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Dear Readers,

We are pleased to share the August issue of our journal with you. In this issue, we present five articles and one case report.

Hypertension, a chronic and major public health concern, remains a subject of intensive interest among all medical professionals. Indeed, every branch of medicine intersects with hypertension in some aspect. However how does the management of anxiety influence outcomes in hypertensive patients? Vatansever and colleagues investigate the impact of adding an SSRI to antihypertensive therapy in patients with uncontrolled blood pressure and comorbid anxiety. Their results once again highlight the importance of considering psychological factors in the management of hypertension.

Could psychiatric symptoms be more prevalent among individuals attending smoking cessation clinics? Özanat and colleagues explore this question. This original study may serve as a basis for future research on how psychiatric symptoms could influence both the success of smoking cessation and adherence to treatment.

Anxiety is a common condition during the antepartum period in pregnant women. In this issue, we also feature the study by Ertaş and Çelik, who demonstrate that listening to Turkish classical music during the third trimester may serve as a safe and effective method for reducing anxiety and stress in primiparous pregnant women. We consider this an interesting contribution.

Two further articles in this issue address, respectively, the relationship between cardiovascular risk knowledge and actual risk, and the effects of COVID-19 on the epidemiological trends of gastric adenovirus and rotavirus infections in children. Both studies report noteworthy findings.

In addition, a case report on delayed puberty is also included in this issue.

I extend my best wishes for an enjoyable reading experience to all our readers, and I would like to thank all the authors, reviewers, and editors who contributed to this issue.

We look forward to meeting you again in the December issue.

M. Reşat DABAK, M.D., Prof.

Editor-in-Chief

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The Relationship between Framingham Risk Score and Cardiovascular Disease Knowledge Level in Adult **Individuals**

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ABSTRACT

Objectives: This study aims to calculate Framingham risk levels in patients aged 40 and above and to examine their relationship with the cardiovascular disease risk factors knowledge level (CARRF-KL) scale.

 $\textbf{Methods:} \ This\ cross-sectional\ and\ analytical\ study\ was\ conducted\ with\ 220\ voluntary\ participants\ aged\ 40-79$ who visited the family medicine outpatient clinic. Participants' knowledge levels were assessed using the CAR-RF-KL, while their 10-year cardiovascular disease (CVD) risk was evaluated using the Framingham risk score. Participants diagnosed with diabetes or CVD were classified as high-risk.

Results: A total of 220 participants were enrolled in the study. The mean age of the participants was 56.8±9.6 years, with 142 (64.5%) being female and 121 (55.0%) having an educational level of middle school or below. The median CARRF-KL score was 23.0 (12.0-28.0). According to the Framingham risk classification, 58 (26.4%) of participants were in the low-risk group, 36 (16.3%) in the moderate-risk group, and 126 (57.3%) in the highrisk group. A significant difference was found between CARRF-KL scale scores according to Framingham risk levels (p=0.031).

Conclusion: The present findings indicate that knowledge of disease risks alone is insufficient for adopting preventive measures or lifestyle changes. Therefore, it is essential to educate and motivate patients in primary healthcare settings regarding the importance of a healthy lifestyle in reducing CVD risk.

Keywords: Awareness, cardiovascular diseases, heart disease risk factors

INTRODUCTION

Cardiovascular diseases (CVD) refer to conditions affecting the heart and/or blood vessels and are among the leading causes of mortality and morbidity both globally and in Türkiye.[1] According to data from the World Health Organization, CVD ranks first among deaths caused by non-communicable diseases, accounting for approximately 18 million deaths annually. [2] Similarly, in Türkiye, CVD was reported as the leading cause of death according to 2019 data from the Turkish Statistical Institute.

The risk of developing CVD can be mitigated by evaluating individuals based on risk factors and addressing modifiable ones.[3] CVD is associated with risk factors, such as smoking, excessive alcohol consumption, high salt intake, obesity, hypertension, diabetes, and physical inactivity. Modifying these lifestyle habits reduces mortality and hospitalization rates while improving quality of life.



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The development of CVD is typically attributed to the interaction of multiple risk factors. These factors' clustering and combined effects in determining atherosclerotic vascular risk in CVD have been well established. Guidelines recommend applying risk assessment tools for CVD prevention, as they facilitate the early identification of individuals at high risk for CVD. In this context, a comprehensive risk factor assessment is crucial for preventive strategies and treatment planning.

Researchers have developed multivariable risk prediction tools that synthesize vascular risk factor data to estimate absolute CVD risk in individual patients. These scoring systems use multiple risk factor equations to estimate an individual's likelihood of developing cardiovascular events. Numerous risk calculation models are available today, with the Framingham risk score being the oldest and most widely used.

The Framingham score evaluates nine risk factors: Gender, age, systolic blood pressure, use of antihypertensive treatment, the level of total cholesterol and high-density lipoprotein-cholesterol, smoking status, presence of diabetes, and a history of CVD (e.g., coronary artery disease, peripheral artery disease, or stroke). Using this model, the 10-year cardiovascular risk score is calculated, and patients are classified into three groups: Low, moderate, and high risk.

Adequate knowledge about CVD risk is a crucial pre-requisite for making informed decisions about disease prevention. Several scales have been developed to assess knowledge levels regarding CVD risk factors. One such instrument is the CVD risk factors knowledge level (CARRF-KL) scale, developed by Arıkan et al., 2009.

This study aims to calculate Framingham risk levels in patients aged 40 and above and to examine their relationship with the CARRF-KL scale.

METHOD

The study population comprised patients aged 40 years and older who visited the family medicine outpatient clinic of a training and research hospital with various complaints between January 2022 and March 2022 and met the inclusion criteria. It was estimated that approximately 800 patients visited the family medicine outpatient clinic during these 2 months. Based on the assumption that 400 patients were 40 or older, the required sample size was calculated as 196 cases to achieve 80% power at an α =0.05 significance level. However, the final sample size was 220 to account for potential dropouts.

Participants included in the study were individuals aged 40–79 who provided informed consent, had no communication problems or cognitive impairments, and had undergone blood tests (lipid panel) within the past 3 months, as recorded in the hospital's automation system.

Each participant was administered a sociodemographic questionnaire prepared by the researchers and the CARRF-KL scale, a validated and reliable instrument consisting of 28 guestions.[10] The scale's first four items assess knowledge about CVD characteristics, their preventability, and the influence of age. Fifteen items evaluate knowledge of risk factors (items 5, 6, 9-12, 14, 18-20, 23-25, 27, and 28), while nine items (7, 8, 13, 15, 16, 17, 21, 22, and 26) assess the consequences of changes in risk behaviors. The items are presented as statements with response options of "Yes," "No," or "I don't know." Six items (items 11, 12, 16, 17, 24, and 26) contain false statements and are therefore reversecoded. The scale's total score ranges from 0 to 28. An internal consistency analysis of the scale revealed that the Cronbach's alpha coefficient for the total CARRF-KL scale was α =0.689, indicating high reliability. This value aligns with the validity and reliability study conducted by Arıkan et al., when they developed the CARRF-KL scale.

Arterial blood pressure measurements were obtained by a physician and recorded in each patient's clinical information form. The Framingham risk score was calculated by a physician using the calculation tool available on the Framingham risk score website, based on the patient's clinical data and lipid panel results obtained from the hospital's automation system within the past 3 months.^[8]

Number Cruncher Statistical System 2007 (Kaysville, Utah, USA) software was used for statistical analyses. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, and maximum) were applied to evaluate the study data. The Kruskal–Wallis test was used for quantitative variables that did not show normal distribution, and the Dunn-Bonferroni test was used for post hoc evaluations. A p<0.05 was considered statistically significant.

RESULTS

A total of 220 participants were enrolled in the study, with a mean age of 56.8±9.6 years. The distribution of the demographic and clinical features is summarized in Table 1.

The median Framingham score of all participants was 15.6 (1.20–30.1). According to the Framingham risk classification, 58 (26.4%) of participants were in the low-risk category, 36 (16.3%) were at moderate risk, and 126 (57.3%) were at high risk.

	n (%)
	11 (70)
Gender	
Female	142 (64.5)
Male	78 (35.5)
Age groups	
≤65 years	170 (77.3)
>65 years	50 (22.7)
Smoking status	
Yes	54 (24.5)
No, I quit	59 (26.8)
No, never smoked	107 (48.7)
Use of antihypertensive medication	97 (44.1)
Diabetes mellitus	85 (38.6)
Cardiovascular disease	19 (8.6)
	Mean±SD
Systolic blood pressure (mmHg)	136.6±22.2
Total cholesterol (mg/dL)	206.6±44.5
HDL cholesterol (mg/dL)	53.8±14.2

An analysis of responses to the CARRF-KL scale revealed that the highest proportion of correct responses was for the statements: "Smoking is a risk factor for heart disease" 213 (96.8%), "Consuming salty foods causes high blood pressure" 212 (96.4%), "Overweight individuals are at increased risk of heart disease" 212 (96.4%), "Regular exercise reduces the risk of heart disease" 212 (96.4%), "High blood pressure is a risk factor for heart disease" 203 (92.3%), and "If blood sugar is controlled in diabetic patients, the risk is reduced" 201 (91.4%). Similarly, participants correctly identified the reverse-coded statements "Fatty foods do not increase blood cholesterol levels" 203 (92.3%) and "Solid fats at room temperature are beneficial for heart health" 207 (94.1%) as incorrect.

Participants most frequently answered incorrectly the following statements: "Slow walking and strolling count as exercise" 87 (39.5%), "If good cholesterol (HDL) is high, there is a risk of heart disease" 86 (39.1%), and "All individuals with high cholesterol levels should be prescribed medication" 103 (46.8%).

The total CARRF-KL scores with a median score of 23.0 (12.0–28.0). CARRF-KL scale scores according to Framingham risk levels are summarized in Table 2. A significant difference was found between CARRF-KL scale scores according to Framingham risk levels, between low- and high-risk groups (p=0.026).

Table 2. CARRF-KL scale scores according to Framingham risk levels

	Fra	Framingham risk level			
	Low risk (n=58)	Moderate risk (n=36)	High risk (n=126)		
CARRF-KL score	23.0 (13.0–27.0)	23.0 (18.0–27.0)	24.0 (12.0–28.0)	0.031	

CARRF-KL score: Cardiovascular disease risk factor knowledge level scale.

Data are presented as median (min-max) as appropriate.

Kruskal–Wallis test.

DISCUSSION

In the present study, the median Framingham score of all participants was 15.6 (1.20-30.1). When participants were categorized into low-, moderate-, and high-risk groups based on their Framingham scores, the majority (126 participants, 57.3%) were classified as high-risk. This result may be related to the fact that disease-specific exclusion criteria were not applied in the present study. In contrast, a study conducted by Tekkeşin et al., on 3,169 participants without CVD or diabetes found that only 9.4% of men and 4.6% of women were classified as high-risk.[1] Similarly, in a study by Dülek et al., involving 258 patients aged 40-72 years who visited a family medicine outpatient clinic and had no known history of CVD, 46.9% were classified as high-risk. [11] Another study conducted in Iran with 2,103 participants aged 40-79 years without a history of CVD found that 26.5% were in the high-risk category.^[12]

The present study's total scores from the CARRF-KL scale were 22.8±2.9. Although it was expected that participants with higher CVD knowledge levels would have a lower CVD risk, the present study found that individuals with higher CARRF-KL scores were more likely to be classified as highrisk rather than low-risk. Several factors may contribute to this finding. Increased knowledge may result from personal exposure to risk factors, the disease, and experiences during hospitalization and treatment. Similar to the present findings, a study by Topuz and Bozdemir on 192 university employees found that individuals with high Framingham risk scores also had high CARRF-KL scores, with the highest CARRF-KL scorers also having the highest Framingham scores.[13] However, a study by Keleşoğlu et al., involving 122 patients aged 40-80 who visited a family medicine outpatient clinic found no significant difference between CARRF-KL scores and SCORE risk distribution.[14] Similarly, Tekin et al., in a study of 390 male patients aged 40-65 years, found a very weak negative correlation between SCORE risk scores and CARRF-KL scores, which was not statistically significant.^[15] The variations in study results may be attributed to differences in patient populations and the risk assessment methods applied.

A limitation of the present study is that participants' lipid levels were evaluated without assessing whether they received treatment for dyslipidemia.

CONCLUSION

Although the CARRF-KL scale scores were generally high in the present study, 57.3% of the participants were classified in the high-risk category based on their Framingham scores. Being knowledgeable about disease risks does not necessarily translate into taking preventive measures. The present findings indicate that participants' knowledge levels did not lead to behavioral changes. Increasing awareness can help prevent or delay the onset of chronic diseases, such as CVD, slow disease progression, and improve survival rates. In this regard, primary healthcare services are crucial in educating the public, promoting healthy lifestyles, and monitoring their implementation. Integrating risk scoring systems into primary care physicians' follow-up screens could be a significant step forward.

Disclosures

Peer-review: Externally peer-reviewed. **Conflict of Interest:** None declared.

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Ethics Committee Approval: Ethical approval for the study was obtained from the Clinical Research Ethics Committee of the University of Health Sciences, Istanbul Fatih Sultan Mehmet Training and Research Hospital (Approval date: December 29, 2021, Approval number: 2021/113). In addition, all participants were informed about the study's content and the voluntary nature of participation, and their written consent was obtained.

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Effects of Selective Serotonin Reuptake Inhibitor Treatment on Blood Pressure in Resistant **Hypertensive Patients with Anxiety Disorder**

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ABSTRACT

INTRODUCTION

Objectives: This study aimed to evaluate the effects of selective serotonin reuptake inhibitor (SSRI) treatment on blood pressure (BP) control in resistant hypertensive patients with anxiety symptoms.

Methods: This interventional study was conducted between January 2021 and March 2022 at a family medicine outpatient clinic. Patients with primary hypertension (HT), uncontrolled with monotherapy, and scoring ≥16 on the Beck anxiety inventory were included. All were switched to combination antihypertensive therapy. Those who accepted SSRI treatment constituted the case group, while those who declined formed the control group. Demographic and clinical characteristics were recorded. BP was measured at baseline and after 1 month.

Results: Ninety-one patients were included, 30 (33.0%) male, the median age was 53.5 (35.0-68.0) years. Of the participants, 72 (79.1%) received combined therapy plus SSRI, while 19 (20.9%) received combined therapy only. After 1 month, systolic BP decreased by 15.0 (1.0-22.0) mmHg and diastolic BP by 13.0 (4.0-18.0) mmHg in the case group, compared to decreases of 8.0 (1.0-17.0) mmHg and 6.0 (2.0-13.0) mmHg in the control group (respectively, p<0.001 and p<0.001).

Conclusion: SSRI therapy provided significantly greater reductions in both systolic and diastolic BP compared with combination antihypertensive treatment alone. Anxiety should be considered an important factor in resistant HT, and psychological as well as pharmacological interventions may enhance treatment outcomes.

Keywords: Antihypertensive agents, anxiety disorders, blood pressure, serotonin reuptake inhibitors

Hypertension (HT) is one of the leading causes of cardiovascular mortality and morbidity and is a global public health problem.[1] The primary aim in the management of HT is to maintain an optimal blood pressure (BP) and prevent these complications, but this cannot be achieved in a group of patients despite appropriate pharmacological treatment.[2] While secondary causes of HT may come to mind in this condition called resistant HT, an important factor that should not be ignored is psychosocial factors, such as anxiety.[3]

Anxiety disorders are frequently observed in the community and may lead to activation of the sympathetic system, which is not desirable in patients with HT, and thus may lead to an increase in BP.[4,5] Sympathetic activation increases cardiac output and also increases peripheral vascular resistance, and shows this effect. Another problem that may complicate BP management in anxious individuals is that these individuals have lower medication compliance



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and unhealthy life preferences, including alcohol, smoking, and poor eating habits, more frequently compared to the general population. In addition, the COVID-19 outbreak increased the anxiety levels of patients and also affected their medical treatment preferences, leading them to move away from medical treatments. [6] In the literature, it is observed that the frequency of HT tends to increase with increasing anxiety level. [7] However, most of the studies conducted on this subject are observational studies, which are not suitable for establishing a causal relationship. The aim of this study was to investigate the effects of the selective serotonin reuptake inhibitor (SSRI) on BP in resistant HT patients with anxiety symptoms.

METHOD

This interventional study was conducted between January 2021 and March 2022 at the Family Medicine outpatient clinic of Maçka Ömer Burhanoğlu Physical Therapy and Rehabilitation Hospital. Patients with primary HT who had been regularly using angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers, or thiazide diuretics for at least 1 month, but who failed to achieve effective BP control with monotherapy, and who scored 16 or higher on the Beck anxiety inventory (BAI), were included in the study. Patients were excluded if they had secondary HT, irregular use of antihypertensive medication, contraindications to current therapy (such as beta-blocker use in asthma), or had recently experienced a major life event that could affect BP control, including severe trauma, new sources of stress, or the loss of a loved one.

Patients who fulfilled the inclusion criteria and consented to be included in the study were first asked for routine follow-up and routine biochemical tests in terms of causes that may suggest secondary HT. At this stage, no patient suggestive of secondary HT was identified. At least 5-day home BP values requested from the patient at the previous visit were analyzed, and all patients also underwent office BP measurement by the same clinician in accordance with the guidelines. Office BP values were recorded as the patient's first systolic and diastolic BP values in mmHg. Patients with discordance between office and home BP measurements were re-evaluated in terms of white coat HT and major life events.

The decision to switch to combination therapy was shared with the patient and an appropriate combination was initiated in accordance with the guidelines, taking into account the patient's comorbidities. Patients who did not accept the treatment were excluded from the study. In addition, an appropriate SSRI group drug was started in patients who

were clinically evaluated and whose BAI scores were moderate/high. The group receiving SSRI treatment was taken as the case group and the patients who did not accept SSRI treatment were taken as the control group. After 1 month of follow-up, office BP values were measured again. Age, gender, height, and weight values of the patients were also recorded.

Data were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) 25.0 (SPSS Inc., Chicago, IL, USA) package program. The conformity of the data to normal distribution was evaluated by the Shapiro–Wilk test. Descriptive statistics were given as median (minmax) for quantitative data and frequency and percentage for categorical variables. The significance of the difference between two groups in terms of median values was analyzed by Mann–Whitney U test and the Pearson Chi-Square test for nominal variables. Spearman correlation analysis was used to evaluate the relationship between continuous variables. Statistical significance level was taken as p<0.05.

RESULTS

The study included 91 participants, 30 (33.0%) male and 61 (67.0%) female. The median age of the participants was 53.5 (35.0–68.0) years, and the median body mass index was 33.5 (27.4–39.3) kg/m2. While 72 (79.1%) of the participants were in the case group, 19 (20.9%) were in the control group. Demographic and clinical characteristics of the participants according to treatment groups are summarized in Table 1.

While 33 (36.3%) of the participants were smokers, 23 (69.7%) of them were in the case group, and 10 (30.3%) of them were in the control group (p=0.095).

At the follow-up visit performed one month later, systolic BP had decreased by 13.0 (2.0–22.0) mmHg and diastolic BP by 11.0 (2.0–18.0) mmHg. These values were 15 (1.0–22.0) mmHg and 13.0 (4.0–18.0) in the case groups, respectively, while they were 8.0 (1.0–17.0) and 6.0 (2.0–13.0) in the control group (respectively, p<0.001 and p<0.001).

No significant relationship was found age between BP measurements, such as first and last systolic and diastolic BP measurements, and systolic and diastolic BP difference (p>0.05). There was a significant relationship found between height and first diastolic BP or diastolic BP difference, while no relationship was found between first and last systolic BP, systolic BP difference, and last diastolic BP (respectively, r=0.223 and p=0.034; r=0.240 and p=0.022; p>0.05). On the other hand, a significant relationship was found between weight and first and last systolic BP, first

	Case group (n=72)	Control group (n=19)	р
Age (years)	53.5 (35.0–68.0)	56.0 (48.0–65.0)	0.086
Height (cm)	162.0 (149.0–180.0)	160.0 (155.0–178.0)	0.739
Weight (kg)	87.5 (75.0-98.0)	88.0 (79.0-98.0)	0.732
First systolic BP (mmHg)	151.0 (135.0-162.0)	155.0 (145.0–163.0)	0.126
First diastolic BP (mmHg)	108.0 (97.0-117.0)	109.0 (97.0-116.0)	0.362
BAI score	26.0 (25.0-37.0)	28.0 (25.0-32.0)	0.066

and last diastolic BP, and diastolic BP difference, while no relationship was found between systolic BP difference (respectively, r=0.342 and p=0.001; r=0.235 and p=0.025; r=0.517 and p<0.001; r=0.264 and p=0.011; r=0.339 and p=0.001; p>0.05). The relationship between BP measurements is summarized in Table 2.

DISCUSSION

This study aimed to investigate the effect of SSRI group drugs on BP control in resistant HT patients with anxiety symptoms. The findings of the study show that SSRI treatment provides significant reductions in both systolic and diastolic BP. These findings support the potential role of SSRI treatment in alleviating the negative effects of anxiety on BP control in patients with anxiety symptoms.

Anxiety is an important psychosocial factor that attracts attention in HT management because of its effects on BP. [8,9] Anxiety causes activation of the sympathetic nervous sys-

tem in the body and thus increased cardiac output and peripheral vascular resistance, and anxious individuals often struggle with behavioral factors, such as low medication adherence and unhealthy lifestyle preferences.^[5,7] Unfortunately, this situation poses a challenge to clinicians in the management of HT. Every clinician should consider these difficulties and possible treatments in HT management.^[10]

The findings of this study are compatible with the existing literature examining the relationship between anxiety and HT. Especially in recent meta-analyses and reviews, this relationship has been emphasized. [11-13] For example, the results of the meta-analysis conducted by Pan et al., in 2015 including 151,389 patients, revealed that anxiety increased the risk of HT and emphasized the importance of early detection and management of anxiety in hypertensive patients. [14] In this study, it was observed that patients with anxiety symptoms had difficulty in BP control, and SSRI treatment improved BP control in these patients.

Table 2. The relations	nip between BP m	neasurements				
	First systolic BP (mmHg)	Last systolic BP (mmHg)	Δ Systolic BP (mmHg)	First diastolic BP (mmHg)	Last diastolic BP (mmHg)	Δ Diastolic BP (mmHg)
First systolic BP (mmHg)	1	r=0.787	r=0.289	r=0.484	r=0.478	r=0.102
		p<0.001	p=0.005	p<0.001	p<0.001	p=0.338
Last systolic BP (mmHg)		1	r=-0.278	r=0.413	r=0.521	r=-0.132
			p=0.008	p<0.001	p<0.001	p=0.212
Systolic BP (mmHg)			1	r=0.057	r=-0.083	r=0.315
				p=0.593	p=0.432	p=0.002
First diastolic BP (mmHg)			1	r=0.684	r=0.479
					p<0.001	p<0.001
Last diastolic BP (mmHg))				1	r=-0.247
						p=0.018
Diastolic BP (mmHg)						1
BP: Blood pressure; Spearm	an correlation test.					

When the literature is reviewed, unfortunately, it is seen that the diagnosis and treatment processes of diseases, such as HT are not sufficiently covered in medical education. However, the etiological questioning of HT, which is seen with a high frequency in society, should be done very well. The findings of this study show that in refractory HT patients in whom the possibility of secondary HT is excluded, the accompanying psychological comorbidities of the patient should be questioned.[15] The findings of this study emphasize the importance of questioning the psychological status of HT patients and developing treatment strategies for selected patients, and including this in medical education. In this respect, this present study, with its prospective nature, is a study that questions the effects of SSRIs on BP in patients with refractory HT and anxiety disorders and can make important contributions to the literature in the field.

This study has some limitations. The limited number of participants, the fact that the data were collected from a single center, and the relatively short follow-up period limit the generalizability of the results. In addition, although SSRI treatment was recommended for all patients, the presence of groups that accepted and did not accept treatment based on patient preference may have affected the study results. Prospective studies with larger sample sizes and longer follow-up periods are needed.

CONCLUSION

In patients with refractory HT, the accompanying psychological comorbidities of the patients should be questioned. The findings of this study emphasize the importance of questioning the psychological status of patients with HT and developing treatment strategies for selected patients. SSRI treatment may improve BP control in resistant HT patients with anxiety symptoms, and these findings should be considered in clinical practice.

Disclosures

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Ethics Committee Approval: Approval for the study was obtained from the Health Sciences University Trabzon Medical Faculty Clinical Research Ethics Committee (Approval date: 25.10.2023, Approval number: 2023-7). Verbal and written informed consent were obtained from all participants before the study and the principles of the Declaration of Helsinki, as revised, were followed at every stage of the study.

Authorship Contributions: Concept – M.V.; Design – O.K.C.; Supervision – O.K.C.; Materials – M.V.; Data Collection and/or Processing – M.V.; Analysis and/or Interpretation – O.K.C.; Literature Search – O.K.C.; Writing – M.V., O.K.C.; Critical Review – M.V., O.K.C.

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Changing Trends of Rotavirus and Enteric adenovirus in Children: Before and After the COVID-19 Pandemic

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ABSTRACT

Objectives: This study aimed to investigate changes in the incidence and seasonal distribution pattern of enteric viruses that are common in children during the COVID-19 pandemic.

Methods: The study included patients aged 0–9 years who were diagnosed with acute gastroenteritis (AGE) in the pediatric emergency department between September 2017 and August 2022.

Results: During the study, 4,244 patients who underwent rotavirus (RV)/enteric adenoviruses (eAV) antigen tests with a diagnosis of AGE were included. Compared with the pre-pandemic period, during the COVID-19 pandemic, RV positivity decreased (479 [16.6%] vs. 167 [12.3%], p<0.001), whereas eAV positivity tended to increase (120 [4.1%] vs. 78 [5.8%], p=0.020).

Conclusion: This surveillance study demonstrates the long-term effects of the COVID-19 outbreak on RV and eAV infections in children. In the early phase of the pandemic, both viruses had almost disappeared, but in the late phase, they returned to the pre-pandemic level.

Keywords: COVID-19, human enteric adenovirus, preventive measures, rotavirus

INTRODUCTION

The COVID-19 virus can be transmitted through droplets and by touching the mouth, nose, and eyes after contact with contaminated surfaces. [1-4] In the fight against the pandemic, strict non-pharmacological measures (NPIs) implemented in primary care have been effective in slowing down the epidemic. [5] It has been reported that primary care measures, especially hand hygiene, social distancing, and mask use, reduce both viral respiratory diseases, such as influenza and respiratory syncytial virus, and the incidence of enteroviral infections. [6-17] Acute gastroenteritis (AGE) is common worldwide, and it is an important cause of death in children <2 years of age, especially in developing countries. Rotavirus (RV) and enteric adenoviruses (eAV) are the most common causes of AGE in children. [18] The incidence of enteroviral infections transmitted by the fecal-oral route was also reduced with the strict application of NPIs in the early phase of the pandemic, but data are limited in terms of the course of enteroviral infections in the late phase of the pandemic. The aim of this was to determine the seasonal frequency of RV and eAV infections in children in the early and late stages of the pandemic and to compare them with the pre-pandemic period.

METHOD

This study was conducted in the pediatric emergency department of a tertiary university hospital in Istanbul, Turkey, with approximately 130,000 patients admitted per year. Patients aged



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between 0 and 9 years who were diagnosed with AGE in the pediatric emergency department and tested for RV and eAV antigen in the stool were analyzed retrospectively. The study period was from September 2017 to August 2022. Based on the start of the pandemic in Turkey, the pre-pandemic period was from September 2017 to February 2020, and the pandemic period from March 2020 to August 2022. The 1st year of the pandemic (from March 2020 to February 2021) was defined as the early pandemic period, and the 2nd year of the pandemic (from March 2021 to February 2022) was defined as the late pandemic period. An AGE diagnosis was made in children who had ≥3 watery stools or vomited ≥2 times in 24 h, and these symptoms persisted for a maximum of 7 days. Patients aged 5 years and younger were classified as preschool children, and patients aged 6-9 years were classified as school-age children.

A total of 4244 patients who met the inclusion criteria and whose records were fully accessible were included in the study. Scanning of the data was done using the hospital's software system for the following International Classification of Diseases 10th Revision codes: A08, Viral and other specified intestinal infections; A09, Diarrhea and gastroenteritis of presumed infectious origin. The decision to perform a fecal rota-adenovirus test was made by the examining physician. According to usual clinical practice, fresh stool samples are placed in clean, sealed boxes and transported to the laboratory within 30 min. The stool samples were investigated for rota-adenovirus antigen positivity using the Combo Rapid Test (Citest Diagnostics, Vancouver, Canada), applying the lateral immunochromatographic method.

Statistical Package for the Social Sciences (SPSS) software version 20.0 (SPSS Inc., Chicago, IL, USA) was used for all statistical calculations and analyses. Descriptive statistical methods, such as frequencies and percentages, were used to analyze demographic data and diagnosis distributions. The Chi-square test was used to compare differences between groups. A p<0.05 was considered statistically significant.

RESULTS

Of the 4,244 patients included in the study, 2891 (68.1%) were admitted in the pre-pandemic period and 1353 (31.8%) in the pandemic period. Compared with the pre-pandemic period, the number of patients decreased by 1538 (53.0%) during the pandemic. The demographic characteristics and frequency of virus positivity are summarized in Table 1.

The frequency of RV and enteric adenovirus was 24 (5.8%) versus 9 (2.2%) in the early pandemic period, respectively, and 60 (11.3%) versus 34 (6.4%) in the late pandemic period (p=0.003 and p=0.002, respectively).

During the entire study, 638 (75.6%) patients were followed up as outpatients, 110 (13.0%) were followed up in the emergency department, and 96 (11.4%) patients were followed up as hospitalization. Clinical courses of RV and eAV infections before and during the pandemic are summarized in Table 2.

Compared with the pre-pandemic period, it was observed that the typical seasonal distribution of RV infection between November and May in the early phase of the pan-

Table 1. The demographic characteristics and frequency of virus positivity					
,	Whole study period (n=4244)	Pre-pandemic period (n=2891)	Pandemic period (n=1353)	р	
Gender					
Male	2373 (55.9)	1594 (55.1)	779 (57.6)	0.135	
Female	1871 (44.1)	1297 (44.9)	574 (42.4)		
Age Groups					
0–5 years	3653 (86.1)	2442 (84.5)	1211 (89.5)	< 0.001	
6–10 years	591 (13.9)	449 (15.5)	142 (10.5)		
Virus positivity					
RV	646 (15.2)	479 (16.6)	167 (12.3)	< 0.001	
eAV	198 (4.7)	120 (4.1)	78 (5.8)	0.020	
Total	844 (19.9)	599 (20.7)	245 (18.1)	0.019	
Co-infection (RV and e	AV) 37 (0.9)	20 (0.7)	17 (1.3)	0.065	

The total period of the study is 60 months, consisting of 30 months in the pre-pandemic period and 30 months in the post-pandemic period. Data is presented as n (%), Chi-square test. eAV: Enteric adenovirus; RV: Rotavirus.

Table 2. Clinical courses of RV and eAV infections before and during the pandemic				
	Pre-pandemic period	Pandemic period	Chi-square	р
Outpatient follow-up	461 (76.3)	177 (73.7)	1.151	0.562
Emergency follow-up	74 (12.2)	36 (15.0)		
Hospitalization	69 (11.4)	27 (11.2)		
Total	604 (100.0)	240 (100.0)		

The total period of the study is 60 months, consisting of 30 months in the pre-pandemic period and 30 months in the post-pandemic period. Data are presented as n (%). Chi-square test. eAV: Enteric adenovirus; RV: Rotavirus.

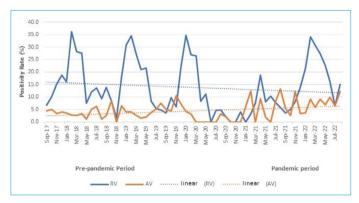


Figure 1. The seasonal distribution of rotavirus and enteric adenoviruses in pre-pandemic and pandemic period.

demic shifted to March–July. The seasonal distribution of RV and eAV in pre-pandemic and pandemic periods is shown in Figure 1.

DISCUSSION

Although COVID-19 spread rapidly, causing a worldwide pandemic, surprisingly, other viral infectious diseases common in children almost disappeared during the pandemic. The enteroviral load was reduced by strict administration of NPIs early in the pandemic. However, data showing the course of enteric viruses in the late phase of the pandemic, when NPIs were relaxed, are limited. In this study, it was found that the seasonality and the frequency of positivity of these viruses changed during the early and late stages of the pandemic.

RV or eAV-positive AGE cases admitted to the pediatric emergency department during the COVID-19 pandemic decreased by approximately 50% compared with the prepandemic period. Many studies conducted in different geographic regions of the world have shown that enteroviral infections decreased during the pandemic, similar to this study. [10-17,19] There may be several explanations for this situation. The most valid explanation is that NPIs, which were strictly applied in the early phase to slow the COVID-19 pandemic, also prevented the transmission of enteric viruses.

[6,18,20] NPIs, which were strictly implemented, included no face-to-face education in schools, use of masks, compliance with hand hygiene, lockdown, and home-office working. In addition, the attention of health personnel in the pandemic was focused on the dominant virus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). Therefore, enteroviral infections, which usually follow a mild course, may have been underdiagnosed. In addition, the concern of parents that SARS-CoV-2 could be transmitted from health institutions played a role in the decrease in hospital admissions of children with AGE. Worried parents may have only brought children with severe AGE to the emergency room.[15,21-23] However, in this study, the need for the frequencies intravenous fluids and hospitalization of patients who attended the pediatric emergency service were similar in pre-pandemic and pandemic. This may be related to the mostly mild-tomoderate clinical course of enterovirus infections.[18]

In this study, the frequency of RV positivity decreased significantly throughout the pandemic compared to the pre-pandemic period. When evaluated according to age groups, RV positivity decreased more significantly in preschool children during the pandemic period. This finding is due to the fact that RV infection is more common in children aged 0-5 years. It was surprising to find that eAV positivity increased and RV positivity decreased significantly during the pandemic compared to before the pandemic. Both enteric viruses are transmitted through the oral-fecal route. NPIs taken to control the COVID-19 epidemic would be expected to reduce positivity similarly for both viruses. To explain this paradox, we compared the early phase of the pandemic, when NPIs were strictly implemented in Turkey, and the late phase of pandemic fatigue, when adherence to NPIs decreased and restrictions were gradually lifted. In the early stages of the outbreak, both eAV and RV positivity rates were close to 0%, especially in the period March-July 2020. In the early period of the pandemic, positivity for both enteric viruses decreased as expected. On the other hand, both RV and eAV virus positivity increased in the late period of the pandemic. Moreover, the rapid increase in eAV positivity in the late period was even higher than in the pre-pandemic period. The increase in eAV during the pandemic was a reflection of this rapid increase at the end of the pandemic. The most important variable affecting the results between the early and late periods of the pandemic is thought to be the strict or loose implementation of the NPI. Late in the pandemic, NPIs were relaxed, and schoolaged children returned to school. Increased close contact at school, decreased compliance with hand washing and general hygiene rules, and an increase in enteric viruses. In a study similar to the results of this study, Liu et al. reported that eAV positivity increased rapidly when NPIs were relaxed.[14] This may also be related to the structural feature of eAV. It suggests that eAV, which is resistant even to nonenveloped and alcohol-containing disinfectants, can only be controlled with strict NPIs.

Similar to this study, other studies have been published showing that RV infection decreased in the early phase of the pandemic and increased in the late phase.[10,14,19] However, Knudsen et al. reported that there was no decrease in RV positivity during the pandemic period compared with the pre-pandemic period. [24] This is related to the fact that the RV vaccine has been administered in the Norwegian national vaccination program since 2014, and has decreased RV gastroenteritis even before the pandemic. In addition, the detection of vaccine strains in stool samples in children who received the RV vaccine may have caused the RV test positivity to remain constant.[24] The RV vaccine is not applied in the national vaccination program in Turkey. Therefore, in this study, RV positivity in the early phase of the pandemic may have decreased more significantly than in countries where vaccination occurs.

As determined in this study, differences in the administration of NPIs affected the incidence of enteroviral infections. [10,14,19] However, in a new study conducted in China, it was reported that norovirus and RV infections increased and returned to pre-pandemic levels, despite the strict application of NPIs in the late phase of the pandemic, but it is thought that the strict NPIs applied during the pandemic are not sustainable in the long term. [25] In contrast, Kuitunen et al. found that, in Finland, the incidence of RV infection, in particular, did not return to the pre-pandemic level and remained at a lower level, despite earlier relaxation of NPIs.[26] This was associated with the low population density in Finland. The results of this study in Istanbul, the most populated city in Turkey in terms of population density, are in parallel with the results of the study conducted in China. The relaxation of NPIs may lead to different outcomes depending on various demographic characteristics, such as population density.

The normal seasonal distribution of RV is that it peaks in winter and spring eAV infections occur sporadically throughout the year. In this study, RV was distributed seasonally and adenovirus sporadically during the winter months, in accordance with the literature data before the pandemic. In the early phase of the pandemic, the seasonal distribution of RV shifted from winter to the spring–summer months and reached lower peak levels. This change was thought to be related to NPIs that were strictly applied in the early period. In the late phase of the pandemic, when NPIs were relaxed, RV returned to pre-pandemic levels in terms of seasonal distribution and peak levels. Liu et al. found that the peak levels of RV decreased during the pandemic, but its seasonal distribution did not change eAV infections were distributed sporadically during the pandemic as well. Italians.

There are some limitations of the study. First, it is a single-center and retrospective study. Second, because RV and eAV tests were not applied to every patient admitted to our emergency department with a diagnosis of AGE, not all cases of RV and eAV could be detected.

CONCLUSION

This study showed that although RV and eAV infections decreased significantly in the early phase of the COVID-19 pandemic, they quickly returned to pre-pandemic levels in the late phase of the pandemic. The most important variable that could cause this difference between the early and late phases of the pandemic was the way NPIs were implemented. In addition, the effectiveness of NPIs may differ with demographic characteristics, such as population density, and health practices, such as national RV vaccination.

Disclosures

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Effectiveness of Music Listening on Anxiety and Stress Levels of Primiparous Pregnant Women in the Third Trimester: A Randomized Controlled Trial

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ABSTRACT

Objectives: This study aimed to evaluate the effect of music listening on the anxiety and stress levels of primiparous pregnant women in the third trimester.

Methods: The study was conducted between December 01, 2019, and August 31, 2020. In the study, 120 primiparous pregnant women in their third trimester were randomized into two groups at a 1:1 ratio. Participants in the music group were given standard prenatal education and a 10-day practice of listening to Turkish music for 20 min a day. Participants in the control group received standard prenatal training. The State and Trait Anxiety Inventory and pregnancy stress rating scale (PSRS) were applied twice to both groups, before and after the practice.

Results: The study included 60 (50.0%) pregnant women in the music group and 60 (50.0%) in the control group. A decrease in state anxiety scores was observed in both the music and control groups (34.5 [15.5] vs. 31.4 \pm 8.6, respectively; p<0.001 in the music group, 37.1 \pm 7.6 vs. 35.0 \pm 7.3, respectively; p<0.001 in the control group). On the other hand, while a decrease was observed in the music group's total PSRS score, no difference was found in the control group (61.9 \pm 28.2 vs. 45.0 [46.8], respectively; p=0.002 in the music group, 59.2 \pm 26.4 vs. 54.8 \pm 28.2, respectively; p=0.1115 in the control group).

Conclusion: Turkish classical music listening can be used safely in primiparous pregnant women to reduce anxiety and stress.

Keywords: Anxiety, emotional stress, music, pregnant women, primiparity, third trimester

INTRODUCTION

Pregnancy is a period in which emotional changes are experienced along with physiological changes. Therefore, anxiety and stress during pregnancy can frequently develop. In the first trimester of pregnancy, the prevalence of anxiety and stress is 15.3%, in the second trimester is 23.6%. The prevalence of anxiety and stress is highest in the third trimester compared to 25%. Similarly, it is known that primiparous pregnant women have higher anxiety and stress levels than multiparous pregnant women because they experience pregnancy and childbirth for the 1st time. The stress is a period in which emotional changes are experienced along with physiological changes. The stress is a period in which emotional changes are experienced along with physiological changes. The stress is a period in the first time.

Music listening is also one of the non-pharmacological methods used during pregnancy. [6] Music listening is defined as using music to support and improve physical, mental, and spiritual well-being. It is found out that music listening relaxes the mother, increases the level of well-being, and improves sleep quality and quality of life when the studies in which music



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Commons Attribution-NonCommer cial 4.0 International License. listening is used in pregnant women are examined. Furthermore, it is reported that it reduces blood pressure, increases birth satisfaction, increases maternal-fetal attachment, and reduces maternal anxiety and stress in pregnant women with preeclampsia.^[7-11]

Considering such studies in the literature, it is seen that interventions to increase the well-being of pregnant women in normal pregnancies where music listening is mainly applied to risky pregnancies are not studied adequately.[7-11] However, it is known that anxiety and stress rates are high even in pregnant women who are not at risk.[3-5] Since this rate reaches the highest level, especially in the third trimester, it is essential to implement midwifery interventions to support the well-being of the pregnant women and the baby in this period.[3] In this way, complications related to anxiety and stress in pregnant women can be prevented. Positive birth results can be achieved by improving the quality of life of the pregnant women and preparing her for birth with positive emotions. In addition, this study can contribute to a positive pregnancy experience within the scope of the Antenatal Care Recommendations on Antenatal Care for a Positive Pregnancy Experience Guide published by the World Health Organization in 2016; with the outputs, we targeted as a result of the music listening application.[12]

With anxiety and stress, the release of catecholamine and corticosteroid hormones in the body increases. [13] In pregnant women, the increase in these hormones can initiate labor by stimulating uterine contractions and may adversely affect delivery outcomes. [14] The positive effects of music can be used to reduce the anxiety and stress of babies. With natural serotonin and acetylcholine, music listening provides a feeling of relaxation, regulates blood pressure and respiratory rhythm, and calms the pregnant women by increasing the oxygenation of the brain. [15]

Pregnant women who are not in the risk group in our country are monitored in primary health care services, the necessary counseling and educational services are provided at this stage. ^[16] The use of different alternative methods such as listening to music during these follow-ups may create positive results such as increasing the diversity of care and pregnant participation. It was thought that our study would bring a different perspective to care services by conducting it in primary health services with healthy pregnant women.

The aim of this study is to investigate the effect of listening to music on anxiety and stress levels in primiparous pregnant women in the third trimester.

METHOD

This randomized controlled experimental study was conducted between December 01, 2019, and August 31, 2020, in a city in the west of Turkey. In this study, primiparous pregnant women in the third trimester who applied to the primary health care center were studied. Pregnant women aged 18 and over, speaking and writing Turkish, having no vision-hearing problems, having and using an internet-supported online site, primiparous, in the third trimester (28 weeks of gestation and above), and volunteering to participate in the study were included in the study. In addition, pregnant women who want to leave at any stage of the research, do not listen to music regularly, and have a chronic disease were excluded from the study.

In the study, a power analysis was used to determine the sample size. Power analysis was calculated by considering 80% power, 5% Type I error, and 50% effect size. According to the power analysis made according to a similar study in the literature, it was calculated that at least 51 people should be included in each group. However, taking into account case losses, a total of 120 pregnant women, 60 (50.0%) in the application group, and 60 (50.0%) in the control group, were planned to be included in the study. The flow chart of participants in the study is shown in Figure 1.

Pregnant women were assigned to the experimental and control groups by randomization method to reduce the

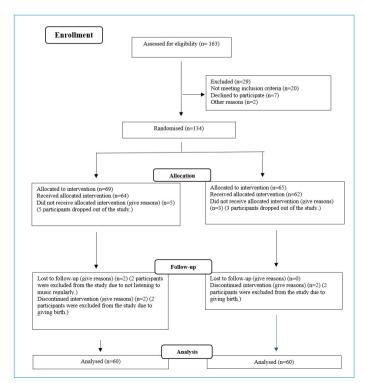


Figure 1. The flow chart of participants in the study.

selection bias and to control the variables that may have an effect on the outcome variables. For this purpose, participants were randomly randomized using the online program using the simple randomization method.[18] For randomization, a random number sequence was created according to the order of participation in the study. In the random number sequence designed, the numbers in the left column and the pregnant women in the music group and the numbers in the right column and the pregnant women in the control group were determined. At the beginning, pregnant women were asked to say a number between 1 and 120. Whichever group the reported number was in, the woman was included in that group. When a number that had been said before was told, he was asked to change the number until the appropriate number was determined. To ensure the reliability of the study, this study was also conducted by an unbiased person who was not in the randomization study. In this study, blinding could not be done because the responsible researchers carried out the intervention.

A personal information form, State and Trait Anxiety Inventory (STAI I-II) and pregnancy stress rating scale (PSRS) were administered to all pregnant women before and after the intervention.

Personal information form

This form consists of questions about pregnant women's socio-demographic and obstetric characteristics.

STAI I-II

The inventory was developed by Spielberger et al., and a validity and reliability study was conducted in Turkish by Öner and Le Compte. ^[19] There are 40 questions in total, 20 questions questioning the feelings of individuals about the situation they live in and 20 questions about the perception and interpretation of general conditions. The range of scores to be taken from the inventory is 0–80. In the evaluation of the inventory, 0–19 points are interpreted as no anxiety, 20–39 points are interpreted as mild anxiety, 40–59 points are interpreted as severe anxiety, and 80 points are interpreted as severe anxiety.

PSRS

The Turkish validity and reliability of the scale, which was developed by Chen, was done by Akin and Erbil.^[20] The scale consists of 36 five-point Likert-type items comprising 5 sub-scales used to define pregnancy-related stress factors. The range of scores to be taken from the scale is 0–144. An increase in the score obtained from the scale is interpreted as an increase in stress.

Interventions

Music Intervention

In this study, pregnant women listened to instrumental classical Turkish music in Neva Magam. Turkish music was preferred in the study because it is a part of the same culture. The sample group was selected only from a city in the west of Turkey to avoid cultural differences. It was also preferred because it gives people a sense of relief, reduces sadness, removes negative thoughts, and gives people feelings of courage, strength, joy, and calmness. According to literature and the consultancy received from Turkish Music Research and Promotion Group (TU-MATA), this music is especially effective on anxiety and stress.[21,22] In the study, the consultancy was received from the TUMATA regarding the type, time, and application of the music used. According to information obtained about the mentioned aspects, pregnant women were requested to listen to music any time from at least 20 min daily for 10 days, from sunrise to afternoon. While listening to the music, pregnant women were asked to be a comfortable sitting position in a guiet, dim place. At the same time, pregnant women were asked loudspeaker to adjust the volume of the sound to a level that he could hear comfortably. The pregnant women were told to focus on their music and let go of their current thoughts. A written instruction was given to the pregnant women about the points that they should pay attention to while listening to music.

Training

In this study, training was given to the participants in the control group by the researcher. The training was carried out live with a maximum of 10 participants on a group basis in different sessions through the internet. The training was carried out through an internet-based platform as the due to COVID-19 pandemic. The training took 40 min. In the training, issues related to anxiety and stress during pregnancy, which are routinely included in the prenatal pregnancy education program, were explained. It also included topics such as training, fear of childbirth, positive thinking, relaxation and breathing techniques, and endorphin massage.

Procedure

Initially, this study was planned to be conducted face-to-face with pregnant women who applied to the primary healthcare center. However, with the start of the COVID-19 pandemic during the study, the study was carried out using online systems with internet access. In this study, music and control groups were formed from the participants, and they were studied for 10 days in two groups. The group

that received music listening was called the music group, and the other group was called the control group. Participants were informed that they were in a music or control group. To ensure the reliability of the study, this study was also conducted by an unbiased person who was not in the randomization study. In this study, blinding could not be done because the responsible researchers carried out the intervention. The procedure applied to both groups is presented below.

Music Group

Before the start of the research, written and oral information was provided by the researcher and online consent was obtained from pregnant women who volunteered to participate in the study and were included in the music group. For 10 days, the study was carried out with the pregnant women included in the music group. Pregnant women filled in the Personal Information Form, STAI I-II, and PSRS online on the 1st day of the study. After filling out the guestionnaire forms, the researcher trained the pregnant women. After the training, pregnant women were asked to listen to the given music for 20 min without using headphones that they were adjusting the music volume to a level where they could comfortably hear through the loudspeaker. They were told to be in a comfortable sitting position in a quiet, dim place while listening to the music. They were focus on music while listening to it and let go of his current thoughts. In addition, written instructions were given regarding these details. Pregnant women were asked to listen to the music given to them every day for 20 min at the recommended time. Pregnant women were contacted through message every day and checked whether they listened to the music. On the 10th day, after listening to the music, the participants filled in the STAI I-II and PSRS again at the end of the study. Furthermore, the pregnant women who filled out the forms were informed that the study was completed.

Control Group

After written and oral information was given by the researcher to the pregnant women in the control group who volunteered to participate in the study, online consent was obtained before starting the study. Pregnant women filled in the Personal Information Form, STAI I-II, and PSRS online on the 1st day of the study. After filled out the questionnaire forms, the researcher trained the pregnant women. On the 10th day, the participants filled in the STAI I-II and PSRS again at the end of the study. Furthermore, the pregnant women who filled out the forms were informed that the study was completed.

Data analysis was performed using the Statistical Package for the Social Sciences (version 24.0). The normality of the data was analyzed with the Shapiro–Wilk test. Descriptive statistical methods such as frequency, percentage, mean, median, standard deviation, and interquartile range were used. In accordance with parametric methods, the "Independent Sample-t" test was used to compare the measurement values of two independent groups and the "Paired Sample-t" test method was used to compare the measurement values of two dependent groups. In accordance with non-parametric methods, Kruskal–Wallis H, Mann–Whitney U, and Wilcoxon were used for data analysis. Moreover, Pearson Chi-square test was used for categorical variables. In the study, p<0.05 value was considered statistically significant.

RESULTS

A total of 120 pregnant women were included in the study, comprising 60 (50.0%) pregnant women in the music group and 60 (50.0%) pregnant women in the control group. Distribution of socio-demographic and obstetric characteristics of pregnant women regarding the groups is summarized in Table 1.

In this study, the state anxiety inventory score was found to be 31.4 ± 8.6 in the music group and 35.0 ± 7.3 in the control group (p=0.014). The trait anxiety inventory score was found to be 39.4 ± 9.6 in the music group and 40.6 ± 8.2 in the control group (p=0.451). The STAI I-II score of pregnant women regarding the groups are summarized in Table 2.

PSRS total score was 45.0 [46.8] in the music group and 54.8±28.2 in the control group (p=0.297). PSRS score regarding the groups are summarized in Table 3.

DISCUSSION

It is known that birth is approach in the third trimester of pregnancy and anxiety and stress increase, especially in primiparous pregnant women due to the effect of this condition. [4] In this study, it was determined that the pregnant women in the music and control groups had mild state anxiety and moderate trait anxiety levels according to their pre-test scores. When studies evaluating the anxiety of pregnant women are examined, it is seen that the level of state and trait anxiety is in the range of mild to moderate. [4,5,10,23,24] According to the findings in this study and the literature, although it is predicted that the anxiety level will be higher in primiparous pregnant women in the third trimester, it was found that the anxiety level in pregnant women is in the light-medium.

	Music group (n=60)	Control group (n=60)	р
Age (years)	27.0±3.7	27.7±3.7	0.269*
Age groups			
18–23 years	11 (18.3)	6 (10.0)	0.417
24–30 years	38 (63.4)	41 (68.3)	
31–37 years	11 (18.3)	13 (21.7)	
Level of education			
High school and below	15 (25.0)	17 (28.3)	0.280
University and above	45 (75.0)	43 (71.7)	
Working status			
Not working	30 (50.0)	24 (40.0)	0.271
Working	30 (50.0)	36 (60.0)	
Level of income			
Income is less than expenses	43 (71.7)	46 (76.6)	0.657
Income exceeds expenses	17 (28.3)	14 (23.4)	
Chronic disease			
No	53 (88.3)	54 (90.0)	0.769
Yes	7 (11.7)	6 (10.0)	
Gestational age			
28–32 weeks	47 (78.3)	45 (75.0)	0.829
33–37 weeks	13 (21.7)	15 (25.0)	
The planned state of pregnancy			
Not planned	9 (15.0)	8 (13.3)	0.793
Planned	51 (85.0)	52 (86.7)	

Table 2. The STAI I-II score of pregnant women regarding the groups

STAI I-II	Music group (n=60)	Control group (n=60)	р
State anxiety			
Pre-test	34.5 [15.5]	37.1±7.6	0.520*
Post-test	31.4±8.6	35.0±7.3	0.014 [†]
р	<0.001 [‡]	<0.001§	
Trait anxiety			
Pre-test	45.2±10.1	43.2±7.9	0.225 [†]
Post-test	39.4±9.6	40.6±8.2	0.451 [†]
р	0.013§	0.003 [§]	

STAI: Stait trait anxiety inventory.

Data are presented as median [IQR] and mean±standard deviation.

*Mann–Whitney U-test; †Independent Sample-t test; †Wilcoxon test; $^{\rm 9}$ Paired sample-t test.

In this study, it was found that music listening applied to primiparous pregnant women in the third trimester significantly reduced the anxiety levels of pregnant women compared to the last test and control groups. According to this result, it was found that listening to music in primiparous pregnant women in the third trimester positively reduced the anxiety level. Similar studies have also reported that music listening reduces the anxiety level of pregnant women.^[10,11,23] According to the data obtained in this study, efficacy of music listening is a positive result that can be used in practice to reduce anxiety in primiparous pregnant women in the third trimester.

In the study, the anxiety level of the pregnant women in the control group decreased significantly in the posttest. In the third trimester, the primary source of anxiety in primiparous pregnant women is the obscurity about childbirth. It has been thought that the training provided

PSRS subscales	Music Group (n=60)	Control Group (n=60)	р
Pregnancy, search for a safe process			
Pre-test	21.1±8.0	20.7±8.6	0.825*
Post-test	17.5 [15.0]	19.0±8.4	0.248 [†]
р	0.002 [‡]	0.064 [§]	
Baby care and changing family relations			
Pre-test	12.0 [10.5]	14.0 [10.0]	0.994 [†]
Post-test	8.0 [14.8]	10.0 [12.8]	0.367 [†]
р	0.011 [‡]	0.058 [‡]	
Motherhood role			
Pre-test	11.5 [10.8]	11.8±6.7	0.629 [†]
Post-test	7.5 [13.8]	11.4±6.9	0.343 [†]
р	0.010 [‡]	0.550 [§]	
Quest for social support			
Pre-test	1.0 [4.8]	1.0 [5.0]	0.998 [†]
Post-test	1.0 [4.8]	1.0 [5.0]	0.710 [†]
р	0.605 [‡]	0.275 [‡]	
Physical appearance and function			
Pre-test	10.0 [10.8]	8.5 [8.0]	0.301 [†]
Post-test	9.0 [9.8]	9.0 [7.8]	0.693 [†]
р	0.037 [‡]	0.993 [‡]	
Total PSRS			
Pre-test	61.9±28.2	59.2±26.4	0.580*
Post-test	45.0 [46.8]	54.8±28.2	0.297 [†]
р	0.002 [‡]	0.115 [§]	

PSRS: Pregnancy stress rating scale.

Data are presented as median [IQR] and mean±standard deviation.

*Independent Sample-t test; †Mann–Whitney U-test; †Wilcoxon test; \$Paired sample-t test.

in this study helps pregnant women to have information about childbirth and therefore reduces anxiety effectively. In studies where prenatal education was given to pregnant women, it was reported that education reduced the level of anxiety. [25,26] It is thought that the education given in this study is effective in reducing the anxiety level due to informing pregnant women about childbirth.

It is reported that the stress level increases in pregnant women in the third trimester.^[27] According to the results of this study, it was determined that primiparous pregnant women in the third trimester experienced a slight level of pregnancy stress. It was found out that the mean scores obtained in other studies in the literature using the same measurement tool were similar to the results of this study.^[7,20,28] Some studies have reported that music listening reduces pregnancy stress. ^[7,8,17] In this study, it was determined that the music played to the pregnant women in the application group significantly

reduced their stress levels compared to the pre-test. However, it was determined that there was no significant decrease when compared with the control group. On the other hand, in two systematic reviews and one study on music listening, it was concluded that music was limitedly effective in reducing stress. [15,29,30] With this study, it is seen that this information is compatible. Music listening was not effective at the desired level in this study to reduce stress. The reason for this may be the type of music, the duration or environmental factors that may affect the practice, as well as the hormones released during pregnancy and physiological changes.

Music listening was not found to be effective for stress in the sub-dimension of seeking social support. Music listening was insufficient on the stress related to the seeking social support experienced by pregnant women. The reason for this is that pregnant women are thought to experience more social isolation with the threat of COVID-19 disease in the pandemic.

Our study was conducted during the pandemic, which may affect the anxiety and stress of pregnant women. It is reported that the pandemic increases anxiety and stress during pregnancy.^[31-33] In the study of Zilver friends, it was emphasized that the proportion of pregnant women experiencing stress due to the pandemic is especially high and it is important to carry out studies to reduce this stress.^[34] In our study, it was found that the anxiety level in pregnant women was significantly reduced by listening to music. However, listening to music is only limited effective in reducing the stress level of pregnant women. These results we have reached suggest that our study may also be related to its implementation, especially during a crisis period such as a pandemic.

Pregnant women listening to music in different environments, listening to music at a certain time interval, and using a single type of music to pregnant women are among the limitations of the study. The results obtained in this study include the results of pregnant women who applied to the place where the study was conducted. These results cannot be generalized to all pregnant women. The accuracy of the research results is based on the self-declaration of pregnant women.

CONCLUSION

In this study, it was found that music listening practice had a positive effect on reducing the level of anxiety in pregnant women but had a limited impact on reducing the stress level. Music listening can be used safely in pregnant women to reduce anxiety and stress due to its low cost, easy application, and no side effects. In future studies, it is recommended to examine the impact of music listening, especially on stress levels. It can be recommended that researchers conduct studies in the future on the effectiveness of music listening, which pregnant women in different cultures and with music suitable for the culture different music.

Disclosures

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Peer-review: Externally peer-reviewed.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

Ethics Committee Approval: The study was approved by the Non-Interventional Clinical Research Ethics Committee of a Kutahya Health Sciences University (Approval date: December 01, 2019, and Approval number: 41997688-402.03.01-E.7757). All procedures in this research were carried out in accordance with the ethical standards set out in the Declaration of Helsinki of 1964 and comparable ethical standards. Written and oral informed consent was obtained from all participants included in the study.

Authorship Contributions: Concept – E.E., N.Ç.; Design – E.E., N.Ç.; Supervision – N.Ç.; Materials – E.E., N.Ç.; Data collection and/or processing – E.E.; Analysis and/or interpretation – E.E., N.Ç.; Literature search – E.E.; Writing – E.E., N.Ç.; Critical review – N.Ç.

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The Frequency of Mental Health according to Smoking Status: A Cross-sectional Study

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ABSTRACT

Objectives: The goal of this study is to compare the frequency of psychiatric symptoms according to smoking status.

Methods: Participants were divided into three groups: 120 active smokers who wanted to quit were assigned to the case group, 120 active smokers who did not want to quit were assigned to control group 1, and 120 non-smokers were assigned to control group 2. The sociodemographic questionnaire and Brief Symptom Inventory were administered by the researcher using a face-to-face interview technique for all participants.

Results: A total of 360 participants were included in the study, and the participants' mean age was 39.7 ± 12.5 years. Somatization was detected in 35 (29.4%) of the case group, 13 (10.8%) of control group 1, and 3 (2.5%) of control group 2 (p=0.001). Obsessive-compulsive disorder was present in 36 (30.0%) of the case group, 15 (12.5%) of control group 1, and 17 (14.2%) of the control group 2 (p=0.001). In addition, depression was found 29 (24.2%) in the case group, 15 (12.5%) in the control group 1, 14 (11.7%) in the control group 2 (p=0.013). Anxiety was observed 21 (17.5%) in the case group, 13 (10.8%) in the control group 1, 8 (6.7%) in the control group 2 (p=0.031). General Severity Index positivity was found 24 (20.0%) in the case group, 11 (9.2%) in control group 1, and 7 (5.8%) in control group 2.

Conclusion: A comprehensive approach should be taken with individuals who want to quit smoking, considering that tobacco addiction is a substance use disorder.

Keywords: Mental disorders, mental health, smoking cessation, tobacco use



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INTRODUCTION

The medical and economic consequences of the worldwide tobacco epidemic demonstrate that tobacco control is a vital public health priority. According to the World Health Organization, nicotine is a psychoactive substance that may not always result in addiction, but it impacts mental processes, such as perception, consciousness, mood, and emotions upon entering the system. In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, tobacco use is categorized as "tobacco use disorder" within the group of substance-related and addictive disorders. This inclusive category covers all forms of tobacco use. Recent studies suggest a relationship between smoking and mental disorders, as individuals with mental disorders have been found to have increased smoking rates and lower smoking cessation success when compared to those without a history of psychiatric illness. And This highlights the potential impact of smoking on mental health. This study aims to compare the frequency of psychiatric symptoms according to smoking status.

METHOD

This case-control study was conducted from November 01, 2022, to March 01, 2023, and included individuals aged 18 years and above who applied to the smoking cessation outpatient clinic (SCOC) and family medicine outpatient clinics (FMOC). The study's sample size was determined by incorporating a 50% frequency, 95% confidence interval and 5% type 1 error margin in an unknown population. The participants were divided into 3 groups. 120 (33.3%) participants who were smokers and applied to the SCOC at the family medicine center were included as the case group, 120 (33.3%) participants who were smokers but did not want to quit and applied to the FMOC were included as the control group 1 and 120 (33.3%) participants who were non-smokers were included as the control group 2.

Patients who refused to participate, had communication disabilities, cognitive impairments, or intellectual disabilities were excluded.

In this study, regular smokers were defined as individuals who, according to the National Health Survey criteria, had smoked at least 100 cigarettes in their lifetime and used at least one tobacco product per day. [5] Individuals who consume alcohol at least once a month, regardless of the amount consumed, were classified as alcohol users.

All participants completed a sociodemographic and medical history questionnaire with 16 questions, prepared by the researchers. Subsequently, the researcher administered a 53-question survey, including the brief symptom inventory (BSI), using a face-to-face interview technique. [6,7] This questionnaire covered topics, such as somatization disorder, obsessive-compulsive disorder (OCD), interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism, and additional items. Additional items included sleep disturbances, appetite problems, thoughts of death, and feelings of guilt. The sociodemographic survey consisted of multiple-choice questions about participants' age, gender, marital status, education level, employment status, income level, chronic illnesses, use of medication, history of psychiatric conditions, smoking habits, history of smoking cessation, alcohol consumption, and substance use status.

BSI is a self-assessment scale used for evaluating psychopathology, which was developed by Derogatis in 1992 based on the symptom checklist-90 (SCL-90). The scale's reliability and validity study was carried out by Sahin and Durak in 2002. The BSI, like the SCL-90, comprises 9 subscales and 3 scales that assess global discomfort. The scale includes three global indices: The general severity index (GSI), the positive symptom

distress index and the positive symptom total. When calculating the GSI, the cutoff value was taken as 1.51 point.

The study data were analyzed using the IBM Statistical Package for the Social Sciences Statistics 28.0. Descriptive values are presented as number, percentages, mean, standard deviation, median, interquartile range. Categorical variables were compared using the Chi-square test. Statistical significance was defined as p<0.05.

RESULTS

A total of 360 participants, 231 (64.2%) males and 129 (35.8%) females, were included in the study. The participants' mean age was 39.7±12.5 years. The socio-demographic characteristics of the participants according to groups are summarized in Table 1.

The mean duration of smoking among participants was 19.8 ± 11.2 years in the case group and 19.6 ± 12.4 years in the control group 1 (p=0.896). The mean number of cigarettes smoked daily in the case group was 24.0 ± 10.7 , meanwhile it was 18.9 ± 11.2 in the control group 1 (p<0.001). The mean smoking cessation time for the case group was 25.5 (118.0) days, while that for the control group 1 was 290.0 (260.0) days (p=0.077). Alcohol use was 29 (24.2%) for the case group and 43 (35.3%) for the control groups (p=0.005). Substance use did not differ significantly between groups (1 [0.8%] vs. 0 [0.0%], p=0.558).

In the case group, 24 (20.0%) of individuals tested positive for GSI, compared to 11 (9.2%) and 7 (5.8%) in the control groups (p=0.013). The frequency of psychiatric symptoms according to groups is summarized in Table 2.

DISCUSSION

Although it is reported previously that smoking behavior is higher in patients with mental disorders, the number of studies on the underlying mechanisms is insufficient.[3,4] In this study, the frequency of prior psychiatric disease diagnosis was higher in the case group. A case-control study by Rosenblum et al., divided participants into three groups similar to this study, indicated that higher levels of cigarette craving and consumption were observed in the first two groups compared to the control group without a psychiatric diagnosis. [8] It is hypothesized that patients in these groups differed from the control group due to the motivation that smoking provides a sense of comfort. Nobile et al., also suggest that people with bipolar disorder have a lifetime prevalence of smoking that is 2-5 times higher than the general population.[9] Second, this study found a statistically significant difference in daily cigarette consumption between the case group and the control group 1.

	Case Group (n=120)	Control Group 1 (n=120)	Control Group 2 (n=120)	р
Age groups				
≤35 years	59 (49.2)	47 (39.2)	60 (50.0)	0.173
>35 years	61 (50.8)	73 (60.8)	60 (50.0)	
Gender				
Male	77(64.2)	77 (64.2)	77 (64.2)	1.000
Female	43 (35.8)	43 (35.8)	43 (35.8)	
Marital status				
Married	72 (60.0)	73 (60.8)	70 (58.3)	0.11
Single	34 (28.3)	38 (31.7)	46 (38.3)	
Widow/divorced	14 (11.7)	9 (7.5)	4 (3.4)	
Education level				
Less than high school	75 (62.5)	52 (43.3)	36 (30.0)	<0.00
More than high school	45 (37.5)	68 (56.7)	84 (70.0)	
Employment status				
Employed	72 (60.0)	91 (75.8)	87 (72.5)	0.01
Unemployed	48 (40.0)	29 (24.2)	33 (27.5)	
Monthly income				
≤450\$	58 (48.3)	41 (34.2)	31 (25.8)	0.00
>450 \$	62 (51.7)	79 (65.8)	89 (74.2)	
Chronic illnesses				
Yes	38 (31.7)	30 (25.0)	27 (22.5)	0.25
No	82 (68.3)	90 (75.0)	93 (77.5)	

	Case Group (n=120)	Control Group 1 (n=120)	Control Group 2 (n=120)	р
Somatization disorder	35 (29.4)	13 (10.8)	3 (2.5)	<0.001
Obsessive-compulsive disorder	36 (30.0)	15 (12.5)	172(14.2)	0.001
Interpersonal sensitivity	24 (20.0)	12 (10.0)	11 (9.2)	0.021
Depression	29 (24.2)	15 (12.5)	14 (11.7)	0.013
Anxiety disorder	21 (17.5)	13 (10.8)	8 (6.7)	0.031
Hostility	29 (24.4)	23 (19.2)	10 (8.3)	0.004
Phobic anxiety	14 (11.7)	1 (0.8)	6 (5.0)	0.001
Paranoid ideation	37 (30.8)	11 (25.0)	11 (12.5)	0.003
Psychoticism	13 (10.8)	6 (5.0)	4 (3.3)	0.045
Additional Items	35 (29.2)	16 (13.3)	8 (6.7)	< 0.001

On the other hand, studies suggest that nicotine addicted smokers are three times more likely to develop alcohol dependence than those who do not smoke. [10] However, one of the limitations of this study is that nico-

tine dependence was not measured in the groups; a significant difference was found between the case group and the control group 1 in the frequency of alcohol use in this study.

A significant difference was detected between the case and control groups in terms of somatization disorder. According to a case-control study carried out by Gulsen and Uygur in individuals who applied to SCOC, somatic symptoms in the case group were found to be significantly different when compared with the control group, who had never smoked.^[3] The findings of high somatization scores in people with high levels of nicotine dependence indicate that nicotine or nicotine dependence may be involved in the etiology.^[3] Examining somatic symptoms in both those who applied to the SCOC and FMOC is what differentiates our approach from previous studies.

In a study conducted in Turkey among clinically followed adolescents with various mental disorder diagnoses, those diagnosed with OCD demonstrated a significantly lower smoking rate compared to those with other psychiatric disorders.[11] A review of the literature reveals that individuals diagnosed with OCD tend to have low rates of smoking.[12] The elevated frequency detected in this study's case group is probably a result of the limited sample size. However, no studies have investigated the incidence of OCD among smokers. This study differs from previous research in its examination of the presence of OCD in smokers reversely. A cohort study conducted by Virtanen et al., in a larger sample revealed that OCD elevates the risk of substance use disorder.[13] Considering that cigarette addiction is also a type of substance abuse, there is a need for studies to clarify its relationship to OCD. In addition, it was found that OCD patients exhibit higher severity of nicotine dependence. In the study, a significant relationship between impulsivity and nicotine dependence was found in the OCD group.

When the participants were analyzed regarding interpersonal sensitivity, a significant difference was observed between the groups. However, according to the case-control study conducted by Gulsen and Uygur, there was no significant difference between the groups.^[3]

In this study, there was a significant difference between all three groups in the analysis of depression. Based on the literature, numerous studies have screened depression among individuals who have applied to SCOC and among those who have quit smoking.^[14,15] However, the inclusion of control groups 1 and 2 distinguishes this study from the existing literature. In a study reported by Velioğlu et al., on patients who applied to SCOC, the relationship between nicotine dependence level and depression was found to be significant.^[16] In a study conducted by Hahad et al., analysis was performed on a 5-year follow-up of smokers and individuals who applied to SCOC.^[17] It has been found that present smokers exhibit a higher prevalence of depressive

symptoms, and there exists a correlation between cigarette pack years and depressive symptoms.[16] However, the absence of measurement of nicotine dependence is a limitation of this study; the comparison of cigarette pack-years and potential depression frequencies between the case and control groups supports these findings. A retrospective analysis by Wooton et al., examined individuals with a history of lifelong smoking and depression and concluded that smoking is a risk factor for the development of depression.[18] Similarly, Gulsen and Uygur found a significant difference between smokers and non-smokers with respect to depression.[3] It is unexpected that the frequencies of potential depression were similar between control group 1 and control group 2 in this study, when evaluated objectively. This is likely due to the fact that depression was the most frequently diagnosed psychiatric disorder in all three groups.

An evaluation of the participants in terms of possible anxiety revealed a significant difference between the groups. A review of the literature reveals a higher prevalence of smoking among individuals with anxiety disorders. [19] It is reasonable to expect that these people would have a higher nicotine dependence than people without anxiety and would seek help from the SCOC; this is thought to be the reason for the difference between the case and control groups in this study.

A significant difference was identified between the groups in terms of their level of hostility. The correlation between nicotine consumption and heightened aggression has been established in previous research.^[20] The findings of this study suggest that the elevated nicotine consumption in the case group might have contributed to these outcomes.

A significant difference was noted between the groups with regard to the presence of possible phobic anxiety. Dahne et al reported that individuals with social phobia had higher smoking frequencies compared to those without psychological comorbidity, with 54.0% being lifelong smokers. There are few studies on the relationship between phobic anxiety and smoking in the literature and this study has enriched the literature in this regard. The cause of the high frequency in the case group compared to the control group 1 can be clarified by examining the object or event considered as phobic in detail with different methods and measurements.

A significant difference between the groups was found when analyzing the participants in terms of paranoid disorder. The study by Gulsen and Uygur found that an increase in nicotine dependence level corresponded with higher levels of paranoid symptoms, while no significant difference was observed between smokers and non-smokers in the same study. In a study by Zvolensky et al., a significant proportion of people with personality disorders were found to be nicotine dependent. However, in cases of paranoid personality disorders, this correlation has been partially attributed to co-occurring anxiety/mood disorders. As the level of nicotine dependence was not assessed in the study, it is not possible to conclude that the high frequency of possible paranoid disorder in the case group is attributable to the relationship between personality disorders and nicotine dependence.

A significant difference was identified between the groups when the participants were analyzed in terms of possible psychoticism. Similarly, Gulsen and Uygur found a significant difference in psychoticism frequencies between smokers and non-smokers in their study.[3] In a study conducted by Lally et al., the positive symptom score was found to be higher among those with high nicotine dependence, regardless of whether they had first-episode psychosis or established psychosis.[4] Mustonen et al., reported that smoking could be a potential risk factor for the development of psychosis.[23] The results of this study indicate a potential correlation between tobacco use and the emergence of psychosis. While acknowledging the limitation of not measuring nicotine addiction in this study, it is crucial to note that the case group had higher levels of cigarette consumption for more years and shorter guit times, resulting in a greater amount of nicotine exposure compared to the control group. Further research is needed to support this hypothesis.

Significant differences were found among the three groups regarding additional items. Since the scale was introduced in 1994 and the use of these additional items has decreased terminologically, present literature lacks studies on the topic. [24] In addition to its psychostimulant effect, smoking is known to cause insomnia and anorexia by disrupting the hypothalamic-pituitary-adrenocortical axis. The research conducted by Gulsen and Uygur revealed a statistically significant difference between smokers and non-smokers in terms of additional items. [3]

The case group had a much higher GSI and this indicates more psychological distress in people seeking smoking cessation treatment. GSI is the most reliable indicator of overall symptom severity. This suggests that these patients have more complex mental health needs. They may need more support than smokers and non-smokers. Prior studies found similar results. They also found higher psychiat-

ric comorbidity and distress in smokers trying to quit. This highlights the role of psychological factors in smoking and relapse. ^[14,17] Therefore, smoking cessation programs should include mental health screening and support. This may improve treatment success and patient well-being.

This study has several limitations. First, the study design is cross-sectional. This prevents conclusions about cause and effect. Second, nicotine dependence was not measured. This limits the evaluation of symptom severity and addiction intensity. Third, differences in socioeconomic status were not fully controlled for. This includes education and income, which may be confounding factors. Finally, self-reported data were used. This may have introduced reporting bias.

CONCLUSION

These findings indicate that patients presenting to smoking cessation clinics frequently experience a higher burden of psychiatric symptoms. This underlines the importance of conducting routine mental health screening during smoking cessation consultations for family physicians. A holistic and multidisciplinary approach that addresses both nicotine dependence and coexisting psychiatric symptoms may improve cessation success and overall patient well-being.

Disclosures

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Detection of Puberty Tarda in a Patient Applied for Screening: A Case Report

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ABSTRACT

Puberty is a critical period in an individual's physical and psychological development. Annual physical examinations are recommended for adolescents, regardless of the presence of symptoms. This report presents the case of a 14-year-old licensed male football player who visited our Education Family Health Unit without any additional complaints and was evaluated for delayed puberty. The discussion emphasizes the importance of adopting and maintaining healthy eating habits during this stage of rapid physiological, psychological, and social growth. A thorough and detailed physical examination is essential for every adolescent presenting to family health centers.

Keywords: Delayed puberty, family practice, nutritional status



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INTRODUCTION

Adolescence, marked by the hypothalamic-pituitary-gonadal axis, is a key growth milestone. If this axis does not work by the age of 13 years in girls or 14 years in boys, delayed puberty may be diagnosed. Although there is no universal definition for puberte tarda, it is commonly thought to occur when puberty signs are >2–2.5 standard deviations below the age average. In the determination of this condition, it can be evaluated that breast budding (breast Tanner stage 2) has not started, even though being at the end of 13 years of age in girls, and testicular volume has not reached 4 mL (genital Tanner stage 2) even though being at the end of 14 years in boys. Puberte tarda is a symptom rather than a diagnosis and may be due to chronic illnesses, excessive thinness, hypogonadotropic hypogonadism, hypergonadotropic hypogonadism, or constitutional delay of growth and puberty.

"Protocol Guide for Infant, Child, and Adolescent Follow-up, published by the Ministry of Health of the Republic of Türkiye recommends annual adolescent follow-ups from 10 to 21 years. [5] Within the scope of the school screening programme, patients in this age group visit their family physicians. These visits should be used for anamnesis, physical examinations, growth assessments, and necessary laboratory tests. Conditions like delayed puberty should be identified early to ensure timely treatment and planning.

In this case report, it was presented a case of puberty tarda in a 14-year-old boy directed to our family health unit within the scope of the school screening programme without any complaints.

CASE REPORT

A 14-year-old male patient visited our family health unit without additional complaints. The patient is also a licensed soccer player. In accordance with national guidelines, anthropometric measurements were taken, a home, education/employment, eating, activities, drugs, sexuality, suicide/depression assessment was conducted, a comprehensive physical examination was performed, and the necessary laboratory tests were ordered.

The anamnesis revealed good school performance; also, he had a history of specific learning disabilities and speech disorders, with no current medication. Anthropometric measurements of the patients and growth percentile values according to Neyzi data are summarized in Table 1.^[6]

Growth retardation was identified. On obtaining consent, a genital examination showed a stretched penile length of 3 cm, suggesting micropenis. Testicular volume was not assessed due to a lack of an orchidometer. There was no axillary or pubic hair, and the patient was evaluated as Tanner Stage-1. Other system examinations were normal. The home, education/employment, eating, activities, drugs, sexuality, suicide/depression, safety (HEEADSSS) assessment was performed, revealing no substance abuse. The patient's socio-economic status was low, with poor protein intake and an irregular diet, as reported by his parents.

The patient, with lagging height and weight percentiles and Tanner Stage 1, was referred through our system to the pediatric polyclinic for further evaluation of delayed puberty and growth retardation. In our patient's data checked through E-nabiz (consent was obtained from the patient and parents), it was seen that he was referred to pediatric endocrinology.

Table 1. Anthropometric measurements of the patients and growth percentile values according to Neyzi data

	Measurements
Height (cm)	146.1 (SDS: –2.61, persentile: 0.45, Age of height: 11.34)
Weight (kg)	36.9 (SDS: –2.35, persentile: 0.94, Age of weight: 10.84)
BMI (kg/m²)	17.29 (SDS: -1.29, persentile: 9.85)
Target height (cm)	161.3 (SDS: -2.42, persentile: 0.78)
Height of mother (cm)	147.3
Height of father (cm)	162.3

BMI: Body mass index; SDS: Standard deviation score.

Complete blood count and lipid profile were also requested, and the results were within normal ranges (checked in our center). Laboratory parameters of the patients are summarized in Table 2. Laboratory test results (checked in another hospital) indicated Vitamin D deficiency. Tissue transglutaminase immunoglobulin was <2 (negative), ruling out celiac disease. Alkaline phosphatase levels, expected to rise during growth periods, were low. Morning cortisol and adrenocorticotropic hormone levels were measured between

Table 2. Labora	ory parameters	s of the patients
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Table 21 Laboratory parameter			
	Patient Value	Reference Value	
25-hydroxy vitamin D (nmol/L)	55	≥50	
Protein (g/L)	67.4	67–84	
Albumin (g/L)	44.83	32-48	
Sodium (mEq/L)	140	132–146	
Potassium (mEq/L)	5.09	3.5-5.5	
Magnesium (mg/dL)	2.28	1.3-2.7	
Calcium (mg/dL)	9.70	9.1–10.3	
Phosphorus (mg/dL)	4.62	3.4-5.9	
ALP (U/L)	109	115–471	
Fasting blood glucose (mg/dL)	87	70–99	
TSH (mU/L)	3.11	0.51-4.94	
Free T4 (mU/L)	1.07	0.83-1.43	
FSH (U/L)	1.6	1.4–18.1	
LH (U/L)	0.1	Tanner Stage-1: <0.02 – 0.5	
		Tanner Stage-2: 0.03 – 3.7	
		Tanner Stage-3: 0.09 – 4.2	
		Tanner Stage-4/5: 1.3 – 9.8	
Estradiol (ng/L)	<11.80	11.8–48.9	
Progesterone (μg/L)	<0.21	0.28-1.22	
17-Hydroxyprogesterone (nmol/	L) 1.25	1.79–10.42	
Prolactin (μg/L)	3.44	3.2-13.5	
Total testosterone (μg/L)	< 0.07	1.448.42	
DHEAS (μg/dL)	44.24	37.3-270.2	
Cortisol (µg/dL)	7.98	5.2-22.4	
ACTH (pg/mL)	15.3	<46	
IGF-1 (μg/L)	106	177–507	
IGFBP-3 (mg/L)	3.6	3.5–10	
IgA (nephelometric) (g/L)	1.450	0.40-3.50	
ACTH: Adrenocorticotronic hormone: ALP: Alkaline phosphatase: DHFAS:			

ACTH: Adrenocorticotropic hormone; ALP: Alkaline phosphatase; DHEAS: Dehydroepiandrosterone sulfate; FSH: Follicle-stimulating hormone; IgA: Immunoglobulin A; IGF-1: Insulin-like growth factor-1; IGFBP-3: Insulin-like growth factor binding protein-3; LH: Luteinizing hormone; T4: Thyroxine; TSH: Thyroid stimulating hormone.

07:00 and 09:00 a.m. The patient's insulin-like growth factor 1 level was below the normal reference range for age and Tanner Stage 1, while the insulin-like growth factor binding protein 3 level was normal.

Bone age was found to be 12.5 years, and calendar age was found to be older than bone age and height. Pelvic ultrasound revealed normal testicular dimensions (right: 16×12×15 mm, left: 15×12×24 mm), with no pubic or axillary hair, confirming Tanner Stage-1. The patient was referred to a dietician; a 2200 kcal high-protein diet was organized, and healthy nutrition recommendations were made; called for follow-up after 3 months to be evaluated in terms of puberty and short stature.

DISCUSSION

Puberty onset can vary based on nutrition, environmental factors, and genetics.[7] Gastrointestinal, endocrinologic, or psychological disorders can affect the puberty process. 62% of puberty tarda cases are constitutional, which have a family history of puberty tarda. 0.7% of the cases are hypergonadotropic hypogonadism patients; for example, gonadal dysfunction due to chemo- or radiotherapy, bilateral cryptorchidism, trauma to the testis, sex chromosomal anomalies like (45 X/46 XY) or Klinefelter syndrome (47 XXY). When all cases were evaluated, 36.8% of the cases were hypogonadotropic hypogonadism patients due to primary chronic or systemic illness (asthma, chronic renal failure, inflammatory bowel disease, celiac disease, anorexia nervosa), excessive exercise or malnutrition, or hypothalamic or pituitary failure/damage. Abdominal pain or changes in bowel habits may suggest inflammatory bowel disease or celiac disease. Symptoms such as weight loss or heat intolerance could indicate thyroid disease. Micropenis with cryptorchidism may suggest hypogonadism. In cases of excessive exercise and dietary restriction, anorexia nervosa should be considered during this period of intense physical and psychological changes. Nutrition has an important effect on puberty progression, for example, pesticide residues are largely found in daily consumed food such as fruits, vegetables, and dairy products. In a review which's about the effects of endocrine disruptors employed in agriculture on puberty, they explored that some of the chemicals can cause a delay in puberty progression of menarche.[8]

Proper nutritional habits are crucial during adolescence, a period influenced by socio-economic and cultural factors, and vital for establishing lifelong behaviors and preventing adult diseases.^[8] Evaluating growth percentiles and monitoring puberty at healthcare visits, with a focus on healthy nutrition, is essential.^[5] Family physicians play a key role in adolescent care through school screenings and regular

visits, as demonstrated by our case, where history, physical examination, growth percentile evaluation, and Tanner staging were crucial for early diagnosis and referral.

CONCLUSION

Monitoring growth and puberty in adolescents is crucial for their health. Any interruption in this monitoring could indicate underlying conditions. Following guidelines, primary care physicians should conduct thorough anamnesis, physical examinations, growth assessments, Tanner staging, and psychosocial HEEADSSS evaluations for every adolescent.

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