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From the Editor

Dear readers,

In the last issue of 2022, we have prepared 9 research articles and a case report that we think will be interesting for you. We hope that these articles will be a guide for healthcare professionals, especially primary care physicians.

We are proud that our journal has the highest citation rate among the primary care journals published in Turkey. Thank you for your growing interest in our journal.

Please stay tuned for the next issue.

Assoc. Prof. Dr. Ahmet Keskin

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Research Article

Ankara Med J, 2022;(4):461-471 // 10.5505/amj.2022.90001

A SURVEY STUDY OF COVID-19 VACCINE HESITANCY OF RELATIVES OF PATIENTS ADMITTED TO A TRAINING AND RESEARCH HOSPITAL IN ISTANBUL

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Abstract

Objectives: Treatment and immunization studies of the COVID-19 infection are still ongoing. Vaccine hesitancy or refusal, which is an important public health problem, has also come to the fore as a factor that negatively affects community immunization during the COVID-19 pandemic. In this study, it was aimed to analyze the thoughts and attitudes of the relatives of patients who were under observation in the hospital due to COVID-19 in the second wave of the pandemic, whether they should have the COVID-19 vaccine or not, and the factors that caused it.

Materials and Methods: The study was carried out between 20.12.2020-20.01.2021 in Başakşehir Çam and Sakura City Hospital COVID-19 Emergency Clinic Yellow Zone. A 25-question questionnaire was applied to a total of 429 relatives of patients who gave consent to the study.

Results: While 40.09% of the participants were considering getting the COVID-19 vaccine, 24.94% were not thinking, and 34.97% were not sure. Those who were positive about getting vaccinated mostly (69%) stated that they were worried about the serious infection of COVID-19 infection, and nearly half of those who did not plan to have the vaccine stated that they made this decision because the content of the vaccine was unknown. When asked which sources they trust more about COVID-19 and its vaccine, they said that they trust the official statements at the highest rate and then their family physician.

Conclusion: The most effective method of protection against COVID-19 infection is vaccination. The fact that family physicians are the second source that people trust should be considered as a great opportunity for vaccine hesitancy and refusal problems.

Keywords: COVID-19, immunization, vaccination refusal, family physician.

Introduction

Vaccines, which have been around for nearly 200 years in the history of medicine, seem to be more effective than treatments in eradicating infectious diseases. Access to clean water has been found to be more effective than vaccines in the fight against infectious diseases.[1] Smallpox has been completely eradicated globally, while infections such as measles, polio, tetanus, and diphtheria have been eradicated locally, with the vaccination studies carried out so far. [2]

Decreased incidence and prevalence of vaccine-preventable diseases are closely linked to vaccination rates. The highness of this rate provides not only direct protection of vaccinated individuals but also provides indirect protection of society from such infections (herd immunity).[3,4] Although vaccination programs are generally accepted, and most of the population is vaccinated, there are individuals or communities who are hesitant or object to these studies. There is a growing literature on vaccine hesitancy, with the most important reasons varying by country, region, subgroups, vaccine type and many related effects. Despite the diversity of reasons for hesitancy across geographic regions and vaccines, there are common themes that emerge globally.[5] The Strategic Advisory Group of Experts (SAGE) on Immunization, affiliated with the World Health Organization (WHO), on vaccine hesitancy, defined as "delaying or refusing vaccination acceptance despite the availability of vaccination services". Vaccine hesitancy is complex, situation-specific, and varies with time, place, and vaccines. It includes hesitation about one or more vaccines.[6] (Table 1). Vaccination refusal is the case of rejecting all vaccines in the literature voluntarily and not having them done. [5,6]

When vaccine hesitancy or refusal is examined, it is seen that this attitude began with the first vaccination studies. Edward Jenner's attempt to popularize smallpox vaccination in England was criticized or rejected by some religious circles and by some parts of society because of the high complication rates (30% mortality, etc., skin scars and blindness) related to the vaccine.[4,7]

COVID-19 Pandemic

Coronaviruses are RNA viruses from the Coronaviridae family and have taken this name because of the crown appearance caused by the spikes on their surfaces. WHO has identified many Coronavirus types since 2002.[8,9] On the other hand, the COVID-19 type was defined for the first time on December 31, 2019, as the causative agent of pneumonia in Wuhan, China, and the cases spread rapidly, first in Wuhan and then throughout the country. The treatment and immunization studies of this epidemic disease, which was declared a "pandemic" by WHO on March 11, 2020, are still ongoing.[10] As in other infectious diseases, vaccine hesitancy or refusal in the COVID-19 pandemic affects immunization studies.

The aim of this study was to analyze the rates of hesitancy and refusal to vaccinate against COVID-19 in the relatives of patients who were under observation in the COVID-19 yellow zone in a tertiary hospital in Istanbul during the second wave of the pandemic and the personal or social factors affecting it.

Table 1. The factors affecting vaccine hesitancy[6]

1. Contextual effects (The effect of historical, sociocultural, environmental, health system / institutional, economic, and political factors)	**2. Individual or group effects (Effects arising from personal vaccination perception or social environment)**	**3. Special issues about vaccine/vaccination**
a. Communication or media	a. Personal, familial, and environmental vaccination experiences, including pain	a. Calculation of risk/benefit (epidemiological or scientific evidence)
b. Effective leaders, anti-vaccine or pro-vaccine lobbies	b. Beliefs and attitudes about health and prevention	b. A new vaccine, a new formulation, or a new recommendation for an existing vaccine
c. Historical effects	c. Knowledge/awareness	c. Form of application
d. Religion/culture/ gender/socio-economical effects	d. Personal experience and confidence with the healthcare system and its providers	d. Vaccination program design / Vaccination campaign method
e. Political effects	e. Risk/benefit perception-intuition	e. Reliability and/or supply of vaccine and/or vaccination equipment
f. Geographic barriers	f. No vaccination required / harmful thought as a social norm	f. Vaccination program
g. Perception of the pharmaceutical industry		g. Costs
		h. Strength of recommendation and/or source of information and/or attitude of health professionals

Materials and Methods

The study was carried out between 20.12.2020 and 20.01.2021 in Başakşehir Çam ve Sakura City Hospital COVID Emergency Polyclinic Yellow Zone. The universe of the study consisted of the relatives of the patients who applied to the COVID-19 Emergency Polyclinic Yellow Zone. Since the number of patients who applied to this area in a month was approximately 1000 at that time, and approximately 80% of these patients had

relatives, our sample size was 360 people at the 95% confidence interval. It was planned to reach approximately 420 patient relatives by calculating the losses. A survey form was applied to 429 patients' relatives in total. The local ethics committee approved the study. All procedures followed the Declaration of Helsinki, and informed consent was obtained from all participants.

The first part of the questionnaire contains sociodemographic information about the relatives of the patients, their general approach to childhood and adult vaccines, and their thoughts on COVID-19 infection and vaccines, the second part of the questionnaire contains questions about the sources of information about the vaccines, with a total of 25 questions. In the survey, the income level question was determined according to a person's subjective opinion.

SPSS-24 (Statistical Package for Social Sciences, IBM) program was used for statistical analysis of the data in the study. In addition to descriptive statistical methods, in comparison of quantitative data, normally distributed parameters were evaluated with Student's t-test, and non-normally distributed parameters were evaluated with Mann Whitney U test. The Chi-square test was used to compare qualitative data. The results were accepted as a 95% confidence interval and statistical significance $p<0.05$.

Results

The mean age of the 429 participants to whom we applied the questionnaire was 33.69 ± 11.47 years old. The female/male ratio was 47.09%/52.91%. The demographic data of the participants, their previous attitudes about getting vaccinated and their thoughts on getting vaccinated for COVID-19 are given in Table 2.

When asked which rules they had the most difficulty following during the pandemic, 41.49% (n: 178) stated that they had difficulty wearing a mask, and then they had difficulty complying with the social distance isolation rules (n: 150, 34.96%) and 134 people (31.23%) stated that they had no difficulty in obeying any rule. When people who are considering or undecided about getting the COVID-19 vaccine were asked about their reasons for choosing to get the vaccine as multiple options, 149 (68.98%) of the 216 respondents answered that they were concerned about the serious infection of COVID-19 infection. The second most important reason for a positive approach to Vaccination was that they did not want to infect their families and loved ones (n: 84, 38.88%), and the positive approach of scientists to vaccination was the third important reason (n: 78, 36.11%).

Table 2. Sociodemographic characteristics of the participants, their knowledge and opinions about previous vaccinations and COVID-19 infection

	n	%		n	%
Gender			**Contact with COVID-19 patient**		
Woman	202	47.09	Yes	273	63.64
Man	227	52.91	No	156	36.36
Total	429	100.00	Total	429	100.00
Education degree			**Compliance with isolation rules**		
Literate or Primary school	77	17.94	Yes	253	58.97
Middle or High school	148	34.50	Partially	168	39.16
Undergraduate- License	184	42.89	No	8	1.87
Graduate	20	4.67	Total	429	100.00
Total	429	100.00	**Influenza vaccination**		
Income level			Yes	42	9.79
Too bad	32	7.46	No	327	76.22
Bad	77	17.95	Sometimes	60	13.99
Medium	241	56.18	Total	429	100.00
Good	74	17.25	**Pneumococcus vaccination**		
Very good	5	1.16	Yes	71	16.55
Total	429	100.00	Not in the risk group, so didn't have done	333	77.62
Marital status			Never done	25	5.83
Married	223	51.98	Total	429	100.00
Single	187	43.59	**Parents' vaccination status**		
Divorced/widow	19	4.43	Yes	196	82.01
Total	429	100.00	No	31	12.97
Having chronic disease			Irregular	12	05.02
Yes	87	20.28	Total	239	100.00
No	342	79.72	**Thought on COVID-19 vaccine efficacy**		
Total	429	100.00	Effective	190	44.29
Regular use of medication			Ineffective	85	19.81
Yes	84	19.58	Not sure	154	35.90
No	345	80.42	Total	429	100.00
Total	429	100.00	**Thinking about getting the COVID-19 vaccine**		
Had COVID-19 infection			Yes	172	40.09
Yes	155	36.13	No	107	24.94
No	232	54.08	Not sure	150	34.97
Not sure	42	9.79	Total	429	100.00
Total	429	100.00			
Hospitalization due to COVID-19 infection					
Inpatient	23	14.84			
Outpatient	132	85.16			
Total	155	100.00			

When the participants were asked the reason for their negative thoughts about the COVID-19 vaccine, about half of the 249 respondents (n:128, 51.40%) said the content of the vaccine was unknown, 116 people (46.58%) had the vaccine imported from a foreign country, and 93 people (37.34%) cited the fact that the Phase-3 studies of the vaccine are still ongoing. The relationship between COVID-19 vaccination intention and sociodemographic characteristics is given in Table 3.

Table 3. Statistical analysis of the factors affecting the thought of getting the COVID-19 vaccine

		COVID-19 Vaccination intentions n(%)			**P***
		Yes	**No**	**Not sure**	
Age	18-30	78(35.94)	64 (29.50)	75(34.56)	**0.047**
	31-50	63(40.38)	33(21.16)	60 (38.46)	
	51 and up	31(55.36)	10(17.86)	15(26.78)	
Gender	Woman	72(35.64)	47(23.27)	83(41.09)	**0.041**
	Man	100(44.05)	60(26.43)	67(29.52)	
Job	Officer	46(40.35)	27(23.69)	41 (35.96)	**0.002**
	Worker	38(33.63)	38(33.63)	37 (32.74)	
	Self-employment	39(55.71)	11(15.72)	20 (28.57)	
	Retired	12(75.00)	1(6.25)	3 (18.75)	
	Housewife	37(31.90)	30(25.86)	49 (42.24)	
Education degree	Literate or primary school	31 (40.26)	17 (22.08)	29 (37.66)	0.820
	Middle or high school	59 (39.86)	40 (27.03)	49 (33.11)	
	Undergraduate-License	71 (38.59)	46 (25.00)	67 (36.41)	
	Graduate	11 (55.00)	4 (25.00)	5 (20.00)	
Marital status	Married	97 (43.50)	49 (21.97)	77 (34.53)	0.381
	Single	70 (37.43)	51 (27.27)	66 (35.30)	
	Divorced/widowed	5 (26.32)	7 (36.84)	7 (36.84)	
Having chronic disease	Yes	48(55.17)	20(22.99)	19(21.84)	**0.003**
	No	124(36.26)	87(25.44)	131(38.30)	
Regular use of medication	Yes	41 (48.81)	20 (23.81)	23 (27.38)	0.153
	No	131 (37.97)	87 (25.22)	127 (36.81)	
Had COVID-19 infection	Yes	80 (51.61)	30 (19.36)	45 (29.03)	**0.007**
	No	80 (34.48)	64 (27.59)	88 (37.93)	
	Not sure	12 (28.57)	13 (30.95)	17 (40.48)	
Compliance with isolation rules	Yes	106(41.90)	66(26.09)	81(32.01)	0.234
	Partially	64(38.10)	37(22.02)	67(39.88)	
	No	2(25.00)	4(50.00)	2(25.00)	
Influenza vaccination regularly	Yes	34(80.95)	5(11.90)	3(7.15)	**< 0.001**
	No	117(35.78)	90(27.52)	120(36.70)	
	Sometimes	21(35.00)	12(20.00)	27(45.00)	
Parents' vaccination status of children	Yes	96(48.98)	31(15.81)	69(35.21)	**0.002**
	No	9(29.02)	11(35.49)	11(35.49)	
	Irregular	6(50.00)	6(50.00)	0(00)	

When asked under what circumstances they would consider getting vaccinated, nearly half of the 240 respondents (n:112, 46.66%) said that they would get the vaccine if a local vaccine was produced, 94 (39.16%) respondents said that they would get the vaccine if the vaccine content was explained clearly, and 85 (35.41%) respondents would get the vaccine if the Phase-3 studies were completed.

Twenty-seven people (11.25%) stated that they do not intend to apply the COVID-19 vaccine under any circumstances. When asked where they follow their information sources about COVID-19 and its vaccine, 347 people stated that they got information from television (80.88%), 253 people (58.97%) stated that they got information from social media and 91 people (21.21%) from forums on the internet.

When asked which sources they trust more about COVID-19 and its vaccine, 286 people (66.66%) stated that they trust the official statements, 131 people (30.53%) stated that they trust their family physician, and 121 people (28.20%) stated that they trust the doctors who appear on television.

Discussion

Vaccine hesitancy or rejection is based on very complicated reasons. In our study, it was aimed to analyze the cases of COVID-19 Vaccination in the relatives of patients under observation in the COVID-19 Emergency Yellow Zone of a training and research hospital and the multifaceted factors affecting it.

In the study, it was seen that male participants were more likely to consider getting the COVID-19 vaccine, while females were more undecided. When the age factor was evaluated, it was seen that those aged 51 and over were thought to be vaccinated statistically significantly compared to those at a younger age. In a study conducted on the Chinese population, the rate of those who intended to have the vaccine was 45.3%, while the rate of those who were undecided was 29.2%, and the rate of those who did not intend to have it was 25.5.[11] In a study conducted in the USA, while the majority of medical students were willing to get the COVID-19 vaccine, nearly a quarter were hesitant.[12] In our study, those considered to have the COVID-19 vaccine were retirees at the highest rate, then self-employed, and the difference was statistically significant. The fact that retirees considered having a high rate of Vaccination were considered as a result compatible with high age. The most undecided group was housewives. This result was also consistent with the female gender being undecided in our study.

Being a parent or having marital status are also factors that can affect vaccination rates and COVID-19 vaccine hesitancy. In a study of Italian parents, only 26.5% of parents stated that they were considering getting the

COVID-19 vaccine. Vaccine hesitancy was due to safety concerns at a rate of 76%. Female gender, younger age and low education level were the negative conditions that affected the positive attitude toward Vaccination. The external factor, on the other hand, only informed by the National Health Authorities had a positive effect on the vaccination rates.[13]

In our study, it was seen that an education degree did not affect vaccine hesitancy. Although the intention to vaccinate was higher in those with postgraduate education, it was not statistically significant. In Fedele's study, low education level was a reason for hesitations about the COVID-19 vaccine.

In a study conducted in Kazakhstan, COVID-19 vaccination hesitancy was approximately 36%. In this study, sociodemographic factors affecting COVID-19 vaccine hesitancy were the female gender, being 30 years old and over, being widowed or divorced, and having children, while the most important external factor was the country where the vaccines were produced.[14] As can be seen, sociodemographic factors affecting vaccine hesitancy vary between countries and cultures. In our study, while gender caused hesitations about Vaccination, marital status did not cause it, and the presence of chronic disease and COVID-19 had a positive effect on Vaccination. In this result, it can be thought that the experiences of those who have had COVID-19 regarding the severity of the infection may have positively affected the Vaccination.

Vaccination against COVID-19 may depend on being vaccinated against other viruses regularly. In our study, the thought of getting COVID-19 Vaccination was found to be statistically significantly higher in individuals who regularly get influenza vaccination every year and in parents who have their children vaccinated regularly. Sociocultural factors play an important role in vaccination hesitancy. In a social study conducted in Pakistan, COVID-19 vaccine hesitancy was found to be as high as 49%. Of the 46% group who wanted to have the vaccine, 42% stated that they would prefer not to have Western vaccines.[15] In a study conducted by Abbas et al. in the same country, while the belief that the vaccine would cause infertility was common in the low-education group, this belief was found to be very low in the graduate group.[16]

The duration of the pandemic also seems to be effective in COVID-19 Vaccination. Our study was carried out in January 2021, towards the end of the COVID-19 second wave. In a Hongkok study, willingness to accept the COVID-19 vaccine was lower in the third wave (34.8%) than in the first wave (44.2%). There appeared to be more concern about vaccine safety in the third wave.[17]

When vaccine hesitancy was investigated in a study conducted in the USA in April 2020, just at the beginning of the pandemic, it was seen that 57.6% were planning to be vaccinated, and 31.6% were undecided. Factors associated with vaccine hesitancy were younger age, lower education level, and no previous year flu vaccination. Reasons for vaccine hesitancy included vaccine-specific concerns, the need for more information, anti-vaccine attitudes or beliefs, and a lack of confidence.[18]

We have some limitations to this study. We applied the study only to the relatives of COVID-19 patients who applied to the emergency department of one hospital.

As a result, clarifying COVID-19 vaccine hesitancy can help effectively design public education campaigns aimed at improving vaccine acceptance behaviors. The fact that family physicians are an important source that people trust should be considered as a great opportunity for vaccine hesitancy and refusal problems.

Ethical Considerations: The study was evaluated at the meeting of the University of Health Sciences Hamidiye Scientific Research Ethics Committee dated 18.12.2020, and permission numbered 28/21 and 20/516 was obtained.

Conflict of Interest: The authors declare no conflict of interest.

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Research Article

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EVALUATION OF KNOWLEDGE, ATTITUDES, AND BEHAVIORS OF MOTHERS WITH 0-6 AGE GROUP CHILDREN ABOUT HOME ACCIDENTS

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Abstract

Objectives: This study was performed to investigate home accidents experienced by children aged 0-6 in the last two weeks, the level of security measures taken by mothers towards home accidents, and the affecting factors.

Materials and Methods: The data were collected through a questionnaire form and "The Scale for Diagnosing the Safety Measures of the Mother for Home Accidents in Children 0-6" with 289 mothers with children aged 0-6 who applied to a pediatric clinic.

Results: The mean score of the scale used in the study was 165.56±16.84. The higher the education level of the mother, the higher the scale score and the relationship between them was found to be statistically significant (p=0.033). The scale means score of working mothers was found to be significantly higher than that of non-working mothers (p=0.006). The mean score of mothers whose children had no home accident was higher than those whose children had a home accident, but the difference was insignificant (p=0.694). It was found that children of 9.00% of the mothers had had a home accident in the last two weeks, and the most common type of home accident was a fall. Most children who had a home accident were between 0-2.

Conclusion: It was determined that demographic characteristics of mothers, such as education and working status, were effective in their knowledge and attitudes about home accidents.

Keywords: Home accidents, prevention, child care.

Introduction

An accident is defined as an event that can be prevented by measures that can be taken that occur in an unplanned and unexpected time, resulting in loss of life and property.[1] Home accidents are defined as accidents that occur inside the home or its surroundings.[2] Home accidents have an important place among public health problems because they are preventable, common, and can cause death or disability.[3] Although the frequency of home accidents varies according to countries and age groups, it constitute 25% of childhood accidents[4] In Turkey, it has been reported that childhood home accidents constitute 18-25% of all accidents.[5] Although home accidents are seen in all age groups, they are an important public health problem, especially for children and the elderly.[6] Children at home, especially in pre-school, are more likely to face home accidents.[7] It has been determined that 45.4% of home accidents in our country are seen in 0-6 age group children. Children in this age group, Since they spend most of their time at home, are curious about exploring and learning about their environment, are constantly moving, are sensitive and open to environmental risks, have the habit of putting everything in their mouth, and their living spaces are not arranged according to the characteristics of children, and they do not have the developmental skills to protect themselves from accidents, they constitute the group with the highest accident rate in the home environment.[8] For children in this age group, the environment they are in should be made safe, and their parents should supervise the safety of their living spaces.[9] Mothers are usually the first to see home accidents and provide first aid to parents. For this reason, the knowledge level of mothers about first aid practices for home accidents is important in reducing the problems that may occur as a result of accidents.[10] Accidents can be prevented with regular training to be given to mothers who spend the most time with their children and make simple arrangements at home.[11]

This study was carried out to determine mothers' knowledge, attitudes, and behaviors about taking safety precautions against home accidents, to evaluate the effects of sociodemographic variables on home accidents in 0-6 age group children, and to determine which subjects mothers need the education to prevent home accidents.

Materials and Methods

This descriptive cross-sectional study was conducted in a training and research hospital pediatrics polyclinics between May 1, 2017, and June 30, 2017, and written permission was obtained from the relevant institution before the research. The universe of the study consisted of mothers with children aged 0-6 years who applied to outpatient clinics. In the study, where the number of individuals in the population is unknown, the sample size was determined as a minimum of 289 people, with a 95% confidence interval, 80% power, and a 5% margin of error resulting from the power analysis. A sample of 289 mothers with children aged 0-6 years who applied to pediatric polyclinics (without emergency medicine and orthopedics and traumatology polyclinics)

between the study dates was formed. During the interview, the mothers were informed about the purpose of the study and the questionnaire and the "Scale for Defining the Safety Precautions of the Mother for Home Accidents in 0-6 Years-Old Children". Questions about the forms were answered by the researcher. The face-to-face interview technique was applied to mothers who had difficulties filling out the forms.

The questionnaire developed in line with the literature included a total of 35 questions questioning the sociodemographic data of the family, the presence of chronic diseases of the child and the mother, the status of the child's home accident, and the characteristics of the accident.[12-15] In the study, the "Scale for Defining the Safety Precautions of the Mother for Home Accidents in Children aged 0-6 years", developed by Çınar, a Turkish validity-reliability study (Cronbach's alpha: 0.8205), was used.[16] The scale, which evaluates the safety measures taken by the mothers to protect their children from falling, burning, poisoning, and drowning, which are the most common home accidents in the home environment, consists of a total of 40 items, including 34 positive and six negative statements. In the five-point Likert-type scale, each item is scored from 1 to 5, and the scores vary according to the answers. In items with positive statements, the answer is always 5 points, most often 4 points, sometimes 3 points, rarely 2 points, never 1 point, whereas in the 6, 9, 23, 26, 30, and 40 items with negative expressions, the scoring is reversed. The minimum score on the scale is 40, and the maximum score is 200. The highest score indicates that the mother takes measures to protect her child from home accidents at the highest level.

Statistical analysis

The data plan to be used in the study was saved in an excel file. Data analysis was performed with the "IBM Statistical Package for the Social Sciences for Windows, Version 24.0 (IBM Corp., Armonk, NY)" program. The nationality, age, birth information, blood parameters of the pregnant women, and sex and birth information of the newborns were summarized using descriptive statistics. A Chi-square test was used to compare qualitative data between groups. The normal distribution suitability of the data was evaluated by analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Comparisons in two groups with parametric conditions were made using the Student's t-test, and comparisons in groups of three or more were made with the One Way Anova test. Data were presented as arithmetic mean ± standard deviation, minimum and maximum value. The Mann-Whitney-U test determined comparisons in the two groups without parametric conditions; comparisons in groups of three or more were made with the Kruskal-Wallis test. Numerical data are presented as median. For statistical significance, the type-1 error level was determined as 0.05.

Results

It was determined that the mean age of the mothers included in the study was 30.28±5.78. The mean age of the children of the mothers included in the study was 2.54±1.97 years. The distribution of children's home accidents according to the descriptive characteristics of mothers is given in Table 1.

Table 1. Distribution of children's home accidents according to the descriptive characteristics of mothers (n=289)

		Children with home accident, n (%)	Children without home accident, n (%)	Total, n (%)	P Value*
Mother's age group	≤30 years old	18 (11.54)	138 (88.46)	156 (53.98)	0.102
	>30 years old	8 (6.02)	125 (93.98)	133 (46.02)	
Mother's educational status	Primary school and below	11 (8.53)	118 (91.47)	129 (44.64)	0.802
	Above primary school	15 (9.38)	145 (90.63)	160 (55.36)	
Mother's working status	Working	4 (8.33)	44 (91.67)	48 (16.61)	0.860
	Not working	22 (9.13)	219 (90.87)	241 (83.39)	
Economical situation	Good	10 (12.99)	67 (87.01)	77 (26.64)	0.351
	Medium	13 (7.78)	154 (92.22)	167 (57.79)	
	Bad	3 (6.67)	42 (93.33)	45 (15.57)	
Number of children	1	11 (12.50)	77 (87.50)	88 (30.45)	0.125
	2	13 (9.56)	123 (90.44)	136 (47.06)	
	≥3	2 (3.08)	63 (96.92)	65 (22.49)	

(*Chi-square Test)

When the scores of the "Scale for Defining the Safety Measures of Mothers for Home Accidents in Children aged 0-6", which measures the knowledge level of mothers about home accidents, were evaluated, the scale score average was found to be 165.56±16.84, and the median value was 166 (min:86, max:199) (Figure 1). The comparison of scale score averages according to the descriptive characteristics of children and mothers is shown in Table 2. In our study, it was observed that the mean score of the scale increased as the educational

status of the mothers increased, and the relationship was found to be significant (p=0.033). The mean scores of the working mothers were higher than the non-working mothers, and the difference was statistically significant (p=0.006). It was determined that the children of 9.00% (n=26) of the mothers included in the study had a home accident in the last two weeks, and 91.00% (n=263) did not have a home accident. The scale score average of mothers whose children did not have a home accident was 165.63±16.70, and the scale score average of mothers whose child had a home accident was 164.85±18.56, and the difference was not statistically significant (p=0.694).

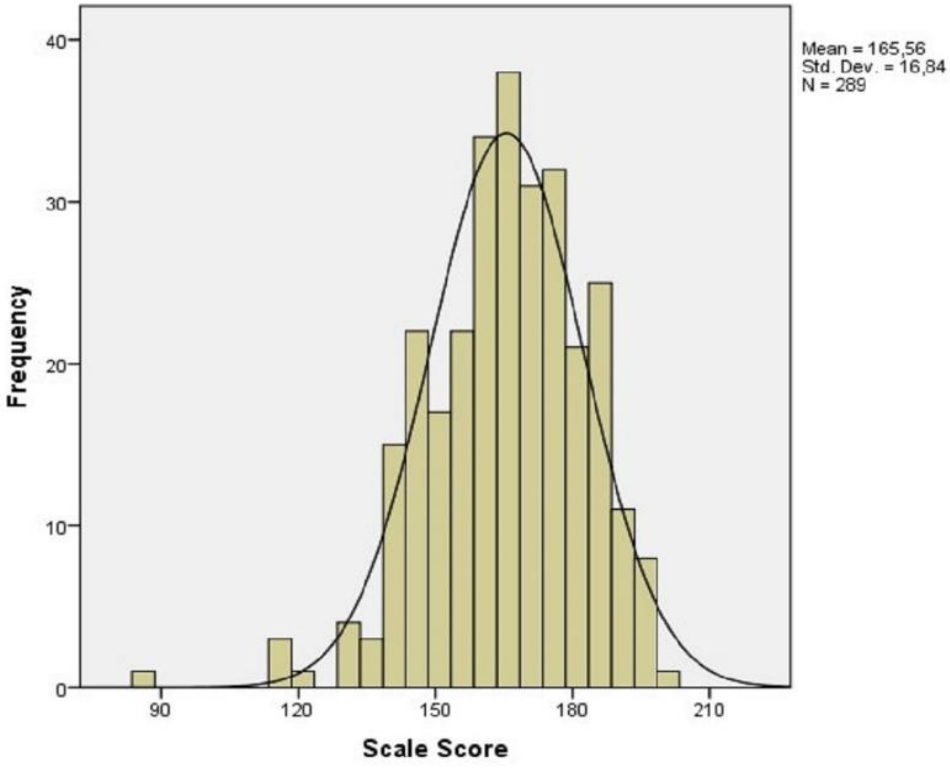

Figure 1. The scale score average for diagnosing safety measures for home accidents

The characteristics of children with home accidents are shown in Table 3. When the types of home accidents experienced by children were examined in the study, they were listed as falls at 65.38%, impacts at 30.77%, and burns at 3.85%. When mothers were asked about the cause of the accidents, 38.46% stated that they were caused by parental neglect and carelessness. When the post-accident health status of the children who had a home accident was examined, it was determined that 88.46% of them showed a full recovery after the injury, and the rest did not have a level of injury that required follow-up.

Table 2. The comparison of scale scores according to the descriptive characteristics of children and mothers (n=289).

		n (%)	Scale Scores, mean±sd	P Value
Gender of the child	Male	148 (51.21)	165.05±17.45	0.601*
	Female	141 (48.79)	166.09±16.27	
Child's age group	0-2	151 (52.25)	165.29±18.31	0.301 †
	3-4	82 (28.37)	164.05±15.85	
	5-6	56 (19.38)	168.50±13.74	
Mother's age group	≤30 years old	156 (53.98)	164.44±15.50	0.219*
	>30 years old	133 (46.02)	166.88±18.26	
Mother's educational status	Illiterate	8 (2.77)	150.00±29.83	**0.033** §
	Literate	11 (3.81)	154.09±13.94	
	Primary school	110 (38.06)	165.43±15.51	
	Middle School	82 (28.37)	165.51±16.98	
	High school	38 (13.15)	166.68±15.46	
	University	40 (13.84)	171.23±16.31	
Mother's working status	Working	48 (16.61)	171.69±16.95	**0.006***
	Not working	241 (83.39)	164.34±16.58	
Economical situation	Very bad	6 (2.08)	169.67±14.35	0.230 §
	Good	71 (24.57)	168.93±18.26	
	Medium	167 (57.79)	164.74±16.78	
	Bad	42 (14.53)	163.07±13.80	
	Very bad	3 (1.04)	158.00±26.00	
Number of children	1	88 (30.45)	167.15±15.58	0.467 †
	2	136 (47.06)	165.39±17.53	
	≥3	65 (22.49)	163.77±17.08	
The person who takes care of the child	Mother own	264 (91.35)	165.02±16.74	0.113 ¶
	Other (caregiver, relative, kindergarten, etc.)	25 (8.65)	171.32±17.15	

(sd: standard deviation, *Student T Test, †One Way ANOVA, §Kruskal Wallis Test, ¶Mann Whitney U Test)

Table 3. Distribution of characteristics related to children's home accidents (n=26)

		n (%)
Gender of the child	Male	11 (42.31)
	Female	15 (57.69)
Child's age group	0-2	16 (61.54)
	3-4	5 (19.23)
	5-6	5 (19.23)
Type of home accident	Fall	17 (65.38)
	Impact	8 (30.77)
	Burning	1 (3.85)
Time of home accident	Morning	5 (19.23)
	Noon	5 (19.23)
	Afternoon	2 (7.69)
	Evening	14 (53.85)
Place of home accident	Kitchen	2 (7.69)
	Living room/Sitting room	10 (38.46)
	Children's room	2 (7.69)
	Balcony/Terrace	3 (11.54)
	Bedroom	2 (7.69)
	Indoor stair	4 (15.38)
	Garden	3 (11.54)
The body area affected by the accident	Head neck	15 (57.69)
	Upper extremity	6 (23.08)
	Lower extremity	5 (19.23)
The person who was with the child during the accident	Friend	5 (19.23)
	Sibling	4 (15.38)
	Mother/Father	15 (57.69)
	Nobody	2 (7.69)
Cause of the accident	Negligence/Carelessness	10 (38.46)
	Lack of protective measures	5 (19.23)
	Play / Mischief	5 (19.23)
	Loss of balance in a child	6 (23.08)
Status of going to the health institution after the accident	Gone, outpatient treatment was given	7 (26.92)
	Gone, hospitalized	1 (3.85)
	Not gone	18 (69.23)
Health status after a home accident	Full recovery	23 (88.46)
	No injuries requiring follow-up	3 (11.54)

Discussion

Home accidents are a public health problem in which society's awareness is important because they are more common among children but because they are preventable. Increasing the awareness of families about the risk factors in home accidents is important to prevent the consequences that may cause disability or death. For this reason, in our study, evaluations were made to question whether the measures against home accidents were taken sufficiently and to understand which measures were preventive in-home accidents.

In the study, the frequency of home accidents in the last two weeks was found to be 9%. In Turkey, the frequency of home accidents in the last two weeks was found to be 14.1% by Kılıç, 18.2% by Boztaş in 0-4 years old, and 19.7% by Karatepe in the 0-6 age group.[17-19] In our study, the incidence of accidents was found to be lower than in other studies. Studies on the subject have shown that essential characteristics of mothers, such as age, educational status, employment status, economic status, and the number of children, affect their children's home accidents.[20-22] In our study, however, no significant difference was found between their children's home accident status according to the mothers' descriptive characteristics (Table 1). In the study of Karatepe, it was shown that the children of mothers who perceived their economic situation as bad had more home accidents.[19] In the study conducted by Kurt, it was determined that the rate of having a home accident was significantly higher for the children of working mothers compared to the children of non-working mothers.[14] The fact that the relationship between the descriptive characteristics of the mothers and the status of their children having a home accident differs in the studies conducted on the subject may be due to the fact that the groups in which the studies were conducted had different socio-cultural and economic characteristics.

In our study, the mean score of the scale for identifying the safety measures of mothers for home accidents was found to be 165.56±16.84. It was found to be 168.00±19.30 in the study of Karatepe, 158.12±1.14 in the study of Erkal, 159.90±14.50 in the study of Altundağ, and it was found be 179.74±12.91 in the study of Gündüz, and this mean scores of the mothers was found to be higher than in our study.[5,15,19,20] When compared with other studies, the scale mean scores of the mothers in our study are similar.

When the mean scale scores of the mothers were compared according to their age groups, it was seen that there was no significant difference between the mean scale scores of the mothers over 30 years of age and the mean scores of the mothers aged 30 years and younger, but it was seen that the mothers over the age of 30 had higher scale mean scores. In the study of Özmen, the mean score of the mothers aged 27 and over was found to be higher than the others.[12] Çiçekler and İnanç also found that the risk of injury in children increased due to the young age of the parents.[23,24] Unlike these studies, in the studies of Erdem and Erkal, a higher mean scale score was observed in young mothers compared to mothers over 30 years of age.[13,20] In our study, when the rates of children who had a home accident in the last two weeks according to the age groups of the mothers were evaluated, it was found that the accident rate was 11.54% in the mothers aged 30 and under, and 6.02% in those over the age of 30. It is known that as the maternal age decreases in childhood accidents, the child's health is at greater risk due to the mother's inexperience.[25] In our study, it was found that mothers whose children had more home accidents were mostly young mothers; At the same time, it was determined that the scale scores were lower.

The study determined that the mean scores of the mothers increased as their education level increased, and the difference was found to be significant. In the study conducted by Boztaş, it was observed that the mean

score of the scale increased as the education level of the mothers increased.[18] In the study of Çiçekler, it was found that mothers who graduated from primary education took more safety precautions for home accidents than mothers who graduated from secondary education and undergraduate education.[23] As the education level of mothers increases, it is expected that children become more conscious about home accidents, predisposing factors for accidents, ways of protection and developmental characteristics of children, and accordingly, their scale score averages are higher than other mothers.

There are different results in studies on the effect of mothers' working status on the scale score averages. In the study of Büyük, it was found that the median score of the mothers who were housewives was higher than that of working mothers, and the difference was significant.[26] In the study of Çiçekler, it was also determined that mothers who are housewives and shopkeepers take more safety precautions against home accidents.[23] In the studies of Karatepe and Şahin, it was found that the working status of the mothers did not affect the mean score of the scale.[19,27] In this study, the scale mean score of working mothers was found to be significantly higher than that of non-working mothers. Similarly, in the study of Gündüz, it is seen that the average scale score of working mothers is higher.[15]

There is no statistically significant difference between the mean score of the mothers whose child is taken care of by persons other than themselves (caregivers, relatives, etc.) and the mean score of the mothers who take care of their child themselves. However, the mean score of the mothers whose children were cared for by persons other than themselves was found to be higher. As it will be remembered, in the study, it was determined that the scale score average of working mothers was significantly higher.

Although the mean score of the mothers whose children did not have a home accident in the last two weeks was higher than the mothers whose children had an accident, the difference was not statistically significant. In the study of Karatepe, the mean score of the mothers of the children who did not have a home accident was found to be higher than that of the mothers of the children who had a home accident.[19] In the study of Özmen, the mean score of the mothers whose children had an accident in the last year was found to be higher.[12] In the studies of Boztaş and Turan, however, no significant difference was found between the status of children having a home accident and the scale mean score of the mothers, as in our study.[9,18] When studies on the subject are evaluated, it can be said that mothers who score higher on the scale take more precautions for accidents and can prevent accidents as a result.

Fall-type accidents are more common in children in this age group due to reasons such as not being mature enough to provide muscle and behavioral coordination despite being active, being open to environmental risks, and not being conscious of dangers.[10,27] When the types of home accidents in children are examined, it has been

found that the most common type of fall accidents is seen in many studies.[4,18,25,28] In our study, it was determined that the most common accident type was falling.

It was determined that the majority of children who had home accidents were in the 0-2 age group. Özmen and Altundağ also found that the incidence of accidents increases as the age of children get younger.[5,12] It is thought that more frequent home accidents in children in this age group may be caused by the fact that they spend more time at home, their curiosity to explore the environment, and their hand skills are not sufficiently developed.

The study found that the head and neck regions and upper extremities of the children who had a home accident were most frequently affected. While the most affected body region was seen as the head region in the studies of Karatepe and Boztaş, it was determined as the hand, arm, and fingers in the study of Kılıç.[17-19] This can be explained by the fact that the most common type of accident in children aged 0-6 years is falling, and the body parts most frequently affected by falls are the head, neck, and upper extremities.[4,18]

In the study, the majority of mothers stated that home accidents were caused by their negligence and carelessness. In their study of Tezcan, it was reported that the cause of the majority of the accidents experienced by the households in the last year was carelessness and inappropriate conditions, respectively; they reported that the most obvious reason for the accidents in the last fifteen days was carelessness.[29] In the studies of Kurt and Karatepe, it was found that accidents often result from parental carelessness.[14,19] It is clear that the risk of home accidents in children will be reduced with the precautions and more attention that families will take at home.[30]

As a conclusion, the study has shown that mothers whose children have not had a home accident have more information about the necessary safety measures to protect their children from home accidents. In addition, it was determined that the awareness of protective measures against home accidents increased with the increase in the education level of the mother. It was determined that the knowledge level of working mothers about the methods of protection from home accidents was higher. It was determined that home accidents were most common in the 0-2 age group. The most frequent home accident was falling, the most common home accident was in the living room, and the head and neck region was most frequently affected by home accidents. Based on this information, considering that the sociodemographic differences of the society affect the risk of home accidents, it is recommended that the child's possible accident probabilities be determined and that the families, especially mothers, play a greater role in the care of their children, should be provided with training that can be given with the relevant professionals about the intervention methods in the face of these situations.

Limitations of the Study

Although we aimed to reduce the limitations related to the recall factor by questioning the home accidents in the last two weeks before the interviews with the mothers, the main limitation of such studies is the collection of information retrospectively, according to the statements of the individuals. In addition, the fact that most of the mothers participating in the study were housewives, so they took care of their children, and the accident status was questioned only on the children brought to the polyclinics may have affected the frequency of accidents.

Ethical Considerations: This study was conducted with the approval of Izmir Katip Çelebi University Non-Interventional Scientific Research Ethics Committee (date:22.02.2017, approval no: 35).

Conflict of Interest: The authors declare no conflict of interest.

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EVALUATION OF THE RELATIONSHIP BETWEEN DEATH ANXIETY AND PERSONALITY TRAITS IN HOSPITALIZED PATIENTS WITH COVID-19

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Abstract

Objectives: Death anxiety is often described as a feeling of panic and/or fear associated with thoughts of death and the afterlife. This impact of death anxiety is often triggered by severe disease or losing someone close. The outbreak of Novel Coronavirus Disease has also affected patients mentally as well as physically. Our study aims to investigate the prevalence of death anxiety among hospitalized patients with COVID-19 and the related factors of this anxiety during the current pandemic.

Materials and Methods: We conducted a study among 283 adult participants to determine their anxiety and depression levels after being hospitalized due to COVID-19 infection by using the Ten Item Personality Inventory (TIPI), Hospital Anxiety and Depression Scale (HADS), and Templer Death Anxiety Scale (DAS).

Results: Death anxiety was significantly higher in females and in patients with prior psychiatric disorders. A positive correlation was found between death anxiety and the risk of anxiety ($p<0.001$ and $r=0.472$) and depression ($p<0.001$ and $r=0.344$). The risk of anxiety and depression was found to increase with DAS scores. Death anxiety was found to be common and associated with three significant personality traits: conscientiousness, extraversion, and emotional stability.

Conclusion: Hospitalized patients with COVID-19 should be closely monitored regarding death anxiety, and awareness should be raised regarding the mental impacts of severe diseases on patients, and these impacts should be identified more often. A professional support system of a psychological call or online guidance should be constituted to identify the affected groups that are vulnerable to mental impacts.

Keywords: Death anxiety, COVID-19, personality traits, anxiety, depression.

Introduction

Death anxiety is often referred to as "emotions like panic, fear, and/or anxiety caused by thoughts of death, disconnection from the world, and thoughts of the afterlife". However, the fields of philosophy, religion, psychology, and psychiatry could not agree upon a common description of it.[1] Death anxiety is related to many socio-demographic variables such as age, gender, educational and marital status, socioeconomic situation, general health condition, religion, cultural level, and some psychopathologies.[2]

The recent outbreak has triggered many physiologic, cognitive, and behavioral responses among the general population. These responses were generally caused by uncertainty, limited information, and the contagious nature of the disease. Individuals diagnosed with Novel Coronavirus Disease (COVID-19) also suffered from excessive stress and fear caused by the possible prognosis of the disease and physical morbidity. Longer quarantine periods, boredom, incomplete information, and social stigmatization were reported to be the origins of stress during the outbreak.[3]

Some studies reported a relationship between some of the personality traits and death anxiety. Some other studies found a positive correlation between neuroticism and death anxiety.[4,5] Additionally, death anxiety was found to have a negative correlation with extraversion, openness to experience, and agreeableness.[4,6]

Our study aims to investigate the prevalence of death anxiety among hospitalized patients with COVID-19 and the related factors of this anxiety during the current pandemic.

Materials and Methods

Study Design and Population

The population of this cross-sectional study consists of COVID-19 in-patients who were being followed between the dates of July 15, 2021, and August 15, 2021, in Ankara City Hospital. In the last three months before the study, nearly 400 patients were hospitalized due to COVID-19 per month, according to the data retrieved from computerized hospital records. The sample size was calculated by using the Epi Info program, and it was aimed to reach out to 197 people with a rate of 50% undefined frequency, 5% deviation, and 95% confidence. The study was conducted among 283 participants who were hospitalized in services due to COVID-19 between the dates of July 15, 2021, and August 15, 2021, in Ankara City Hospital, a central hospital for the pandemic. Informed consent was taken from the patients. Patients answered the questionnaires themselves via paper rather than doing it face-to-face with an authorized person to keep their distance and reduce the risk of infection. The study patients' age range was between 18 and 65 years. We have followed these patients due to

COVID-19 in pandemic units and these patients managed to fill out the questionnaire completely. Patients over 65 years, intensive care unit patients, and illiterates were excluded from the study.

Data Collection Tools

In our research, we benefited from the Personal Information Form, Ten Item Personality Inventory (TIPI), Hospital Anxiety and Depression Scale (HADS), and Templer's "Death Anxiety Scale" (DAS).

Personal information form had data on the patient's age, educational and marital status, chronic diseases, COVID-19 vaccine details, history of COVID-19 infection, alcohol consumption, smoking status, presence of any psychiatric disease, and the use of any psychiatric medicine at the time of hospitalization. The patients were also asked to specify their illness severity from the least severe (1) to the most severe (10) and their sleep quality from the worst (1) to the best (10).

Gosling et al. (2003)[7] developed a 10-item inventory called TIPI, which was later adapted to Turkish by Atak (2013).[8] The 10-item inventory has five critical personality traits. These five dimensions of personality are: 1) openness to experience, 2) conscientiousness, 3) extraversion, 4) agreeableness, and 5) emotional stability. The inventory is a Likert-type scale and has the following options: 1=disagree strongly to 7=agree strongly. The Cronbach's Alpha reliability coefficient for the sub-dimensions was reported to range from 0.81 to 0.86 in its adaptation study, which meant that the inventory's reliability was acceptable, and in our study, it was found to be 0.62.

HADS was developed by Zigmond and Snaith (1983)[9], and its reliability and validity analysis was carried out by Aydemir et al. (1997).[10] The HADS is used to evaluate the symptoms of anxiety and depression in hospitals and is filled out by the patients. It is a four-point Likert-type scale with a total of 14 questions, 7 (odd numbers) of which analyze the risk of anxiety, and the remaining 7 (even numbers) analyze the risk of depression. The cut-points were ≥7 for the depression subscale and ≥10 for the anxiety subscale. The Cronbach alpha coefficient was reported to be 0.85 and 0.77 in the anxiety and depression subscales, respectively. Whereas, in our study, it was reported to be .82 and 0.72, respectively.

Templer (1970)[11] developed a 15-item inventory called DAS, which was later adapted to Turkish by Şenol (1989). As a result of the validity and reliability analysis conducted by Akça and Köse (2008), test-retest reliability was found to be 0.79, while the reliability coefficient calculated by using the Kuder-Richardson formula was found to be 0.75.[12] In our study, Cronbach alpha coefficient was reported to be 0.60. The scale is a 15-item, true/false, two-point Likert-type scale that is used to determine the degree of death anxiety. True answers get 1 point, and false answers do not get any points. The scale has a point range of between 0 to 15,

and higher points mean an increase in death anxiety. Seven points out of a point range of 0 to 15 indicate high rates of death anxiety.[12]

Data Analysis

We used Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM Corp., Armonk, New York, USA) to analyze data. Basic descriptive statistics and frequencies were used for the description of all variables. Mean ± standard deviation, median, ranges (minimum value–maximum value), and numbers (%) were used to express the results and the usage depended on whether the data was parametric or non-parametric. The chi-squared test was used to compare the quantitative data. The t-test was used to examine the comparison of means between two groups for normally distributed data and the Mann- Whitney U Test was used for the non-normally distributed data. ANOVA was used for normal distributions and the Kruskal-Wallis test (post-hoc Dunn-Bonferroni test) for non-normal distributions. The statistical significance level was $p<.05$. Correlation analyses were conducted for two statistically significant variables. Logistic regression models were carried out to analyze the relationship among independent variables, such as demographic characteristics, psychiatric disease history, personality traits, and risk of anxiety and depression and to calculate the odds ratio (OR) and confidence interval (CI).

Ethical Issues

Approval was taken from the local Ethics Committee. The study patients were informed about the aim of the study and voluntarily signed informed consent.

Results

Of all the patients (n=283), 57.95% (n=164) were male, and 42.05% (n=119) were female. The mean age was 48.22±10.57. Of all the patients, 22.26% had a COVID-19 vaccine, 20.49% (n=58) previously had COVID-19 infection, and 15.55% (n=44) had lost someone due to COVID-19 and related complications. Of the participants, 11.31% had a prior diagnosis of a psychiatric disorder and 9.89% (n=28) were still on prescribed psychiatric medicine. The demographical and clinical data of the patients are shown in Table 1.

Table 1. Demographical and clinical data of the patients (n=283)

		n	%
Gender	Male	164	57.95
	Female	119	42.05
Marital Status	Married	222	78.45
	Single	28	9.89
	Divorced	16	5.65
	Widowed	17	6.01
Educational Status	Literate	20	7.07
	Primary School	86	30.38
	High School	60	21.21
	University	91	32.15
	MBA and higher	26	9.19
Chronic Diseases	Existent	108	38.17
	Non-existent	175	61.83
COVID-19 Vaccine	Vaccinated	63	22.26
	Unvaccinated	220	77.74
Previous COVID-19 Infection	Yes	58	20.49
	No	225	79.51
Lost someone due to COVID-19	Yes	44	15.55
	No	239	84.45
History of a mental disorder	Yes	32	11.31
	No	251	88.69
Current psychiatric treatment	Yes	28	9.89
	No	255	90.11

The mean disease severity and sleep quality of the patients were 6.86±2.44 and 4.49±2.51, respectively. Of our patients, 58.29% (n=165) had a high rate of death anxiety and 57.24% (n=162) had a high risk of depression. Table 2 demonstrates the scores for the perceived severity of the disease, sleep quality, risk of anxiety-depression, death anxiety, and personality traits of the cases.

Death anxiety was found to be significantly higher in females than in males ($p<0.001$). Patients with prior psychiatric disorders were found to have higher death anxiety compared to those without a history of any psychiatric disorder ($p=0.026$). No significant difference was found between death anxiety and age ($p=0.269$), education status ($p=0.088$), presence of chronic disease ($p=0.212$), vaccination ($p=0.511$), and history of having COVID-19 infection ($p=0.09$). Similarly, no significant difference was found between death anxiety and the loss of someone due to COVID-19 infection ($p=0.344$), psychiatric medicine use ($p=0.944$), perceived severity of disease ($p=0.546$), and sleep quality ($p=0.271$) (Table 3).

Table 2. Age, perceived disease severity, sleep quality, risk of anxiety-depression, death anxiety, and personality traits of the participants (n=283)

	n	%	Mean ± Standard Deviation	Median (min-max)
Age			48.22 ± 10.57	50 (19-65)
Disease Severity			6.86 ± 2.44	7 (1-10)
Sleep Quality			4.49 ± 2.51	4 (1-10)
Templer DAS Scale Score			7.51 ± 3.47	7 (1-15)
Low	118	41.71	4.19 ± 1.46	4 (1-6)
High	165	58.29	9.87 ± 2.36	9 (7-15)
HADS Anxiety Risk			7.19 ± 4.25	7 (0-19)
Yes	79	27.92	12.57 ± 2.42	12 (10-19)
No	204	72.08	5.11 ± 2.72	5 (0-9)
HADS Depression Risk			7.04 ± 3.96	7 (0-20)
Yes	162	57.24	9.79 ± 2.67	9 (7-20)
No	121	42.76	3.36 ±1.81	3 (0-6)
Extraversion			9.78 ± 3.14	10 (2-14)
Agreeableness			10.57 ± 2.68	11 (2-14)
Conscientiousness			11.27 ± 2.92	12 (2-14)
Emotional Stability			9.82 ± 2.78	10 (2-14)
Openness to experiences			8.71 ± 2.67	8 (2-14)

Table 3. Comparison of socio-demographic characteristics regarding low and high death anxiety (n=283)

		Low Death Anxiety n (%)	High Death Anxiety n (%)	p
Gender	Male	80 (48.78)	84 (51.22)	0.005
	Female	38 (31.93)	81 (68.07)	
Marital Status	Married	90 (40.54)	132 (59.46)	0.452
	Single	28 (45.89)	33 (54.11)	
Educational Status	Literate	3 (15)	17 (85)	0.088
	Primary School	34 (39.53)	52 (60.47)	
	High School	26 (43.33)	34 (56.67)	
	University	41 (45.05)	50 (54.95)	
	MBA and higher	14 (53.85)	12 (46.15)	
Chronic Disease	Existent	40 (37.04)	68 (62.96)	0.212
	Non-existent	78 (44.57)	97 (55.43)	
COVID-19 Vaccination	Yes	24 (38.09)	39 (61.91)	0.511
	No	94 (42.73)	126 (57.27)	
Previous COVID-19 Infection	Yes	18 (31)	40 (69)	0.090
	No	100 (44.4)	125 (55.6)	
Lost someone due to COVID-19	Yes	15 (34.09)	29 (65.91)	0.344
	No	103 (43.09)	136 (56.91)	
History of a mental disorder	Yes	7 (21.87)	25(78.13)	0.026
	No	111 (44.22)	140 (55.78)	
Current psychiatric treatment	Yes	11 (39.29)	17 (60.71)	0.944
	No	107 (41.96)	148 (58.04)	
		Median (min-max)	**Median (min-max)**	**p**
Age		49 (23-65)	50 (19-65)	0.269
Disease Severity		7 (1-10)	7 (1-10)	0.546
Sleep Quality		5 (1-10)	4 (1-10)	0.271

A positive correlation was reported between death anxiety and the risk of anxiety ($p<0.001$ and $r=0.472$) and depression ($p<0.001$ and $r=0.344$). The risk of anxiety and depression was found to increase with DAS scores.

No significant difference was found between death anxiety and agreeableness ($p=0.57$) and openness to experiences ($p=0.16$) regarding the relationship between death anxiety and personality traits determined by TIPI; however, a significant relationship was found between death anxiety and the other three traits (conscientiousness, extraversion, and emotional stability), and thus a correlation analysis was conducted. As a result of the analysis, death anxiety was reported to decrease with increasing extraversion ($p=0.002$, $r=-0.215$), conscientiousness ($p<0.001$, $r=-0.292$), and emotional stability ($p=0.007$, $r=-0.231$) (Table 4).

Table 4. Relationship between death anxiety and personality traits (n=283)

Personality Traits	**r***	**p**
Extraversion	-0.215	<0.001
Agreeableness	-0.034	0.571
Conscientiousness	-0.292	<0.001
Emotional stability	-0.231	<0.001
Openness to experiences	-0.083	0.163

(*Spearman correlation)

Of the study population, 57.24% (n=162) and 27.92% (n=79) scored above the depression cut-off point and the anxiety cut-off point regarding HADS cut-off points, respectively. Females were found to have higher mean anxiety ($p=0.002$) and mean depression scores ($p=0.016$) when compared to males. No significant difference was found between anxiety and depression scores and age ($p=0.31$), educational status ($p=0.091$), presence of chronic diseases ($p=0.18$), and history of losing someone due to COVID-19 ($p=0.36$). No significant relationship was found between the perceived severity of disease and anxiety ($p=0.48$) and depression ($p=0.37$) scores; however, a statistically significant relationship and a negative correlation were found between sleep quality and the scores of anxiety ($p=0.001$, $r=-0.190$) and depression ($p=0.005$, $r=-0.168$). No significant relationship was found between depression scores and prior psychiatric disorder history and current psychiatric medication use, and the patients with prior history of a psychiatric disorder ($p=0.011$) and those who were still on psychiatric medicine ($p=0.021$) were found to have higher anxiety scores.

The scores for anxiety were found to decrease with the increase in the following traits: agreeableness ($p=0.003$, $r=-0.173$), extraversion ($p<0.001$, $r=-0.306$), conscientiousness ($p<0.001$, $r=-0.444$), and emotional stability ($p<0.001$, $r=-0.433$). No significant relationship was found between openness to experiences and anxiety scores. All of the subscales of these personality traits were found to have a significant relationship with depression risk. Depression scores were reported to decrease with the increase in the following traits:

agreeableness (p=0.004, r=-0.170), extraversion (p<0.001, r=-0.341), conscientiousness (p<0.001, r=-0.376), emotional stability (p<0.001, r=-0.351), and openness to experiences (p=0.001, r=-0.195).

Logistic regression analysis was carried out for the anxiety risk factors and revealed that the female gender (OR = 1.930, 95% CI 1.055–3.530, p=0.033) increased the anxiety risk, and the risk of anxiety decreased with an increase in conscientiousness (OR = 0.780, 95% CI 0.702–0.868, p<0.001), emotional stability (OR = 0.790, 95% CI 0.698–0.894, p<0.001), and sleep quality (OR = 0.858, 95% CI 0.755–0.976, p<0.001) (Table 5). Logistic regression analysis was done for the risk factors for depression and revealed that the increase in conscientiousness (OR = 0.859, 95% CI 0.768–0.961, p=0.008), emotional stability (OR = 0.882, 95% CI 0.792–0.983, p=0.023), extraversion (OR = 0.835, 95% CI 0.756–0.921, p<0.001), and sleep quality (OR = 0.882, 95% CI 0.792–0.981, p=0.021) decreased the depression risk. Contrary to its effect on anxiety risk, gender was found to have no effect on depression (Table 6).

Table 5. Risk factors for anxiety

Risk Factors	**OR (%95 CI)**	**p-value**
Gender		
Male	1 (reference)	0.033
Female	1.930 (1.055-3.530)	
Sleep Quality	0.858 (0.755-0.976)	0.020
Emotional Stability	0.790 (0.698-0.894)	<0.001
Conscientiousness	0.780 (0.702-0.868)	<0.001

Table 6. Risk factors for depression

Risk Factors	**OR (%95 CI)**	**p-value**
Sleep Quality	0.882 (0.792-0.981)	0.021
Emotional Stability	0.882 (0.792-0.983)	0.023
Conscientiousness	0.859 (0.768-0.961)	0.008
Extraversion	0.835 (0.756-0.921)	<0.001

Discussion

Death anxiety is common, and it is triggered by incidents associated with death. An uncertain period started with the pandemic, and since then, people have been feeling insecure about their health and safety.[13] Our study aims to investigate the relationship among death anxiety, personality traits, anxiety, and depression risks of the adults who needed treatment after being hospitalized due to COVID-19 infection during the pandemic. We reported high death anxiety rates in more than half of our patients. In their comparative study, Cağlar and Kaçer reported that followed COVID-19 in-patients had a death anxiety rate as high as myocardial infarction patients.[14] In our study, we reported higher rates of death anxiety among females when compared to males

who had been supported by previous studies.[2,5,15] Females are usually getting more affected by stress hormones and they are not likely to use adaptive coping strategies. They have a higher tendency to make negative evaluations during emergencies.[15] These are the factors that contribute to the differences between genders. Additionally, this finding also can be explained by gender roles in society and that it is more acceptable for women to express their emotions (sadness, fear, etc.) in society, whereas men are generally taught to suppress their emotions. In the literature, death anxiety was reported to decrease with younger age, higher level of education, and better physical and psychological health[4]; however, our study surprisingly did not find any significant differences between these variables and death anxiety. Our study did not report any significant differences between age and death anxiety, this might be because COVID-19 affects all age groups and younger age is not a protective factor. Death anxiety and various psychiatric disorders (e.g., anxiety, depression, schizophrenia) were found to have a significant relationship in some studies in the literature.[16,17] There is data on various mental disorders having high and low death anxiety rates. Death anxiety is accepted to be the main fear that underlies the development, progress, and course of many mental situations.[18] So, it is not surprising that we found increased death anxiety in those who had a prior psychiatric disease.

During the pandemic, studies in the literature reported a relationship between poor sleep quality and depression and anxiety.[19] Similarly, the multivariate logistic regression model that we conducted has revealed an increase in sleep quality with a decrease in depression and anxiety risk. During the pandemic, it might be helpful to use cognitive-behavioral techniques like suggestions for helping to stay calm before bedtime, the awareness of the negative results of sleeplessness, and finding alternative thoughts.

Previous studies showed that some personality traits strengthen or sensitize people against stress and the benefits or disadvantages of stress.[20] Our study also reported that some personality traits were related to increased death anxiety and that death anxiety decreased when the following traits increased: extraversion, conscientiousness, and emotional stability. Individuals with neuroticism experience sudden changes in their emotional states, and people without neuroticism has emotional stability. A personal trait, neuroticism, is characterized by emotional instability, nervousness, sadness, and anxiety. So, the awareness of death might be more triggering for many who are more neurotic as they generally feel more anxious and become sad more easily.[9] Emotionally unstable people (individuals with high neuroticism) were considered to show increased emotional reactivity because of their maladaptive coping strategies such as avoidant coping.[20] Conscientiousness is believed to be associated with the increase in the ability to manage and tolerate stress and avoid stress.[21] High levels of conscientiousness were associated with better-perceived health, higher life satisfaction, and positive impact.[22] So, our finding regarding the association between high conscientiousness levels and decreased death anxiety was not surprising. In a study conducted among university students in Turkey by Yıldız and Bulut in 2017, no significant relationship was found between conscientiousness and death anxiety.[5] In the same study, a negative relationship was reported between openness to experiences and death

anxiety[5], in our study, however, we did not find any statistically significant association between these two variables. People with high openness to experiences have high adaptability to new social environments and they easily accept new ideas. A dissertation research reported a weak, negative correlation between openness to experiences and death anxiety, relatedly, these people were found to get lower scores in the death anxiety questionnaires due to being more liable to discover abstract concepts.[23] Introverted neurotic individuals were reported to have higher death anxiety when compared to extroverted neurotic individuals due to being more inclined to overthink past and future events.[24] Our result is compatible with this literature finding regarding decreasing death anxiety with increasing extraversion.

In dynamic models, depressive disorders are associated with more than one trait. Each personality trait is associated with depression in different ways.[25] In our study, three out of five personality traits (emotional stability, extraversion, and conscientiousness) were specifically found to be a predictive factor for depressive mood. The most examined trait, neuroticism, was a risk factor for depressive mood, while conscientiousness and extraversion were protective factors toward depressive mood. Conscientiousness was considered to trigger depression by increasing exposure to negative life events.[25] Naragon-Gainey et al. found a relationship between social anxiety symptoms and four personality traits of extroverts (ascendance, sociability, positive emotionality, fun-seeking) whereas only low positive emotionality was found to have a strong relationship with the severity of depressive symptoms.[26]

Stressful conditions such as the coronavirus pandemic have a mechanism of "resilience," which creates an association between personality and psychological functionality.[27] For example, conscientiousness can have a positive effect on people's mood by making people get social support more often and by providing adaptiveness and extroversion and it can also affect all components of high durability through flexible coping. In a study investigating whether personality traits were predictors of durability, agreeableness and openness to experiences were found not to be the significant predictors of Resilience.[28] Similar to the findings in the literature[29], we also believe that agreeableness and openness to experiences are not predictors of depressive mood, which can be explained by the concept of "Resilience".

In a study evaluating anxiety levels in the Turkish population during the COVID-19 pandemic, females were found to have higher anxiety levels than males.[30] In our study, multivariable logistics regression analysis found a higher risk in females than in males regarding the development of anxiety. Among the reasons for this finding were biological reasons and woman's gender role in society.

The limitations of our study were: the lack of healthy controls, the evaluations upon subjective perceptions rather than objective clinical classifications regarding the variables, such as patients' disease severity and sleep quality, and the inability to carry out face-to-face interviews for questionnaires. We believe further studies

should be carried out among larger sample groups that evaluate anxiety during challenging conditions caused by the COVID-19 pandemic and examine the individuals regarding "resilience" and "coping styles" along with their personality traits. Our study is the first study in the literature that analyzes the relationship between the personality traits in patients hospitalized due to COVID-19 infection and death anxiety.

As a result, death anxiety was found to be high among our study population. Death anxiety might be a triggering factor in many different mental disorders during the COVID-19 pandemic. So, death anxiety coping strategies are recommended to be included in mental health programs for patients with COVID-19. Death anxiety was found to decrease with cognitive-behavioral therapy. Further studies are needed to analyze whether long-term results are successful and whether progression has come to a halt in vulnerable populations. More evaluation tools should be developed, and training is necessary for the awareness and management of the mental impacts of COVID-19 in society. A professional support system like mental health helpline or online guidance should be constituted to identify and help the mentally vulnerable groups during the pandemic.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

Ethical Considerations: The study complied with the Declaration of Helsinki and was approved on July 14, 2021, with an approval number of E221-587 by the Republic of Turkey Ministry of Health, the Institutional Review Board of the Ankara City Hospital, and the Ethics Committee of the Ankara City Hospital.

Conflict of Interest: The authors have no conflicts of interest to declare. There are no external funding sources for this study.

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Research Article

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THE EFFECT OF TREATMENT METHODS AND CONTINUITY OF FOLLOW-UP ON SUCCESS RATES IN PATIENTS FOLLOWED IN THE SMOKING CESSATION POLYCLINIC

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Abstract

Objectives: Smoking causes addiction with physical and psychosocial factors. This study aimed to reveal factors that affected the success rate and continuity of follow-up in people who presented to the smoking cessation polyclinic

Materials and Methods: The study included 154 patients who presented to the smoking cessation polyclinic (SCP) of a training and research hospital between September 1st, 2018, and February 28th, 2019. Varenicline or nicotine replacement therapy (NRT) was given to eligible patients, along with cognitive behavioral therapy (CBT). The demographic characteristics, number of cigarettes smoked daily, number of outpatient visits, treatment received, Fagerström Test for Nicotine Dependence (FTND) results, and treatment success at the end of the third month and first year were examined retrospectively in all patients.

Results: Among those who received pharmacotherapy, 33 (21.43%) received varenicline and 37 (24.02%) had NRT. As a result of the analysis, the smoking cessation rate in the entire group was 33.11% at the end of 3 months and 20.78% at the end of 1 year. Three-quarters (75.76%) of patients using varenicline and 54.05% of patients using NRT quit smoking. Although the rate of quitting in patients using varenicline was higher than in those using NRT, it was not statistically significant (p=0.059).

Conclusion: According to the results of this study, there was no significant difference between varenicline + CBT and NRT + CBT in smoking cessation. Male sex, receiving treatment, and regular follow-up visits are factors that increase the chances of success.

Keywords: Cessation of treatment, smoking cessation, clinic visits, pharmacotherapy, addiction.

Introduction

Tobacco use is one of the greatest public health threats to which humanity is exposed. Tobacco is implicated in chest diseases, cardiovascular diseases, more than 20 different types of cancer, and many other health problems, which cause the death of more than 8 million people in the world annually. The nicotine found in tobacco is highly addictive and there is no safe level of exposure. Smoking is the most common form of tobacco use worldwide.[1] According to the Global Adult Tobacco Survey 2016 data, 19.2 million adults (31.6%) use tobacco products in Turkey and the frequency of use is 44.1% in men and 19.2% in women.[2]

The Framework Convention on Tobacco Control, which is the first international agreement, was adopted and implemented by our country. The World Health Organization (WHO) has published a series of measures under the name of the 'MPOWER policy package' to control the spread of tobacco use. According to this series of measures, there are two main interventions for users to quit their tobacco habit. The first of these is a consultancy service that includes face-to-face meetings with physicians and other healthcare professionals, integrated into primary healthcare services, as well as easily accessible free telephone helplines. The second is access to low-cost drug therapy.[2] Quitting smoking ensures a longer, healthier, and more productive life. Health costs will decrease due to chronic disease, and socially productive years and quality of life will increase.[3] Most smokers want to quit and providing effective means of quitting increases the likelihood of a successful quit attempt. There is strong evidence that behavioral education and pharmacotherapy are effective in smoking cessation, and the combination of the two modalities produces better results.[4,5]

In the SCP, a detailed anamnesis is taken, and physical examinations and necessary medical examinations are performed. Afterward, behavioral training is given to each patient, and pharmacologic treatment, which will continue for at least three months, is started for eligible patients. Patient follow-ups are conducted face-to-face, at least once in the first 15 days, monthly for up to 3 months, and once every three months until the end of 1 year. This study aimed to contribute to reducing the rates of tobacco addiction, which is an important public health problem, by evaluating the reasons that affect treatment attendance and success rates in people who present to quit smoking.

Materials and Methods

Participants and Procedures

Our study was approved by the scientific research ethics committee of a university (Approval No: 20/75). The study was conducted among people who presented to the SCP and were included in the treatment program from September 1st, 2018, when our SCP started, until February 28th, 2019. In our study, whether the subjects

quit smoking at the end of the 3rd and 12th months was evaluated both by scanning the file data and by contacting them by phone.

Patients whose smoking cessation was not recorded and could not be reached by phone were excluded from the study and 154 were included in the study. In the period when the patients used both pharmacotherapy methods (varenicline and NRT) in a similar way along with behavioral education, the demographic characteristics of the individuals, the number of cigarettes smoked daily, the number of applications to the polyclinic, the treatment they received, their nicotine addiction status, and their effects on the success of the treatment were retrospectively examined.

The nicotine addiction status of individuals is measured using the Fagerström Test for Nicotine Dependence (FTND), which is widely used in the SCP, and the results are routinely available in patient files. The Turkish validity and reliability study of the FTND was performed by Uysal et al. and it was concluded that it could be used as a measurement method in the evaluation of nicotine addiction in smoking cessation.[6]

Smoking cessation rates were determined from the files in the third month when the pharmacologic treatments of the individuals ended and after the 1st year when the routine follow-up period ended. The patients who stopped the follow-up were contacted by phone and asked about their smoking cessation status and the reasons for quitting the follow-up.

Statistical Analysis

In the study, descriptive data are shown as number (n), percent (%) values for categorical data, and mean ± standard deviation and median minimum-maximum values in continuous data. The Chi-square test was used to compare categorical data. Cross-tables were created to show the smoking cessation status of individuals according to their treatment method. Because the percentage of expected values less than 5 was higher than 20%, except those who only received cognitive behavioral therapy from the treatment methods were cross-tabulated with a 2x2 regular basis and the p-value was given.

Measurement data were tested using the Kolmogrov-Smirnov test for the assumption of normal distribution. The Mann-Whitney U test and Kruskal-Wallis tests were used as appropriate for the comparison of measurement data that did not show normal distribution. For data showing normal distribution, the t-test and one-way analysis of variance (ANOVA) were used in independent groups, where appropriate. $P<0.05$ was accepted as statistical significance in all analyzes. Analyses were performed using the IBM © SPSS program version 20.

Results

Of the 154 people included in the study, 69 (44.80%) were female and 85 (55.19%) were male. The mean age was 40.1±12.1 years. When the number of cigarettes smoked per day was grouped, the majority was between 11 and 20. Treatment was started in 75 (48.70%) patients, 79 (51.30) individuals left the follow-up before deciding on the treatment method or did not use the recommended treatment at all. Of the 75 people who were given treatment, 33 (21.43%) received varenicline, 37 (24.02%) had NRT, and five (3.25%) received CBT only. When the FTND score was classified as low, moderate, or high, those with a medium score (4-6) were in the majority (Table 1) (Figure 1).

The participants were divided into two groups according to their smoking cessation status and compared again (Table 2). No significant difference was found between the mean age and education level in both groups, but a significant difference was found in terms of smoking cessation rate by sex, which was higher in males (p=0.271, p=0.065, and p=0.044, respectively). When the number of cigarettes smoked per day was grouped as ≤10, 11-20, and >20, the distribution was similar between the two groups (p=0.828). When we divided the FTND scores into three groups, low, moderate, and high, and took the average, there was no significant difference in the quitter and non-quitter groups (p=0.687).

The quit rate of participants who used any method to quit smoking was significantly higher than those who did not receive treatment (p<0.001). Three-quarters (75.76%) of our patients using varenicline and 54.05% of patients using NRT quit smoking. Although the rate of quitting in patients using varenicline was higher than in those using NRT, it was not found to be statistically significant (p=0.059). The mean number of physician follow-up visits was significantly higher in the group who quit smoking (p<0.001). The rate of smoking cessation in the entire group was 33.11% at the end of 3 months. The quit rate of these patients at the end of 1 year was 20.78%; the relapse rate was 12.33%.

Seventeen (11.04%) of the participants regularly came for follow-up visits. When the reasons for the patients who discontinued SCP follow-up were questioned, 29 (21.17%) were due to personal reasons (inability to get leave from work, stress, loss of motivation), 27 (19.71%) quit smoking, 18 (13.14%) could not find medicine, 17 (12.41%) were related to problems with the recommended method (drug adverse effects and ineffectiveness), 11 (8.03%) were reported as bureaucratic reasons (unable getting an appointment or not reaching health institutions) (Figure 2).

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Table 1. Sociodemographic data and smoking factors of the patients

Group	n	%
Age (mean ± standard deviation)	40.11±12.13	
Sex		
Female	69	44.80
Male	85	55.19
Educational status		
Under primary education	37	24.02
Primary education	31	20.13
High school	40	25.97
University	46	29.87
Number of cigarettes per day		
≤10	19	12.34
11-20	85	55.19
>20	50	32.47
Status of receiving treatment		
Received	75	48.70
Not received	79	51.30
Treatment Method		
Varenicline	33	21.43
NRT	37	24.02
Only CBT	5	3.25
FTND score		
Low (0-3)	19	12.34
Moderate (4-6)	64	41.56
High (≥7)	71	46.10

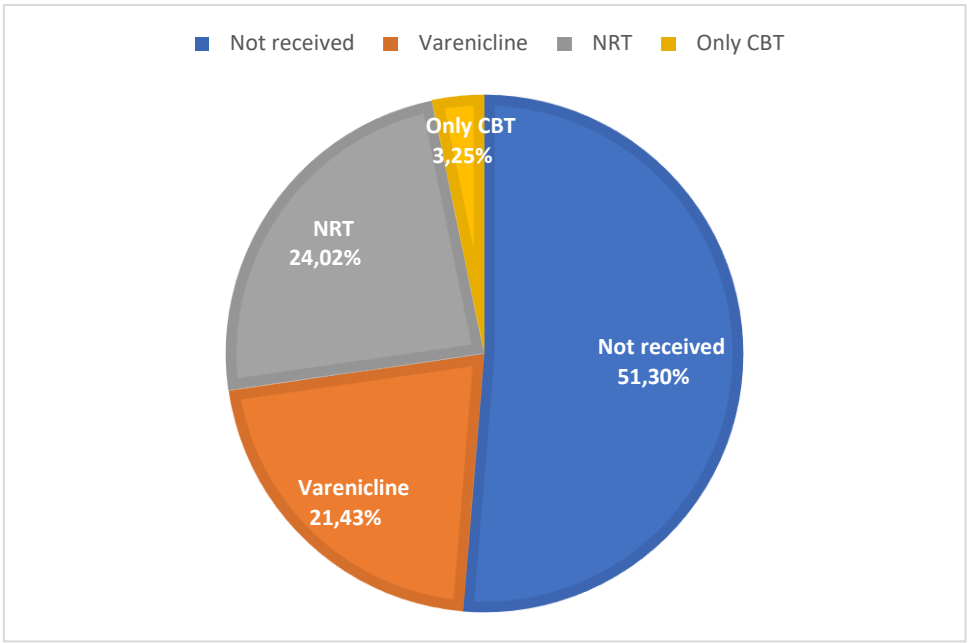

Figure 1. Status of Receiving Treatment and Method

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Table 2. Characteristics of the Participants According to Whether They Quit

	Smoking Status		
	Quit	Did not Quit	p
Group	**n (%)**	**n (%)**	
Age [median (min-max)]	38.0 (18.00-65.00)	40.0 (20.00-67.00)	0.271
Sex			
Male	34 (40.00)	51 (60.00)	0.044
Female	17 (24.64)	52 (75.36)	
Status of receiving treatment			
Received	49 (65.33)	26 (34.67)	<0.001
Not Received	2 (2.53)	77 (97.47)	
Treatment method			
Varenicline	25 (75.76)	8 (24.24)	0.059
NRT	20 (54.05)	17 (45.94)	
FTND			
Low	7 (36.84)	12 (63.16)	0.687
Moderate	23 (35.94)	41 (64.06)	
High	21 (29.58)	50 (70.42)	
FTND [median (min-max)]	6.0 (1.00-10.00)	6.0 (0.00-10.00)	0.559
Educational status			
Under primary education	9 (24.32)	28 (75.67)	0.065
Primary education	6 (19.35)	25 (80.64)	
High school	18 (45.00)	22 (55.00)	
University	18 (39.13)	28 (60.87)	
Number of cigarettes per day			
≤10	7 (36.84)	12 (63.16)	0.828
11-20	29 (34.12)	56 (65.88)	
>20	15 (30.00)	35 (70.00)	
Follow-up visits [median (min-max)]	3.00 (1.00-6.00)	1.00 (1.00-6.00)	<0.001

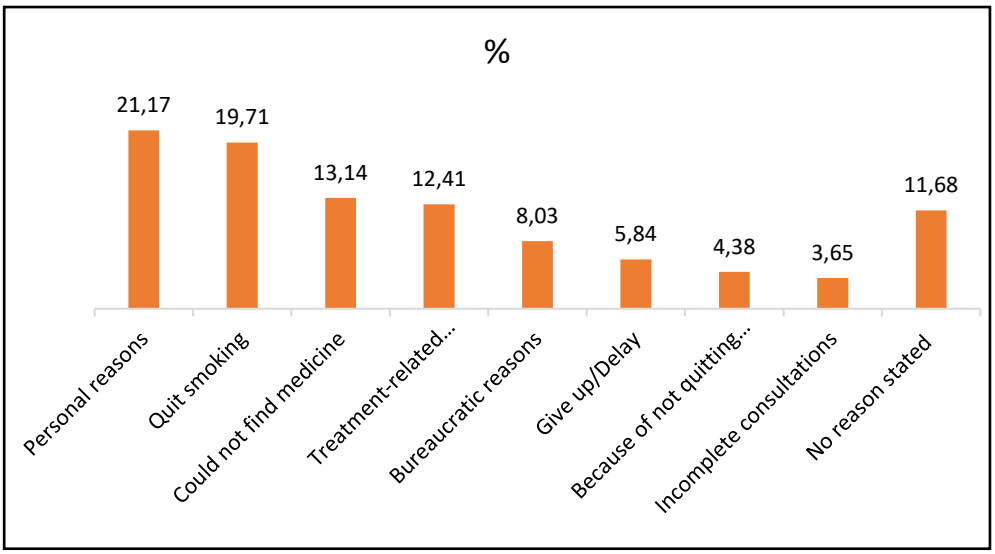

Figure 2. Distributions of reasons for not coming to follow-up visits (%)

Discussion

The number of smoking cessation clinics in our country is increasing and this systematic program increases the chance of success in eliminating tobacco addiction.

Behavioral education is as important as pharmacologic treatment in this smoking cessation process, which can be perceived as chronic and repetitive by patients. In our study, the smoking cessation rate was 33.11% at the end of the third month and 20.78% at the end of the 1st year. Different rates have been reported in studies evaluating the success of smoking cessation in our country. In the third month, the quit rates were found to be between 34% and 54%.[7–9] In studies conducted in our country that evaluated smoking cessation success at the end of the 1st year, rates between 19.3% and 45.3% were reported.[8,10–14] The 3-month success rates in our study were similar to Yılmaz et al., and 1st-year quit success rates were similar to those of Kanatsız et al. In both studies, success was associated with continued treatment and follow-up.[9,11] In our study, it was observed that the number of physician follow-up visits and the rate of continuation of treatment were low in the group that failed to quit smoking.

Different results have been obtained regarding the effects of age and sex on smoking cessation success. Monso et al. stated that advanced age and male sex increased the success of quitting.[15] Although sex was not significant in some studies and the success of quitting at an advanced age was high[8,9], age and sex were not found to be significant in other studies.[7,10,14] In our study, just as in Sağlam's study, age was not found to be a significant factor, but the male sex was found to have a positive effect on quitting success.[13]

In some studies, it has been shown that higher education level increases the success of quitting.[16,17] In the study of Monso et al., it was found that education level was ineffective in quitting success, but it was thought that this might be due to the high level of education of the participants included in the study.[15] Consistent with some studies conducted in our country, our study also found that education level had no significant effect on quitting success.[7,10,14,18]

In the study of Niu et al., the number of cigarettes smoked daily and the increase in the risk of nicotine addiction were highly correlated.[19] On the other hand, some studies show that the number of cigarettes smoked daily has a significant effect on the success of quitting[7], whereas others claim it has no effect.[12] Studies state that only the FTND score affects quitting success,[9,10,13,14] as it has been shown that patients who smoke a high number of cigarettes daily with high FTND scores have low quitting success.[15] In our study, the number of cigarettes smoked daily and FTND score levels were not found to be effective in the success of smoking cessation, similar to the findings of Salepçi et al.[8]

In some studies in the literature, it has been reported that the success of smoking cessation is higher in patients using varenicline than with NRT.[20–23] In multicenter studies, the variability of subjects, such as completed treatment, behavioral support, how drug efficacy is perceived, and adverse effect management, appear as confounding factors.[21] In our study, the rate of smoking cessation in patients using varenicline was found to be higher than in those using NRT, but this difference was not statistically significant (p=0.059). In some studies, although the success of varenicline users in the fourth week of treatment was higher than with NRT, there was no significant difference between the two methods in the follow-ups after treatment.[24,25]

Another point that draws attention is that only 11,04% of our patients attended their follow-ups regularly. The most frequently reported reasons for discontinuation were not being able to take time off from work, loss of motivation, quitting smoking, and not being able to find drugs. In a similar study, the most common reasons for discontinuing follow-up were the thought that the treatment did not work, the occurrence of adverse effects, and smoking cessation, and 54% of those using NRT reported that they terminated the treatment in less than four weeks. Smokers are typically resistant to receiving treatment for the recommended amount of time. However, stopping treatment early in the belief that they have been successful in quitting smoking seems to be a mistake many can make. Encouraging smokers to participate more actively in their treatment can increase their success in quitting.[26]

In smoking cessation clinics, giving free drugs increases participation in programs. However, difficulties experienced from time to time in finding drugs may cause patients to quit their follow-up. Some studies argue that telemedicine or online interview-based counseling is similar to the standard face-to-face smoking cessation interview in the clinic.[27] In addition to face-to-face meetings, alternative methods can be applied to manage smoking cessation programs. Situations that make it difficult to meet face-to-face with a physician, such as the pandemic, may also create additional reasons for the necessity of using these methods.

It is thought that increasing the number and duration of face-to-face meetings with physicians, as well as making physicians' work schedules suitable for telephone and/or online visits, and facilitating access to drugs will increase the success rates of smoking cessation clinics.

Limitations

The smoking cessation status of the individuals was not evaluated using a breath carbon monoxide monitor, and only their verbal statements were recorded. This may have resulted in the patients having difficulty declaring that they are still smoking and misdirecting the physician. The single-center nature of the study is also among the limitations. Multicenter studies with a higher number of participants and continuous communication with the consent of the participants will reveal valuable results on smoking cessation and treatment.

Ethical considerations: Our study was approved by the scientific research ethics committee of Health Sciences University (Date: 28.02.2020, Approval No: 20/75).

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Research Article

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EFFECT OF MARITAL TYPOLOGY, REPRODUCTIVE COERCION, AND CONTRACEPTIVE METHODS IN ABORTION RATE, ISTANBUL 2021

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Abstract

Objectives: Abortion is both a reason for maternal mortality and a consequence of unintended pregnancies. This study aimed to propose the effect of marital typologies, reproductive coercion, and contraception methods on abortion presence among married Turkish women.

Materials and Methods: An observational study including married women was done in the family medicine clinic of a tertiary hospital in İstanbul. It was completed between 15 May 2021 and 15 June 2021. A survey was applied to supply sociodemographic data, asking about contraceptive method use, reproductive coercion scale, and marital typology scale questions.

Results: In the reproductive history of the 199 women whose mean age was 37.32±7.54 years, abortion and unintended pregnancy frequencies were found to be 35.17% and 37.18%. The reproductive coercion score was 0.47±0.82 out of a total of 5 points. The most common contraceptive methods were condom use (59.79%) and withdrawal (41.70%), whose success depended more on the male partner. Logistic regression analyses identified young age, early childbearing mother age and unintended pregnancy presence as predictors of abortion presence (OR=0.914; 95% CI: 0.863-0.968; p=0.002, OR=0.862; 95% CI: 0.778-0.954; p=0.002 and OR=5.413; 95% CI: 2.487- 11.780; p<0.001, respectively).

Conclusion: In light of this study, one out of three married women had a spontaneous or induced abortion history, regardless of the contraceptive method, marital typology, and reproductive coercion score. Therefore, the physician must be aware of the high abortion risk and the information needed for both healthy pregnancy and safe abortion care for a young married woman with an unintended pregnancy.

Keywords: Abortion, coercion, contraception, pregnancy, reproductive history.

Introduction

Worldwide, 26% of women of reproductive age want to prevent or delay pregnancy but do not use any modern method.[1] Although women in Turkey know modern contraception techniques, the prevalence of withdrawal among traditional methods continues to be a general problem for unintended pregnancies.[2] Legalizing induced abortion by the Population Law in 1983 was a critical and controversial step for Turkey's public health and reproductive rights.[3] However, recent evidence suggests that the provision of abortion in public hospitals has diminished significantly.[4] According to 2020 data, only 10 of 295 public hospitals in Turkey (Ankara, Amasya, Bayburt, Burdur, Hakkari, Şanlıurfa, Tekirdağ, and Tunceli) provide optional abortion services without any conditions.[4]

Complications of abortion are the fourth leading direct cause of maternal mortality globally, accounting for 7.9% of maternal deaths.[5] It has been reported that unintended pregnancies are mainly caused by not using or falsely using contraceptive methods or extra-marital sex, forced sexual intercourse, sexual violence, exposure to incest and rape, and adolescent marriages, which are directly related to access to family planning centers.[6] Based on data from the WHO Global Database on Prevalence of Violence Against Women, it was found that 27% of all ever-partnered women aged 15–49 years had experienced physical or sexual intimate partner violence since the age of 15 years.[7]

Researchers have demonstrated mechanisms that may underlie the association between intimate sexual partner violence and poor reproductive health, including forced or coerced sex.[8] Since contraception knowledge in adolescents is both unknown and undesirable, adolescent marriages commonly cause unintended pregnancies and induced abortions. Therefore, modern and traditional society's marital perspective is an essential distinction in women's reproductive and marital health decisions.[9]

A family medicine specialist is a reproductive health counselor who recognizes the female patient before her pregnancy and has a management role.[10] This present study aimed to explain how marital typologies, reproductive coercion, and contraception methods affect the abortion presence among married Turkish women.

Materials and Methods

A cross-sectional (observational) study was completed, including married women admitted to the family medicine clinic of a Gaziosmanpaşa Training and Research Hospital between 15 May 2021 and 15 June 2021. One hundred ninety-nine participants aged between 18 and 49 years and accepted to participate in this study were included unless pregnant or planning to get pregnant. Female patients under the age of 18 years,

participants without the ability to fill out the online survey by phone, and participants without active sexual life were excluded from the study.

The study sample size was obtained using a single population proportion formula. The estimated rate of abortion based on the literature was accepted at 22.00%, with a power level of 95% and a margin of error of 5%.[11] The final sample size required for the study was a minimum of 154 taking a non-response rate of 10%. An online survey link with forty-five questions by phone was applied, including voluntary consent, sociodemographic data, contraceptive method use, reproductive coercion scale, and marital typology scale. The permissions for the use of the scales were obtained from the corresponding authors.

The Marital Typhology Scale is a five-point Likert-type scale consisting of 30 items with a Cronbach Alpha coefficient of 0.920 in the validity and reliability analysis. It was conducted by Çatal et al. in 2018 on married individuals in Turkey. Three sub-dimensions are in the scale; the traditional type marriage (TM) subscale consists of questions 2, 6, 8, 14, 16, 19, 25, 27, 30, dependant-autonomous type Marriage (DAM) subscale consists of questions 1, 3, 4, 5, 9, 10, 12, 13, 15, 17, 21 , 22, 26, 28 and the autonomous type marriage (AM) subscale consists of questions 7, 11, 18, 20, 23, 24, 29 questions.[12] There is no reverse scoring and no total score on the scale. The sub-scale scores are calculated separately. In TM, couples' views on life are similar. The spouses believe that self-independence must be sacrificed for their marriage. They avoid conflicts and only deal with important issues. In the DAM, openness in marriage life is considered, and the spouses are not pressured to negotiate. Conflict is experienced. The wife and husband believe in the equality of man and woman in the family. AM gives great importance to autonomy. The self-individual development is ahead of her marriage. Partners talk very little about their marriages.[12]

The Reproductive Coercion Scale was developed by McCauley et al. in 2017. [8] It has a 5-question tool translated into Turkish by Öztürk et al. in 2020. It has a Cronbach Alpha coefficient of 0.720 in its validity and reliability analysis. The total score is calculated as yes (1) points, no (0) points, and the increased score indicates increased reproductive coercion; there is no specific cutoff value.[13]

Statistical Analysis

Data were given as mean, standard deviation, median, frequency, and percentage. Variables with normal distribution between the two groups were analyzed using the t-test in independent groups and the Mann-Whitney U test for those that were not normally distributed. Categorical variables were evaluated with Chi-square tests. Binary logistic regression analysis was performed to determine the variables affecting abortion presence. The limit of significance was taken as $p<0.05$. Analyzes were performed using the NCSS 10 (2015. Kaysville, Utah, USA) software program.

Results

The reliability coefficients (Cronbach's alpha coefficients) of the marital typology total scale, and TM, DAM, and AM subscales were found to be 0.920, 0.823, 0.889, and 0.729, respectively. The reliability coefficient of the reproductive coercion scale was observed as 0.821. Cronbach's alpha number for all scales used in this study was between 0.700 and 0.950, which is considered reliable.[14]

As shown in Figure 1, the most common contraceptive method used was first; condom use (59.79%), second withdrawal (41.70%), and third; oral contraceptive pill (24.62%). Vasectomy was the method never used.

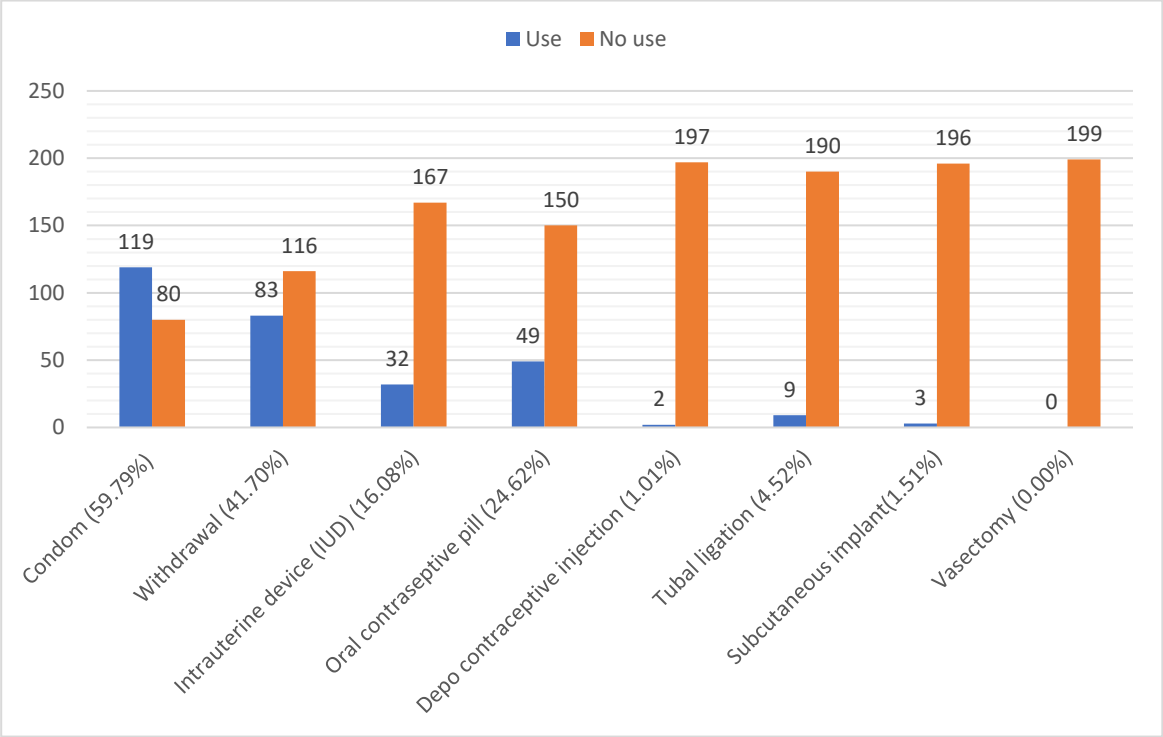

Figure 1. Distribution of the contraceptive methods used by the participants

Data comparison between women with and without abortion history has shown in Table 1. The mean age of the participants was 25.38±3.81 years, 65.79% were university graduates, and 37.14% were housewives. The RC score was 0.47±0.82 out of a total of 5 points. TM score, DAM score, AM score, reproductive coercion score, marital age, and childbearing mother age were statistically similar (p=0.252, p=0.649, p=0.251, p=0.070, p=0.925, p=0.073, respectively). The unintended pregnancy rate in the abortion (+) group (62.86%) was three

times higher than the rate (23.26%) in the abortion (-) group, significantly (p<0,001). Having two or more children was significantly higher in the abortion (+) group than in those with one or no child (p= 0.023).

Table 1. Evaluation of the women with and without abortion in obstetric-gynecological health history in terms of family planning

Variables	**Total score**	**Abortion (+) group** Mean±SD Median	**Abortion (-) group** Mean±SD Median	**t; Z; X^2 value**	**p-value**
Continuous Variables					
Age	37.32±7.54	41.0±7.43	35.33±6.84	t=5.418	**<0.001**
Marital age	25.38±3.81	25.41±4.49	25.36±3.40	t=0.094	0.925
Childbearing mother age	27.79±4.60	28.62±5.19	27.23±4.09	t=1.806	0.073
Reproductive coercion score	0.47±0.82	0.64±0.98	0.38±7.09	Z=-1.814	0.070
Traditional Type Marriage score	34.64±5.58	34.03±6.04	34.98±5.30	Z=-1.148	0.252
Dependent Autonomous Type Marriage score	57.64±7.84	57.81±8.34	57.55±7.58	Z=-0.649	0.649
Autonomous Type Marriage score	24.53±4.47	24.26±4.08	24.67±4.67	t=-0.628	0.251
Categorical Variables	Groups	**Abortion (+) group** n (%)	**Abortion (-) group** n (%)	**X^2 value**	**p-value**
Education level	Primary/Secondary school	11 (15.71%)	9 (6.98%)	3.929	0.140
	High school	13 (18.57%)	24 (18.60%)		
	University	46 (65.79%)	96 (74.42%)		
Occupation	Working	44 (62.86%)	97 (75.19%)	2.773	0.096
	Housewife	26 (37.14%)	32 (24.81%)		
Income level	Low	18 (25.72%)	21 (16.28%)	2.591	0.274
	Medium	33 (47.14%)	70 (54.26%)		
	High	19 (27.14%)	38 (29.46%)		
Pregnancy intend	Intended	26 (37.14%)	99 (76.74%)	30.466	**<0.001**
	Unintended	44 (62.86%)	30 (23.26%)		
Number of children	No child	7 (10.00%)	32 (24.81%)	7.522	**0.023**
	One child	27 (38.56%)	50 (38.76%)		
	≥2 children	36 (51.44%)	47 (36.43%)		
Condom use	User	36 (51.42%)	83 (64.34%)	3.147	0.076
	Non-user	34 (48.58%)	46 (35.66%)		
Withdrawal use	User	29 (41.43%)	54 (41.86%)	0.003	0.953
	Non-user	41 (58.57%)	75 (58.14%)		
Oral Contraceptive Pill use	User	19 (27.14%)	30 (23.26%)	0.190	0.663
	Non-user	51 (72.86%)	99 (76.74%)		
Intrauterine Device (IUD)	User	15 (21.43%)	17 (13.18%)	1.718	0.190
	Non-user	55 (78.57%)	112 (86.82%)		
Depo contraceptive injection	User	0 (0.00%)	2 (1.55%)	0.190	0.542
	Non-user	70 (100.00%)	127 (98.45%)		
Tubal ligation	User	4 (5.72%)	5 (3.86%)	0.355	0.723
	Non-user	66 (94.28%)	124 (96.14%)		
Subcutaneous implant	User	1 (1.43)	2 (1.55)	0.005	0.946
	Non-user	69 (98.60%)	127 (98.45%)		

(Chi-square test and Mann-Whitney U test results)

Evaluation of age, RC, and marriage types in Table 2 showed no relationship between RC and TM score, DAM score, AM score (p=0.473, p=0.808, p=0.065, respectively). Although not statistically significant (p= 0,056, r=-0.135), there was a clinically probable correlation between early age and traditional type marriage score.

Predictors of abortion presence have been calculated by logistic regression analysis and are presented in Table 3. It was identified age, childbearing mother age and unintended pregnancy presence as a predictor of abortion presence (OR=0.914; 95% CI: 0.863-0.968; p=0.002, OR=0.862; 95% CI: 0.778-0.954; p=0.002 and OR=5.413; 95% CI: 2.487- 11.780; p<0.001, respectively). As a result, it was observed that the presence of unintended pregnancy increased the risk of abortion by 5.4 times. Additionally, younger age and earlier childbearing mother age were also other abortion risk factors by 1.09 and 1.16 times, respectively.

Table 2. Evaluation of relationships of age, reproductive coercion, and marital typology

Variables	Age	Reproductive coercion score	Traditional Type Marriage score	Dependent-Autonomous Type Marriage score	Autonomous Type Marriage score
Age	-	r=-0.018 p=0.798	r= -0.135 p= 0.056	r= -0.125 p= 0.078	r= -0.120 p= 0.091
Reproductive coercion score	r=-0.018 p=0.798	-	r= -0.051 p= 0.473	r= -0.017 p= 0.808	r= -0.131 p= 0.065
Traditional Type Marriage score	r= -0.135 p= 0.056	r= -0.051 p= 0.473	-	r= 0.589 **p< 0.001**	r= 0.544 **p< 0.001**
Dependent-Autonomous Type Marriage score	r= -0.125 p= 0.078	r= -0.017 p= 0.808	r=0.589 **p<0.001**	-	r= 0.710 **p< 0.001**
Autonomous Type Marriage score	r= -0.120 p= 0.091	r= -0.131 p= 0.065	r= 0.544 **p< 0.001**	r= 0.710 **p< 0.001**	-

(Spearman correlation test. r: Spearman's rho)

Table 3. Evaluation of risk factors for abortion presence by logistic regression analysis

Variables		**P value**	**OR (95%C.I.)**
Age		**0.002**	0.914 (0.863-0.968)
Childbearing mother age		**0.004**	0.862 (0.778-0.954)
Reproductive coercion score		0.091	1.585 (0.929-2.703)
Condom	User	Ref.	-
	Non-user	0.334	0.684 (0.316-1.478)
Pregnancy intend	Intended	Ref.	-
	Unintended	**<0.001**	5.413 (2.487- 11.780)
Occupation	Working	Ref.	-
	Housewife	0.940	0.962 (0.354-2.615)
Education	Primary/Secondary school	Ref.	-
	High school	0.302	2.170 (0.498-9.453)
	University	0.353	2.019 (0.458-8.905)
Number of children	No child	Ref.	-
	One child	0.127	7.884 (0.556- 111.850)
	≥2 children	0.274	4.335 (0.313- 60.059)

(Binary Logistic Regression test, OR: Odds ratio, C.I.: Confidence Interval, Ref: reference value)

Discussion

This present study was conducted with married women admitted to a tertiary hospital outpatient clinic. The relationships and the effects of MT, RC, and contraception methods on women's reproductive health were evaluated**.** Young age, early childbearing mother age, and unintended pregnancy presence were predictors of abortion. Contraceptive methods such as condoms and withdrawal, whose success depends more on the male partner, were the most used method as a risk for unintended pregnancy that may be related to abortion. MT and RC scores had no effect on abortion or unintended pregnancy rate, and women had a low coercion score in our study.

Among all pregnancies, 85 million unintended pregnancies occurred in the world in 2012, of which 50% resulted in abortion.[15] In the studies of İzmir, Ankara, Kayseri, Hatay, Diyarbakır, Erzurum, and Manisa, it was determined that the rates of unintended pregnancy in women ranged between 15% and 47%.[16] To prevent abortions, unintended pregnancies should be prevented with birth control methods. According to the 2018 data from the Turkey Demographic and Health Surveys (TNSA), the unexpected and unintended pregnancy rate in married women aged 15-49 years is a total of 25.0%.[17] The frequency of using any contraceptive method is 70.0%, rated as 49.0% modern and 21.0% traditional ways. The rates of those using modern methods are as follows: Pill 5.0%, IUD 14.0%, injection 1.0%, condom 19.0%, tubal ligation 10.0%.[17] In a study describing family planning method use among women aged between 15-49 in Samsun province, it was found that modern method use was 68.36% of women's contraception whereas traditional protection method use, such as primarily withdrawal, was 31.64%.[18] In our study, withdrawal as a traditional protection use rate was 41.7%. The most common modern method was the condom. Nearly 60% of participants were using a condom in our study sample. Male-based contraceptive methods may be affected by factors such as infection and premature ejaculation, which is especially high (36%) in Turkey, so male-based contraceptive methods are the risk of unintended pregnancies.[19]

On the other hand, sexual partner violence is another risk of condom use in unintended pregnancies. Women aged 18-24 years old, women with restrictive health conditions, pregnant women, and women under financial stress are at high risk for sexual partner violence, which may cause abortions.[20] Reproductive coercion is a newly identified but commonly experienced form of domestic violence with potentially severe consequences for women's health. Findings suggest that sexually coercive men may be more attracted to women with characteristics associated with sexual vulnerability. In addition, men perceive women differently based on their attachment styles, and sexually coercive men may perceive women differently than other men.[21] An Indian study has demonstrated that women's experience of reproductive coercion was associated with poor marital quality at 18 months. Women's experience of sexual partner violence was also negatively associated with men's self-reported marital quality. However, among men, the spouse's marital quality was positively associated with

their own rating of marital quality.[22] In light of this search, it was thought that marital typology may be related to reproductive coercion and may cause a high unintended pregnancy rate. But, we did not find a relationship between RC scores and MC scores. Additionally, the analyses of women with and without abortion history were similar on RC and MC scores.

We found both young age and early childbearing mother age are at risk of abortion rate. Early marriage age was not significant in abortion presence; the reason for this result was that early marriages usually occur through religious practices without formal documentation.[23] In adolescent marriages, women are also victims of physical violence.[23] Despite adolescent pregnancies being affected by large families and lower levels of education. Contrary to expectations, pregnant adolescents in Turkey reported no greater incidence of psychological problems. This may be due to a sociocultural perception of the functional value of motherhood in the country and a positive attitude toward adolescent pregnancies.[24] In our study, education level or financial status was not risk of abortion rate versus unintended pregnancy, young age, and early childbearing mother age.

Especially the pandemic and the associated economic and social support uncertainties will factor into many women's decisions to obtain an abortion.[25] In the following days, unintended pregnancies and related abortions will increase. Therefore, contraception methods and safe abortion services have gained even more importance after the Covid-19 outbreak. As a reproductive counselor in a family medicine center, the family physician should know that a young married woman with an unintended pregnancy needs a healthy pregnancy and safe abortus information depending on her high abortion risk.

Limitations

The result of this search is not a generalizable comment because most women prefer not to talk about abortion history depending on cultural and religious reasons. We had to ask for either spontaneous or induced abortion presence in one question without distinction. Abortion stigma or the negative attributes assigned to women seeking or having had abortions may be an underlying cause.

Ethical Considerations: This study's ethics committee approval was received from the Ministry of Health Istanbul Provincial Health Directorate Gaziosmanpaşa Training and Research Hospital Clinical Research Ethics Committee with the approval letter dated 28/04/2021 and decision numbered 270. Informed consent was obtained from all participants.

Conflict of Interest: The authors declare no conflict of interest.

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THE IMPACTS OF DIABETES ON FAMILIES WITH A CHILD DIAGNOSED WITH TYPE 1 DIABETES MELLITUS AND INFLUENCING FACTORS

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Abstract

Objectives: This study aimed to determine the impacts of diabetes on families with a child diagnosed with Type 1 Diabetes Mellitus (DM) and influencing factors using the Diabetes Family Impact Scale (DFIS).

Materials and Methods: The population of our study, which is a descriptive cross-sectional type, consists of the parents of 289 school-aged children diagnosed with Type 1 DM and followed for at least one year in the Department of Pediatric Endocrinology of Sivas Cumhuriyet University Faculty of Medicine. The study questionnaire was completed in a face-to-face interview with the parents of 121 of the 289 children who volunteered to participate in the study. The first 21 questions of the research questionnaire were related to sociodemographic data, and the following 14 questions, which included some characteristics of the disease, were related to DFIS.

Results: The mean DFIS scale score of the participants was 14.60±10.82. In our study, the mean DFIS scale score and the mean scores of the School and Work subscales were significantly higher in families with a child who had a high mean HbA1c and had been hospitalized for diabetes in the last year. It was also found that the DFIS scale score was significantly higher in low-income families than in high-income families. While there was a negative correlation between the DFIS scale score and the child's age with Type 1 DM, and the mother's age, there was a positive correlation between the DFIS scale score and the HBA1c values.

Conclusion: The impact of Type 1 DM on families is widespread and multifactorial. In our study, as the diabetic control deteriorates and the age of the child decreases, the level of influence of the families in different aspects increases.

Keywords: Type 1 diabetes mellitus, diabetes family impact scale, family.

Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by chronic hyperglycemia caused by inadequate insulin function and/or secretion.[1] Type 1 DM is a common form of DM caused by damage to pancreatic β-cells in children and adolescents.[2,3] According to American Diabetes Association, about 1.25 million people in the United States are diagnosed with Type 1 DM, and about 40,000 children are diagnosed each year.[4] About 25,000 children diagnosed with Type 1 DM continue to be followed in Turkey, and about 2500 children are newly diagnosed each year.[5,6] Type 1 DM affects not only the children with the disease but also the family members (i.e., parents and siblings). They face financial, social, emotional, behavioral, cognitive, and psychological pressures, and these effects last for a long time.[7] Family members and caregivers play an essential role in diabetes management.[8] Therefore, parents should acquire new knowledge and skills to manage their children's diseases.[9]

On the other hand, Type 1 DM can hurt school attendance and academic success.[10] Although the impact of Type 1 DM on the family has been investigated in some studies, the number of studies assessing this issue with valid and reliable scales is limited.[7,10,11] In Turkey, there are also studies investigating the impact of Type 1 DM on children with the disease, their school life, family financial situation, and family relationships. [12-15] Our study is the first known study conducted in our country using the Diabetes Family Impact Scale (DFIS). The DFIS was developed in 2015, and its Turkish validity and reliability study was done in our country in 2020.[10,16] This study aims to determine the impacts of diabetes on families with a child diagnosed with Type 1 DM and the influencing factors using the DFIS.

Materials and Methods

Type of the study

This study is a descriptive cross-sectional study.

Design

The population of the study consists of the parents of 289 children of school-age (6-18 years) who have been followed up in the Department of Pediatric Endocrinology at Sivas Cumhuriyet University Faculty of Medicine (SCUFM) with a diagnosis of Type 1 DM for at least one year. Parents of 112 of the 289 children who visited the outpatient clinic of Pediatric Endocrinology between November 2020 and February 2021 and agreed to participate in the study were included. The research questionnaire was administered to the participants by one

of the researchers in a face-to-face interview. Before the interview, participants were informed about the study, and their informed consent was obtained.

Data collection tool

The data form used in the study consisted of a total of 35 questions. The first 21 questions of the questionnaire were related to sociodemographic data and some characteristics of the disease, and the following 14 questions were related to Diabetes Family Impact Scale (DFIS).[10,16] HbA1c levels in children with Type 1 DM were classified as HbA1c <7.0%, 7-9%, and >9% according to the International Guidelines Society for Pediatric and Adolescent (ISPAD) Diabetes Clinical Practice Consensus Guidelines 2018.[17]

We asked parents how often their child had hypoglycemia (<50 mg/dl, 50-70 mg/dl, and frequency of loss of consciousness due to hypoglycemia).[17] In addition to these questions, height, weight, body mass index, blood pressure, and HbA1c levels (%) in the last year were retrospectively retrieved from the hospital information management system in the children of parents who gave informed consent (61.2%; n=74).

Diabetes Family Impact Scale was developed by Katz et al. in 2015. [10] The Turkish validity study of the scale was performed by Çetintaş.[16] The scale consists of 14 items and is a 4-point Likert-Type with scores ranging from 0 to 3 (0 = never, 1 = sometimes, 2 = often, 3 = always). The Cronbach's alpha value was 0.881 for the internal consistency analysis of the data belonging to the scale's Turkish validity and reliability study. The scale consists of 4 sub-dimensions (School, Work, Financial Status, and Well-Being). The reliability coefficients of the four sub-dimensions of the scale ranged from 0.703 to 0.857. In the School subscale, questions were asked about the impacts of diabetes on the child's school performance, while in the Work subscale, questions were asked about the impacts of diabetes on the work areas of the child's family members. While the subscale Financial Situation included questions about the effect of diabetes on the family's financial situation, the subscale Well-Being included questions about sleep duration and family relationships of the child's family members with Type 1 DM. The higher the total score of the scale or sub-dimensions/dimensions, the greater the negative impact of diabetes on the family.

The collected data were analyzed using the SPSS program (Statistical Package for Social Sciences) for Windows Version 25 package. Normality analysis of numerical data was performed using the Shapiro-Wilk test. Firstly, a descriptive statistical analysis of the data was carried out. Frequencies for categorical data and measures of central distribution (Mean ± Standard Deviation) for numerical data were calculated. Independent Samples T-test was used to analyze whether normally distributed numerical data means differ significantly between two independent groups. The one-way ANOVA test analyzed whether there was a significant difference between more than two independent groups, whereas a chi-square test compared categorical data. Pearson Correlation

test was conducted to analyze the relationship between scale and sub-dimension scores and different numerical data. A p-value of less than 0.05 was considered statistical significance, with a 95% CI.

Results

Demographic data and characteristics of the family

Parents of 121 children were included in the study; the mean age of these children was 12.32 ± 3.24 years (minimum: 6.01- maximum: 17.71). The mean age of the mothers of the children was 38.57 ± 6.25, and the mean age of the fathers was 42.44 ± 5,68. The demographic data of the 121 children are shown in Table 1.

Table 1. Demographic data of the children

	n	%
Sex		
Girl	72	59.57
Boy	49	40.54
Family structure		
Nuclear family	85	70.24
Extended family	31	25.63
Parents separated	5	4.23
Mother's educational status		
Primary Education	54	44.65
High School	35	28.91
University and above	32	26.53
Father's educational status		
Primary Education	18	14.99
High School	70	57.90
University and above	33	27.21
Family income level		
Below minimum wage	54	44.63
2500-5000 TL	41	33.92
> 5000 TL	26	21.55
Mother's age (M/SD)	38.57	6.249
Father's age (M/SD)	42.44	5.667

Data on the health status of the children

22.33% (n=27) of the children had a chronic disease in addition to Type 1 DM. Considering the insulin use patterns, 88.41% (n=107) were using pens, and 11.69% (n=14) were using pumps. They measured blood glucose at a median of 7.00 (min:2 - max:15) times per day. Our study examined how often blood glucose levels

of children with type 1 DM fell below 50, how often they ranged between 50 and 70, and whether they experienced hypoglycemia at a level that would cause loss of consciousness**.** 89.30% (n=108) of the families of children participating in the study reported that their children did not experience hypoglycemia at a level that would lead to loss of consciousness (Table 2). Table 2 shows the frequency of children experiencing hypoglycemia.

Table 2. Frequency of patients experiencing hypoglycemia

	Blood Glucose between 50 – 70 mg/dl **n(%)**	Blood Glucose below 50 mg/dl **n(%)**	Loss of consciousness due to hypoglycemia **n(%)**
Never	6 (5.01%)	43 (35.51%)	108 (89.30%)
1-2 times a month	22 (18.20%)	43 (35.53%)	10 (8.25%)
1-2 times a week	74 (61.23%)	33 (27.34%)	2 (1.73%)
1-2 times a day	19 (15.66%)	2 (1.72%)	1 (0.82%)

43.01% (n=52) of children were hospitalized for Type 1 DM within the last year. Of these, 75.90% (n=44) were hospitalized for blood glucose regulation, 20.71% (n=12) for diabetic ketoacidosis, and 3.42% (n=2) for hypoglycemia.

When asked about children's of children physician visits due to Type 1 DM, the proportion of those who came for check-ups at intervals of more often than six months was 87.6% (n=106), and the proportion of those who came for check-ups at intervals of longer than six months was 12.40% (n=15).

The proportion of parents of children who gave consent for their children's data to be studied from the system was 61.20% (n=74). Mean values for height, weight, body mass index, systolic/diastolic blood pressure, and HbA1C for the last year of children of consenting parents are given in Table 3.

Scale scores and comparisons

The mean DFIS scale score of participants was 14.60±10.82. The school subscale mean score of the participants was 3.22±3.12, the job subscale mean score was 2.42±3.01, the financial status subscale mean score was 4.73±3.12, the well-being subscale mean score was 4.12±3.61. In our study, the mean scores of the DFIS total scale ($p=0.007$) and subscales on work ($p=0.040$), school ($p=0.014$), and financial situation ($p<0.001$) were significantly higher in low-income families than in high-income families. Among children with Type 1 diabetes DM, the mean score of the DFIS scale was significantly higher (21.41±11.92) in the families of those who had

other chronic diseases in addition to diabetes than in those without additional diseases (12.72±9.73) (p<0.001). Similarly, in all subgroups of the scale, mean scores were significantly higher in patients with additional diseases (p<0.05). Total DFIS (p=0.043), school (p=0.002), and work (p=0.015) subscale scores of families who received support from a caregiver in child care were significantly higher compared to those who received no support or support from their family. There was no significant difference between the education level of the mother and the total DFIS score (p=0.262). The school subscale scores of mothers with university or higher education were significantly lower than those of primary school graduates (p=0.026). Table 4 compares various sociodemographic data of families of diabetic children with their DFIS scale total scores.

Table 3. Percentile values and mean HbA1C values of the patients

	M ± SD	Min	Max
Height (SDS)	-0.41 ± 1.145	-2.41	2.51
Height (percentile)	39.07 ± 30.984	0.80	99.40
Weight (SDS)	-0.30 ± 1.275	-2.63	2.77
Weight (percentile)	42.30 ± 32.252	0.43	99.72
BMI (SDS)	-0.195 ± 1.245	-2.42	2.15
BMI (percentile)	46.19 ± 33.462	0.78	98.46
Systolic BP (mm/Hg)	105.35 ± 12.169	80	130
Diastolic BP (mm/Hg)	63.59 ± 9.716	50	90
HbA1C (%)*	8.71 ± 2.310	5.10	15.50
HbA1C (IFCC)*	71.43 ± 23.367	33.10	123.70

* The mean of the last 1-year values was taken. (SD: Standard deviation)

In our study, no significant association was found between the mean score of the DFIS scale in the families and insulin use patterns of the child with Type 1 DM (p=0.900) and frequency of self-monitoring blood glucose per day (p=0.937). Those with HbA1c >9% had a significantly higher DFIS mean score (p=0.026), Work subscale score (p=0.024), and Financial Status subscale score (p=0.047) than those with <7%. Those who lost consciousness due to hypoglycemia more than 1-2 times a month or more often had significantly higher DFIS score mean (p=0.011), school subscale, score (p<0.001), and work subscale score (p=0.009) compared to those never. The DFIS score means (p=0.009), the school subscale score (p=0.012) and the Financial Status subscale score (p=0.004) were significantly higher in those who had a history of hospitalization in the last year compared to those who did not. The comparison of DFIS scores with different variables related to the child's disease DM Type 1 is given in Table 5.

While there was a negative correlation between the DFIS scale score and the child's age with Type 1 DM, the mother's age and the father's age, there was a positive correlation with the mean HBA1c values (%) (Table 6). In addition, there were significant negative correlations between the age of the child and all subscales (p<0.05).

Table 4. Comparison of Diabetes Family Impact Scale (DFIS) with family sociodemographic characteristics

	DFIS scores	p
Sex		
Girl	14.21±11.521	0.629
Boy	15.22±9.913	
Mother's education level		
Primary education	16.01±11.013	0.262
High School	14.82±11.414	
University and above	12.01±9.856	
Father's education level		
Primary education	13.61±10.443	0.337
High School	15.82±11.787	
University and above	12.68±8.865	
Family structure		
Nuclear family	13.43±10.221	0.159
Extended family	16.95±11.263	
Parents separated	20.29±16.584	
Family income level		
Below minimum wage	17.10±10.923	**0.007[a]**
2500-5000 TL	14.92±11.458	
Above 5000 TL	9.04±7.814	
Childcare support		
No one	14.21±10.858	**0.043[b]**
Family elder	12.92±8.813	
Caregiver	22.73±13.454	
Child chronic disease		
Present	21.43±11.954	**<0.001**
Absent	12.79±9.736	

DFIS: Diabetes Family Impact Scale, TL: Turkish liras
Bonferroni post hoc analyses; a: 2500–5000 TL, b: family elder-caregiver

Table 5. Comparison of Diabetes Family Impact Scale (DFIS) and its subscales with different variables related to child's disease with DM type 1

	DFIS scores	p
Insulin use patterns		
Pump	15.02±7.434	0.900
Pen	14.61±11.289	
Frequency of self-monitoring blood glucose per day		
≤ 6 times	14.77±11.454	0.937
> 6 times	14.56±10.512	
HbA1c (%)		
<%7	9.30±11.103	**0.026**[a]
%7-9	13.72±10.058	
> %9	19.12±12.046	
Frequency of hypoglycemia (50-70 mg/dl)		
1-2 times a month or less	14.62±12.912	0.548
1-2 times a week	15.27±10.268	
1-2 times a day	12.24±10.098	
Frequency of hypoglycemia (<50 mg/dl)		
Never	12.47±11.178	0.249
1-2 times a month	15.58±10.387	
1-2 times a week or more often	16.29±11.135	
Loss of consciousness due to hypoglycemia		
Never	13.72±10.614	**0.011**
1-2 times a month or more often	21.89±10.969	
Hospitalization in the last year		
Yes	17.54±10.813	**0.009**
No	12.43±10.458	
The frequency of physician visits due to DM		
at intervals 6 months or more often	14.74±11.78	0.764
at intervals longer than 6 months	14.01±8.554	

DFIS: Diabetes Family Impact Scale
Bonferroni post hoc analyses; a: HBA1c (%) between >9 % and <7 %

Table 6. Correlation of Diabetes Family Impact Scale and its sub-scales with different variables

	DFIS	
	r	p
Child's age (year)	-0.270	**0.003****
Mother's age (year)	-0.204	**0.025***
Father's age (year)	-0.254	**0.005****
Duration of DM (month)	-0.194	0.091
Frequency of self-monitoring blood glucose per day	0.147	0.107
HbA1c (%)	0.298	**0.009****

DFIS: Diabetes Family Impact Scale; DM: Diabetes mellitus type 1; HbA1c: Hemoglobin A1c
** Correlation is significant at the 0.01 level (2-tailed)
* Correlation is significant at the 0.05 level (2-tailed)

Discussion

Although there are several studies on the impact of a child with Type 1 DM on the family, our study is the first known study conducted in our country using the DFIS scale.[10,18,19]

Parents of children with Type 1 diabetes are exposed to severe stress and burden. In the study by Herbert et al., families of school-aged children with Type 1 DM reported that they felt most stressed when their children were exposed to intensive medical treatment for various diseases.[20] In our study, parents of children with additional chronic diseases besides diabetes had higher DFIS scores. This situation is consistent with the literature. In the study conducted by Harrington et al., the parents of a child with Type 1 DM stated that the most common problem they perceived as a burden of diabetes was the child's hypoglycemic episodes.[21] Haugstvedt et al.'s study revealed that parents of children with hypoglycemic episodes, especially with nocturnal hypoglycemia and loss of consciousness, experience higher diabetic burden and emotional stress.[22] In a qualitative study by Commissariat et al., some families with a child with Type 1 DM mentioned that they were concerned about the occurrence of hypoglycemic episodes in their children and delays in treatment.[23] However, no significant association was found in our study between the frequency of hypoglycemia and DFIS score; in contrast, a significant increase in the scale score for severe hypoglycemic episodes with loss of consciousness due to DM was found, similar to the literature.

In the qualitative study of Abolhassan and his friends, the situation that families are most worried about for their children with diabetes; stated that there was a possibility of falling into a coma due to changes in blood sugar.[24] In the qualitative study of Wennick et al., they stated that the most affected issue for family members with children with diabetes is the changes (sudden rises and falls) in their children's blood sugar levels. In the same study, it was determined that the level of anxiety in families increased with the type and frequency of insulin use.[7] In our study, however, there was no significant difference between the type of insulin use and DFIS.

In the study conducted by Emre et al., it was determined that the school performance of children with poor diabetic control was more affected.[13] In a different study, they stated that the parents of adolescent children with diabetes thought the most about their children's academic success at school and future anxiety.[25] In our study, students with high HbA1c scores were found to be higher than those with low school subscale scores, although there was no significant difference. This situation is compatible with the literature.

Our study observed that families with a child who had a high HbA1c mean and had been hospitalized for diabetes in the last year had a significantly higher mean DFIS score and higher scores in the School and Work subscales. In a study conducted with diabetic children under the age of seven, the child's uncontrolled diabetes with Type 1 DM and risk of diabetes complications were among the issues of greatest concern to families.[21] In

another study, families of children hospitalized for diabetes were found to have high levels of anxiety and worry, especially about school.[20]

In Harrington et al.'s study, the only study in the literature that used the DFIS scale, families with a child diagnosed with Type 1 DM reported experiencing limitations in their workspace due to childcare.[21] Katz et al. pointed out that children with Type 1 DM affect their families, primarily in the areas of work, finances, and school absenteeism.[24] In our study, the Work subscale score of the DFIS increased significantly, especially among families with children with a high HbA1c mean. This finding suggests that families with diabetic children may experience different work-related problems.

Several studies have determined that the effect of diabetes on the family increases with the decreased age of the child diagnosed with Type 1 DM.[8,20] Our study also had a negative correlation between the child's age and the DFIS total score and all subscale scores except the school score, which is consistent with the literature.

In the study by Haugstvedt et al., it was concluded that parents whose child has Type 1 DM and who self-monitor their child's blood glucose levels more frequently have a higher perceived burden and psychological distress related to diabetes. The same dissertation study also found that better glycemic control was achieved as the mother's educational level increased, but the child's perception of social constraints increased.[22]

In the study conducted by Kobos et al. in Poland, it was shown that mothers with a low level of education felt more burdened by their diabetic children. In the same study, parents whose fathers do not work and whose income level is low were more affected.[8] Similarly, in our study, the DFIS score was higher in parents whose mothers had low education levels and whose income was below the minimum wage.

In our study, there was no significant difference between the frequency of going to the hospital controlled due to diabetes and DFIS. In the study conducted by Wennick et al., they found that families who regularly go to check-ups every three months due to their diabetes were affected positively by this situation because they contacted the diabetes team at the hospital more frequently.[7]

The impact of Type 1 DM on families is widespread and multifactorial. The main finding of our study is that children with poorly controlled diabetes and Type 1 DM affect their families in different ways the younger they are. Recognizing and addressing the impact of children with Type 1 DM on their families not only affects the quality of life of family members but can also provide them with the support and resources they need to better care for their children. Parents can also help adapt their children to diabetes. Social support and ongoing education are also paramount in adapting to a chronic illness. Therefore, it is crucial to set up psychosocial support groups where families of children with Type 1 DM can be educated together and talk about their problems. In this way, diabetics and families can expect better blood glucose control in the future.

Limitations

Although our study is the first study conducted in our country using DFIS, the results cannot be generalized to the whole country as it was conducted in a single center. There is a need for multicenter studies on this topic.

Ethical Considerations: The Ethics Committee of Cumhuriyet University for noninvasive clinical research approved the study (2020/10-09). Permission to use the scale in our study was obtained from Çetintaş via email.

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EVALUATION OF LARGE UNSTAINED CELLS (LUC) AND NITRIC OXIDE IN DIABETES MELLITUS

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Abstract

Objectives: The large unstained cells (LUC) is a differential count parameter measured by routine hematology analyzers and reflects activated lymphocytes and peroxidase-negative cells in leukocytes. Nitric oxide (NO) is produced in all tissues in enzymatic and non-enzymatic ways. This study aimed to determine the levels of LUC and NO products (nitrite and nitrate) and to evaluate the LUC/NO ratio in patients with Diabetes Mellitus (DM).

Materials and Methods: The study included 103 DM patients and 84 healthy controls. HbA1c, LUC/%LUC and total NO levels were measured. All the statistical calculations were performed using the Statistical Package for Social Sciences (SPSS) software program.

Results: Nitric oxide levels of the patients were statistically significantly lower compared with the control group (p=0.004). LUC levels, LUC% values, LUC/NO, and LUC%/NO ratios were significantly higher in the DM group (p=0.002, p=0.009, p= <0.001, and p= <0.001, respectively). Statistically significant correlations were observed between HbA1c and nitrite, nitrate, NO, LUC/NO ratio, and LUC % /NO ratio.

Conclusion: In this study, we determined the LUC/NO percent ratio and LUC%/NO percent ratio for the first time, according to our knowledge. We predict that these two parameters may be useful markers in the diagnosis and the follow-up of the disease and may provide target pathways for further studies that may contribute to the etiopathogenesis of the disease.

Keywords: Diabetes Mellitus, inflammation, LUC, NO.

Introduction

Diabetes mellitus (DM) is a carbohydrate metabolism disorder that is increasing in prevalence worldwide and manifests itself with hyperglycemia due to the underuse of glucose. Acute complications of DM are often serious, but long-term micro- and macrovascular complications of the disease are responsible for most of the morbidity and mortality in patients with DM.[1,2] Hemoglobin A1c (HbA1c) is a parameter used in the evaluation of glycemic status for both diagnosis and follow-up of DM and is a marker that shows glucose tolerance and glucose regulation in DM, formed by slow and non-enzymatic glycosylation of hemoglobin. HbA1c reflects the risk of developing diabetic complications and the quality of diabetic care, together with demonstrating glycemic control in DM.[3] While HbA1c reflects the mean plasma glucose of erythrocytes for 120 days. It is also the parameter that best correlates with the mean plasma glucose over the previous 8-12 weeks.[4] In 2009, the American Diabetes Association (ADA) approved the use of HbA1c level of ≥ 6.5% for the diagnosis of DM.[5] Also in our country, according to the guideline published by the Turkish Endocrinology and Metabolism Society in 2020, HbA1c levels of ≥6.5% (≥48 mmol/mol) make the diagnosis of overt DM. In the same guideline, people with HbA1c levels of 5.7-6.4% (39-47 mmol/mol) were considered to be a high-risk group for DM.[6]

Large unstained cells (LUC) are large peroxidase-negative cells that could not be determined as large lymphocytes, virocytes, blasts, or stem cells on the automatic cell counters. The percentage of LUC (%LUCs) is a count test measured by hematology analyzers automatically and shows activated lymphocytes and peroxidase-negative cells in leukocytes.[7,8] Increased levels of LUCs may be related to some viral and fungal infections, inflammation, or leukemia.[8]

Nitric oxide (NO) is produced in all tissues in enzymatic and non-enzymatic ways. NO is mostly produced from L-arginine by nitric oxide synthase (NOS) enzymes. NO plays an important role in the regulation of metabolism, energy balance, food intake, and insulin sensitivity. High morbidity and mortality rates of DM may be due to the early development of atherosclerosis in these patients.[9] NO affects endothelial permeability for macromolecules and also the proliferation and migration of vascular smooth muscle cells.[10,11] The concept of impaired NO activity for increased cardiovascular complications in DM is gaining more and more support.[12] Traditionally, nitrate and nitrite (NOx) were assumed to be inert derivatives of NO production.[13] The last stage in the NO pathway is an electron transfer from nitrite to NO. This nitrite reduction is catalyzed by deoxyhemoglobin, deoxymyoglobin NOS, cytochrome P-450, xanthine oxidase, and the mitochondrial electron transfer complexes. This reaction occurred in hypoxic conditions. The alternative NO generation pathway limits the production of NO from NOS under hypoxia and oxidative stress conditions.[14]

DM leads to endothelial dysfunction and accelerates the progression of atherosclerosis. Inflammation is known to play a key role in atherosclerosis.[9] This study aimed to determine the levels of LUC indicating inflammation

and nitric oxide products nitrite and nitrate (NOx), which are markers of endothelial dysfunction, and to evaluate the LUC/NO ratio in patients with DM.

Materials and Methods

In the study, the subjects were divided into two groups according to their HbA1c levels patients with DM (HbA1c≥6.5%) and control (HbA1c<5.7%). Our study included 103 patients with DM over the age of 18 who applied to the internal medicine outpatient clinic of our hospital and 84 healthy volunteers as the control group. Blood samples were collected from the patients and healthy volunteers into two separate tubes, EDTA (ethylenediaminetetraacetic acid) containing tube and a serum separator tube used for routine biochemical tests. HbA1c values were measured by Atellica CH 930 Analyzer (Siemens Healthineers, Erlangen, Germany) with the principle of latex agglutination inhibition assay in our laboratory. The %LUC values were calculated automatically with the Advia2120 (Siemens Healthcare Diagnostics, Forchheim, Germany) fully automatic blood count analyzer. Nitrite, nitrate, and NO levels were measured using the spectrophotometric method. Briefly, samples were initially deproteinized. Then, nitrite levels were measured with the Griess reaction. Total nitric oxide (nitrite and nitrate) was measured after the conversion of nitrate to nitrite by cadmium granules by a spectrophotometer at 545 nm.[15] A standard curve was established with sodium nitrite, and this curve was used to calculate the unknown sample concentrations. The results were expressed as micromoles per liter plasma (μmol/L).

Our study was approved by Ankara City Hospital Ethics Committee number E-19-022.

The conformity of continuous variables to normal distribution was examined using Kolmogorov–Smirnov test). Variables were evaluated considering their distribution using statistical tests. Since continuous variables showed normal distribution, the results were presented as mean and standard deviation. Categorical variables are given as numbers and percentages (%). Categorical variables were evaluated by the Chi-square test. Group comparisons (control group vs. patient group) were made using Student's t-test. Correlation analyses were performed using Pearson's correlation. The analysis of the cut-off value, sensitivity, and specificity of tests was done by the receiver operating characteristic (ROC). SPSS software program (v22 IBM, Armonk, NY, USA) was used for the statistical analysis, and a *P* value less than 0.05 was set as statistically significant for all analyses.

Results

Our study included 103 patients with the diagnosis of DM (52 females (50.48%), 51 males (49.52%)) and 84 healthy controls (41 females (48.80 %), and 43 males (51.20%)). The mean age of the patients and the control group were similar. Nitric oxide levels of the patients were statistically significantly lower than healthy controls

(p=0.004). LUC levels, LUC% values, LUC/NO and LUC%/NO ratios were significantly higher in the DM patient group (p=0.002, p=0.009, p= <0.001, and p= <0.001, respectively) (Table 1, Figure 1).

Table 1. Laboratory findings of individuals in study groups.

Parameters	**Group**	**Mean ± SD**	***p*-value**
HBA1c (%)	Control	5.05 ± 0.33	<0.001
	DM	8.58 ± 1.93	
FG (mg/dL)	Control	78.17 ± 9.11	<0.001
	DM	176.74 ± 80.41	
PG (mg/dL)	Control	89.33 ± 21.55	<0.001
	DM	286.79 ± 125.03	
LUC (x10^9/L)	Control	0.11 ± 0.03	0.002
	DM	0.15 ± 0.07	
LUC (%)	Control	1.5 ± 0.43	0.009
	DM	1.82 ± 0.65	
Nitrite (µmol/L)	Control	3.23 ± 0.68	0.011
	DM	2.81 ± 0.51	
Nitrate (µmol/L)	Control	8.06 ± 0.76	0.039
	DM	7.66 ± 0.7	
NO (µmol/L)	Control	11.29 ± 1.02	0.004
	DM	10.51 ± 1.06	
LUC/NO ratio	Control	0.97 ± 0.28	<0.001
	DM	1.4 ± 0.47	
LUC %/NO ratio	Control	13.16 ± 3.9	<0.001
	DM	17.39 ± 6.11	

(FG: fasting glucose; PF: postprandial glucose; LUC: large unstained cells; SD: standard deviation.)

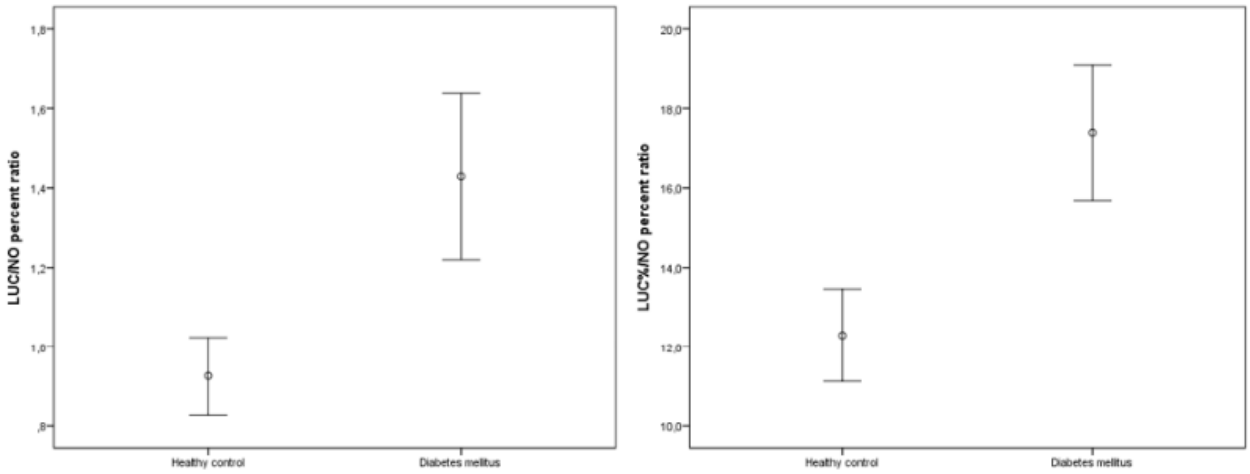

Figure 1. The alteration of LUC/NO and LUC%/NO percent ratios in Diabetes Mellitus and healthy control groups.

According to ROC analysis performed to evaluate the possible contribution of the tests to prediction, LUC/NO ratio and LUC%/NO ratio parameters provided the highest contribution (Table 2, Figure 2.). The cut-off level for LUC/NO ratio was 1.01, the sensitivity was 73.10%, and the specificity was 60.90%. The optimal cut-off level for the LUC%/NO ratio was 13.05, the sensitivity was 75.00 %, and the specificity was 65.20 %.

Table 2. The value of the tests in predicting cases of Diabetes Mellitus

Parameters	AUC %	Std. Error	95% CI	*p*-value
LUC	66.9	0.062	0.547-0.792	0.014*
%LUC	64.1	0.065	0.515-0.768	0.065
NO	69.8	0.063	0.574-0.822	0.006*
LUC/NO Ratio	78.2	0.052	0.679-0.884	<0.001*
%LUC/NO Ratio	78.4	0.052	0.683-0.885	<0.001*

(AUC: area under the curve; CI: confidence interval; LUC: large unstained cells)

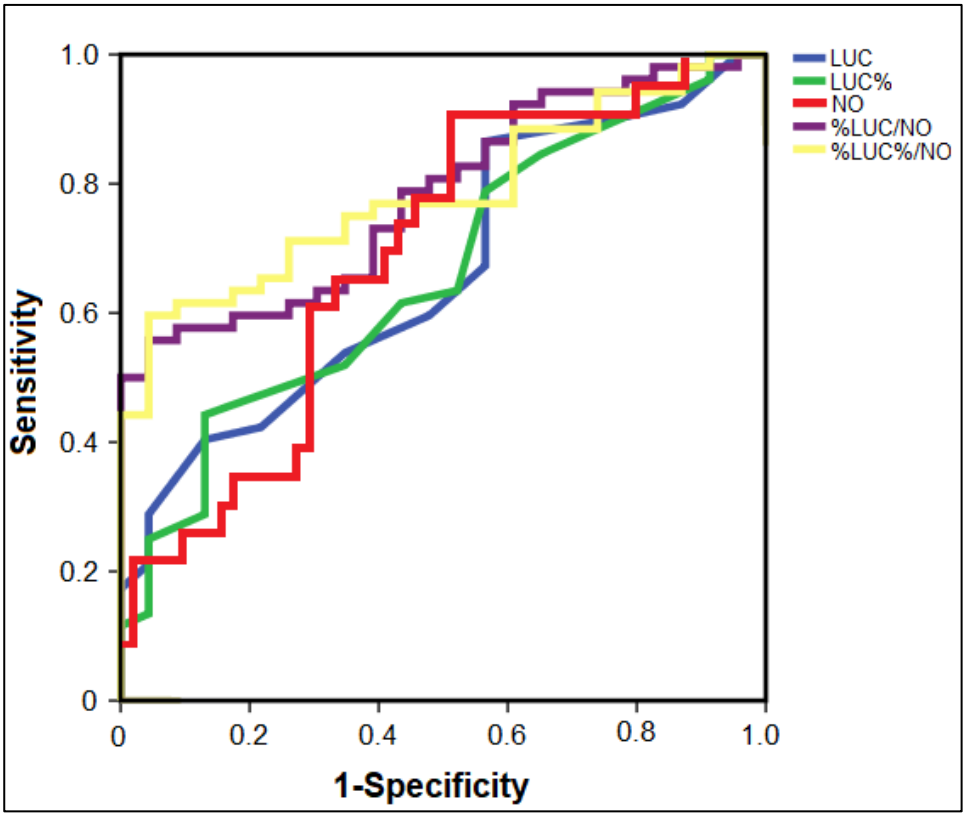

Figure 2. ROC curve of tests predicting Diabetes Mellitus

While statistically significant correlations were observed between HbA1c and NO_2, NO_3, NO, LUC/NO ratio, and LUC % /NO ratio, no correlation was found with LUC and LUC % levels (Table 3).

Table 3. The relationship between the HbA1c levels and other laboratory parameters.

		LUC	%LUC	NO_2	NO_3	NO	LUC/NO Ratio	%LUC/NO Ratio
HbA1c	*r*	0.115	-0.005	-0.507	-0.396	-0.547	0.261	0.239
	p	0.281	0.961	<0.001*	<0.001*	<0.001*	0.024*	0.038*

Discussion

DM is a chronic metabolic disorder that the metabolism of carbohydrates, fats, and proteins is disrupted due to insulin deficiency or defects in the effect of insulin on the target organs. Oxidative stress is thought to be associated not only with DM complications but also with the progression of insulin resistance. [6,16] DM leads to endothelial dysfunction and accelerated progression of atherosclerosis.[17] Inflammation is known to be a component of DM.[18] Another parameter that has recently been shown to be related to inflammatory markers is LUC. It has been emphasized in previous studies that LUC levels are significantly positively correlated with inflammatory biomarkers.[19]

LUCs are larger than lymphocytes and may be abnormal lymphocytes, peroxidase-negative blasts, or myeloperoxidase-deficient cells. Aberrations in the number of LUCs may be an indicator of some viral infections or leukemia.[7,20] In a study, it was determined that leukocyte and neutrophil counts were higher and lymphocyte counts were lower in patients with DM.[21] According to our knowledge, there is not enough information about LUC levels in patients with DM. Therefore, it is important to evaluate the relationship between DM and LUC levels. In our study, we found increased LUC levels in DM patients when compared to healthy controls. DM is an inflammatory disease.[22] The increase may be associated with the inflammation status in DM patients. The results of the study of Vozarova B et al. [23] support our findings, and it can be said that elevated leukocyte levels and elevated LUC levels can be indicators of inflammation in DM.

Another parameter associated with the development of DM is nitric oxide, which is known to be important in the maintenance of vascular endothelial functions. NO plays an important role in the regulation of systemic metabolism, energy balance, and insulin sensitivity. Endothelial dysfunction and increased oxidative stress in DM are suggested as common mechanisms in the development of the metabolic syndrome and insulin resistance.[24,25] An imbalance of oxidant-antioxidants in the body results in oxidative stress, which contributes to impaired bioavailability of nitric oxide and vascular dysfunction. It has been shown that endothelial cells cannot produce enough NO in patients with DM and do not relax in response to some vasodilators, such as

endothelium-dependent acetylcholine and bradykinin.[26,27] With these findings, it can be said that oxidative and nitrosative stress has a potential contribution to the pathogenesis of complications related to DM, where glycemic control cannot be achieved.[28] In the study of Paolo Tessari et al., it was shown that whole-body NOx synthesis was decreased in patients with type 2 DM and was not stimulated appropriately by hyperinsulinemia. In this study, it has also been shown that there is a decrease in whole-body NOx synthesis and the conversion of arginine to NOx in DM in response to insulin.[29] Similarly, in our study, we found lower NO levels in DM patients indicating impaired NOS activity and decreased NO production. Lower NO levels in our study indicated endothelial dysfunction in DM patients in accordance with the literature. The stimulation of NOS activity downregulates the effect of insulin; and, insulin resistance may be associated with decreased nitric oxide production in DM.[30]

When the healthy controls and DM patients were compared, LUC, LUC%, NO, and the oxidation products of NO (nitrite and nitrate) were statistically significant. In this study, we determined the LUC/NO percent ratio and LUC%/NO percent ratio for the first time, according to our knowledge. LUC/NO percent ratio and LUC%/NO percent ratio were also statistically significant. Various visual and statistical analyzes were performed to evaluate the effectiveness of these parameters for the diagnosis of DM. According to the analyzes performed, LUC/NO percent ratio and LUC%/NO percent ratio parameters provided the highest contribution to the diagnosis of DM patients (Table 2 and figure 2). In addition, significant correlations were observed between HbA1c, which is an important test in the diagnosis of DM, and NO, the oxidation products of NO, LUC/NO percent ratio, and LUC%/NO percent ratio parameters (Table 3).

In line with these findings, the LUC/NO percent ratio and LUC%/NO percent ratio parameters are remarkable, as they are found to be significantly higher in DM patients, making the highest contribution to the diagnosis of DM. We predict that these two parameters may be useful markers in the diagnosis and the follow-up of the disease and may provide target pathways for further studies that may contribute to the etiopathogenesis of the disease.

Ethical Considerations: The study was approved by Ankara City Hospital Ethics Committee (Date: 05.09.2019, Approval number: E-19-022).

Conflict of Interest: Authors declare that there is no conflict of interest

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Research Article

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THE RELATIONSHIP OF NEUTROPHIL AND PLATELET MARKERS WITH CLINICAL VARIABLES AND DISEASE ACTIVITY IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Abstract

Objectives: The aim of this study is to show the relationship between neutrophil and platelet levels and clinical criteria such as disease activity and pain in ankylosing spondylitis (AS) patients.

Materials and Methods: The study included 48 AS patients (Group 1) and 47 healthy controls (Group 2). Clinical and laboratory evaluations, including the measurement of the hemogram, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR), were performed. The AS patients were divided into two subgroups according to their disease activity was evaluated by using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score (≥4 high activity, <4 low activity).

Results: Mean age of the patients was 42.44 ±12.32 years in Group 1 and 46.30 ± 9.10 years in Group 2 and showed no significant difference between groups (All p values >0.05). The ESR, CRP, NLR, PLR, and plateletcrit (PCT) values were significantly higher in Group 1, while the hemoglobin values were significantly lower in Group 2 (All p values <0.05). The platelet count was significantly higher in the subgroup with high disease activity according to the BASDAI score (All p values <0.05). A significantly negative weak correlation was found between MPV and BASMI and MPV and ESR (r=-0.303, p=0.037; r=-0.492, p<0.001, respectively). According to the receiver operating characteristic (ROC) analysis, PLR and MPV had diagnostic value in demonstrating disease activity.

Conclusion: While NLR, PLR, and PCT can be used in the initial evaluation of inflammation in AS patients, PLR and MPV were found effective in demonstrating disease activity.

Keywords: Ankylosing spondylitis, mean platelet volume, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, plateletcrit.

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Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that primarily affects the sacroiliac joint and spinal segment and is characterized by joint and extra-articular involvements.[1] While its etiopathogenesis is unknown, the disease is usually seen in young men, with a prevalence varying between 0.15-1.4% in the general population.[1,2]

In addition to clinical findings and imaging methods, the acute phase reactants C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are frequently used to determine disease activity and inflammatory progression in rheumatic diseases.[1] It has been reported that CRP and ESR levels may increase in approximately 50 to 70% of AS patients.[2] In addition, it is known that some cytokines and biological markers used in determining the disease activity and prognosis in AS increase with inflammation. However, these markers are not routinely used since they are difficult and expensive to obtain.[3]

Recently, an association between the neutrophil, lymphocyte, platelet, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) count (an indicator of the number of platelets in a unit volume of blood) and inflammation has been established.[4-6] It has been reported that MPV is decreased in active clinical conditions of rheumatological diseases and can be used as a negative acute phase reactant[7,8], while NLR is effective in demonstrating systemic inflammation in rheumatic diseases such as rheumatoid arthritis.[9] In addition, it has been proposed that the NLR can be used as a subclinical inflammatory marker in familial Mediterranean fever and in predicting the development of amyloidosis.[10] In line with this information, the number of studies evaluating the relationship of NLR and PLR with disease activity in rheumatic diseases has increased, confirming the use of these parameters as an indicator of disease activity.[9-11]

In previous studies, the relationship of neutrophil and platelet parameters with disease activity and the functional index was evaluated, but the relationship of these parameters with quality of life, metrological index and enthesitis index in AS patients was not investigated. The aim of this study is to show the relationship between neutrophil and platelet levels and clinical criteria such as disease activity, pain, quality of life, enthesitis index, functional index, and metrological index in patients with AS.

Materials and Methods

Forty-eight patients who applied to the Department of Physical Medicine and Rehabilitation of our hospital between January 2016 and January 2020 and were previously diagnosed with AS according to the Modified New York criteria were included as the patient group (Group 1). The control group (Group 2) was comprised

of 47 age- and sex-matched healthy patients. Patient data were analyzed retrospectively. Ethical approval was obtained from the University Clinical Research Committee (Date: 23/12/2020, Decision No: 370) prior to the study. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The patients who have been observed with the diagnosis of AS for at least one year were included in the study. Exclusion criteria: Patients with hypertension, diabetes mellitus, coronary artery disease, thyroid disease, chronic obstructive pulmonary disease, asthma, malignancy, liver or kidney failure, inflammatory bowel disease, or local or systemic infection, current smokers or with a history of smoking in the past year were not included in the study. Patient data regarding demographic features (age, gender, and body mass index), laboratory examination results, and the duration of the disease were recorded. Healthy controls were formed from the patient relatives who did not meet the exclusion criteria.

Hemoglobin (g/dL), leukocyte ($\times 10^9$/L), lymphocyte ($\times 10^9$/L), neutrophil ($\times 10^9$/L), thrombocyte ($\times 10^9$/L), MPV (fL), PCT (%), and PDW (fL) values were obtained simultaneously from complete blood count. NLR was determined by dividing the absolute neutrophil count by the absolute lymphocyte count and PLR was determined by dividing the absolute platelet count by the absolute lymphocyte count. The CRP (mg/L) and ESR (mm/hour) acute phase reactants were also evaluated. Clinical and laboratory evaluations of the patients were performed simultaneously on the same day.

BASDAI, BASFI, BASMI, enthesitis index, and ASQL scales are routinely performed in patients with Ankylosing Spondylitis, and data were obtained from patient files in a retrospective review. In the AS group, the disease activity was evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), which consists of six questions, including fatigue, spinal pain, pain and/or swelling in peripheral joints, areas of localized tenderness, and the duration and severity of morning stiffness. The total score ranges from 0 (best) to 10 (worst).[12]

The functional status of the patients was checked with the Bath Ankylosing Spondylitis Functional Index (BASFI). The index is evaluated on a 10-cm-long visual analog scale (VAS), with a total of 10 questions, eight of which include activities of daily living and two questions evaluating the patients' ability to cope with daily life. The total score was calculated between 0 and 10.[13]

Spinal mobility of AS patients was evaluated using the Bath Ankylosing Spondylitis Metrology Index (BASMI), which includes measurements regarding cervical rotation, tragus to wall distance, lumbar lateral flexion, lumbar anterior flexion (modified Schober test), and intermalleolar distance. Total scores range from 0 to 10, with a lower score denoting better spinal mobility.[14]

Quality of life was assessed using the Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire. This questionnaire consists of 18 yes/no items designed to measure the impact of AS on health-related quality of life, with lower scores indicating better quality of life.[15]

The Maastricht Ankylosing Spondylitis Enthesitis Score (MASES) was used to evaluate the degree of enthesitis in the patients. MASES bilaterally evaluates the first and seventh costochondral joints, posterior and anterior iliac spines, iliac crest, and Achilles attachment site and determines whether the fifth lumbar spinous process is sensitive to pressure. Tenderness in all regions was recorded as absent (0 points) or present (1 point), with the total score ranging between 0 and 13.[16]

Day and night pain evaluations of the patients were performed using a 10-cm-long VAS.

Comparison of the patient and control group data and intergroup comparison of the AS patients according to their BASDAI score (≥4 high activity, <4 low activity) were performed.

Statistical analyses

Power analysis and sample size calculation were performed using the PASS version 11.0 software (NCSS LLC, Kaysville, UT, USA). Accordingly, the study power was 0.990 with alpha=0.005, beta=0.00956, standard deviation 1 and 2=0.1, and, k=2, and a total of n=76. According to the power analysis, there should be at least 38 patients in each group. As we reached the target patient number at that point, we terminated the study, and in total, we completed recruitment. Totally 95 patients were included in the study.

Statistical analyses were performed using IBM SPSS (IBM SPSS Statistics Version 22.0. Armonk, NY: IBM Corp.) software. While descriptive statistics were used to determine the characteristics of the patients and controls, a comparison of the groups was carried out using Fisher's exact chi-square test, independent samples t-test, and the Mann-Whitney U test. Correlation analyses were performed using the Pearson correlation coefficient. Receiver operating characteristic (ROC) analysis was performed to examine the diagnostic values of the NLR, PLR, MPV, PCT, and PDW parameters. According to the ROC analysis, appropriate sensitivity and specificity values were determined and the according to threshold value was found by calculating the lowest value according to the $Distance=(1-sensitivity)^2+(1-specificity)^2$ formula based on the Pythagorean theorem. Since MPV and PDW were negatively correlated with BASDAI, ESR, and CRP, the analysis was performed by considering the decreasing values in the ROC analysis more significant for positive results. The results were expressed as number (percent) and mean±standard deviation (mean±SD). A p-value less than 0.05 was considered significant in the statistical analyses.

Results

The mean age of the patients was 42.44 ±12.32 years in Group 1 and 46.30 ± 9.10 years in Group 2. The groups showed similarity in terms of age, gender and body mass index. The mean duration of the disease was 12.92 ±11.91 years in the patient group. Group 1 had significantly higher ESR, CRP, NLR, PLR, and PCT values and significantly lower hemoglobin values than the control group (All p values <0.05). The comparison of the demographic data and laboratory findings of AS patients and healthy controls and their evaluations regarding disease activity index, quality of life, enthesitis, and pain are given in Table 1.

According to the BASDAI score, 29 patients had a high level of disease activity (BASDAI≥4), while 19 had a low level of activity (BASDAI<4). Platelet count was found to be significantly higher in the group with high activity (p=0.022). The comparison of the laboratory values of the AS patients divided into groups according to disease activity is given in Table 2.

The correlation analysis among the patients' NLR, PLR, and MPV values and their age, BASDAI, BASFI, BASMI, ASQoL, MASES, day VAS, night VAS, VAS patient's global assessment, VAS physician's global assessment, ESR, and CRP parameters demonstrated a statistically significant, negative weak correlation between MPV and BASMI and between MPV and ESR (r=-0.303, p=0.037 and r=-0.492, p=<0.001 respectively). There was no correlation between NLR and PLO with all the above-mentioned parameters and no correlation was found between MPV and the above parameters except BASMI and ESR (Table 3).

The ROC analysis results for the diagnostic values of NLR, PLR, MPV, PCT, and PDW based on the threshold values of BASDAI ≥4, ESR>20 mm/hour, and CRP >5 mg/dl are shown in Table 4. According to the ROC analysis results, the diagnostic value of PLR was 71.0% (area under the curve: 0.710) and the diagnostic value of MPV was 72.3% (area under the curve: 0.723) according to the ESR>20 mm/hour threshold. While PLR had a sensitivity of 68.8%, specificity of 81.3% and a cut-off value of>161.50, MPV had a sensitivity of 75.0%, specificity of 62.5%, and a cut-off value of<9.90. The diagnostic values of both parameters were statistically significant (p=0.019 and p=0.013, respectively). The results of the ROC analysis of other parameters revealed no statistical significance for their diagnostic values. The cut-off graph for platelet and lymphocyte parameters in patients with ankylosing spondylitis based on the threshold values of ESR>20 mm/hour is shown in Figure 1.

Table 1. Demographic data and laboratory findings of the study groups and the disease activity index, quality of life, enthesitis, and pain evaluation results of ankylosing spondylitis patients.

Parameters	AS patients n=48)	Controls (n=47)	p
Age (years)	42.44±12.32	46.30±9.10	0.056†
BMI (kg/m²)	26.84±5.10	27.76±5.01	0.377†
Sex (female/male)	13/35	10/37	0.509
Duration of the disease (years)	12.92±11.91	-	-
BASDAI	4.50±1.99	-	-
BASFI	3.55±2.49	-	-
BASMI	2.48±1.99	-	-
ASQoL	9.46±5.56	-	-
MASES	3.56±3.63	-	-
VAS night	3.54±3.56	-	-
VAS day	3.67±2.92	-	-
VAS patient GA	4.33±2.33	-	-
VAS physician GA	3.63±1.78		
ESR (mm/hour)	17.94±14.38	11.47±7.40	**0.035***
CRP (mg/L)	9.48±10.08	4.70±3.02	**<0.001***
Hemoglobin (g/dL)	13.94±1.85	14.80±1.44	**0.008***
Leukocyte (×10⁹/L)	8.06±1.90	7.77±1.45	0.655*
Neutrophil (×10⁹/L)	5.15±1.47	4.64±1.08	0.053†
Lymphocyte (×10⁹/L)	2.22±0.88	2.38±0.59	0.053*
Platelet(×10⁹/L)	288.67±61.64	270.72±66.87	0.177†
NLR	2.72±1.38	2.03±0.63	**0.017***
PLR	148.97±67.36	118.13±37.11	**0.014***
MPV (fL)	9.81±1.19	9.72±1.54	0.820*
PCT	0.27±0.05	0.25±0.06	**0.040†**
PDW (fL)	16.02±0.35	16.08±0.38	0.381†

(AS: ankylosing spondylitis, ASQoL: Ankylosing Spondylitis Quality of Life, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, BMI: body mass index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, MASES: Maastricht Ankylosing Spondylitis Enthesitis Score, MPV: mean platelet volume, NLR: neutrophil to lymphocyte ratio, PCT: plateletcrit, PLR: platelet to lymphocyte ratio, PDW: platelet distribution width, VAS: visual analog scale.)
*Mann-Whitney U test, †Student's t-test. The data are shown as n, % or mean±standard deviation. Significant p values are written in bold.

Table 2. Comparison of ankylosing spondylitis patients according to BASDAI values.

Parameters	BASDAI <4 (n=19)	BASDAI≥4 (n=29)	p
ESR (mm/hour)	14.21±9.35	20.38±16.59	0.268*
CRP (mg/L)	9.33±10.50	9.58±9.98	0.599*
Hemoglobin (g/dL)	14.33±1.93	13.69±1.78	0.249†
Leukocyte ($\times10^9$/L)	8.28±2.03	7.92±1.84	0.527†
Neutrophil($\times10^9$/L)	5.11±1.53	5.19±1.46	0.856†
Lymphocyte($\times10^9$/L)	2.37±0.99	2.12±0.80	0.877*
Platelet($\times10^9$/L)	265.74±43.50	303.69±67.61	**0.022**†
NLR	2.57±1.35	2.81±1.41	0.473*
PLR	129.59±51.89	161.66±73.92	0.132*
MPV (fL)	10.09±1.34	9.63±1.07	0.195†
PCT	0.27±0.05	0.28±0.06	0.405†
PDW (fL)	16.11±0.37	15.96±0.33	0.134†

(BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, MPV: mean platelet volume, NLR: neutrophil to lymphocyte ratio, PCT: plateletcrit, PLR: platelet to lymphocyte ratio, PDW: platelet distribution width.)

*Mann-Whitney U test, †Student's t-test. The data are shown as mean±standard deviation. Significant p values are written in bold.

Table 3. Correlations of the clinical and laboratory parameters in ankylosing spondylitis patients.

		Age	BASDAI	BASFI	BASMI	ASQoL	MASES	VAS night	VAS day	VAS patient	VAS physician	ESR	CRP
NLR	r	-0,077	0.001	0.186	0.099	0.005	0.143	0.117	0.091	-0.101	0.081	0.176	0.249
	p	0.605	0.992	0.207	0.503	0.972	0.333	0.428	0.538	0.493	0.584	0.232	0.088
PLR	r	-0.069	0.064	0.076	0.179	0.102	0.140	0.217	0.098	-0.019	0.198	0.268	0.014
	p	0.643	0.666	0.606	0.223	0.488	0.344	0.139	0.509	0.896	0.177	0.066	0.927
MPV	r	-0.157	0.086	-0.077	-0.303	0.118	-0.053	-0.018	0.032	0.079	-0.015	-0.492	-0.046
	p	0.286	0.559	0.601	**0.037**	0.423	0.718	0.905	0.830	0.593	0.921	**<0.001**	0.756

(ASQoL: Ankylosing Spondylitis Quality of Life, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, BASMI: Bath Ankylosing Spondylitis Metrology Index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, MASES: Maastricht Ankylosing Spondylitis Enthesitis Score, MPV: mean platelet volume, NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, VAS: visual analog scale.)

Table 4. Receiver operating characteristic curve analysis results of platelet and lymphocyte parameters in patients with ankylosing spondylitis based on BASDAI, ESR, and CRP thresholds.

	Sensitivity	Specificity	AUC	Cut-off	Likelihood ratio	p
BASDAI						
NLR	0.586	0.526	0.542	>2.22	1.24	0.628
PLR	0.759	0.526	0.630	>120.99	1.60	0.132
MPV	0.621	0.579	0.588	<10.05	1.47	0.307
PCT	0.621	0.579	0.583	>0.26	1.47	0.337
PDW	0.586	0.579	0.620	<16.05	1.39	0.164
ESR						
NLR	0.750	0.594	0.646	>2.30	1.85	0.101
PLR	0.688	0.813	0.710	>161.50	3.67	**0.019**
MPV	0.750	0.625	0.723	<9.90	2.00	**0.013**
PCT	0.563	0.594	0.504	>0.27	1.38	0.089
PDW	0.563	0.719	0.633	<15.85	2.00	0.088
CRP						
NLR	0.650	0.571	0.584	>2.30	1.52	0.326
PLR	0.600	0.607	0.588	>144.95	1.53	0.301
MPV	0.650	0.607	0.621	<9.90	1.66	0.155
PCT	0.500	0.571	0.488	>0.27	1.17	0.884
PDW	0.400	0.643	0.535	<15.85	1.12	0.683

(AUC: area under the curve, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, MPV: mean platelet volume, NLR: neutrophil to lymphocyte ratio, PCT: plateletcrit, PLR: platelet to lymphocyte ratio, PDW: platelet distribution width.)

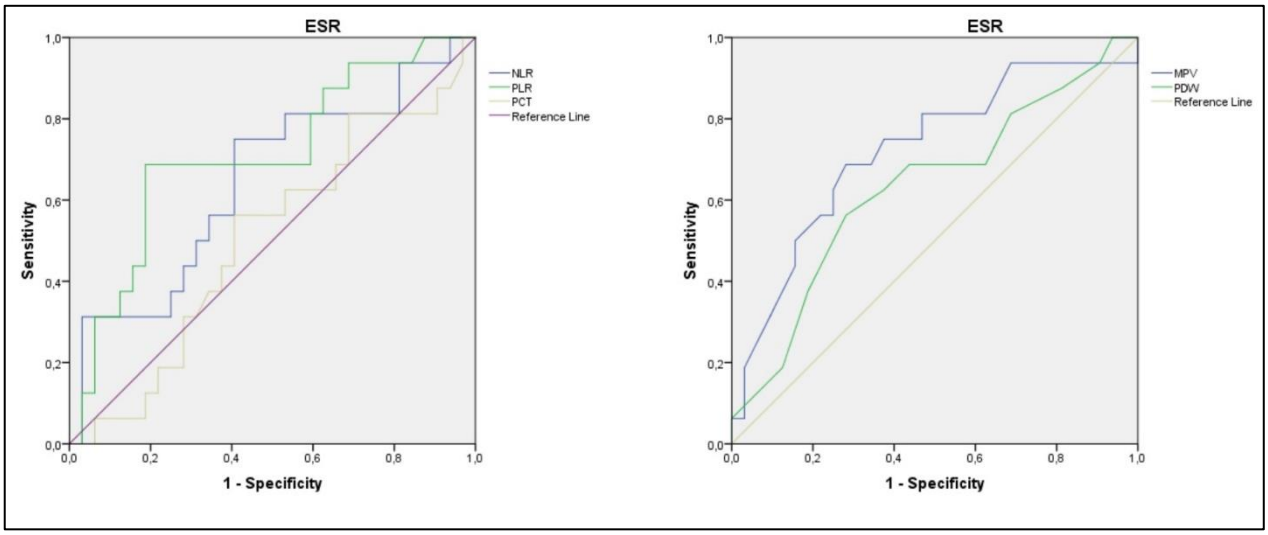

Figure 1. The cut-off graph for platelet and lymphocyte parameters in patients with ankylosing spondylitis based on the threshold values of ESR >20 mm/hour

Discussion

In the current study, AS patients had significantly higher ESR, CRP, NLR, PLR and PCT parameters but lower hemoglobin values than the control group. The platelet count was higher in the subgroup with high disease activity. A negative correlation was observed between MPV and BASMI and between MPV and ESR in the patient group. In addition, PLR and MPV had diagnostic value in demonstrating disease activity.

The literature on neutrophil and platelet markers in AS patients has presented inconsistent results. While NLR and TLR values were high in some studies[17-19], they were similar to those of the control group in others.[11,20] In a study of 30 AS patients and 35 healthy controls, Bozan et al. reported higher NLR values in the study group and similar PLR values.[18] Gokmen et al. also recounted higher NLR values in their patient group.[21] In another study of 103 AS patients, NLR and PLR values were found to be similar to those of the control group.[19] In studies examining the relationship of disease activity with NLR and PLR, it was reported that NLR and PLR values were higher in the group with high disease activity according to BASDAI.[19,20] The NLR and PLR values were found to be similar when 216 AS patients were divided into groups according to disease activity.[17] In our study, NLR and PLR values were found to be significantly higher in AS patients than in the control group. When we evaluated disease activity according to BASDAI, we found that 29 patients showed high activity. The group with high disease activity had higher NLR and PLR values than the group with low disease activity, but this elevation did not reach statistical significance.

In systemic inflammation, changes occur in circulating leukocytes, erythrocytes, and thrombocyte counts. The best known of these changes are normochromic anemia, thrombocytosis, and the relative decrease in lymphocyte count accompanying the increase in the neutrophil count.[11] In inflammatory conditions, platelets are stimulated and significant changes occur in their structure and function. Low MPV levels have been reported in patients with an increased inflammatory response, such as rheumatoid arthritis. In inflammatory diseases, large-size platelets migrate to and are consumed in the inflammation area, and, in addition to this, platelet production is stimulated by increasing the number of platelets in the circulation.[26] When we examined the relationship of these parameters to an acute inflammatory process in our study, MPV's threshold value was <9.4, sensitivity 71.9% and specificity 68.7%, while PLR's threshold value was 161.50, sensitivity 68.8% and specificity was 81.3%.

It has been reported that thrombocyte and MPV values are higher in AS patients than in non-AS patients.[22] In another study[23], platelet values were high in 30 AS patients, while MPV values were low. The same study also reported an increase in MPV values after TNF treatment. Sahin et al. reported that low MPV levels could be used as a negative acute phase reactant.[8] While some studies reported that MPV has a negative[23] or positive[24] correlation with BASDAI in AS patients, others stated otherwise.[21,25] Byun et al. reported that there was no

relationship between MPV values and BASDAI, BASFI, and ASDAS.[25] Al-Osami et al. reported that platelet count was high in the active group in 132 AS patients in comparison to the low activity group, classified according to BASDAI.[20] Similarly, the platelet count was high in the group with BASDAI ≥4 in another study.[7] In our study, platelet and MPV values were found to be similar between AS patients and the control group. While the platelet count was high in the group with high disease activity, MPV values were similar. However, there was a negative correlation between MPV and ESR, confirming that MPV is a negative acute phase reactant. We also found a negative correlation between MPV and BASMI. This situation explains the limitation of spine motion during the active disease period.

Platelet distribution width is an indicator of variability in platelet size.[27] Studies on PDW have mostly been conducted in rheumatoid arthritis patient groups.[28] In their study of 216 AS patients, Illeez et al. found that the PDW values were significantly lower in the AS group, while they were similar in active remissory AS patients.[17] In contrast to this study, PDW values were similar in the AS and control groups in our study, but similarly, there was no difference between the groups in terms of disease activity.

The number of studies on PCT in AS patients are limited in the literature. In a study evaluating 46 AS patients, Luo et al. reported that the PCT value was higher than the control group.[29] In patients with axial spondyloarthropathy, a positive correlation was found between PCT levels and ASDAS but not with BASDAI.[30] In our study, PCT values were higher in the patient group. However, there was no difference between the groups according to the BASDAI.

In an examination of the relationship between clinical findings and laboratory parameters of AS patients, Sezgin et al. divided patients into two groups according to BASDAI and MPV and reported no difference between the groups in terms of morning stiffness or the number of swollen and tender joints.[22] Similar to this study, when the patients were divided into two groups according to BASDAI, we observed that there was no difference between them in terms of enthesitis index, quality of life, pain, VAS patient and physician global evaluations, BASMI and BASFI in our study.

The confirmation of increased systemic inflammation in AS patients are important in terms of demonstrating both serious disease activity and possible comorbid conditions. Therefore, it is important to practically determine the degree of inflammation in these patients.[20] The PLR and MPV values, which we found to have diagnostic value in demonstrating disease activity according to the results of ROC analysis, together with ESR and CRP, are useful markers in demonstrating the inflammatory response and disease activity in AS patients.

The superiority and dissimilarity of our study to other studies are that while just the relationship between lymphocyte and platelet parameters with BASDAI and BASFI was evaluated in other studies, the relationship between enthesitis index, quality of life, BASMI, patient and doctor global evaluation with these parameters

was also investigated. The most important limitations of our study were its retrospective design and the use of disease-modifying drugs, which may affect the complete blood count. In addition, we could not confirm whether the patients received any medical treatment that may affect platelet functions during the evaluation period. Prospective controlled and long-term studies will be useful to understand the relationship between AS patients and hematological parameters, and their effects on the disease. In addition, we think it would be beneficial to group patients in terms of the treatments they receive and, if necessary, using imaging techniques for enthesitis.

In conclusion, we determined that the NLR, PLR, and PCT parameters, which can be easily obtained from complete blood count, can be used in the initial evaluation of inflammation in AS patients. In addition, PLR and MPV were found to be effective in demonstrating disease activity. However, parameters other than PLR and MPV exhibited no significant relationship with clinical criteria. Platelets and neutrophils can be used as inexpensive and early diagnostic markers in AS patients to confirm inflammation.

Ethical Considerations: Approval was obtained from University Clinical Researches Ethics Committee (Date: 23/12/2020, Decision No: 370).

Conflict of Interest: The authors declare no conflict of interest.

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PREDICTORS OF EARLY-ONSET OVERT HYPOTHYROIDISM IN HYPERTHYROID PATIENTS TREATED WITH RADIOIODINE

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Abstract

Objectives: Radioiodine (RAI) treatment with iodine-131 is a safe and effective approach that is widely used for treating hyperthyroidism. Although euthyroidism is the optimal outcome of this treatment, some patients will eventually develop hypothyroidism requiring hormone replacement. In this context, we aimed to investigate the predictive factors for early-onset overt hypothyroidism developing within two months after the RAI treatment.

Materials and Methods: All hyperthyroid patients treated with RAI between March 2019 and March 2022 were screened retrospectively. Patients with thyroid function tests within two months after the treatment were included in the final analyses. Baseline clinical characteristics, including pre-treatment imaging modalities and laboratory tests, were retrieved from the institutional database. Predictors of early-onset overt hypothyroidism were determined with a multivariable logistic regression model.

Results: Seventy-two patients (44% female, median age 42 years) were included in the study. Twenty-four patients (33.3%) developed overt hypothyroidism within two months after the treatment. Multivariable logistic regression analysis revealed that the appearance of a diffuse goiter in ultrasound (OR= 4.33, 95% CI= 1.15–16.28, p= 0.030) and the dose of RAI per thyroid volume (OR= 4.30, 95% CI= 1.38–13.45, p= 0.012) were independently associated with the risk of early-onset hypothyroidism after RAI treatment.

Conclusion: The RAI dose per thyroid volume and the appearance of a diffuse goiter in ultrasound were significantly associated with an increased risk of early-onset overt hypothyroidism after RAI treatment. If validated in larger cohorts, these parameters could have a role in predicting the need for early hormone replacement in hyperthyroid patients treated with RAI.

Keywords: Hyperthyroidism, radioiodine, overt hypothyroidism.

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Introduction

Hyperthyroidism is a prevalent thyroid disorder seen in up to 2% of women (tenfold more than men) in iodine-replete communities.[1] The current therapeutic strategies for treating hyperthyroidism include antithyroid drugs (ATDs), radioiodine (RAI) and thyroidectomy. RAI treatment with iodine-131 (I-131) has been increasingly used as a safe and effective approach for treating hyperthyroidism ever since its introduction in 1941.[2-4] I-131 is a radioactive isotope of stable iodine that demonstrates thyroidal uptake with the same uptake mechanism and leads to cellular damage and volume reduction by emitting radioactive beta particles. These physical and biological features of I-131 make it an ideal radionuclide for treating all major causes of hyperthyroidism.[5]

The optimal dose of RAI should be high enough to cure hyperthyroidism and low enough to avoid the risk of RAI-induced hypothyroidism.[6] Empirical fixed-dose approach has been the most practical and the most common method for dose planning. Accordingly, I-131 is administered at a dose of 10-15 mCi in case of Graves' disease,[5] and the dose is increased to 15-30 mCi in cases of toxic nodular or multinodular goiter.[7] To date, empirical high-dose has been the most preferred approach in many centers to cure hyperthyroidism at the expense of developing hypothyroidism and to prevent the necessity of a second RAI treatment.[8,9] Maintaining stability with hormone replacement in case of RAI-induced hypothyroidism is a common and manageable practice. However, it makes the patient perpetually dependent on thyroid hormone replacement.

Regular follow-up after the RAI treatment involves periodical thyroid function tests (TFTs) and thyroid ultrasound (US). The practice guidelines by the Turkish Society of Endocrinology and Metabolism and the Turkish Society of Nuclear Medicine suggest the assessment of thyroid functions at two months following RAI treatment.[10,11] However, outcomes of the treatment can occasionally develop even sooner, and some patients may require early hormone replacement for improved management.

In this context, we sought to evaluate the frequency of overt hypothyroidism onsetting within two months after the RAI treatment and to investigate the predictors of this phenomenon.

Materials and Methods

Patient Selection

Hyperthyroid patients that received RAI treatment in our institution between March 2019 and March 2022 were screened retrospectively. Patients who underwent TFTs within two months (60 days) after the treatment were included in the study. Exclusion criteria were (a) receiving more than one episode of RAI treatment during the study period, (b) absence of TFTs within two months after treatment, and (c) failure to access baseline clinical characteristics. The records of thyroid ultrasonography, scintigraphy and radioiodine uptake (RAIU) test, as well as the levels of thyroid stimulating hormone (TSH), free thyroxine (fT4) and free triiodothyronine (fT3) within the two months after treatment was pulled from the institutional database. Informed consent was obtained from all participants included in the study. The institutional ethics committee approved the study (Approval no: E2-22-2069).

Estimation of Pre-treatment Thyroid Volume

The volume of each lobe of the thyroid gland was estimated according to the previously suggested formula:[12]

[Volume (mL) = Length (cm) × Depth (cm) × Width (cm) × $\pi/6$] by using the dimensions derived from pre-treatment US. The total thyroid volume was found by adding the volumes of both lobes, with the isthmus not being taken into account. The RAI dose per thyroid volume was calculated by dividing the total administered dose by the volume of the thyroid gland.

Administration of Radioiodine

The dose of RAI was determined empirically for each patient and varied between 7 and 25 mCi, with a median (IQR) of 15 (10 – 20) mCi. The most frequently administered dose was 10 mCi (n=31, 43.06%), followed by 15 mCi (n=28, 38.89%). Patients were placed on an iodine-restricted diet starting two weeks before the treatment to ensure adequate RAI uptake. Pharmaceuticals that could potentially affect the accumulation of RAI in the thyroid tissue were discontinued before the treatment (e.g., ATDs, corticosteroids, iodized compounds). Patients were tried to be made euthyroid before the treatment to prevent a possible thyroid storm that may develop due to RAI-induced cell damage. All patients fasted for 4-6 hours before the treatment. RAI was administered orally and patients were released from the hospital after two hours.

Treatment Outcomes

The primary outcome was the onset of overt hypothyroidism according to levels of TSH, fT4 and fT3 within two months after RAI treatment. Overt hypothyroidism was defined as the presence of clear hypothyroidism

characterized by an increase in TSH level along with a decrease in fT3 and fT4 levels. All TFTs were performed using the same immunoassay system throughout the study period. The limit of detection for TSH was 0.008 mU/L. The results below this value were assigned the value of 0.008 for the sake of statistical analyses. The accepted normal ranges for TSH and fT4 were 0.55 – 4.78 mU/L and 0.89 – 1.76 ng/dL, respectively. None of the patients had undergone multiple TFTs within the study period, so the selection of a particular assay was not required.

Statistical Analyses

Continuous variables are expressed as median (interquartile range, IQR), and categorical variables as frequency (percentage). The two samples T-test was used to compare independent means. A multivariable logistic regression model was built using the variables that demonstrated substantial association in the univariable analysis. Statistical analyses were performed using the R statistical package (R Foundation for Statistical Computing, Vienna, Austria) and Stata/MP 16 (Stata Corporation, College Station, Texas, USA) software. A p-value below 0.05 was considered statistically significant.

Results

Patient Characteristics

A total of 72 patients (61% female) were included in the final analyses. The median (IQR) age was 42 (36–55) years. The characteristics of the study population are presented in Table 1. The median (IQR) values of baseline TSH, fT4 and fT3, were 34 (8 – 662) mU/L, 1.14 (0.96 – 1.31) ng/dL and 3.40 (3.02 – 3.93) ng/dL, respectively.

All patients had undergone thyroid US within 12 months before the RAI treatment. The median (IQR) time between the US and the RAI treatment was 90 (56 – 172) days. Baseline thyroid volume ranged between 5.09 and 88.61 mL, with a median (IQR) of 17.31 (12.94 – 22.75) mL. According to baseline US findings, 33 patients (45.83%) had diffuse goiter, while 16 patients (22.22%) had a solitary nodular goiter and 23 patients (31.95%) had a multinodular goiter.

Thyroid scintigraphy was performed in 47 patients (65.28%) within 12 months before RAI treatment. The median (IQR) time between the scintigraphy and the RAI treatment was 56 (24 – 124) days. Accordingly, 25 patients had a diffusely active gland, four had toxic adenoma, and 11 had a multinodular goiter. Twenty-five patients (34.72%) had undergone a radioiodine uptake test (RAIU) within two months before the treatment. The median (IQR) time between RAIU and the treatment was 17 (13 – 25) days. The median (IQR) values of RAIU at 4- and 24-hours were 46% and 67%, respectively.

Table 1. Characteristics of the study population (n=72)*

Sociodemograhics (n=72)	
Age, *years*	42 (36 – 55)
Sex	
Male	28 (38.89)
Female	44 (61.11)
Baseline Thyroid Functions (n=72)	
TSH, *mU/L*	34 (8 – 662)
Free T4, *ng/dL*	1.14 (0.96 – 1.31)
Free T3, *ng/dL*	3.40 (3.02 – 3.93)
Baseline Ultrasound (n=72)	
Thyroid Volume, *mL*	17.31 (12.95 – 22.76)
Diffuse Goiter	33 (45.83)
Solitary Nodular Goiter	16 (22.22)
Multinodular Goiter	23 (31.94)
Number of Nodules	1 (0 – 2)
Baseline Scintigraphy (n=47)	
Normal	7 (14.89)
Diffuse Active	25 (53.19)
Toxic Adenoma	4 (8.51)
Multinodular Goiter	11 (23.40)
Baseline Radioiodine Uptake Test (n=25)	
Uptake at 4 hours, *%*	46 (43 – 60)
Uptake at 24 hours, *%*	67 (59 – 86)

*Continuous variables are presented as median (interquartile range) and categorical variables are presented as frequency (percentage).

Treatment Outcomes

An overview of dosimetric parameters and treatment outcomes is presented in Table 2. The median (IQR) levels of TSH, fT4 and fT3 within two months after the RAI treatment were 28.71 (4.64 – 438.51) mU/L, 1.05 (0.69 – 1.36) ng/dL and 2.67 (2.07 – 3.68) ng/dL, respectively. The early outcome of RAI treatment was specified as overt hypothyroidism in 24 patients (33.33%), subclinical hypothyroidism in 28 patients (38.89%), euthyroidism in 4 patients (5.56%), subclinical hyperthyroidism in 3 patients (4.17%) and overt hyperthyroidism in 6 patients (8.33%). Seven patients could not be classified as any of these clinical conditions, as 5 of them had a low fT4 and normal TSH, while two had elevated values for both fT4 and TSH.

Table 2. Dosimetric parameters and early treatment outcomes*

Dosimetric Parameters (n=72)	
RAI Dose, *mCi*	15 (7 – 25)
RAI Dose per Volume, *mCi/mL*	0.77 (0.52 – 1.08)
Post-treatment Thyroid Functions (n=72)	
TSH, *mIU/L*	28.71 (4.63 – 438.51)
Free T4, *ng/dL*	1.05 (0.69 – 1.35)
Free T3, *ng/dL*	2.67 (2.07 – 3.68)
Early Treatment Outcomes (n=72)	
Overt Hypothyroidism	24 (33.33)
Subclinical Hypothyroidism	28 (38.89)
Euthyroidism	4 (5.56)
Subclinical Hyperthyroidism	3 (4.17)
Overt Hyperthyroidism	6 (8.33)
Other	7 (9.72)

*Continuous variables are presented as median (interquartile range) and categorical variables are presented as frequency (percentage).

Predictors of Early-Onset Overt Hypothyroidism

Table 3 shows the comparison of parameters between the patients that did and did not develop overt hypothyroidism within two months after the RAI treatment. The mean RAI dose per thyroid volume was significantly higher in patients with early-onset overt hypothyroidism (1.11 vs. 0.79 mCi, p=0.023). Other parameters, including the total RAI dose or the thyroid volume alone, were not significantly different across the two groups.

A multivariable logistic regression model was built using the parameters that could hypothetically have an impact on the treatment outcomes (Table 4). The scintigraphic uptake pattern and RAIU test were excluded from the model due to a large amount of missing data. Accordingly, the RAI dose per thyroid volume (OR= 4.345, 95% CI= 1.382 – 13.664, p= 0.012) and the appearance of a diffuse goiter in the baseline US (OR= 3.680, 95% CI= 1.003 – 13.505, p= 0.030) were independently associated with increased risk of early-onset overt hypothyroidism after the RAI treatment.

Table 3. Comparison of patients that did and did not develop overt hypothyroidism within the study period.*

	Early-Onset Overt Hypothyroidism		p-value
	Yes (n=24)	No (n=48)	
Age, *years*	44 (37.5 – 54)	42 (35 – 58)	0.620
Male	8 (33)	20 (42)	0.490
RAI Dose, *mCi*	15 (10 – 15)	15 (10 – 15)	0.460
Thyroid Volume, *mL*	21.11 (21.17)	20.45 (10.62)	0.860
RAI Dose per Volume, *mCi/mL*	1.11 (0.78)	0.79 (0.41)	0.023*
Diffuse Goiter in Ultrasound	14 (58)	19 (40)	0.130
Uptake at 4 hours, *%*	54.11 (17.06)	48.01 (18.88)	0.450
Uptake at 24 hours, *%*	73.17 (16.76)	70.00 (18.52)	0.680

* Continuous variables are presented as median (min-max) and categorical variables are presented as frequency (percentage).

Table 4. Multivariable logistic regression model for identifying the predictors of early-onset overt hypothyroidism after the RAI treatment

Parameter	Odds Ratio	95% Confidence Interval	p-value
Age	1.011	0.963 – 1.060	0.664
Sex	1.039	0.270 – 3.993	0.755
RAI Dose per Volume, *mCi/mL*	4.345	1.382 – 13.664	0.012*
The appearance of Diffuse Goiter in US	3.680	1.003 – 13.505	0.049*
Diffuse Active Gland in Scintigraphy	2.179	0.608 – 7.811	0.232
Baseline fT4, *ng/dL*	0.107	0.010 – 1.103	0.060

Discussion

In this study, we investigated the predictive factors for overt hypothyroidism developing within two months after the RAI treatment and found that the RAI dose per thyroid volume and the appearance of a diffuse goiter in US were independently associated with this phenomenon. Other characteristics, including age, sex and baseline TFTs, did not demonstrate significant association with the study outcome.

RAI treatment is a long-known, safe and effective approach that is widely used for treating hyperthyroidism through radiation-induced volume reduction.[5] Although higher doses of RAI will necessarily improve treatment success by leading to better volume reduction. An increased dose is also associated with the risk of RAI-induced hypothyroidism.[13] According to our results, the RAI dose alone or the baseline thyroid volume

alone were not associated with the development of early overt hypothyroidism. Instead, an alternative measure, the RAI dose per unit volume of the thyroid gland, was significantly associated with an increased risk of early-onset overt hypothyroidism. This parameter was derived by dividing the total RAI dose by the volume of the thyroid gland in an attempt to have a better insight into the radiation burden of the thyroid gland. There have been previous studies reporting the separate roles of higher RAI dose and smaller thyroid volume in the development of post-treatment hypothyroidism.[14] To the best of our knowledge, this is the first study incorporating the relative RAI dose with respect to thyroid volume as a parameter for predicting post-treatment hypothyroidism.

The appearance of a diffuse goiter in the pre-treatment US was yet another predictive parameter for the early development of overt hypothyroidism after the RAI treatment. Diffuse goiter is defined as the uniform enlargement of the thyroid gland and differs from multinodular goiter by the absence of nodules. In the literature, data revealing the effect of diffuse goiter and nodularity on the outcome of hypothyroidism are not sufficient. Generally, the relationship between nodule volume and treatment success or the effect of RAI treatment on nodule volume has been investigated. Schiavo et al. reported that nodule volume was inversely correlated with the treatment efficacy.[15]

According to our results, the baseline levels of TSH and fT4 were not associated with the risk of early-onset overt hypothyroidism after the RAI treatment. These findings are in line with previous studies investigating the association between baseline TFTs and treatment outcomes.[16-18] There are several other factors that could potentially have an impact on the outcome of the RAI treatment, e.g., use of ATDs, corticosteroids, age of onset, adherence to low-iodine diet or smoking habits. These covariates will usually be influenced by the clinical condition and the age of the patient. Nevertheless, further studies are needed to investigate their independent impact on early treatment outcomes.

Almost one-fourth of the patients in our cohort (n=20, 27.7%) did not develop overt or subclinical hypothyroidism within the study period. However, it has been previously shown that the transition to hypothyroidism may continue in the following months. Ahmad et al. shared that the overall cumulative incidence of hypothyroidism following the RAI treatment was 38.2% after six months and increased to 55%, 66%, 69% and 86% after 1, 3, 5 and 10 years, respectively.[19] A gradual increase in the incidence of post-RAI hypothyroidism was reported in several other studies.[13,20,21] Further studies may focus on developing clinical nomograms to predict the time of onset for the treatment outcomes.

Our results should be interpreted in the context of some limitations. Firstly, the relatively small size of the study population may fail to represent the true nature of the general population. These results should be validated with larger multi-centric cohorts. Secondly, we were unable to include scintigraphic findings and RAIU values

in the prediction model due to a substantial amount of missing data. Lastly, this was a retrospective, observational study that could be prone to recall bias.

In conclusion, our results indicate that the RAI dose per thyroid volume and the appearance of a diffuse goiter in baseline US were significantly associated with an increased risk of developing overt hypothyroidism within two months after the RAI treatment. If validated in larger cohorts, these parameters could have a role in predicting the need for early hormone replacement in hyperthyroid patients treated with RAI.

Ethical Considerations: Informed consent was obtained from all individual participants included in the study. The institutional ethics committee approved the study (Approval no: E2-22-2069).

Conflict of Interest: The authors declare no conflict of interest.

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Case Report

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ONE OF THE CAUSES OF RECURRENT URINARY TRACT INFECTION: BIFID COLLECTING SYSTEM- A CASE REPORT

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Abstract

Although genitourinary system anomalies are frequently diagnosed in childhood, they are also clinically important in the adult population. Patients with these anomalies are at risk for recurrent urinary tract infections and also obstructions. Urinary system anomalies should be considered in the patients who come with recurrent urinary tract infection complaints to the family medicine outpatient clinic. In this article, a case with recurrent urinary tract infections, which were later diagnosed with a double collecting system, is presented.

Keywords: Ureter, urogenital abnormalities, cystitis.

Introduction

Bifid collecting systems are one of the most common anomalies of the urinary system. [1] The incidence of duplication of the renal collecting system and ureter ranges from 0.5% to 3%.[1,2] Detection rate of such renal anomalies in childhood has increased thanks to advanced fetal imaging facilities markedly; however, a significant number of undiagnosed adults still exist.[1] Although duplication of the ureter may remain asymptomatic in adults, it can cause recurrent urinary tract infections (UTIs) or stones and also can result in injury during pelvic surgeries. [1,3] In this article, we present an adult female patient with recurrent UTIs who was diagnosed with a bifid collecting system after imaging, and she was referred to the urology department

Case Report

A 31-year-old female patient with no known history of internal disease visited our family medicine outpatient clinic with a complaint of a change in urine odor for a week. The patient stated that she did not measure her temperature but also sweating enough to change underwear at night. It was learned from the patient's history that she got married two months ago and visited an outpatient clinic with the complaint of a burning sensation while urinating one month ago. Urinary tract infection was detected, and she received fosfomycin and ciprofloxacin treatment. In her medical history, there was no history of urology visits or recurrent UTIs in childhood. On physical examination, vital signs were normal (fever: 36.6 °C, blood pressure: 125/82 mmHg, pulse:76 bpm, spo2: 96%). Abdominal examination revealed no tenderness, defense, or organomegaly. She had no costovertebral angle tenderness. Other system examinations were normal. No pathological finding was detected. Urinalysis revealed pyuria and bacteriuria (Full urine analysis pH: 5.0 Density: 1.014 Leukocyte: 60 HPF Nitrite: ++). The patient was treated with a single dose of fosfomycin 3 g/day. In the control examination, the patient stated that there was no regression in her complaint. Thus, urine culture, whole blood, sedimentation and C-Reactive Protein (CRP) were requested from the patient. No leukocytosis, sedimentation and CRP increase was observed in blood tests.(leukocyte: 5.0 x10^3/µL(4.1-11.2 x10^3/µL) , lymphocyte count: 1.8x10^3/µL(1.2) -3.6x10^3/µL), neutrophil count: 2.5 x10^3/µL(1.8-6.4 x10^3/µL), lymphocyte%:35.3% (18.8-50, 8%), neutrophil %: 50.4% (39.9-73%), CRP: 0.531 mg/dL, (0-0.8 mg/dL) sedimentation (ESR) : 10 mm /hour (0-25 mm/hour). 100,000 cfu/mL Escherichia coli isolated in urine aerobic culture.

Nitrofurantoin 200 mg/day was given to the patient according to the antibiogram analysis. In addition, due to the presence of recurrent urinary tract infections in the last three months, urinary system ultrasound imaging was planned to investigate the etiology and for renal system control.

Ultrasound examination revealed a right extrarenal pelvis and duplicated left renal collecting system. The patient was consulted by the urology department based on the current ultrasound finding. Computed tomography (CT) urography was requested by the urologist in terms of other accompanying urinary system complications. CT urography showed that both kidneys were normal in terms of size, localization, parenchymal thickness and filtration functions; hydroureteronephrosis, urolithiasis, solid or cystic mass and no ureteral filling defect were reported (Figure 1). It was learned that annual urology control in the outpatient clinic was recommended to the patient.

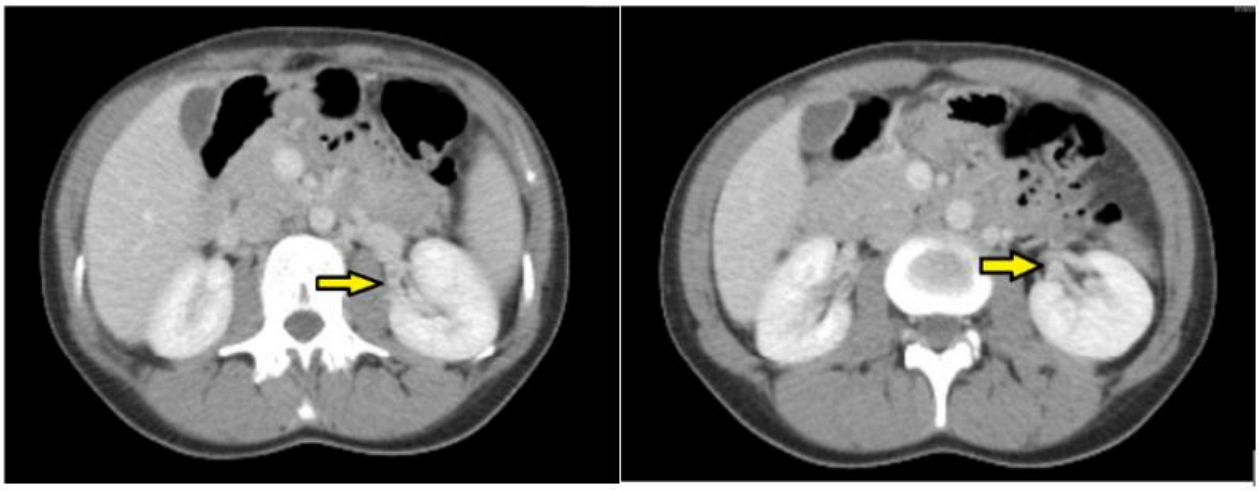

Figure 1. A bifid collecting system emerging from the left kidney is seen in CT urography transverse sections.

Discussion

A recurrent UTI is typically defined as three or more UTIs in the last 12 months or two or more infections in the last six months.[4] Sexual intercourse three or more times a week, use of spermicide, new or multiple sexual partners, and having a UTI before the age of 15 have been shown to be independent risk factors for recurrent UTI in premenopausal women.[4] In addition to these factors, it is also important to confirm whether there is an anomaly of the genitourinary system as a facilitating factor.[4]

The ureters form as a bud from the mesonephric duct during the 4th to 5th weeks of pregnancy. Ureteral duplication occurs when suppression of ectopic ureteral bud development fails during metanephros development.[1] The most common congenital anomaly of the genitourinary system is the bifid collecting system and is slightly more common in women, with an approximate ratio of 1.6:1.[5] The incidence of unilateral

duplications is six times higher than bilateral duplications [3] Unilateral duplications are seen equally on the right and left sides. [5]

While the detection of such kidney anomalies in childhood is gradually increasing due to the developments in fetal imaging methods, unlike the literature, it was detected in our case at the age of 31. Although frequent sexual intercourse is a risk factor for urinary system infections in women, the recurrence of infection after treatment in our case suggested that we should also question other underlying factors. Duplex systems may predispose to complications such as obstructive uropathy, stone formation, ureterocele and vesicoureteral reflux.[1] Early detection of this anomaly helps to prevent comorbidities and complications. In all cases, imaging is essential to confirm the diagnosis. Urinary system ultrasound should be performed as an initial diagnostic test. CT urography is important in visualizing the course of the duplex collecting system, visualizing the distal opening, and detecting ectopic kidney, infection, or other associated genitourinary malformations.

Conclusion

Undiagnosed genitourinary system anomalies should also be considered in the approach to adult patients presenting with recurrent urinary system complaints in primary care, and necessary tests should be requested.

Ethical Considerations: Informed consent has been obtained from the patient.

Conflict of Interest: The authors declare no conflict of interest.

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