis and Donepezil due to memory problems, despite not being diagnosed with dementia. The history of patient revealed that she had fallen four times in the last three years and was conscious at the time of the fall and she had balance problems while walking. She had a history of hypertension, and major depressive disorder for 4 years, without a history of family psychiatric or substance abuse. In the psychiatric examination; depressive mood, anhedonia, avolition, difficulty in falling asleep, decreased speech fluency, psychomotor retardation, attention and memory impairment were found. In the neurological examination; hypomimia, hypophonia, bilateral bradykinesia, bilateral rigidity, postural instability, bilateral supranuclear gaze paralysis and slowed saccadic eye movements were detected. Laboratory tests of the patient were found to be normal, the patient got 24/30 points from the Standardized Mini Mental Test. Cranial MRI revealed midbrain-mesencephalon atrophy. Hummingbird appearance was observed in sagittal section (Figure-1).

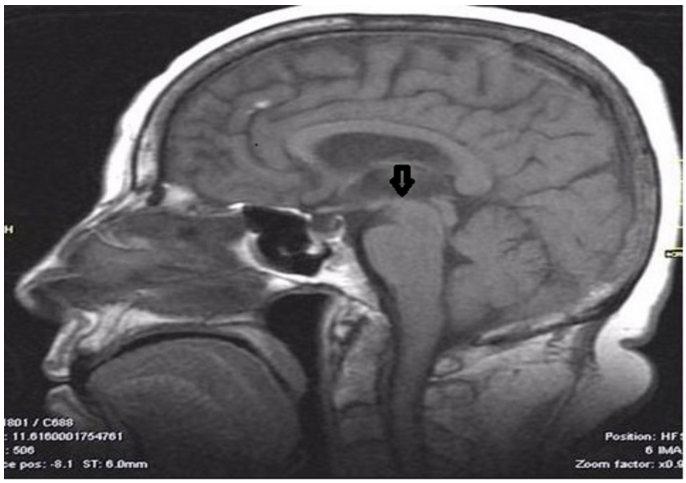

Figure 1. Hummingbird sign; Mid-sagittal T1-weighted sequence MRI brain showing atrophy of the midbrain tegmentum, with a relatively preserved pons, decreased midbrain to pons ratio with a superior aspect concavity, resembling the head and body, respectively, of a hummingbird

After the current clinical picture and imaging tests, the patient was referred to neurology with the prediagnosis of probable PSP, diagnosis was made according to the National Institute of Neurological Disorders and Stroke and Society for Progressive Supranuclear Palsy (NINDS-SPSP) diagnostic criteria and then L-Dopa was started at 500 mg / day. Her psychiatric treatment was arranged as Sertraline 100 mg / day and Zopiclone 7.5 mg / day. The patient who responded poorly to L-Dopa treatment had a partial regression in her depressive mood and insomnia during the follow-up period, and her response status was determined by clinical evaluation and a 25% decrease in the Hamilton Depression Scale score compared to the baseline score. The patient's follow-up continues in neurology and psychiatry outpatient clinics. Written consent was obtained from the patient for publishing case report.

DISCUSSION

Treatment-resistant depression and sleep disorder started about 4 years before the diagnosis of PSP. Although there is a high possibility of depression in patients with PSP in the following years, there are also cases that present with psychiatric symptoms and are later diagnosed with PSP (5). It has been stated that psychiatric symptoms are quite common in these individuals due to the involvement of the frontal-subcortical circuits, and therefore patients can also be diagnosed with psychiatric disorders in the early period (3). Although many neurobiological models related to the frontal lobe and its functions have been proposed, the fronto-subcortical loops start from the cortex and follow a path from the cortex to the striatum, globus pallidum and dorso-medial thalamus. It is thought that there are five cycles following the mentioned path starting from the frontal cortex, two of them are related to eye movements and the other three are closely related to the behavioral dimension. These 3 pathways closely related to the behavioral dimension are the anterior cingulate loop, orbito-frontal loop and the dorsolateral prefrontal loop, and the damage in the pathway is clearly reflected in the clinic (6). Supranuclear gaze paralysis diagnosed in the neurological examination of our patient was indicating fronto-subcortical circuit dysfunction which is responsible from eye movements. The loss of energy and motivation, depressive mood and apathy detected during the psychiatric examination attributed to involvement of the anterior cingulate loop. Difficulty in focusing and maintaining attention, cognitive impairment, and decrease in speech fluency occurred as a result of the involvement of the dorsolateral prefrontal cycle which is associated with executive functions.In Parkinson's disease and Huntington's disease, the involvement of subcortical pathways is asserted to be responsible from the dementia accompanying movement disorders (7). In our case, the findings and neuroimaging results support the diagnosis of progressive supranuclear palsy. The hummingbird sign image is diagnostic for the diagnosis of PSP and has 100% of sensitivity (8). It has

been reported that falls usually occur within three years after the onset of the disease, and MRI findings correlate with the stage of the disease (9). Apathy was reported to be the most common neuropsychiatric symptom in PSP and it is difficult to distinguish it from depression. It has been stated that apathetic individuals generally describe their own moods as happy and pleasant unlike individuals with depression, and depression and apathy may coexist very often. It has been reported that apathy can be treated with antidepressant treatment when depression accompanies apathy (10,11). In the literature, it has been stated that PSP does not respond or respond poorly to L-Dopa treatment, and insomnia is a common symptom in PSP, patients have prolonged sleep latencies and have difficulty in maintaining sleep at the same time, REM sleep is shortened while the rate of sleep-related movement disorders and sleep apnea is increased (12,13). It has been stated that Zolpidem can positively contribute to motor functions and supranuclear gaze paralysis in PSP, and it has positive contributions to sleep disorders in Parkinson's patients. Since Zolpidem is not available in our country, Zopiclone, which is another nonbenzodiazepine GABA agonist, was started (14,15).

CONCLUSION

Considering the patient's clinic and neuroimaging findings, we thought that PSP started years ago with psychiatric presentation since depression symptoms and insomnia did not respond to psychiatric treatment for many years and patient's parkinsonism symptoms didn't respond to L-Dopa treatment. Psychiatrists should be more careful in terms of neurodegenerative diseases in patients with atypical symptoms such as the onset of depressive symptoms at an advanced age, resistance to treatment and the presence of accompanying neurological findings, as in our patient. It should also be kept in mind that neurodegenerative diseases may also present with psychiatric symptoms and that depression and insomnia may be the first symptom of neurodegenerative diseases.

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MEDICAL RECORDS-International Medical Journal

Olgu Sunumu/ Case Report

Psychotic Depression Related to Hashimoto's Thyroiditis: A Case Report

Hashimoto Tiroiditine Bağlı Psikotik Özellikli Depresyon: Bir Olgu Sunumu

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Abstract

Hashimoto's thyroiditis can lead to depression, anxiety disorder, and sleep problems. However, this autoimmune disease has been reported to be less related to psychotic depression. The case applied to our outpatient clinic with introversion, anhedonia, and guilt thoughts. The patient was admitted to our clinic with a preliminary diagnosis of psychotic depression. TSH value was found to be high in the patient's hormone analysis. Afterward, treatment was started with the diagnosis of Hashimoto's thyroiditis according to the patient's anti-TPO value and thyroid USG results. After levothyroxine treatment, the patient's depression scores, TSH, and anti-TPO values decreased.

Keywords: Hashimato's thyroiditis, psychotic depression, hypothyroidism

Öz

Hashimoto tiroiditi depresyona, anksiyete bozukluğuna ve uyku sorunlarına yol açabilir. Bununla birlikte, bu otoimmün hastalığın psikotik özellikli depresyonla daha az ilişkili olduğu bildirilmiştir. Olgu içe dönüklük, zevk alamama ve suçluluk düşünceleri ile polikliniğimize başvurdu. Hasta psikotik özellikli depresyon ön tanısı ile kliniğimize yatırıldı. Hastanın hormon analizinde TSH değeri yüksek bulundu. Ardından hastanın anti-TPO değeri ve tiroid USG sonuçlarına göre Hashimoto tiroiditi tanısı ile tedaviye başlandı. Levotiroksin tedavisi sonrası hastanın depresyon skorları, TSH ve anti-TPO değerleri düştü.

Anahtar Kelimeler: Hashimoto tiroiditi, psikotik özellikli depresyon, hipotiroidi

INTRODUCTION

Hashimoto's Thyroiditis (HT) is an organ-specific autoimmune disease characterized by lymphocytic infiltration in the thyroid gland. HT is the most common cause of hypothyroidism, but it may rarely be present with hyperthyroidism. Thyroid-stimulating hormone (TSH) level increases in patients with HT-induced hypothyroidism and sub-clinical hypothyroidism. Higher levels of anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin antibodies in serum are more sensitive to HT diagnosis (1).

HT can cause symptoms of many psychiatric diseases. The most common psychiatric symptoms of HT are psychomotor retardation, depressive mood, anxiety, and sleep disturbances. Additionally, psychotic and manic/hypomanic symptoms are relatively less common in patients with HT (2).

The relationship between HT and psychiatric diseases has been mentioned in many studies. In case reports in the literature, acute psychosis, affective psychosis, and epileptic seizures have been reported together with HT encephalopathy (3-5). In a study, thyroid autoantibodies were found to be higher in bipolar disorder (6). Acute manic episodes have been described with HT (7).

While depression in HT patients with subclinical hypothyroidism is frequently encountered in the literatüre (8,12), information on psychotic depression is limited in HT patients with subclinical hypothyroidism.

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The authors aimed to report psychotic depression in an HT patient with subclinical hypothyroidism.

CASE REPORT

A 37-year-old female patient was referred to the psychiatric outpatient clinic with anhedonia, social isolation, crying, guilty thoughts, and sleep disturbances. She was married for ten years and had two children. She had no psychiatric disease or treatment history in the past. She was diagnosed with HT about ten years. She was irregularly using levothyroxine sodium 75 mcg per day. Her husband reported that she was depressed and anhedonic last month. At the same time, she had crying episodes and was talking to herself. According to the mental state examination of the patient, she had poor self-care and depressive affect. Her eye contact was decreased, and she was reluctant to communicate along with the examination. The patient had guilty delusion and described auditory hallucination. The psychotic symptoms were consistent with the patient's mood.

Beck Depression Inventory (BDI) and Brief Psychiatric Rating Scale (BPRS) scores of the patient were 22 and 45, respectively. According to the results of laboratory tests, the TSH level of the patient was 18.54 uIU/MI. fT3 and fT4 were normal (respectively 1.92 and 0.67). The Anti-TPO level of the patient was 769.7 IU/mL. There were no other abnormal laboratory findings, including hemogram, CRP, sedimentation, and electrolytes. Ultrasound scan of thyroid gland showed diffuse heterogeneity in the parenchyma. We did hospitalize the patient in the psychiatry inpatient unit and internal medicine consultation for the patient. After the patient was hospitalized in the psychiatry inpatient unit, venlafaxine 75 mg, levothyroxine 125 mcg, and olanzapine 10 mg were administered per day. With this treatment, the psychotic and depressive symptoms of the patient were decreased two weeks later. BDI and BPRS scores of the patient were 10 and 19 two weeks later. At the end of two weeks, TSH and anti-TPO levels of the patient were declined 0.91 uIU/MI and 609.5, respectively.

At the psychiatric examination one month later, the patient's psychotic symptoms had disappeared. The patient was able to make eye contact during the psychiatric examination and was willing to be interviewed. The patient had a decrease in guilt thoughts. There was an improvement in the patient's sleep and appetite. The patient's self-care and depressive affect also improved. Venlafaxine 75 mg and olanzapine 10 mg treatment was continued. The patient continued to receive levothyroxine 125 mcg treatment from the internal medicine outpatient clinic. During the 6-month follow-up period, the patient did not have any active psychiatric complaints. The patient's olanzapine treatment was gradually tapered and discontinued. The patient's venlafaxine treatment was tapered and stopped at the end of 1 year. The patient did not have any additional psychiatric complaints during this period.

DISCUSSION

It has been reported that disarrays in the hypothalamus-pituitary-thyroid (HPT) axis may play a role in the pathogenesis of psychiatric diseases. It is thought that in depression, the response of thyroid-releasing hormone (TRH) to TSH decreases, TRH levels increase in the cerebrospinal fluid and the blood level of antithyroid antibodies increases. Therefore, hypofunction of the thyroid gland located in HPT axis can lead to depression and cognitive disorders (9). However, the association of psychosis with thyroid dysfunction is less frequently reported (10). A scarce psychotic picture known as myxedema psychosis in the literature can be seen together with HT (11).

HT can be seen together with autoimmune diseases such as rheumatoid arthritis, vitiligo, alopecia areata, Type 1 diabetes, autoimmune liver diseases, ankylosing spondylitis, and ulcerative colitis. HT usually manifests weakness, fatigue, cold intolerance, decreased sweating, hoarseness, edema, amenorrhea, weight gain, forgetfulness, and constipation. In untreated cases, depressive complaints can be added to the table (12).

Many studies and case presentations have reported that HT can accompany depressive symptoms (13-16). Krysiak et al. reported depressive symptoms at a rate of 59% in HT patients with subclinical hypothyroidism and 37% in euthyroid HT patients in their study (17). On the other hand, psychosis is rarely seen in patients with HT due to hypothyroidism. However, there is limited information about psychotic depression that is related to HT. This case report has shown that HT can accompany psychotic depression. The case report has indicated that clinicians should be alert for different manifestations of HT.

Being female and middle-aged is considered a risk factor for the development of hypothyroidism (7). In this case, the rapid disappearance of psychotic and depressive symptoms with levothyroxine treatment and the acute onset of the psychiatric complaints suggested that HT may have caused this condition. Anti-TPO value and psychiatric symptom severity decreased aligned with levothyroxine treatment. The fact that the patient did not have a history of psychiatric illness and did not describe psychosocial stressors increased our evidence that the psychiatric complaints of our case were associated with HT. In addition, no depressive, manic, or psychotic episodes were detected in our patient's 1-year follow-up. Our case was a known HT patient, and therefore thyroid hormone replacement therapy was started early. Routine testing of thyroid hormones in patients with psychotic or affective symptoms with risk factors can improve treatment outcomes.

CONCLUSION

Although HT is a disease that is followed up in endocrinology outpatient clinics, it can present with different manifestations due to the variety of

neuropsychiatric symptoms it causes. It is clear that the application of thyroid function tests in acute psychotic symptoms, as in this case, has clinically significant results.

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