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From the Editor

Dear readers,

In the first issue of 2022, we proudly announce that our journal is officially indexed in Scopus, in addition to the other respected indexes. Secondly, beginning from this issue, the only accepted manuscript language will be English in Ankara Med J.

In this issue, we have prepared 14 original research articles and a case report for you.

Unsurprisingly, your interest is our most significant source of motivation to carry our quality to a higher level.

Please stay tuned for the next issue.

Assoc. Prof. Dr. Ahmet Keskin

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ASSESSMENT OF PREGNANCY FOLLOW-UPS FOR CASES REGISTERED IN A FAMILY HEALTH CENTER

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Abstract

Objectives: Our research aimed to evaluate the antenatal care (ANC) and pregnancy outcomes for pregnant cases registered with a family practice unit providing primary health services.

Materials and Methods: Data for 385 pregnant cases aged 18 to 40 years registered with a family health center from 15/07/2010 to 01/02/2019 were screened from the "Family Practice Information Management System" database. Data regarding antenatal visits were statistically investigated and the p-value below 0.05 was accepted as significant.

Results: The mean age was 28.66±5.36 years. The mean pregnancy week of first attendance was 9.59±5.52. Of pregnant cases, 89.61% received iron, 47.79% vitamin D and 63.63% folic acid supplements. Of the patients, 81.81% had the first trimester, and 76.88% had second-trimester screening tests. 71.42% of patients had gestational diabetes screening, and 88.83% had detailed ultrasonography. 78.44% of patients had tetanus-diphtheria vaccination, while no pregnant case had influenza vaccination. The age and gravida did not affect receiving ANC, vitamin D, iron supplementation and tetanus-diphtheria vaccination status. Vitamin D use was higher in groups receiving education compared to those not receiving education. When the educated group was assessed among themselves, the use of supplements reduced as the educational level increased.

Conclusion: There is a need to increase referrals for iron, vitamin D, and folic acid supplementation and for screening during antenatal follow-up. The tetanus-diphtheria vaccination rate was observed to be lower than ideal. Additionally, it appears administration of seasonal flu vaccines is deficient, and necessary steps should be taken to reduce concerns related to vaccination.

Keywords: Antenatal care, family physician, pregnancy.

Introduction

Maternal and infant health is among the most important indicators of social welfare levels. Pregnancy and labor are the periods with the most frequent morbidity and mortality for women worldwide. In Turkey, antenatal care (ANC) services are provided by family clinicians and family health workers in "Family Health Centers". The 'safe motherhood' movement, begun by the World Health Organization (WHO) in 1987, created management guides for antenatal care. The aim of antenatal care is to provide health care services to women during pregnancy and labor, to identify risk groups and additionally organize care plans for these groups. In Turkey, the 'Antenatal Care Management Guide' was created by the Ministry of Health and is updated at regular intervals.[1] Antenatal care is one of the best outputs indicating the development of health care services and ensures reductions in maternal and fetal mortality. Globally, nearly 810 women die due to pregnancy and related reasons every day. Of all maternal deaths, 94% occur in low- and moderate-income countries.[2] The definition of maternal mortality encompasses deaths occurring from the start of pregnancy until the 42nd day after birth. Among women with live births, the rate of those dying within one year after birth is given per 100,000 live births. For the world in general, 2015 data show mean maternal deaths were 216/100,000. Within the same year, the deaths of more than 300,000 women were included in the definition of maternal mortality. In Turkey, this number was reported as 13.6 for 2018.[3] Care plans in the Ministry of Health ANC Management Guide are implemented by family clinicians and their teams. Within the framework of this plan, the number of pregnancy check-ups and elements that require attention during these check-ups are defined in detail in the guide. The guide reports four check-ups are required within the first 14 weeks of pregnancy and in weeks 18-24, 26-32 and 36-38, and defines the anamnesis, examinations, laboratory tests, measurements and counseling services that should be provided in detail. According to WHO data, 75% of pregnant cases receive sufficient ANC in the world, while this rate is 88.9% for our country.[2] The vaccination, pregnancy, infant and child check-ups that family clinicians are responsible for are considered within the scope of the performance assessment for family health centers, and disciplinary measures to be applied if these responsibilities are not fulfilled are stated in the legislation.

The aim of the research was to assess the antenatal care services and pregnancy outcomes since the beginning of the family clinician system in a family health center based on retrospective data.

Materials and Methods

The population for the study comprised pregnant cases registered with Ankara Keçiören Şevkat-1 Family Health Center Family Clinician unit number 0617052 from 15/07/2010 to 01/02/2019. The sample comprised 385 pregnant cases aged from 18-40 years registered with family clinician unit number 0617052 in the family health center who were pregnant between these dates. The study was designed to be retrospective, and data

for women included in the study were screened from the Neuroogle Family Practice Information Management System (NAHBS) database. Women pregnant between these dates who did not attend check-ups were interviewed, and also data for women were evaluated by accessing the 'e- nabız' information system.

The NAHBS database, Republic of Turkey Ministry of Health' e- nabız' database and interviews were women were used to record the date of first attendance, the number of check-ups, demographic data (educational status, age, age of marriage, consanguinity, date of pregnancy, smoking, height, maternal weight during first pregnancy check-up and fourth check-up, gravida, parity, abortus/stillbirth history, blood group), systemic disease history (thyroid function disorder, diabetes, hypertension, asthma, epilepsy and others), the status of receiving antenatal care and the number of check-ups, check-up parameters (iron, vitamin D and folic acid supplementation, first trimester (double marker screening test) and second trimester (triple test) screening results, secondary stage obstetric ultrasonography (USG) results, oral glucose screening test, tetanus inoculation) and birth outcomes (type of birth, week of birth, place of birth, live/stillbirth, birth weight). Statistical analyses were performed.

All analyses in the research were completed with the SPSS 25.0 program. Continuous numerical variables are given as mean ± standard deviation, median (minimum-maximum) values, while categoric variables are given as number (percentage) style. The normal distribution of numerical data was checked with the Shapiro-Wilk test. When the assumption of normal distribution was met, comparisons of continuous numerical data between two groups used the independent samples t-test and ANOVA test, while the Mann Whitney U test and Kruskal Wallis test were used if the assumption of normal distribution was not met. For comparisons between groups, the Bonferroni correction was used. Comparison of distributions between groups of categoric variables used the Pearson chi-square and Fisher's exact test. Comparison of continuous variables used the Pearson or Spearman correlation coefficient according to the status of fit to normal distribution. For statistical significance, p values below 0.05 were accepted as the limit.

Results

The mean age of the 385 women included in the study was 28.66±5.36 years, with the mean age of marriage 22.72±4.52 years. Of women in our research, 115 were primary-middle school graduates (29.87%), 114 were high school graduates (29.61%), 86 were university and master-degree graduates (22.33%), three had not received education (0.77%), and information about educational status could not be reached for 67 women (17.40%). While 77 women smoked (20%), 286 women did not smoke (74.28%), and information about smoking status could not be reached for 22 women (5.71%). For 344 women, information about consanguinity could be reached, and 48 women were married to relatives (12.46%). The mean height of women in our research group was 162.70 ± 5.52 (147-176) cm. Weight at the start of pregnancy was 65.11±11.43 kg (39-

127), and weight at the end of pregnancy was 76.28±11.41 kg (47-130), with a mean weight increase during pregnancy of 11 kg. The mean body mass index (BMI) was 24.63 kg/m^2 at the start of pregnancy and 28.81 kg/m^2 at the end of pregnancy. High BMI at the start of pregnancy was associated with gestational diabetes (p=0.021), while BMI of 19 and above were associated with an increase in neonate birth weight (p=0.46).

The mean week of pregnancy, when patients attended the first check-up, was 9.59±5.52, and the mean number of antenatal check-ups was 3.28±1.38. There was positive significance between ANC and gravida (p=0.021), with the highest ANC rates observed in the group with 2-3 pregnancies. Age and educational status did not affect receiving ANC. Mean ANC check-up numbers were lower for women during their first pregnancy (3±161) compared to women in their second or third pregnancies (3.53±1.24) (p=0.031). The pregnancy check-up numbers for women with four or more pregnancies were not different compared to the other groups.

Of women participating in the study, 89.61% received oral iron, 47.79% vitamin D and 63.63% folic acid supplements. Among patients, 81.81% had performed first-trimester screening tests, and 76.88% had performed second-trimester screening tests. While 71.42% of patients had gestational diabetes screening performed, 88.83% had 2nd stage USG performed. During check-ups, 78.44% of patients had tetanus-diphtheria (Td) vaccination; however, no participant had influenza vaccination. Analysis of parameters investigated during pregnancy check-ups is presented in Table 1. The iron supplementation of pregnant cases was not affected by age, educational status and number of pregnancies, with no statistically significant correlations between iron supplementation with age (p=0.546), educational level (p=0.192) and the number of pregnancies (p=0.762). There were no statistically significant correlations between vitamin D use with gravida and age, but there was a correlation with educational status (p=0.009) (Table 2). The group not receiving education had lower vitamin D use, while in-group analysis of the educated group observed that the group with the least vitamin D supplementation had an educational level of doctorate or above (Table 2). There were no statistically significant correlations identified between Td inoculation status with age (p=0.521), educational status (p=0.817) and gravida (p=0.888) (Table 2).

The mean week of birth for patients included in the study was 37.31±5.54, with a mean neonate weight of 3177.13±572.60 g. Of patients, 49.09% had a cesarean birth, and 70.90% of patients gave birth in a medical faculty or educational hospital, 13.50% in a private hospital and 12.50% in a state hospital. Among patients, information about birth centers could not be reached for 12 cases (3.11%).

Table 1. Analysis of participation in pregnancy check-ups

	Yes n (%)	No n (%)	No information n (%)
Oral iron supplement	345 (89.61)	40 (10.39)	
Vitamin D supplement	184 (47.79)	201 (52.20)	
Folic Acid supplement	245 (63.63)	140 (36.36)	
First trimester screening test	315 (81.81)	67 (17.40)	3 (0.77)
Second trimester screening test	296 (76.88)	85 (22.07)	4 (1.03)
Gestational diabetes screening	275 (71.42)	107 (27.79)	3 (0.77)
Secondary stage ultrasonography	342 (88.83)	40 (10.38)	3 (0.77)
Td (Tetanus-Diphtheria) Vaccination	302 (78.44)	83 (21.55)	

Table 2. Distribution of antenatal care, iron supplementation, vitamin D supplementation and Tetanus-diphtheria (Td) vaccination according to age, gravida and educational status

	Received antenatal care			**Iron supplement**			**Vitamin D supplement**			**Tetanus-diphtheria vaccination**		
	Yes	**No**		**Yes**	**No**		**Yes**	**No**		**Yes**	**No**	
	n (%)	**n (%)**	**p**	**n (%)**	**n (%)**	**p**	**n (%)**	**n (%)**	**p**	**n (%)**	**n (%)**	**p**
Age												
<30	223 (65.58)	30 (66.66)	0.886	225 (65.21)	28 (70.00)	0.546	117 (63.58)	136 (67.66)	0.331	196 (64.90)	57 (68.67)	0.521
≥30	117 (34.42)	15 (33.34)		120 (34.79)	12 (30.00)		67 (36.42)	65 (32.34)		106 (35.10)	26 (31.33)	
Educational status												
None	3 (1.06)	0	0.438	3 (1.06)	0	0.192	3 (1.85)	0	**0.009**	3 (1.19)	0	0.814
Primary-middle school	99 (35.23)	16(43.24)		102 (36.04)	13 (37.14)		54 (33.33)	61 (39.10)		88 (34.92)	27 (40.90)	
High school	105 (37.36)	9 (24.32)		97 (34.27)	17 (48.50)		49 (30.24)	65 (41.66)		92 (36.50)	22 (33.33)	
Associate-undergraduate degree	70 (24.91)	12 (32.43)		78 (27.56)	4 (11.42)		53 (32.71)	29 (18.58)		66 (26.19)	16 (24.24)	
Doctorate and above	4 (1.42)	0		3 (1.06)	1 (2.85)		3 (1.85)	1 (0.64)		3 (1.19)	1 (1.51)	
Gravida												
1	99 (29.11)	23 (51.11)	**0.021**	109 (31.59)	13 (32.50)	0.762	64 (34.78)	58 (28.85)	0.330	96 (31.78)	26 (31.32)	0.888
2-3	194 (57.05)	15 (33.33)		189 (54.78)	20 (50.00)		98 (53.26)	111 (55.22)		165 (54.63)	44 (53.01)	
≥4	47 (13.82)	7 (15.55)		47 (13.62)	7 (17.50)		22 (11.95)	32 (15.92)		41 (13.57)	13 (15.66)	

Positive and weak correlations were identified between maternal weight at the beginning of pregnancy (p=0.001, r=0.198) and at the end of pregnancy (p=0.001, r=0.246) with neonate birth weight. Maternal age, pregnancy and birth numbers did not affect neonate birth weight; however, smoking caused an increase in low birth weight (LBW) among neonates (p=0.036). The number of pregnancies did not differ according to the educational status of women; however, most women with four or more pregnancies were women with primary-middle school education, and most women in the uneducated group had four or more pregnancies. In our research, 84.15% of pregnant cases (324) received breastfeeding training.

There were no statistically significant correlations identified between the first-trimester screening test, second-trimester screening test, secondary stage ultrasonography screening and gestational diabetes screening with educational level, age and gravida number. Details are shown in Table 3.

Table 3. Distribution of first trimester (double marker), second trimester (triple test), gestational diabetes screening and detailed ultrasonography according to age, gravida and educational status

	First-trimester screening test			Second-trimester screening test			Gestational diabetes screening			Secondary stage ultrasonography		
	Yes	No		Yes	No		Yes	No		Yes	No	
	n (%)	n (%)	p	n (%)	n (%)	p	n (%)	n (%)	p	n (%)	n (%)	p
Age												
<30	208 (66.03)	43 (64.17)	0.772	199 (67.22)	52 (61.17)	0.299	178 (64.72)	73 (68.22)	0.518	222 (64.91)	57 (68.67)	0.339
≥30	107 (33.96)	24 (35.83)		97 (32.78)	33 (38.83)		97 (35.28)	34 (31.78)		120 (35.08)	26 (31.32)	
Educational status												
None	3 (1.13)	0	0.128	3 (1.21)	0	0.817	3 (1.31)	0	0.747	3 (1.05)	0	0.326
Primary-middle school	85 (32.07)	29 (50.87)		87 (35.36)	27 (38.57)		80 (34.93)	34 (34.63)		97 (34.15)	17 (51.51)	
High school	98 (36.98)	16 (28.07)		89 (36.17)	25 (35.71)		81 (35.37)	33 (33.67)		101 (35.56)	13 (39.39)	
Associate - undergraduate degree	77 (29.05)	10 (17.54)		65 (26.42)	16 (22.85)		63 (27.51)	19 (19.38)		79 (27.81)	3 (9.09)	
Doctorate and above	2 (0.75)	2(3.50)		2 (0.81)	2 (2.85)		2 (0.87)	2 (2.04)		4 (1.40)	0	
Gravida												
1	104 (33.01)	17 (25.37)	0.380	98 (33.10)	22 (25.88)	0.347	93 (33.81)	28 (26.16)	0.344	113 (33.04)	8 (20.00)	0.915
2-3	169 (53.65)	38 (56.71)		159 (53.71)	48 (56.47)		145 (52.72)	62 (57.94)		184 (53.80)	23 (57.50)	
≥4	42 (13.33)	12 (17.91)		39 (13.17)	15 (17.64)		37 (13.45)	17 (15.88)		45 (13.15)	9 (22.50)	

There was a statistically significant correlation identified between the birth center and educational status (p=0.001). All three uneducated pregnant cases, 72.17% of 115 primary-middle school graduates (83 cases),

74.50% of high school graduates (85 cases), 52.43% of undergraduates (27 cases) and 50% of cases with a doctorate or above (4 cases) gave birth in education-research hospitals or faculty hospitals. The group with undergraduate and higher education were observed to have higher rates for births in private hospitals compared to other groups (p=0.001).

Discussion

In this study, the pregnancy check-ups performed in a family health center after initiating the family clinician system with changes to Turkey's health system were retrospectively assessed. Of the 385 women included in the study, the mean age was 28.66±5.36 years, the mean pregnancy week of first attendance was 9.59±5.52, and the mean number of check-ups before birth was 3.28±1.38. Of the patients participating in the study, 89.61% used oral iron, 47.79% used vitamin D and 63.63% used folic acid supplementation. In terms of scans, 81.81% of patients had the first-trimester screening, and 76.88% had the second-trimester screening performed. While 71.42% of patients had gestational diabetes screening performed, 88.83% had 2nd stage USG performed. Tetanus-diphtheria vaccination was given to 78.44% of patients during follow-up. Age and gravida did not affect attending ANC, vitamin D, iron supplementation and Td vaccination status. Educational status did not affect any variable, apart from vitamin D supplementation. The educated group had higher vitamin D use than the uneducated group, but when the educated group was assessed within-group, the use of supplements reduced as the educational level increased.

National and international guidelines recommend that the first check-up during pregnancy should occur within the first 10-14 weeks of pregnancy.[1] This was the case in our center, with the mean number of ANC check-ups lower for women during their first pregnancy than women in their second and third pregnancies. In countries with high development levels, 98% of pregnant cases attend ANC at least once, while this rate is 65% for less developed countries (73,74). According to Turkish Demographic and Health Survey (TNSA) data, in 1993, the ANC rate was 62%, with 54% attending ANC in the first three months and 36% attending ANC check-ups four or more times. According to 2018 data, the ANC rate was 96%, with 90% attending in the first three months and attending four or more ANC check-ups.[4,5] According to United Nations International Children's Emergency Fund (UNICEF) data, globally, 86% of pregnant women from 15-49 years of age receive care from health personnel at least once before birth, while only 61% receive care at least four times. The rate of women aged 15-49 years attending at least four antenatal care appointments during pregnancy was 50% from 2006-2012, while this rate was stated to be 65% between 2013-2018.[6,7] As family medicine practice targets tight control and organization of pregnancy check-ups at 100% rates, pregnant cases are automatically registered with the family clinician system when they receive a pregnancy diagnosis from any health organization and pregnancy check-ups begin. In our unit, nearly all registered and pregnant women (97-100%) had pregnancy identified and all of our monitored pregnant cases were given ANC services. In our research, the mean value of the first

check-up week of pregnancy was 9.6, which abides by the Ministry of Health ANC management guide; however, the mean number of check-ups was 3.3, and efforts should be made to ensure each pregnant case attends at least four check-ups.

According to the Ministry of Health Antenatal Care Management Guide, under normal conditions, supplementation of 40-60 mg/day iron from the 16th week, 1200 IU/day vitamin D from the 12th week and 400-800 µg/day folic acid beginning one month before pregnancy and continuing to the 12th week should be given.[1] According to WHO 2019 data, the frequency of anemia is 36.5% in pregnancy.[8] Regions with the highest anemia rates in pregnant women are India (50.1%) and countries in central Africa (45-59%).[8] Mean hemoglobin level during the first check-up for pregnant cases participating in our study was 12.52 g/dL, and mean hemoglobin level at final check-up was 11.73 g/dL. In our research group, the number of pregnant cases who were anemic (hemoglobin <11 g/dL according to WHO criteria) was 65 at the start of pregnancy (16.8%) and 158 at the end of pregnancy (41.03%). A study assessing ANC services in Turkey in 2015 found that 229 (88.0%) of the pregnant women participating in the research (total 260) were using oral iron supplements, while 231 (88.8%) were using multivitamin preparations.[9] Iron supplementation rates vary in national studies,[10,11,] while the TNSA 2018 study reported 81% of women in the 15-49-year age group used iron supplementation during their last pregnancy.[4] In our research, the rate of pregnant cases using iron supplements was 89.61%. The iron supplementation rates among our pregnant cases are similar to the national figures but appear inadequate. This inadequacy is thought to be related to treatment compliance.

In this study, the vitamin D supplementation rate was 47.79%. Though the same guidelines are followed, this rate displays regional differences in society.[11,12] These differences may be the result of sociocultural differences reflecting societal trends. In the uneducated group, vitamin D use was low. However, when the educated group was assessed, the lowest vitamin D supplementation rate was observed in the group with doctoral education or above. As education increases, compliance with family medicine check-ups and treatments reduce. Apart from family clinicians performing pregnancy check-ups, doctors do not reflect the insistence on iron and folic acid supplementation for vitamin D use. For folic acid use, social differences are reported; different studies found folic acid use rates vary from 48-79%. In our research group, 63.63% of pregnant cases used folic acid supplements during the first trimester. When assessed based on guideline recommendations, the iron, vitamin D, and folic acid supplementation rates for pregnant cases included in the study did not appear to be at the targeted levels.

In our research, 81.81% of women had a first-trimester screening, 76.88% had a triple screening, 71.42% had gestational diabetes screening (oral glucose tolerance test, OGTT), and 88.83% had detailed USG during pregnancy. The rates for screening tests in our study are similar to the averages for the country. A study comparing before and after the changes in the health service in 2014 found that the rates for double, triple and

quadruple tests were 45% before the transformation in health and 77% after the transformation.[14] OGTT rates were 33% before the transformation in health and 88% after the transformation.[14] OGTT rates are lower than other screening tests, and this is reported to be affected by unchecked speculative explanations not based on science made by unqualified individuals about the topic in the national written and visual media.[15] Additionally, when the reasons for not doing the OGTT test are examined among pregnant cases, 56.3% thought the test was not necessary, 21.5% thought the test was harmful to themselves or the fetus and 17.4% stated they did not do the test as their doctor did not recommend it.[16] In our study, nearly 90% of cases had a detailed ultrasound performed, showing that pregnant cases were sufficiently informed and directed toward screening for radiological anomalies and the high implementation rates. Additionally, in our study, there were no statistically significant correlations identified between first-trimester screening, second-trimester screening, GDM screening and detailed USG with educational status, age and gravida. This situation shows that pregnancy screening is implemented in ANC services independent of education, age and gravida.

According to the Ministry of Health ANC Management Guide, Td vaccination should be administered from the 12th week (16th week according to vaccination calendar) and other doses performed according to the vaccination calendar. According to the TNSA 2018 study, 81% of mothers with last live birth within the previous five years had Td vaccinations within the scope of ANC.[4] On 24 April 2009, the WHO declared that maternal and neonatal tetanus was eliminated in Turkey.[17,18] In our research, 78.4% of pregnant cases had Td vaccination, which is close to the average for the country; however, higher rates should be targeted. In our research, there were no statistically significant correlations identified between Td vaccination status with age (p=0.521), educational status (p=0.817) and gravida (p=0.888). A study researching factors affecting vaccination in 2005 observed that as the educational status increased, the vaccination rate increased; however, a study with a similar population in 2015 found that as educational status increased, vaccination rates fell.[19,20] It appears that anti-vaccination has begun to find a place among the educated population through the years.

It was determined that 49.09% of pregnant cases gave birth with cesarean section. According to TNSA 2018 data, Turkey had a cesarean birth rate of 52%. According to TNSA 1993, the cesarean rate was 7%, while it increased through the years to reach 48% according to TNSA 2013 before the increase rate slowed compared to previous years and reached 52% in TNSA 2018. In our research population, cesarean rates were similar to the country average; however, it is much above the targeted level. Though the decision about the form of birth is not made in primary stage services, in addition to ANC services, studies to reduce fears related to vaginal birth of candidate mothers and labor preparation work will reduce cesarean surgeries performed for social reasons.

The pregnancy numbers did not differ according to the educational status of women; however, most women with four or more pregnancies comprised women with primary-middle school education and most women in

the uneducated group had four or more pregnancies. The TNSA 2018 study found that the total fertility rate in Turkey was 2.3 children per woman. While the total fertility rate was highest among uneducated women or women who did not finish primary school,[2,5] was lowest among women with high school or higher education.[1,4,23]

The increase in LBW rates for mothers who smoke was shown in our research results. In parallel with many studies, smoking caused low birth weight in our research.[24] From this perspective, if not provided before pregnancy, mothers should be given detailed information about smoking, and efforts should be made to ensure they try to quit or reduce the habit at the start of pregnancy.

According to the Ministry of Health ANC Management Guide, breastfeeding and breastmilk counseling should begin after the 28th week.[1] Providing breastfeeding counseling and early beginning of breastfeeding are essential in maternal and infant health. In our research, the education rate was high (84.2%); however, the target is that all monitored pregnant cases be given education.

In conclusion, it appears the number of pregnancy check-ups in primary services approaches the levels targeted. It was concluded that there is a need to support vitamin and mineral supplementation recommended in pregnancy. Additionally, in spite of being a study in a metropolitan center, the screening tests did not appear complete. The causes of these inadequacies should be researched, and patients' compliance with screening tests should be increased. Additionally, some patients had complete vaccination for tetanus suppression, while some remained inadequate due to not wanting the vaccination. Though seasonal flu vaccines are recommended in the ministry guidelines, it is thought-provoking that none were administered. Awareness and referrals should be provided about this topic when necessary. Generally, the necessary organization should be provided by identifying if the inadequacy of necessary follow-up and tests performed outside the primary healthcare settings in this study of an educated section of society without poor welfare levels is due to reasons such as lack of awareness among patients or appointment congestion, etc. Contrary to previous studies, educational level was revealed not to affect vaccination and screening positively. This may be due to changes in access routes to information and data without scientific support being reached by the educated group. If this topic is not rapidly resolved, anti-vaccination will be an unavoidable threat to social health in epidemics like COVID-19 affecting the whole world for nearly two years.

Ethical considerations: Ethical approval was taken from local ethics committee on 19/12/2018 with number 26379996/320. The approval dated 05/03/2019 and numbered 604.02-E.147 was received from Ankara Provincial Health Directorate.

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

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EVALUATION OF THE GENERAL DEMOGRAPHIC CHARACTERISTICS OF COLON CANCER PATIENTS: IS THERE A DIFFERENCE BETWEEN MALE AND FEMALE PATIENTS?

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Abstract

Objectives: Colon cancer (CC) is seen in both sexes at the third frequency, and it is the cause of cancer-related deaths at the second frequency despite the advances in diagnosis and treatment. This study, it was aimed to evaluate the patients diagnosed with CC and their general demographic features in Bolu.

Materials and Methods: CC patients' gender, age, body mass index (BMI), the primary location of the tumor, pathological diagnosis, grade, staging, location of metastasis and treatments administered were recorded retrospectively.

Results: Those diagnosed with CC constituted16.54% of all cancer patients during the study period. 199(60.49%) of 329 patients included in the study were male, and 130 (39.51%) were female. The median diagnosis age in men and women was 64 years, the maximal age range of diagnosis was 60-69 years (32.66% and 32.22%, respectively). It was found that 6.53% of men and 26.15% of women were obese. The pathological diagnosis of 317 (96.35%) of the patients was adenocarcinoma, and the highest Grade 2 tumors subsisted (48.63%) (p= 0.696). The most diagnosed stage was stage III in men (36.68%) and stage II in women (38.46%) (p=0.044). While the appeal with the metastatic stage was 25.13% in men, it was seen at 17.69% in women (p=0.044).

Conclusion: In Bolu, CC is among the cancers in the early stage diagnostic screening program. It is important to increase the training and participation in these programs and to provide healthy nutrition and exercise training to avoid obesity which plays an important role, especially in women, in CC etiology. In addition, prospective studies should be carried out to prevent data loss and to reach healthy statistical results in our country.

Keywords: Colon cancer, gender, demographic features.

Introduction

Colon cancer is seen as the third most common cancer after prostate and lung cancer in men and breast and lung cancer in women and cause of death at the second common.[1]

Obesity, inflammatory bowel diseases, diabetes mellitus, smoking and alcohol use, processed red meat consumption, polyp, family history, genetic factors can be counted in CC etiology.[2] Colon adenomas are more common in men and lead to an increased risk of CC. Although the reasons for this are not fully known, gender differences in exposure to hormones and risk factors are thought to be the possible cause.[3]

Obesity is a very important risk factor in the development of CC. It is more common in Western Europe, America and Australia than in India and Africa, suggesting that calorie consumption and nutrition play a role in cancer formation. At the same time, obesity-related insulin resistance, diabetes, and hyperlipidemia also increase the risk of developing CC.[4] The most important determinant factor of prognosis in CC is TNM staging which is done according to the depth of the tumor in intestinal layers (T), lymph node involvement (N) and presence of metastasis (M). It can be shown that other prognostic factors include histology of the tumor, grade, and anatomical localization of the tumor.[4]

This study aimed to evaluate the general demographic characteristics of patients who applied to the medical oncology clinic with the diagnosis of CC in Bolu and whether there is a difference between male and female patients.

Materials and Methods

After obtaining the ethical approval, the data of patients who applied to the medical oncology clinic of our hospital dates between 01.01.2012 and 31.12.2017 were analyzed retrospectively through the file and computer records. Gender age, body mass index (BMI), tumor location, pathological diagnosis, grade, stage, metastasis and treatments administered were recorded. The patients were evaluated as BMI <18.5 underweight, BMI 18.5 – 24.9 normal, BMI 25 – 29.9 overweight, BMI >30 obese. Patients whose files were not available, who had missing file data and were under 18 were excluded.

Statistical analysis

Statistical analyzes were performed by using SPSS version 20 software. The suitability of convenience to normal distribution was examined by visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov / Shapiro-Wilk tests). The men and women groups were compared with the Mann-

Whitney-U test (nonparametric variables) or Student T-test (parametric variables) for continuous variables. Continuous variables were shown as median (minimum-maximum) or mean±SD according to be nonparametric or parametric, respectively. Whether there is a difference in terms of frequency between groups was compared by using chi-square or Fisher tests (where the values observed in cells do not provide chi-square test assumptions) accordingly. The p-value below 0.05 was evaluated as statistically significant.

Results

It was observed that 332 (16.54%) of 1039 male and 968 female patients totally 2007 patients who applied to our hospital's oncology outpatient clinic, were diagnosed with CC**.** One patient was not included in the study because he was younger than 18 years old, and the file data of 2 patients could not be accessed. Data of 329 patients diagnosed with CC were received for consideration.

It was determined that 199 (60.49%) of the patients were male, and 130 (39.51%) were female. The median age of all patients was 64 (min 26-max 87) years, the median age for men was 64 (min 26-max 87), and the median age in women was 64 (min 30-max 87) years.

When the patients were evaluated according to age groups, 106 (32.22%) patients' age were between at most 60-69 age group. There was no difference between men and women. Both sexes were at most 60-69 years old (p=0.160).

When the patients were examined in terms of body mass index (BMI), men who had normal BMI was 34.17%, and women who were overweight was 30.00% constituted the majority. While 13 (6.53%) patients were obese in men, 34 (26.15%) patients were obese in women. The bodyweight index of 96 of the patients could not be calculated since (29.18%) were unknown the patients' weight and height data before diagnosis. The distribution of patients by age groups and BMI are shown in Table 1.

The most common location in men and women was the rectum (38.69% and 45.38%). There was no difference between groups in terms of the location of the primary tumor (p=0.778).

When the histo-pathological diagnosis of CC patients was examined, it was found that 317 (96.35%) of the patients were diagnosed with adenocarcinoma and ring cell carcinoma followed this histology with seven patients (2.17%). There was no difference between the groups in terms of histopathological diagnosis (p=0.394). When the tumor grades of the patients were evaluated, it was found that the most common grade with 160 (48.63%) patients was grade 2. There was no difference between the groups in tumor grade (p=0.959).

Table 1. The distribution of patients according to age and body mass index

	Male (N=199)		Female (N=130)		Total (N=329)		P*
Age (years)	64 (26-87)		64 (30-87)		64 (26-87)		0.916
Age Groups	n	%	n	%	n	%	
< 40 aged	5	2.51	3	2.31	8	2.43	
40-49 aged	9	4.52	13	10.00	22	6.69	
50-59 aged	56	28.14	30	23.08	86	26.14	0.160
60-69 aged	65	32.66	41	31.54	106	32.22	
70-79 aged	52	26.13	28	21.54	80	24.32	
80 aged≤	12	6.03	15	11.54	27	8.21	
BMI (kg/m^2)	25.0±3.7		28.2±5.3		26.4±4.7		<0.001
Weak	3	1.51	1	0.77	4	1.22	
Normal	68	34.17	25	19.23	93	28.77	
Overweight	50	25.13	39	30.00	89	27.05	<0.001
Obese	13	6.53	34	26.15	47	14.29	
Unknown	65	32.66	31	23.85	96	29.18	

BMI: Body mass index: * male, female

When the patients were evaluated according to their stages at the time of diagnosis, the stage diagnosed the most was stage III with 119 (36.17%) patients. Stage III disease with 73 (36.68%) patients in men and stage II with 50 (38.46%) patients in women was more. It was found that in 50 patients with the metastatic stage in men, admission was seen in 50 (25.13%) patients in men and 23 (17.69%) in women. When the patients were evaluated according to the locations of metastases at the time of diagnosis, 42 (12.77%) patients had liver, 10 (2.13%) patients had lungs, 3 (0.90%) patients (ovarian, bone and peritoneum), 19 (5.78%) patients had multiple metastases, and there was no metastasis in 256 (77.81%) patients. The most common site of metastases in male and female patients was the liver.

After the diagnosis of CC, surgical intervention was done to 301 (91.49%) patients. After the diagnosis of CC, curative surgery was done to 254 (77.20%). It was found that 47 patients (14.29%) out of 73 patients in the metastatic stage had palliative surgery, and 28 (8.51%) patients had not any surgical intervention. There was no difference between the groups (p=0.321). The tumor location, pathological diagnosis, grade and stage of the patients are shown in Table 2.

It was observed that there was no treatment indication for 46 (13.98%) of the patients, and 38 patients (11.55%) refused the treatment although they were indicated for chemotherapy. There was no difference between the groups (p=0.572).

Table 2. Distributions of the tumor location, pathological diagnosis, grade and stage of the patients

	Male (N:199)		Female (N:130)		Total (N:329)		P*
	n	%	n	%	n	%	
Location of tumor							
Cecum	18	9,05	13	10,00	31	9,42	0,778
Ascending Colon	19	9,55	10	7,69	29	8,81	
Transverse Colon	8	4,02	6	4,62	14	4,26	
Descending Colon	17	8,54	11	8,46	28	8,51	
Sigmoid Colon	55	27,64	30	23,08	85	25,84	
Rectum	**77**	38,69	**59**	45,38	136	41,34	
Synchronous Tumor	5	2,51	1	0,77	6	1,82	
Pathological Diagnosis							
Adenocarcinoma	194	97.49	123	94,62	317	96.35	0.394
Signet ring cell carcinoma	3	1.51	4	3.08	7	2.17	
Others	2	1.01	2	2,31	5	1.48	
Grade							
1	49	24.62	34	26.15	83	25.23	0.959
2	95	47.74	65	50.00	160	48.63	
3	16	8.04	11	8.46	27	8.21	
Unknown	39	19.60	20	15.38	59	17.93	
Stage							
I	26	13.07	11	8.46	37	11.25	0.044
II	50	25.13	50	38.46	100	30.40	
III	73	36.68	46	35.38	119	36.17	
VI	50	25.13	23	17.69	73	22.19	
Surgical intervention							
Curative	148	74.37	106	81.54	254	77.20	0.321
Palliative	30	15.08	17	13.08	47	14.29	
Unavailable	21	10.55	7	5.38	28	8.51	
Chemotherapy							
No indication	28	14.07	18	13.85	46	13.98	0.572
Chemotherapy	151	75.88	97	72.31	245	74.47	
Treatment Rejection	20	10.05	18	13.85	38	11.55	

*male, female

Discussion

Todays, CC continues to be an important cause of morbidity and mortality all over the world and in our country. According to statistics of Public Health Institution of Turkey, CC is seen with the rate 9% after lung and prostate cancer in men, and after breast and thyroid cancer in women, CC is seen in 3. place with the rate 8%.[5] In our study, it was seen that the patients diagnosed with CC were at a higher rate than this study. As a reason, it was thought that the patients who applied to the only outpatient clinic could be evaluated, and the elderly population could be high in Bolu.

The lifetime risk of CC is higher in men, with a rate of 4% than in women.[1] In our study, it was found that men were 1.5 times more than women. Obesity was significantly higher in women in accordance with the literature. The rate of obese %26.15 and overweight %30 was higher in female patients than in males. Particularly, while the rate of the CC patients aged 80 years and older was 11.54% for women, this rate was 6.03% for men. The reason for this was thought to be that women lived longer than men.

It is known that the incidence of CC increases gradually after 50.[1] In a study in the USA related to this issue, it was found that 89% of the patients were over 50 years old.[6] In our study, the age range mostly seen in CC was 60-69 age range.

CC is generally more common in men than in women.[7] In a study in which ten centers participated in the USA, CC was seen in men with the rate of 49.4%, and the rate was 50.6% in women.[8] In a study conducted by Liu and his friends In China, it was found that 57.5% of patients were male and% 42.4 were female.[9] Similarly, we found that men more than women.

In a study conducted in the Aydın region, 33.1% of CC patients were determined to be female, and 66.9% of patients were male.[10] In a study performed in the Southeastern Anatolia Region, it was found that 57.1% of CC patients were male, and 42.9% were female.[11] In our study, it was found that male patients were more diagnosed with CC than women, similar to Turkey and the world literature.

It is known that obesity increases the risk of the development of CC. In fact, it is thought that the degree of obesity and the risk of developing CC has a correlational relationship among themselves and increases the mortality associated with CC.[12] In a study conducted in Kütahya, it was found that 43.6% of CC patients had high BMI, and there was no significant difference between the overweight patients in terms of distribution of males and females.[13] In our study, it was found that male CC patients were more overweight than women.

In a study with CC patients in England and Scotland evaluating the location of the CC, the most common site of uptake was in the rectum.[14] In the study of Loree and her friends, it was seen that the most common location was sigmoid colon, rectum and caecum in both men and women.[15] In another study performed in Samsun, it was seen that the most common location of cancer was rectum in both men and women.[16] Similar to these studies, in our study, it was found that there was a sigmoid colon involvement after the most common rectum involvement and the least involvement was the transverse colon.

In the study conducted with CC patients in Thailand, the most common CC type was detected as adenocarcinoma of histological subtype.[17] In a study conducted in Jordan, it was observed that the most common was signet ring cell carcinoma following adenocarcinoma of histological subtype.[18] Similar to these

studies, adenocarcinoma was found to be the most common histological subtype with signet ring cell carcinoma, and no significant difference were found between the genders.

Although various methods are used in literature in grading CC, the method used more commonly is the degree of gland formation. Grade (G) 1 tumors were defined as well-differentiated, G2 tumors were moderately differentiated, and G3 tumors were poorly differentiated.[19] In a study conducted with CC patients in Egypt, it was seen that %87.7 of patients had grade 2 tumors.[20] In another study conducted in Ankara, it was found that grade 2 was the most common grade and then grade 3 and grade 1 were seen in CC patients.[21] Similar to the literature, in our study, it was observed that the highest number of patients with CC was grade 2.

The most frequently used system in CC staging is the TNM staging system. It is important to determine treatment and prognosis.[22] In a study conducted in the Netherlands, 17% of CC patients were found to be stage 1, and 23% were stage 4.[23] In our study, it was seen that the rate of men in the advanced stage was higher than women. While stage 3 was more common in men, stage 2 was more common in women.

The most commonplace of metastasis in CC patients is the liver. It is seen lung metastases following liver metastasis in patients.[24] In a study conducted in Sweden, after lung, peritoneal and bone metastases, the liver was observed in both men and women as the most common site of metastases of CC patients.[25] Another study performed by Hugen and his friends it was found that liver metastasis was seen the most commonly and after that lung and peritoneal metastasis.[26] In our study, the liver was the most common site of metastasis.

Surgery is generally the first choice in the treatment of CC, and it can be performed for curative and palliative purposes.

In a study conducted in Istanbul, it was seen that 83.4% of the patients who had surgical intervention due to CC were operated as elective, and 16.6% of patients were as palliative.[27] In another study carried out in Mersin, %86.2 of patients had an operation in elective conditions and %13.8 of patients had an operation for palliative purposes.[28] In our study, similar results were obtained.

In a study performed by Kumar and his friends, it was found that 9.8% of the patients refused treatment despite the indication of chemotherapy.[29] In the study conducted in İzmir, it was observed that 9.3% of CC patients did not receive any treatment.[30] In our study, the rate of refusing treatment was similar.

As a result, in Bolu, CC is more common in men and diagnosed at a higher grade than in women. Though CC is among the cancers being in the early stage diagnostic screening program, the education related to CC screening programs and enhancement of participation of these programs will help to diagnose in the early stage since the patients are diagnosed at a metastatic stage of approximately %25. It was also concluded that it is important

to give healthy nutrition and exercise educations for avoiding obesity, especially those that play a significant role in CC etiology. In addition, prospective studies were thought to be important in order to prevent data losses and reach healthy statistical results in our country.

Ethical considerations: For this study, following the permission of the hospital management on 02.05.2016, numbered 68246970 / 903.99, it was gained ethics committee approval from Bolu Abant İzzet Baysal University Faculty of Medicine ethical committee numbered 2017/63 dated 26.05. 2017.

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

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DETERMINATION OF PHYSICAL ACTIVITY LEVELS OF PATIENTS WITH DIABETES MELLITUS AND EVALUATION OF ITS RELATIONSHIP WITH TREATMENT COMPLIANCE

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Abstract

Objectives: Physical activity is a crucial component of the treatment of Diabetes Mellitus (DM). This study aimed to determine the physical activity levels of patients with DM and evaluate the relationship between their adherence to treatment.

Materials and Methods: The study was designed as a single-center, prospective, analytical study. It was conducted with patients who applied to the Family Medicine Outpatient Clinic for any reason, those who had a diagnosis of DM for at least one year. Sociodemographic data, anthropometric measurements, fasting blood glucose, and HbA1C levels were recorded. Physical activity levels were assessed using the General Practice Physical Activity Questionnaire (GPPAQ) and the International Physical Activity Questionnaire (IPAQ). The levels of compliance with drug treatment were assessed using the Modified Morisky Medication Adherence Scale-8 (MMMAS-8).

Results: The mean age of 237 people included in the study was 51.32 ± 8.62 years (25-65), and most were women (n=141; 59.49%). The majority of the participants were physically inactive. (according to IPAQ n=143, 60.34%; GPPAQ n=161, 67.93%). 55.70% (n=132) had a moderate-high level of treatment compliance. No statistically significant correlation was determined between both scales measuring physical activity level and compliance of individuals to drug treatment (p=0.110 for GPPAQ; p=0.714 for IPAQ).

Conclusion: No significant correlation was found between the physical activity levels of patients with DM and their compliance with drug therapy. However, it has been observed that the results obtained with GPPAQ, a new measurement tool that can be easily applied in primary care, are also instructive.

Keywords: General Practice Physical Activity Questionnaire, Diabetes Mellitus, Physical Activity, Modified Morisky Medication Adherence Scale-8, Medication Adherence, International Physical Activity Questionnaire.

Introduction

Diabetes Mellitus (DM) is a chronic metabolic disorder that requires continuous medical care, in which the organism can not adequately benefit from carbohydrates, fats, and proteins due to insulin deficiency or defects in the effect of insulin.[1] In many diseases, including DM, lack of physical activity is an important and modifiable risk factor.[2] Physical activity, structured by determining personal goals and performed regularly, is known to help regulate DM and delay the development of complications.[3] Therefore, physical activity, together with drug therapy, medical nutrition therapy, and patient education, are counted among the constant elements of DM treatment.[4] Studies evaluating physical activity in patients with DM in the literature have shown that a majority of patients lead a sedentary life.[5-7]

In order for the medical treatments applied to the patients to be beneficial, the concept of "adherence to treatment," known as taking the prescribed treatment in the recommended form, at the appropriate time and dose, and ensuring continuity in the process determined for the treatment, is important.[8] A few studies concluded that adherence to drug therapy is insufficient in type 2 DM patients.[9-11] When the level of adherence to treatment is low in patients with DM, the effectiveness of the treatment decreases, and the course of the disease is adversely affected. This condition may lead to the development of complications, the occurrence of other diseases, and death.[12-14]

Many methods can be used to evaluate the physical activity levels of individuals and their compliance with treatment.[15] Although there are studies in the literature in which physical activity and adherence to treatment are evaluated separately in patients with DM, to our knowledge, there is no study examining the relationship between these two concepts.

This study aimed to evaluate the relationship between the physical activity levels of patients with DM and the level of compliance with the treatment given.

Materials and Methods

Study population and study design

This analytical study was designed as a single-center and prospective study. It included 237 patients between the ages of 18-65, admitted to the Family Medicine Outpatient Clinic of a tertiary hospital for any reason, between February 15th and June 15th, 2020, who had a diagnosis of DM for at least one year and agreed to participate in the study.

Those aged <18 and those aged>65 years, those who had a history of severe cardiovascular disease, advanced stage pulmonary diseases, a musculoskeletal disease that prevents physical activity, gestational diabetes mellitus, those diagnosed with DM less than one year ago, those who were pregnants, those who breastfeed, and those with communication barriers were excluded.

According to the calculation result made by using the G-Power program, when considering the 1st type error as 5% (bidirectional) and the 2nd type error as 5% (95% power), with the percentage of being physically active as determined by the scale in the sample literature, a total of at least 172 cases was found to be suitable to include.

Data collection tools

Patient information form:

A patient information form was formulated by us using the literature, which included the participants' sociodemographic characteristics (age, gender, marital status, educational level, working status), information on DM disease (type of DM, duration of DM, treatment used, presence of complications related to DM, type of complication, hospitalization in the last year, adherence to diet) and general health status (presence of additional diseases, medication, alcohol and cigarette use) were questioned. The participant's blood pressure (mmHg), waist circumference (cm), height (m), weight (kg), and BMI (Body Mass Index, kg/m^2) values were measured and recorded. Previously measured fasting blood glucose (FBG, mg/dl) and HbA1C (%) levels were noted as well.

General Practice Physical Activity Questionnaire

General Practice Physical Activity Questionnaire (GPPAQ), the first of the scales used to determine the physical activity levels of the participants, was developed in 2002 by The London School of Hygiene and Tropical Medicine in England to evaluate the physical activity level of adults in primary care.[16] Turkish validity and reliability study was performed by Noğay et al. in 2019 (Cronbach α=0.74).[17] The scale consists of 3 parts and seven questions. In the first part, the activities of the participants at work are questioned. In the second part, physical exercises, walking, cycling, hobbies, and housework in the last week, how many hours a week are done, and in the last part, walking speeds are asked. Walking, housework, gardening, and hobby activities are not considered as they are not significant and reliable when calculating total physical activity. People are divided into four groups according to their physical activity levels as active, moderately active, less active, and sedentary.[16,17]

International Physical Activity Questionnaire

The International Physical Activity Questionnaire (IPAQ), the second scale used to determine the physical activity levels of the participants, was developed by Craig et al. in 2003.[18] The Turkish validity and reliability study of the short and long forms of the questionnaire was performed by Sağlam et al. in 2010.[19] The scale consists of 4 parts and seven questions. In the first part, whether the participant did a vigorous physical activity and if it was done, the duration of it is questioned. In the second part, whether moderate physical activity is done, and if it was done, its duration is evaluated. In the third part, it is questioned whether the participant walked for more than 10 minutes in the last week and if it was done, its duration is questioned. The fourth part consists of a single question evaluating the time spent sitting. In evaluating the results, MET-min (Metabolic Equivalent) score is used. While calculating the total MET value of the participant, the minutes of sitting (1.5 MET-min), walking (3.3 MET-min), moderate-intensity physical activity (4 MET-min), and vigorous physical activity (8 MET-min) within one week were used. It is categorized as inactive if the total MET-min/week value is below 600, minimally active if 600-3000 MET-min/week is detected, and active if it is above 3000.[18,19]

Modified Morisky Medication Adherence Scale-8

The treatment adherence levels of the participants were evaluated with the Modified Morisky Medication Adherence Scale-8 (MMMAS-8) prepared for DM patients in 2006 by Morisky et al.[20] The validity and reliability study of the scale was performed by Sayıner et al. in 2019.[21] The scale consists of 8 questions. Answering "no" to the first four questions, sixth and seventh questions, and "yes" to the 5th question, never/rarely to the 8th question score 1 point. Other answers do not receive points. While 8 points are considered as high adherence to treatment, 6-7 points indicate moderate adherence, and below 6 points indicate low adherence.[20,21]

Statistical analysis

The IBM SPSS Statistics 22 program was used for statistical analysis. The compliance of the parameters to normal distribution was evaluated with the Shapiro-Wilk test. In addition to descriptive statistical methods (mean, standard deviation, frequency) in more than two-group comparisons, one-way ANOVA was used when numerical variables showed normal distribution, and the Tukey HDS test and Tamhane's T2 test determined the group that caused the difference. The Kruskal-Wallis test was used when there was no normal distribution, and Dunn's test was used to determine the group that caused the difference. Mann-Whitney U test evaluated the comparisons of non-normally distributed parameters between two groups. The Chi-square test and Fisher Freeman Halton test compared qualitative data. Pearson's correlation analysis was performed to examine the relationships between parameters that conform to a normal distribution, and Spearman's rho correlation analysis examined relationships between parameters that did not conform to a normal distribution. The statistical significance was considered at the level of $p<0.05$.

Results

The mean age of the 237 participants included in the study was 51.32±8.62 years (min:25, max:65), and 59.49% were female (n=141). Table 1 presents the sociodemographic characteristics of the participants.

The mean height of the participants was 1.63±0.09 m, the mean weight was 83.88±15.49 kg, and the mean BMI was 31.75±5.7 kg/m^2. The mean value of participants' waist circumference measurement was 106.24±12.58 cm. The participants had the diagnosis of DM for an average of 6.63±5.47 (min:1, max:30) years. The mean FBG values were 173.87±92.6 mg/dl, and the mean HbA1C values were 8.37±2.38 %. While 57.81% (n=137) had used only OAD in the treatment of DM, 38.40% (n=91) had combined therapy. 61.60% (n=146) had additional drug use due to another disease. It was found that 74.30% (n=176) had no previous complications. As complications, retinopathy (34.43%; n=21) and neuropathy (32.79%; n=20) were reported the most. While 28.69% (n=68) were active smokers, 6.75% (n=16) reported that they used any amount of alcohol. The anthropometric measurements of the participants, their general health status, and information about diabetes are presented in Table 2.

The total MET values of the participants ranged from 180 to 8490 minutes (mean 1304.11±960 min). While 60.34% (n=143) of the participants were inactive according to IPAQ, 35.44% (n= 84) were minimally active and 4.22% (n=10) were very active. According to GPPAQ, 8.02% (n=19) was active, 14.35% (n=34) was moderately active, 9.70% (n=23) was less active and 67.93% (n=161) were considered sedentary. The mean score of the MMTUS-8 was 5.74±2.05, and 55.70 % of the participants (n=132) had a moderate-high level of treatment compliance.

Table 1. Sociodemographic characteristics of the study population

		Min-Max	**Mean±SD**
Age (years)		25-65	51.32±8.62
		n	**%**
Gender	Female	141	59.49
	Male	96	40.51
Education status	Illiterate	40	16.88
	Primary school	131	55.27
	Middle school	25	10.55
	High school	34	14.35
	University	7	2.95
Marital status	Married	205	86.50
	Single	32	13.50
Working status	No	154	64.98
	Yes	83	35.02

According to the results obtained from the scales used, the distribution of the physical activity levels and treatment compliance levels of the participants is summarized in Table 3.

No statistically significant correlation was determined between both scales measuring physical activity level and adherence to drug therapy (p:0.110 for GPPAQ; p:0.714 for IPAQ). Table 4 shows the relationship between the physical activity levels of the patients and their compliance with drug treatment according to the results obtained from the scales.

Table 2. Health status, characteristics of diabetes, and anthropometric measurements of the participants

		Min-Max	**Mean±SD (median)**
BMI (kg/m²)		18.99-59.58	31.75±5.7
Waist circumference (cm)		70-160	106.24±12.58
Diastolic BP (mmHg)		50-100	76.84±8.19 (80)
Systolic BP (mmHg)		90-180	123.42±12.71 (120)
FBG (mg/dl)		77-743	173.87±92.6 (140)
HbA1c (%)		5.2-17	8.37±2.38 (7.6)
Duration of disease (years)		1-30	6.63±5.47
		n	**%**
DM Medication	OAD	137	57.81
	Insulin	9	3.80
	Combined	91	38.40
DM Complication (n=61)	Retinopathy	21	34.43
	Nephropathy	18	29.51
	Neuropathy	20	32.79
	Diabetic foot	2	3.28
History of hospitalization	No	232	97.89
	Yes	5	2.11
Diet compliance	Yes	111	46.84
	Partially	73	30.80
	No	53	22.36
Smoking status	Active smoker	68	28.69
	Ex-smoker	60	25.32
	Non-smoker	109	45.99
Alcohol Use	Yes	16	6.75
	No	221	93.25
Additional chronic diseases	No	76	32.07
	Yes	161	67.93
Additional drug use	Yes	146	61.60
	No	91	38.40

BMI: body mass index (kg/m²). BP: Blood Pressure, DM: Diabetes Mellitus, FBG: Fasting Blood Glucose.

Table 3. Distribution of participants' physical activity levels and medication adherence levels according to the results obtained from the scales used

		Min-Max	Mean±SD (median)
IPAQ Sub-dimensions (min/week)	**Vigorous MET**	0-2880	48.95±323.55 (0)
	Moderate-int. MET	0-4800	206.5±567.6 (0)
	Walking MET	0-6930	505.44±650.92 (346,5)
	Sitting MET	0-1260	543.23±261.34 (540)
	Total MET	180-8490	1304.11±960.14 (1035)
MMMAS-8 score		0-8	5.74±2.05 (6)
		N	**%**
Activity levels According to IPAQ	**Inactive**	143	60.34
	Minimally active	84	35.44
	Active	10	4.22
Activity levels According to GPPAQ	**Active**	19	8.02
	Moderately active	34	14.35
	Less active	23	9.70
	Sedentary	161	67.93
Treatment compliance	**Low**	105	44.30
	Moderate	66	27.85
	High	66	27.85

Data presented as Mean±SD and min-max. GPPAQ: General Practice Physical Activity Questionnaire, IPAQ: International Physical Activity Questionnaire, MET: Metabolic Equivalent, MMMAS-8: Modified Morisky Medication Adherence Scale-8.

Table 4. The relationship between the physical activity levels of the participants and their compliance with treatment

MMMAS-8					
		Score Mean±SD (median)	**Level of adherence to treatment n (%)**		
Activity levels			**Low**	**Moderate**	**High**
GPPAQ	**Active**	5.95±2.01 (7)	8 (42.11%)	5 (26.32%)	6 (31.58%)
	Moderately active	5.44±2.41 (6)	15 (44.12%)	10 (29.41%)	9 (26.47%)
	Less active	4.78±2.17 (5)	14 (60.87%)	6 (26.09%)	3 (13.04%)
	Sedentary	5.91±1.92 (6)	68 (42.24%)	45 (27.95%)	48 (29.81%)
		p: 0.110	***p: 0.700**		
IPAQ	**Inactive**	5.82±1.97 (6)	62 (43.36%)	41 (28.67%)	40 (27.97%)
	Minimally active	5.6±2.12 (6)	40 (47.62%)	22 (26.19%)	22 (26.19%)
	Active	5.8±2.62 (6.5)	3 (30.00%)	3 (30.00%)	4 (40.00%)
		p: 0.714	***p: 0.825**		

Data presented as Mean±S and n (%). * Chi-Square Test
GPPAQ: General Practice Physical Activity Questionnaire, IPAQ: International Physical Activity Questionnaire, MMMAS-8: Modified Morisky Medication Adherence Scale-8.

Discussion

The present study investigated the relationship between physical activity and adherence to treatment of patients with DM. Although the physical activity levels of the majority of patients with DM were low, it was observed that their treatment compliance was moderate to high. No significant relationship was found between physical activity levels and compliance with treatment.

DM is a disease with an increasing frequency in society, with a high rate of morbidity and complications. In order to achieve success in the treatments given, the patient's compliance with the treatment is critical. In addition, adequate physical activity is an essential component of DM treatment.[3,4]

There are many studies in the literature evaluating physical activity in patients with DM. In these studies, different results, which were thought to be due to the sociodemographic characteristics of the patients and physical activity measurement methods, were obtained. Physical activity was mostly evaluated by using UFAA, and there are also studies using different measurement tools.[6,7]

In the study of Duarte et al. using IPAQ, 8.7% of diabetes patients were very active, 60.6% minimally active, and 30.7% inactive[6]. Similarly, Çolak et al. evaluated the patients as 39.5% inactive, 51.9% moderately active, and 8.5% active.[7]

Consistent with the literature, the results obtained from both physical activity assessment scales (IPAQ and GPPAQ) used in our study were compatible with each other, and it was determined that the majority of the patients were inactive according to IPAQ and sedentary according to GPPAQ.

Previous studies have demonstrated that the sociodemographic characteristics of the patients can affect the level of physical activity.[22,23] It has been observed that the level of physical activity decreases with increasing age. In a study performed in Sri Lanka, the level of physical activity decreased according to UFAA with increasing age, but no significant difference was determined.[22] In our study, while there was no significant difference in terms of activity levels and mean age according to IPAQ, the difference between GPPAQ and mean age was statistically significant. The results were thought to be determined in this way due to the increase in chronic diseases and decrease in the effort capacity of the patients as the age progresses.

Different results were obtained about gender. In a study in which the physical activity levels of diabetic patients were measured and the calories they spent weekly were calculated, no significant relationship was found between the level of physical activity and gender.[23] However, men were significantly more active than women

in our study. It is thought that women can spend most of their time at home as they undertake more household chores and childcare, thus causing physical activity to appear low.

The positive effects of physical activity on BMI and waist circumference are known.[24,25] In an experimental study performed with type 2 diabetes patients, a significant decrease was found in the BMI of the physical activity program compared to the control group.[24] In another study, a significant inverse relationship was found between physical activity and waist circumference, but no relationship was found with BMI.[25] The results obtained from our study were similar to most studies in the literature.

Many studies have revealed that physical activity positively affects the decrease in HbA1C and BG.[26-28] A literature review determined that a 100-minute weekly increase in physical activity resulted in an average of 0.16 % decrease in HbA1C and a 4.71mg/dl decrease in FBG.[26] In another study, a significant decrease was determined in HbA1c at 3 and 6 months in the group that underwent physical activity and nutrition interventions compared to the control group.[27] A meta-analysis revealed that in addition to a structured physical activity program, only suggesting physical activity resulted in a decrease in HbA1C.[28] Although a significant relationship was found between physical activity and HbA1C and FBG levels in the literature, no significant relationship was found between physical activity levels and HbA1C and FBG levels in our study. It is thought that this may be due to the inability to standardize many factors that may cause deterioration in DM regulation, such as adherence to diet, additional chronic disease, and the presence of additional drugs used.

When previous studies were examined, it was indicated that good adherence to treatment, as well as exercise, positively affected the course of diabetes, reduced the need for medication, and decreased HbA1C and BG.[13,14,29] In a study performed in 2017, HbA1C and treatment compliance levels were followed up for one year, and the HbA1C levels of the intervention group decreased significantly compared to the control group[14]. Similar to HbA1c, Özkaptan et al. found a negative correlation between treatment adherence and FBG levels.[29] The study of Fadare et al. revealed that adherence to treatment did not have a significant effect on the instantaneous BG level.[30]

Our study determined that HbA1C levels were higher in patients with low treatment compliance, which was consistent with the literature. There was no significant difference between treatment compliance level and FBG. In medical treatments, it is known that drugs must reach a certain dose in the blood in order to be effective. Compliance with treatment is vital to provide and maintain an effective dose. In this context, it was concluded that HbA1C values were found to be lower in patients with better adherence to treatment. On the other hand, FBG can be affected by variables that can affect blood sugar in a short time, apart from the general course of diabetes. Since these variables could not be controlled, it is thought that no difference was detected.

In addition, in our study, the relationship between the physical activity level of the patients and their compliance with drug treatment was investigated. While 55.70% of the patients were found to have a high or moderate level of treatment compliance, it was observed that the majority were included in the inactive and sedentary group. However, there was no statistically significant relationship between the participants' physical activity levels and their adherence to the treatment. To our knowledge, there is not yet a study in the literature investigating the relationship between physical activity levels of patients with DM and adherence to drug treatment. We think that in the primary care follow-up of patients with diabetes, physical activity recommendations should be repeated at each meeting with the patient, personal goals should be determined, and patients should be encouraged.

Limitations of the study

Our study has some limitations. Firstly, since the number of Type 1 DM patients that can be reached is limited, only Type 2 DM patients were studied. Latter, it is thought that the results of the low activity levels obtained from the physical activity scales are not only related to the diagnosis of DM but also related to the sociocultural level and lifestyles of the participants who could be reached in the study.

In this study, in which we aimed to evaluate the relationship between physical activity levels and adherence to treatment in patients with Type 2 DM, it was observed that the majority of the patients had low physical activity levels, and their compliance with drug treatment was at a moderate-high level. However, no significant relationship was found between physical activity levels and adherence to drug therapy. Moreover, although not statistically significant, it was concluded that since the results obtained with GPPAQ, which is a short and easy-to-understand new measurement tool that can be easily applied in primary care, are also instructive, it can be used more frequently in determining the level of physical activity in primary care.

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Ethical Considerations: Ethical permission to perform this study was obtained from the Local Ethics Committee (Approval No:29; Date: 05.02.2020). The study was conducted under the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants.

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Research Article

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DIFFERENCES BETWEEN OFFICE AND AMBULATORY BLOOD PRESSURE MEASUREMENTS IN PATIENTS USING TRIPLE ANTIHYPERTENSIVE TREATMENT

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Abstract

Objectives: It has been suggested that blood pressure (BP) measurements in the office/clinic may fall short of detecting phenomena such as a white coat or masked hypertension (HT). In this cross-sectional study, we aimed to evaluate the differences in office and ambulatory BP measurements (ABPM) and investigate the secondary causes in patients using triple antihypertensive medication.

Materials and Methods: Of the included 57 patients using triple antihypertensives, 28 had high office BP measurements (HOM-HT group), whereas 29 had normal office BP values (NOM-HT group). Both groups underwent an ABPM. Also, serum biochemistry, 24-hour urine tests, Epworth Sleepiness Scale, and renal artery Doppler assessments were performed to detect secondary causes of HT. Groups were compared regarding ABPM values, tests, scale results, and secondary causes.

Results: No significant differences were found between the demographics and serum tests. According to the ABPM, white coat HT was detected in 15 patients (53.67%) in the HOM-HT group, whereas five (17.24%) in the NOM-HT group had masked HT (p=0.018). In three patients, secondary causes were detected (hyperaldosteronism, renal artery compression, and sleep apnea), all of whom were in the HOM-HT group. The groups did not differ significantly regarding the frequency of secondary causes (p=0.112). In contrast to when the ABPM is taken into account (16.66% vs. 0% p=0.028).

Conclusion: Data of the present study showed that ABPM is necessary to detect white coat and masked HT. Also, depending on ABPM rather than office/clinic measurements may save time and expenses when investigating secondary causes.

Keywords: Ambulatory blood pressure, office blood pressure, resistant hypertension, white coat, masked.

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Introduction

Hypertension (HT) is one of the most important causes of mortality and morbidity in the aging population. Although the incidence of HT may vary according to age, gender, or race, the crude prevalence was estimated to be approximately 20% in adults worldwide according to the "Seventh Joint National Committee" (JNC-7) criteria published in 2003.[1] However, the prevalence in the current reports is even higher, reaching up to 31.1% as published by the "American Heart Association" (AHA) in 2018.[2] Moreover, the "American College of Cardiology" (ACC)/(AHA) lowered the threshold values of HT from 140/90 to 130/80 mmHg in 2017, which boosted the prevalence in the American population up to 46%.[2] In Turkey, the prevalence of HT in the adult population has been reported as 31.8%, close to AHA.[3]

While most patients with primary HT respond to one or two antihypertensive drugs, in some patients, lifestyle changes and appropriate drug selection may not suffice to manage HT. These patients may constitute the resistant HT, which is defined as the blood pressure (BP) ≥ 140/90 mmHg despite three antihypertensive drugs in maximum tolerable doses, one of which is a diuretic, or can only be controlled with at least four or more antihypertensive medications.[4] Although different rates for resistant HT were reported probably due to different study designs; most studies gave a prevalence of 10-15% for resistant HT.[2,5-7] The diagnosis of resistant HT necessitates further clinical and laboratory tests and inevitably increases health care expenditures.

Although there is a well-accepted definition of resistant HT, the rationale of its threshold is not strongly evidence-based. Moreover, the values determined in single or multiple measurements in the office/clinic may be unreliable. Therefore, we sought to assess the patients who fall in the resistant HT category and those who have their BPs in target levels in office/clinic measurements using ambulatory blood pressure monitoring (ABPM) and compare the frequency of secondary hypertension.

Materials and Methods

Patients

This study is planned as a cross-sectional study. The eligibility criteria for study inclusion were as follows: Being over the age of 18, having HT and using ≥ three antihypertensive agents of different classes, at least one of which is a diuretic applied to the Internal Medicine or Cardiology outpatient clinics of Gülhane Training and Research Hospital between December 2010 and June 2011. BPs were measured between 08:00 and 11:00 in the morning, at both arms after five minutes of rest. Then, a second measurement was made on the side with a higher value, and the average of both measures was recorded. Before the measurements, we confirmed that

the patients had taken their morning antihypertensive regimens. Patients with office BP values ≥140/90 mmHg that was thought to have resistant HT were assigned to the "High Office Measurement" hypertensive (HOM-HT) group. In comparison, others (office BP <140/90 mmHg) constituted the "Normal Office Measurement" hypertensive (NOM-HT) group. Participants were excluded with chronic renal or hepatic insufficiency, malignancy, acute infection, pregnancy, and contraindication in diuretics. The local ethics committee approved the study. All procedures followed the Declaration of Helsinki, and informed consent was obtained from all participants.

Assessments

The sociodemographic data of all participants were evaluated in detail, including body mass index (BMI) and waist circumference. For the detection of secondary HT causes, a whole blood count, routine biochemistry (including fasting blood glucose, urea, creatinine, electrolytes, total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglyceride, aldosterone, plasma renin activity, thyroid-stimulating hormone (TSH), as well as 24-hour urine analysis including microalbumin, protein, sodium, vanillylmandelic acid (VMA), 5-hydroxy indole acetic acid (5-HIAA), metanephrine, normetanephrine, adrenaline, and noradrenaline levels were investigated. Additionally, 24-hour ABPM was performed in all participants. Cut-off values of <130/80mmHg for 24 hours, <135/85mmHg for daytime, and <120/70mmHg for nighttime were taken for the ABPM. Participants with higher mean values in either of these cut-offs were considered to have an abnormal ABPM (9). Besides, electrocardiography and renal ultrasound, and renal artery Doppler imaging were performed in all patients. The "Epworth Sleepiness Scale" (ESS) was applied to screen obstructive sleep apnea (OSA). High scores in ESS were confirmed by polysomnography (PSG).

Statistical analysis

The sample size of the present study was calculated based on the previous study and preliminary data. The estimated difference between the groups regarding high BP values in the ABPM was 35%, with an estimated WCH of 50% and masked HT of 15%. With 5% type-1 error (two-tailed) and 80% power, 27 patients were needed in each arm". Visual histograms and the Kolmogorov-Smirnov test analyzed the distribution of the data. Quantitative data are given as mean/median or SD/min-max. Concerning group comparisons with continuous variables, independent samples t-test or Mann-Whitney U test was used according to the distribution of the data. Chi-square or Fisher's exact tests compared nominal data. A 2-sided p-value of <0.05 was considered significant. SPSS Statistics 22.0.0 (SPSS Ltd., Chicago IL) was used for statistics.

Results

A total of 57 patients were included in the study, 28 of whom had HOM-HT. No significant difference was found between the groups regarding age (p=0.342), sex (p=0.509), BMI (p=0.363), and waist circumference (p= 0.690) (Table 1).

As an enrollment criterion, all the patients were taking diuretics. With respect to other antihypertensive medication, the percentage of patients treated with angiotensin receptor blockers, calcium channel blockers, beta-blockers, angiotensin-converting enzyme inhibitors, alpha-blockers, aldosterone antagonists, and centrally acting antihypertensives was 82.46, 80.70, 63.16, 17.54, 3.51, 3.51, and 1.75%, respectively. No significant difference was found in terms of the evaluated serum biochemistry. 24-hour urine assessments revealed significant differences for normetanephrine, adrenaline, and noradrenaline, but these did not indicate any secondary cause such as pheochromocytoma (Table 2).

Table 1. Distribution of sociodemographic characteristics of the groups.

	HOM-HT group (n=28)	NOM-HT group (n=29)	P
	Mean±SD	Mean±SD	
Age, years	60.64±9.28	58.10±10.58	0.342
Male sex, n (%)	10 (35.71)	8 (27.59)	0.509
Antihypertensive treatment duration, years	12.73 (7.79)	11.34 (9.76)	0.572
Waist circumference, cm	96.54±8.80	97.52±9.42	0.690
BMI, kg/m^2	30.77±5.38	32.11±5.52	0.363
BMI, kg/m^2 n(%)			
≤ 24.9	3 (10.71)	1 (3.44)	0.543
25-29.9	9 (32.14)	9 (31.03)	
>30	16 (57.14)	19 (65.52)	
Smoking, n			
Non-smoker	18	20	0.921
Current smoker	7	6	
Quitted	3	3	
Accompanying chronic illness			
Hyperlipidemia	11 (39.28)	10 (34.48)	0.707
Type-II DM	9 (32.14)	11 (37.93)	0.647
Coronary artery disease	3 (10.71)	2 (6.90)	0.610

HOM-HT: high office measurement; NOM-HT: normal office measurement; BMI: body mass index; cm, centimeter; DM: Diabetes Mellitus.

Table 2. Comparison of the serum and 24-hour urine assessments of the groups.

	HOM-HT group (n=28)	NOM-HT group (n=29)	P†
	Mean±SD	Mean±SD	
Serum parameters			
Fasting glucose, mg/dL	128±58.66	105.66±15.28	0.522
Urea, mg/dL	31.90±10.64	31.79±7.62	0.960
Creatinine, mg/dL	0.96±0.215	0.88±0.14	0.052
Na, mmol/L	137.95±10.44	140.80±2.81	0.114
K, mmol/L	4.36±0.46	4.28±0.32	0.454
Total cholesterol, mg/dL	211.13±51.19	202.52±32	0.461
LDL cholesterol, mg/dL	132.58±43.94	124.82±28.50	0.439
Triglycerides, mg/dL	180.85±117.72	158.07±105.45	0.447
HDL cholesterol, mg/dL	49.69±109.90	48.48±10.10	0.654
TSH, mikroIU/mL	1.20±1	1.59±1.37	0.251
Urine parameters			
Microalbuminuria, mg/day	7. 29 (3.60-6678)‡	9.60 (4.40-80.40) ‡	0.237
Proteinuria, mg/day	105 (44-8260)‡	105 (48-180) ‡	0.260
Urine Na, mmol/day	161.96 ±68.53	188.69 ±82.91	0.242
VMA, mg/day	3.28 ±1.40	4.18 ±2.29	0.109
5-HIAA, mg/day	2.96 ±1.77	3.52 ±1.83	0.288
Homovalinic acid, mg/day	4.18 ±2.45	3.32 ±1.54	0.174
Metanephrine, mcg/day	118.83 ±146.19	84.85 ±50.15	0.992
Normetanephrine, mcg/day	289.85 ±342.05	405.91 ±496.94	0.047*
Adrenaline, mcg/day	2.88 ±1.54	5.26 ±4.29	0.042*
Noradrenaline, mcg/day	34.10 ±15.90	51 ±28.64	0.021*

HOM-HT: high office measurement; NOM-HT: normal office measurement; Na: sodium; K: potassium; LDL: low-density lipoprotein; TG: triglyceride; HDL: high-density lipoprotein; TSH: thyroid-stimulating hormone; VMA: Vanilla mandelic acid; 5-HIAA: 5-Hydroxy indole acetic acid.

† Independent samples t-test

‡ Median (min-max)

*p<0.05

Secondary causes of HT were identified in three patients, all of whom were in the HOM-HT group (10.71%). They were diagnosed with hyperaldosteronism, OSA, and a mass compressing the renal artery, respectively. Of note, the patient with a mass pressuring renal artery was operated on and subsequently became normotensive without medication. None in the NOM-HT group had secondary causes, but this difference was not significant (10.71% vs. 0%, Fisher's exact test p=0.112). However, when the patients were re-grouped according to the ABPM, patients with accurate resistant HT (n=18) differed significantly in the frequency of secondary causes (16.66% vs. 0%, Fisher's exact test p=0.028).

In total, 18 (31.58%) of all patients (n=57) were detected to have true resistant HT according to the ABPM values. Significant differences were found between the groups regarding ABPM (Table 3). Within the HOM-HT group, only 13 (46.43%) had ABPM values consistent with the definition of resistant HT; the remaining 15

(53.67%) failed to fulfill the definition of resistant HT. In the NOM-HT group, 5 (17.24%) were had resistant HT assessed by ABPM (p=0.018). There was no significant difference in circadian BP measurements between the groups (systolic BP, p=0.109; diastolic BP, p=0.104, Table 3).

Table 3. Ambulatory/office BP values and circadian patterns of the groups.

		HOM-HT group (n=28)	NOM-HT group (n=29)	P
		Mean±SD	Mean±SD	
ABPM and office measurements				
Average 24-hour, mmHg	SBP	126.43 ±15.39	114.90 ±10.00	0.001†**
	DBP	74.75 ±11.90	69.21 ±7.00	0.036†*
Average daytime, mmHg	SBP	128.43 ±15.50	117.90 ±10.03	0.003†**
	DBP	77.07 ± 12.62	71.71 ±7.30	0.054†
Average nighttime, mmHg	SBP	122.46 ±17.34	108.90 ±10.20	0.001†**
	DBP	70.04 ±11.39	63.72 ±6.27	0.012†*
Office BP, mmHg	SBP	153.63 ±17.33	124.48 ±12.50	<0.001†**
	DBP	88.59 ±11.58	75.60 ±5.90	<0.001†**
Circadian SBP, n (%)				
Extreme dipper		0 (0)	0 (0)	0.109‡
Dipper		3 (10.71)	6 (20.69)	
Non-dipper		16 (57.14)	20 (68.96)	
Raiser		9 (32.14)	3 (10.34)	
Circadian DBP, n (%)				
Extreme dipper		0 (0)	0 (0)	0.104‡
Dipper		14 (50.00)	7 (24.14)	
Non-dipper		8 (28.57)	15 (51.72)	
Raiser		6 (21.43)	7 (24.14)	

HOM-HT: high office measurement; NOM-HT: normal office measurement; SBP: systolic blood pressure; DBP: diastolic blood pressure: BP: blood pressure.
† independent samples t-test
‡ Chi-square test
*p<0.05
**p<0.01

Discussion

Patients using at least three antihypertensive medications in this study were assessed using an ABPM. Our results revealed a significant disagreement between office/clinic and ABPM measurements, indicating the existence of white coats and masked HT within the groups.

Whitecoat hypertension (WCH)

The (WCH) is a fundamental cause for false resistance defined as >20 / 10 mmHg increase in SBP/DBP values measured in the doctor's office compared to home or ABPM.[4,8] The white coat effect is more common in patients

with resistant HT than in the general hypertensive population.[5] The prevalence of false resistance is 20-45% in all hypertensive patients[5,9], including WCH in the hypertensive population. In Turkey, the reported rates vary in a wide range of 17-72%.[10,11]

The incidence of conversion of WCH to permanent HT is between 1-5% per year with ABPM.[12] Concerning the WCH, studies have found that these individuals have a higher cardiovascular risk than normotensive people but lower than those with persistent and masked HT.[13-15] In our study, the result that at least half of the HOM-HT group (53.67%) supposed to have resistant HT were found to have normal values measured by ABPM. This striking result is attributed to WCH, considering that our study design controlled other causes of false resistance such as inappropriate measurement and office settings, lack of rest, failure of taking the morning pill, etc. Moreover, the physician effect may inflict an additional contribution on this high rate since a physician performed the measurements, but not a nurse, in agreement with the studies that the white coat effect created by physicians is higher than that of nurses.[13] Detecting WCH is crucial to avoid unwanted adverse effects caused by excessive treatment and avoid unnecessary, expensive, and sometimes invasive approaches to investigate secondary causes of HT. Thus, the diagnosis of resistant HT is supposed to be confirmed with ABPM before further steps for the treatment and therapy are taken.[4,12]

Masked hypertension

Another finding of our study is that 17.24% of the NOM-HT group had masked resistant HT. While the prevalence of masked HT is between 10-26% in community studies, it may range from 14% to 30% in studies among normotensives,[16-18], according to the frequency obtained in our study. Unlike WCH, individuals with masked HT have similar cardiovascular risk and all-cause mortality rates as those with permanent HT. Secondary causes may also be found in patients with masked HT. However, in our study, none of the patients with masked HT had a secondary reason, probably due to the small sample size. On this basis, ABPM may be employed in routine clinical assessments not to miss the masked HT.

Secondary causes

Studies show that there may be underlying secondary causes of HT in 10-20% of hypertensive patients.[19] In our study, secondary causes of HT were detected in three patients, which constituted 10.71% of the HOM-HT group and was not significantly different from the NOM-HT, which had no such patients. The low rate of above threshold BP levels with ABPM, i.e., high rate of WCH in the HOM-HT group, is a potential explanation of this result. Indeed, this percentage increased to 16.66% (3 out of 18) within the true resistant patients (according to ABPM) and was significantly higher compared to patients with normal ABPM values (p=0.028). Of those three patients, one had primary hyperaldosteronism, which was reported to be found in 5-10% of HT patients, and around 20% in resistant HT.[20] We detected OSA in another patient who had a high score in the ESS and

confirmed by PSG. OSA prevalence in resistant HT is relatively high (>80%)[21,22], unlike our finding with one patient. This may be due to the low sensitivity of the ESS, which we used as a screening test.[23,24] In another patient, renal Doppler imaging revealed a mass was compressing the renal artery. The association between renal masses and hypertension is known with a frequency of 1-2%, which aligns with our finding.[25] This patient became free from HT after the removal of the mass. The BP values of these three patients with secondary HT were 164/107 mmHg, 161/103 mmHg, and 155/102 mmHg. Although it is not universally accepted, the threshold for HT was determined as >130/80 mmHg in the latest guideline published by the ACC/AHA in 2018.[26] Our study applied the threshold of ≥140/90 mmHg recommended by the European Society of Cardiology and Hypertension (ESC/ESH) in-office measurements. In our patients with detected secondary causes, BP values were well above the threshold given in both guidelines (systolic 20-30 mmHg more). This allows the conclusion that it may be helpful to investigate secondary causes in individuals with values far above the threshold.

Another issue considered in our study was the differences in circadian BP patterns between the groups. SBP "dipper" rate was two times higher in the NOM-HT group than the HOM-HT group, whereas the SBP "raiser" rate was three times higher in the HOM-HT group than the NOM-HT group. However, these differences were non-significant, probably due to the small sample size (type-2 error). Determining the dipping / non-dipping profile in ABPM is valuable because it predicts the prognosis associated with organ damage that may result in consequences such as cardiovascular mortality, microalbuminuria, left ventricular hypertrophy, and arterial stiffness.[27]

Study limitations

The limitations of our study that may be potential sources of bias should also be mentioned. The most important limitation is the small sample size. As mentioned before, the insignificant difference between the groups regarding the secondary causes may also be influenced by the power of the study and the presence of WCH in HOM-HT. Also, it is generally recommended to repeat ABPM within three to six months to confirm the diagnosis in individuals with WCH, which was not done in our study.[28] Given that HT is a progressive disease, it is possible for patients evaluated as WCH to convert to true resistant HT in the future. However, the opposite may also be likely.[29] Therefore, the study's cross-sectional design and the lack of confirmation with follow-up ABPMs are shortcomings. Also, as stated above, the ESS used for sleep apnea screening may be insufficient to detect OSA patients. Moreover, it has been shown that the patients' plasma renin and aldosterone levels may have been affected by antihypertensive usage.[30] Thus, renin and aldosterone levels should be interpreted with caution. On the other hand, obtaining information in standardized face-to-face interviews and investigating secondary HT causes in all patients are the strengths of our study.

In conclusion, in this study, around half (53.67%) of the patients supposed to have resistant HT in-office measurements had WCH, and 17.24% of the patients who were thought to be under control with treatment had masked HT as measured by ABPM. Our findings add to a growing corpus of research showing that ABPM predicts cardiovascular risks better than office measurements, can detect WCH, masked HT, non-typical circadian changes in BP, prevents unnecessary tests for the secondary causes, and should be performed before the diagnosis of resistant HT. Future research with a larger sample size in the Turkish population is needed to validate our findings.

Ethical considerations: All research procedures were evaluated and accepted by the Research Ethics Committee of Gülhane Military Medical Faculty Hospital, (date: 22.07.2010, decision number: 1491-957-10/1539) and were conducted in agreement with the ethical standards specified in the Declaration of Helsinki. Written informed consent was obtained from patients before they participated in this study.

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

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THE POSITIVITY RATE OF COVID-19 PCR TEST PERFORMED FOR SCREENING BEFORE THYROID FINE NEEDLE ASPIRATION BIOPSY

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Abstract

Objectives: Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome. Coronavirus 2 (SARS-CoV-2) is spreading rapidly around the world. Asymptomatic infection is highly contagious, potentially leading to viral spread. We aimed to determine the rate of patients positive for COVID-19 PCR performed for safety measures before thyroid fine-needle aspiration biopsy (FNAB).

Materials and Methods: The patients applied to Ankara City Hospital, Endocrinology and Metabolism Clinics between 15.03.2020 and 15.08.2020 and underwent routine COVID-19 PCR test before FNAB were evaluated retrospectively. Age, gender, history of hypertension and Type 2 Diabetes Mellitus (T2DM), use of levothyroxine (LT4) or antithyroid drug, 25-hydroxyvitamin D3 [25(OH)D3], TSH, freeT3 (fT3), free (fT4) levels, FNAB results were obtained from the records.

Results: Asymptomatic COVID-19 infection was detected in 29 (2.43%) of 1195 patients who underwent FNAB. There was no statistically significant difference between patients with COVID-19 PCR test positive asymptomatic and negative patients in terms of age, gender, median values of 25(OH)D3, TSH, fT3, fT4, the ratio of hypertension and T2DM.

Conclusion: The healthcare professionals work devotedly against COVID-19 infection, demonstrating a great example of struggle worldwide. FNAB is an invasive procedure requiring close contact. It should be known by the clinician that COVID-19 infection is associated with a high risk of transmission in asymptomatic patients. The rate of 2.43% in the population cannot be underestimated and indicates the importance of the use of personal protective equipment and taking infection prevention measures.

Keywords: SARS-CoV-2, COVID-19, asymptomatic infection, FNAB, screening.

Introduction

COVID-19, which emerged on 12 December 2019, spread rapidly and became the cause of the pandemic. From then until January 2022, there were over 340 million cases and over 5 million deaths of COVID-19. SARS-CoV-2 is the etiological agent in this pandemic disease, an enveloped, positive-sense, single-stranded RNA virus. COVID-19 infection presents with clinical symptoms ranging from asymptomatic infection to mild upper respiratory tract disease and severe interstitial pneumonia, and it may cause mortality in some patients. COVID-19 is a life-threatening condition with the highest infection rate and a long and slow incubation period.[1-2] The source of the massive community spread of SARS-CoV-2 is rapid viral spread, particularly by asymptomatic or pre-symptomatic carriers. Nasopharyngeal and oropharyngeal sampling is considered the gold standard method in diagnosing upper respiratory tract infections. RT-PCR is the most widely used test to diagnose COVID-19.[3] Thyroid nodules are a common clinical problem. Ultrasound-guided FNAB is the most accurate and essential method for detecting malignancy and monitoring thyroid nodules.[4]

Materials and Methods

Patients who applied to our Endocrinology and Metabolism Clinics between March 2020 and August 2020 for multinodular goiter (MNG), nodular goiter (NG), papillary thyroid cancer (PTC), follicular thyroid carcinoma (FTC), medullary thyroid carcinoma (MTC), noninvasive follicular thyroid neoplasms (NIFTP), operated recurrent MNG who underwent FNAB and who underwent routine COVID-19 PCR test for screening beforehand were retrospectively analyzed. During the study, all patients were tested within 72 hours before their planned FNAB. Real-time reverse transcription-quantitative PCR (RT-qPCR) testing analysis was performed from upper respiratory tract, nasopharyngeal and oropharyngeal swab samples. Patients' COVID PCR test results, age, gender, autoimmunity status (antithyroid peroxidase, antithyroglobulin, thyrotropin receptor antibody), history of hypertension, T2DM, and TSH, fT3, fT4, 25(OH)D3 levels, FNAB results were noted from the records. FNAB has been reported by the Bethesda System for Reporting Thyroid Cytopathology; a sampled nodule is classified as Bethesda I: Nondiagnostic, Bethesda II: Benign, Bethesda III- follicular lesion of undetermined significance (FLUS) or atypia of undetermined significance (AUS), Bethesda IV: Follicular neoplasm or suspicious for a follicular neoplasm, Bethesda V: Suspicious for malignancy, and Bethesda VI: Malignant.

Statistical analysis

The continuous variables were presented as median (minimum-maximum), and the categorical variables were presented as number and percentage. Normality analyzes of continuous variables were performed with the Kolmogorov-Smirnov Goodness of Fit Test. The data analysis that did not fit the normal distribution between

the two groups was performed with the Mann-Whitney U-test. Chi-square test and Fisher's exact test were used to compare categorical data. Analyzes were performed with IBM SPSS Package Program version 22.0 (IBM Corporation, Armonk, NY, USA). A p-value of < 0.05 was considered statistically significant.

Results

Asymptomatic COVID-19 infection was detected in 29 (2.43%) of 1195 patients who underwent FNAB. While the median age of asymptomatic patients was 53 (23-80) years, others were 50 (20-88) years. Female patients were in the majority in both groups. Although autoimmunity rates were higher in COVID-19 PCR positive asymptomatic patients (44.82%) than in patients with negative COVID-19 PCR (36.10%), the difference was not statistically significant (p=0.335). The mean 25(OH)D3 level of asymptomatic patients was 21.5 ng/ml. No statistically significant difference was found between patients with positive and negative COVID-19 PCR test in terms of age, gender, median values of 25(OH)D3, TSH, fT3, fT4, rates of hypertension, and T2DM (Table 1).

Table 1. The comparison of clinical and biochemical features of patients with COVID-19 PCR positive asymptomatic and negative patients

	COVID-19 PCR negative (n=1166)	**COVID-19 PCR positive asymptomatic (n=29)**	***p***
Age (years) [median (min-max)]	50 (20-88)	53 (23-80)	0.579*
Gender (n,%)			
female	898 (77.01)	22 (75.86)	0.826**
male	268 (23.80)	7 (24.13)	
25(OH)D3 (ng/ml) [median(min-max)]	18 (4-80)	21.5 (7-46)	0.168*
TSH (mU/L) [median (min-max)]	1.32 (0.1-48)	1.36 (0-17)	0.709*
fT3 (ng/L) [median (min-max)]	1.19 (0.3-2.29)	1.23 (1-2.04)	0.198*
fT4 (ng/dl) [median (min-max)]	3.22 (1-33.30)	3.30 (2-5)	0.166*
Autoimmunity (n,%)			
Negative	745 (66.16)	16 (55.17)	0.335**
Positive	421 (36.10)	13 (44.82)	
Hypertension (n,%)			
No	869 (74.52)	23 (79.31)	0.669**
Yes	297 (25.47)	6 (20.68)	
Type 2 Diabetes Mellitus (n,%)			
No	934 (80.10)	25 (86.20)	0.636**
Yes	232 (19.89)	4 (13.79)	

* Mann-Whitney U-test
** Fisher's exact test

The distribution of the clinical diagnoses of the patients in both groups is shown in Table 2. Among COVID-19 PCR-negative patients, 58% were euthyroid MNG, 7.4% were PTC, in COVID-19 PCR-positive asymptomatic patients, 58.6% were euthyroid MNG, 17.2% were PTC. MNG subtypes are shown in figure 1. 22.5% of COVID-19 PCR negative patients were using levothyroxine, 6.7% were using thyromazole, 20.7% of PCR positive

asymptomatic patients were using levothyroxine, and 10.3% were using thyromazole (Table 3). FNAB results of COVID-19 PCR positive asymptomatic patients and negative patients are indicated in the graphics (Figure 2-Figure 3).

Table 2. Distribution of clinical diagnoses of patients with COVID-19 PCR positive asymptomatic and negative patients

Clinical Diagnoses (n,%)		
	COVID-19 PCR negative (n=1166)	**COVID-19 PCR positive asymptomatic (n=29)**
MNG	1012 (86,79)	23 (79,31)
NG	22 (1,88)	1 (3,44)
PTC	86 (7,37)	5 (17,24)
MTC	2 (0,17)	0 (0,0)
FTC	1 (0,08)	0 (0,0)
NIFTP	1 (0,08)	0 (0,0)
Operated recurrent MNG	42 (3,60)	0 (0,0)

* Chi-square test

Table 3. Patients' thyroid drug use status

Thyroid medication (n,%)	**COVID-19 PCR negative (n=1166)**	**COVID-19 PCR positive (n=29)**	***p***
No medications	822 (70,6)	20 (69,0)	0.884*
Levothyroxine (LT4)	262 (22,5)	6 (20,7)	
Propylthiouracil (PTU)	2 (0,2)	0 (0,0)	
Methimazole (MMI)	78 (6,7)	3 (10,3)	

* Chi-square test

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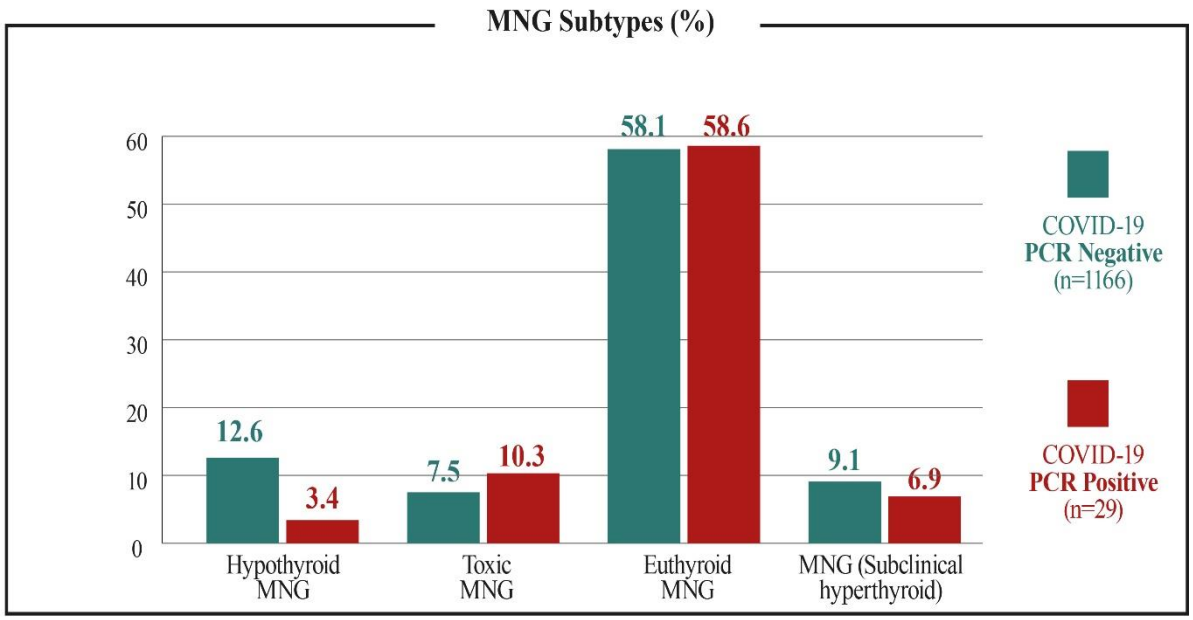

Figure 1. The patients with MNG were clinically grouped as hypothyroid MNG, toxic MNG, euthyroid MNG, MNG with subclinical hyperthyroid

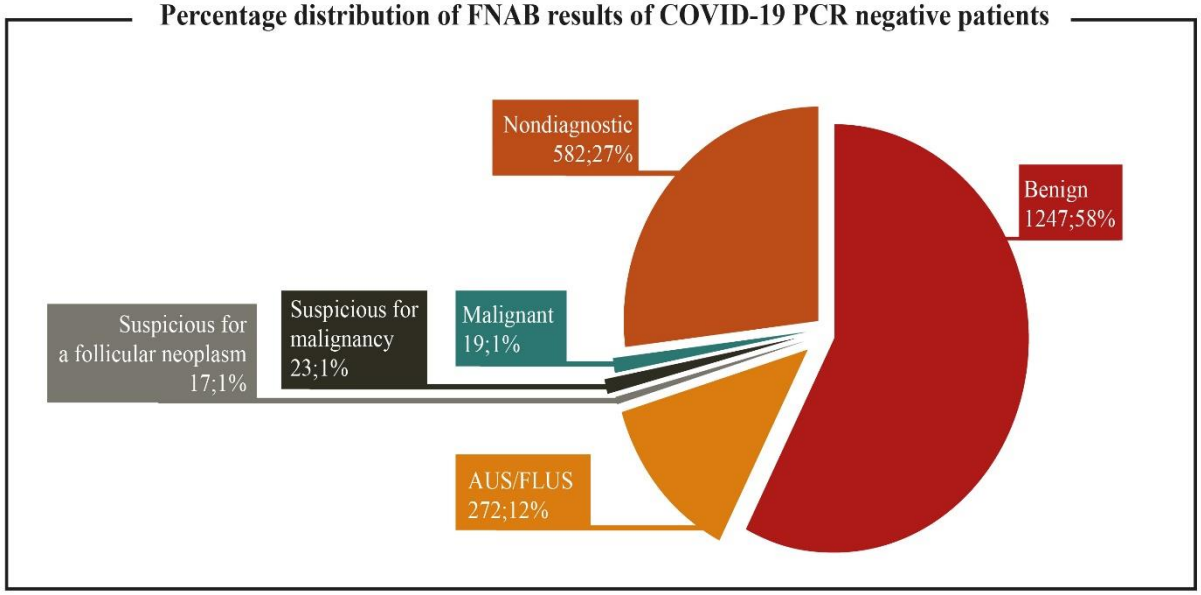

Figure 2. Results of 2160 nodules fine-needle aspiration biopsies, obtained from 1166 patients with COVID-19 PCR negative according to the Bethesda system. (The frequency of each Bethesda class was as follows: Bethesda I: 27%, Bethesda II: 58%, Bethesda III: 12%, Bethesda IV: 1%, Bethesda V: 1%, Bethesda VI: 1%)

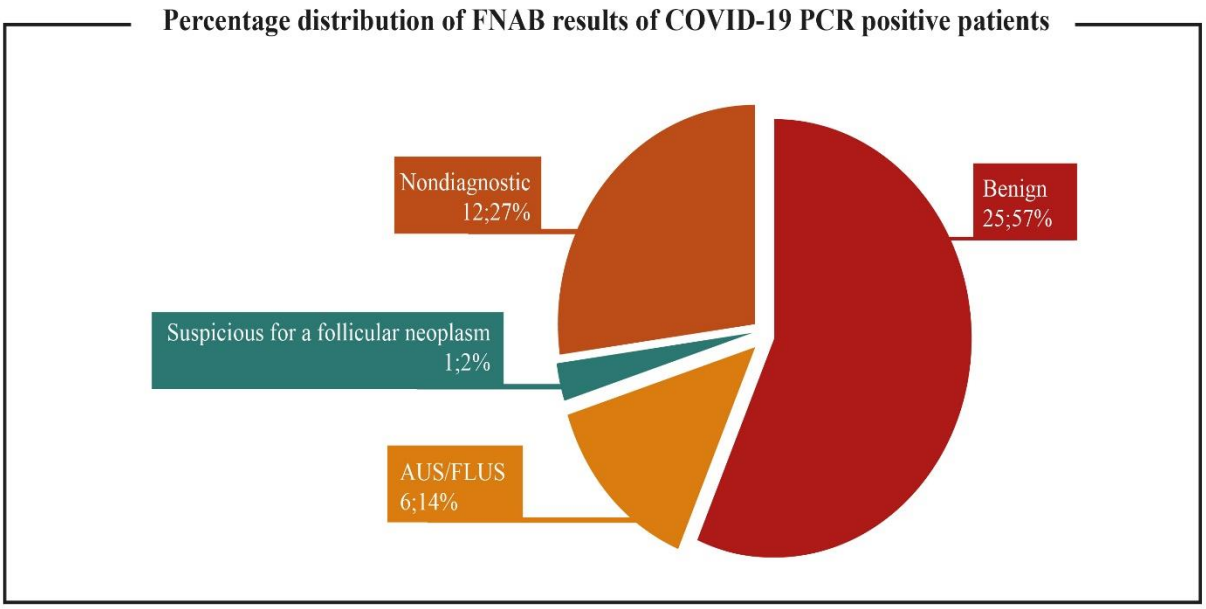

Figure 3. Results of 44 nodules fine-needle aspiration biopsies, obtained from 29 patients with COVID-19 PCR positive according to the Bethesda system. (The frequency of each Bethesda class was as follows: Bethesda I: 27%, Bethesda II: 57%, Bethesda III: 14%, Bethesda IV: 2%, Bethesda V: 0%, Bethesda VI: 0%)

Discussion

Our study found the rate of asymptomatic COVID-19 infection as 2.43% in 1195 patients for whom FNAB was planned. FNAB is an invasive procedure requiring close contact, and sometimes the contact time is prolonged depending on the number of nodules. The clinician should know that COVID-19 infection is associated with a high risk of transmission in asymptomatic patients, and this risk is also high in the early stages of the disease. Healthcare workers worldwide are working with great devotion against the COVID-19 infection and displaying a great example of struggle, which brings with it the risk of infection. In SARS-CoV infection, the transmission of infection to healthcare workers by infected patients is very common (33%-42%).[5] SARS-CoV-2 genome sequences have 79.5% similarity to the SARS-CoV genome sequence. The difference of COVID-19 from other coronavirus infections is that it has a less severe course but has a higher transmission rate.[6] Compared to asymptomatic patients with influenza, asymptomatic individuals with influenza had a shorter viral spread and lower viral load in their secretions.

Contrary to influenza, in a study, asymptomatic COVID-19 infection was defined as the achilles tendon of pandemic control to emphasize the importance of asymptomatic infection control.[7] Li et al.'s study, which compared patients with mild symptoms and asymptomatics in a cabin hospital in Wuhan, found that 74

(29.4%) patients in a total of 252 were asymptomatic. They detected pneumonia on CT imaging of 36 asymptomatic patients. This study found that the median transmission duration was seven days in asymptomatic and mildly symptomatic patients. This study, which showed that asymptomatic patients have the same risk of transmission as symptomatic patients, emphasizes the importance of quarantining asymptomatic individuals in disease control.[8] Han et al. in the study, asymptomatic and symptomatic patients with COVID-19 infection were compared, and it was found that asymptomatic patients had faster virus turnover, higher numbers of lymphocytes, T cells, B cells and natural killer cells, and low IgM, low LDH levels, and normal liver function tests. These results show that viral clearance is faster in asymptomatic patients because the viral load was determined at the same rate in both groups. The incubation period for COVID-19 infection can be up to 29 days.[9] The clinician should consider that COVID-19 infection is associated with a high risk of transmission in asymptomatic patients and only in patients with atypical presentations such as headache and fatigue, and this risk is at the same level in the early stages of the disease.[10] In a meta-analysis of 41 studies with 50.155 confirmed COVID-19 patients, the percentage of asymptomatic infection was 15.6%.[11] In a study, the prevalence of asymptomatic patients and the rate of COVID-19 asymptomatic infection in the cancer population was extremely low (4%).[12] The asymptomatic COVID-19 infection rate in pregnant women, a specific group, was determined as 5%.[13] A study carried out in the Obstetrics and Gynecology Department of Ankara City Hospital found that 3 (1.4%) of 206 pregnant women had asymptomatic PCR positive COVID-19 infection. These asymptomatic PCR-positive pregnancies were high-risk pregnancies.[14] In various studies, the rate of asymptomatic COVID-19 infection varies between 0.6-35.5%, although it varies by region. It has been determined that the rate of asymptomatic infection is low in China.[15] The rate of 2.43% in the population can not be underestimated and indicates the importance of using personal protective equipment and taking infection prevention measures for healthcare workers.

Significant destruction of thyroid follicular and parafollicular cells was observed in autopsies of patients with SARS, but no virus was detected in the thyroid. Studies have shown that thyroid dysfunction is not permanent.[16-17] Chang C. et al., in their study, 1811 FNAB cases between 2019-2020 and 1567 FNAB cases between 2020-2021 were screened. While a decrease was detected in FNAB cases in the pandemic, it was observed that the rate of atypical, suspicious and malignant cases decreased by only 5%. It was observed that the abnormal case rate was maintained before and during the pandemic.[18] In our study, there were 1195 FNAB cases within six months from the onset of the pandemic in our clinic. Nowadays, the number of FNAB performed in our clinic is 900 per month. When we compare it with the first period of the pandemic, there is an increase in monthly biopsies. With the recent emergence of the omicron variant, the number of asymptomatic cases seen in the last month has reached 30 patients. Although there is an increase in the number of patients undergoing a biopsy, there is also an increase in the number of asymptomatic patients. The fact that the number of asymptomatic patients seen in the last month and the number of asymptomatic patients seen in the first six months of the pandemic is approximately the same, indicates the high transmission rate of the omicron variant.

SARS-CoV-2 enters the host cell via ACE2 and TMPRSS2 receptors. These receptors are highly expressed in the thyroid gland. Thyrotoxicosis negatively affects the clinic of COVID-19 infection. Thyrotoxic patients with COVID-19 developed atrial fibrillation (32%) and thromboembolic events (16%).[19] Our study found that asymptomatic COVID-19 infection can also be detected in thyrotoxic patients under medical treatment. Thyroid hormones play essential roles in innate and adaptive immunity.[20] In a meta-analysis that included 21 studies and a total of 31339 patients, it was found that thyroid abnormalities and hypothyroidism were associated with worsening COVID-19, the age of the patient was important, but there was no such relationship in hyperthyroidism.[21] There are no data to suggest that patients with autoimmune thyroid disease are at higher risk for COVID-19. Treatment of asymptomatic or mildly symptomatic patients should be continued in the same dose.[22] In a systematic review of seven studies to evaluate the prevalence of thyroid dysfunction in COVID-19 patients, including 1237 COVID-19 patients, there was heterogeneity between studies, most COVID-19 patients were euthyroid, and there was a positive correlation between thyroid dysfunction and clinical severity of COVID-19.[23] In our study, there was no difference between the two groups in terms of TSH, fT4, fT3 values, and these values were within normal limits. We found that the most common diagnosis of our patients was euthyroid MNG.

This is the first study in the literature to determine the risk of asymptomatic COVID-19 infection in the group of patients scheduled for FNAB due to a thyroid nodule. The patient group planned for FNAB with a thyroid nodule is a specific but common population. It is an important study in which the rate of asymptomatic COVID-19 patients, the demographic characteristics, clinical and laboratory findings, and FNAB results are determined cross-sectionally in these days when the pandemic continues and the number of cases increases. Asymptomatic patients carry a risk of transmission for both healthcare workers and the community, and protocols are needed to manage asymptomatic patients to control the pandemic.

Ethical Considerations: Our cross-sectional study protocol was approved by the Ethics Committee of Ankara City Hospital (Signature number: E1-20-1106).

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

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Research Article

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ASSESSMENT OF SMOKING HABITS OF HEALTHCARE PROFESSIONALS DURING THE COVID-19 PANDEMIC PERIOD

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Abstract

Objectives: Our study aimed to assess the smoking habits of healthcare professionals who are at the forefront of the coronavirus disease-2019 (COVID-19) pandemic and are most exposed to the risk of getting infected and the factors affecting those habits.

Materials and Methods: All of 285 healthcare professionals who are 18 years old and over and are still smoking or quit smoking during the pandemic or started smoking during this period were included in the study. A sociodemographic data form, a questionnaire containing categorical questions on smoking behaviors and Beck's Anxiety Inventory were administered to the participants through face-to-face interview method.

Results: All of 31 participants (10.88%) did not smoke in the pre-pandemic period but started smoking during the pandemic period, 230 participants (80.70%) were smokers in the pre-pandemic period and still continued to smoke, and 24 (8.42%) participants quit smoking due to the pandemic while they were smoking in the pre-pandemic period. It was observed that healthcare professionals considering whether or not to quit smoking and considering that smoking increased deaths from COVID-19 infection experienced more anxiety (respectively p=0.012; p=0.027). It was also observed that healthcare professionals who had a COVID-19 infection and lost someone close to them due to COVID-19 significantly reduced the daily amount of cigarettes they smoked (respectively p=0.001; p=0.003).

Conclusion: Anxiety scores were found to be high among healthcare professionals who had COVID-19 and those who lost someone close to them due to COVID-19. It has been determined that the number of cigarettes smoked by healthcare professionals with high anxiety scores has decreased significantly.

Keywords: Anxiety, COVID-19, healthcare professional, smoking.

Introduction

According to the World Health Organization, smoking addiction is a situation that must be tackled globally. Smoking is one of the leading causes of preventable death worldwide. In our country, approximately 100,000-110,000 people lose their lives every year due to smoking-related diseases.[1]

The Severe Acute Respiratory Syndrome (SARS-CoV-2; COVID-19) virus, which emerged in China and spread all over the world, was declared as a COVID-19 pandemic by the World Health Organization in March 2020.[2-3] It is well-known that smoking increases the risk of respiratory viral and bacterial infections and is associated with worse outcomes in possible infections.[4-7] Moreover, it is believed that behavioral factors related to smoking (e.g., regular hand-to-mouth movements) may increase SARS-CoV-2 infection and transmission in smokers.[8]

Since healthcare professionals play an active role in the treatment of nicotine addiction and constitute a professional group that people may look up to, they have a special place in tobacco control studies. Therefore, the smoking status of healthcare professionals is essential. Pandemics also lead to many negative psychological consequences for healthcare professionals. Ignoring the psychological stress that healthcare professionals are exposed to causes significant negative consequences in the capacity of health services at both individual and societal levels.[9]

Our study aimed to assess the smoking habits and affecting factors in healthcare professionals who face increased workload, anxiety, stress and disease risk during the COVID-19 pandemic period.

Materials and Methods

This descriptive study was conducted between the dates of 1st of March and 31st of April 2021 at Ankara Training and Research Hospital and its affiliated district polyclinics. A total of 285 healthcare professionals of 18 years old and above who are currently working and still smoking or quit smoking during the pandemic or started smoking during the pandemic period were included in the study.

Non-smokers, including pre-pandemic and pandemic periods, were not included in the study.

The sociodemographic data form and a questionnaire aiming to determine the behavioral characteristics of the participants on their smoking habits were administered to the participants through face-to-face interview method. In the sociodemographic data form, participants were asked their age, gender, marital status, educational level, whether they have chronic diseases, whether they take medication regularly, whom they live

with at home, their COVID-19 status, length of hospital stay, whether they have complaints after COVID-19, whether there were any deaths due to COVID-19 among their household members, first-degree relatives or close circle outside of their family. Regarding their smoking habits, 20 questions were asked, including how their smoking status changed based on the pre-pandemic and post-pandemic period, the change in the number of cigarettes smoked, the age of first smoking, how many cigarettes smoked regularly, the number of cigarettes smoked per day, whether smoking increases the risk of COVID-19 infection, whether smoking increases death rates from COVID-19 infection and whether they consider quitting smoking. In addition, Beck's Anxiety Inventory consisting of 21 items, was applied to determine anxiety levels.[10]

The data collected during the research were transferred to the SPSS 25 software (Statistical Package for Social Sciences, version 25), and statistical analysis was performed. The normal distribution test was conducted using Kolmogorov-Smirnov and Shapiro-Wilk tests. The student's T-test was used to compare means between groups for those consistent with normal distribution, and the Mann Whitney-U test was used for those inconsistent with normal distribution. The Kruskal Wallis test was used for the statistical significance of the means between multiple dependent groups. The Chi-square test was used to compare categorical parameters. p-value<0.05 was considered statistically significant.

Results

A total of 285 healthcare professionals were involved in the study, including 95 (33.33%) doctors, 97 (34.04%) allied health professionals (nurses, midwives, health technicians, health officers, emergency medical technicians) and 93 (32.63%) other healthcare professionals (security personnel, cleaning staff, and clinical support personnel). Out of the participants, 123 (43.16%) were female, and 162 (56.84%) were male. Some sociodemographic characteristics of the participants are presented in Table 1.

While 52 (18.25%) of the participants had a chronic disease, 233 (81.75%) stated that they did not have any chronic disease. One hundred fourteen people (40%) smoked 0-10 cigarettes per day, 120 people (42.11%) smoked 11-20 cigarettes per day, 43 people (15.09%) smoked 21-30 per day, and eight people (2.81%) smoked more than 31 cigarettes per day.

When we look at the smoking status of the participants during the COVID-19 pandemic; 31 participants (10.88%) did not smoke in the pre-pandemic period but started smoking during the pandemic period, 230 participants (80.70%) used to smoke in the pre-pandemic period and continued to smoke, and 24 (8.42%) participants quit smoking due to the pandemic while they were smoking in the pre-pandemic period (Table 3).

Table 1. Sociodemographic Characteristics of the Participants

Sociodemographic Characteristics		**n**	**%**
Gender	Female	123	43.16
	Male	162	56.84
Marital Status	Married	169	59.29
	Unmarried	86	30.18
	Divorced	30	10.53
Education Level	Elementary	14	4.91
	Secondary	4	1.41
	High School	68	23.86
	Two-year degree (Associate)	51	17.89
	University and above	148	51.93
Professional Status	Doctor	95	33.33
	Allied Health Professionals	97	34.04
	Other Healthcare Professionals	93	32.63
Who does s/he live with at home	Alone	70	24.56
	Family or friend	215	75.44

Table 2. Disease, COVID-19 and Smoking Status of the Participants

Chronic Disease, COVID-19 and Smoking Status		**n**	**%**
Chronic disease	Yes	52	18.25
	No	233	81.75
Cigarettes/pieces smoked per day	0-10 pieces	114	40
	11-20 pieces	120	42.11
	21-30 pieces	43	15.09
	31+	8	2.81
COVID-19 infection status	Yes	71	24.91
	No	214	75.09
Hospitalization due to COVID-19	Yes	4	1.40
	No	281	98.60
Ongoing complaint after COVID-19 infection	Yes	20	28.17
	No	51	71.83
Death of someone close due to COVID-19 infection	Yes	47	16.49
	No	238	83.51

Table 3. The Smoking Status of Healthcare Professionals during the Pandemic Period

Smoking Characteristics		**n**	**%**
Smoking status	I was not a smoker in the pre-pandemic period, but I am now.	31	10.88
	I used to smoke in the pre-pandemic period, and I still do.	230	80.70
	I used to smoke in the pre-pandemic period, and now I do not, I quit.	24	8.42
The amount of smoking	The number of cigarettes I smoke has increased.	80	28.07
	The number of cigarettes I smoke did not change.	147	51.58
	The number of cigarettes I smoke has decreased.	58	20.35

While 213 (74.74%) of the participants thought that smoking increased deaths due to COVID-19, 72 (25.26%) stated that they did not think that smoking increased deaths due to COVID-19. Furthermore, while 181 (63.51%) of the participants were considering quitting smoking, 104 (36.49%) stated that they did not want to quit smoking.

The Beck's Anxiety Inventory mean score was found to be 10.32±9.19 (min=0, max=43). It was determined that 142 people (49.82%) did not have anxiety; 70 (24.56%) had mild anxiety, 53 (18.59%) had moderate anxiety, and 20 (7.02%) had severe anxiety. While no significant relationship was found between their anxiety status and age, it was observed that the number of cigarettes smoked increased significantly as the mean age declined (p=0.007). Anxiety scale scores were found to be significantly higher in female healthcare professionals (p=0.001). The anxiety scale scores of primary school graduates were high, and the anxiety scores of high school graduates were low (p=0.036).

Anxiety scores were significantly higher in healthcare professionals who lost someone close to them due to COVID-19 infection and in participants who smoked 21 or more cigarettes per day (respectively p=0.001; p=0.026). The anxiety levels of the participants who reduced the number of cigarettes they smoked daily during the pandemic period were found to be higher than those who did not change the amount of smoking and those who increased it, and this result was statistically significant (p=0.023). It was determined that healthcare professionals who considered quitting smoking experienced more anxiety than the other participants who did not (p=0.012). Moreover, it was found statistically significant that participants who thought that smoking increased death rates from COVID-19 infection had higher levels of anxiety (p=0.027).

It was observed among the participants that "other healthcare professionals (security, cleaning, clinical support)" decreased the number of cigarettes they smoked during the pandemic period more than doctors, and allied health professionals did, and this difference was significant (p=0.014). It was observed that healthcare professionals who had COVID-19 infection and lost someone close to them due to COVID-19 reduced the

number of cigarettes they smoked daily, and this result was significant (respectively p=0.001; p=0.003). It was observed that healthcare professionals who did not have COVID-19 infection increased the amount of smoking more than those who had infection did (p=0.001).

Among the participants, those who thought that smoking increased the risk of being infected by COVID-19 significantly reduced their daily cigarette consumption more than the other participants did (p<0.001). Healthcare professionals who thought that smoking increased death rates due to COVID-19 infection significantly reduced the amount of smoking compared to other participants (p<0.001). Healthcare professionals who were considering quitting smoking also reduced the number of cigarettes significantly that they smoked during the pandemic period (p<0.001).

Discussion

Our study assessed some biopsychosocial characteristics related to the smoking habits of healthcare professionals who work in a training & research hospital during the COVID-19 pandemic period.

In the study of Elling et al. on the general population named "Tobacco smoking and smoking cessation in times of COVID-19"; while 68% of the smokers indicated that the coronavirus did not influence the number of cigarettes smoked per day, 19% indicated that they smoked fewer cigarettes during the pandemic and 14% smoked more cigarettes per day due to the coronavirus.[11] In another study conducted by Arpacıoğlu et al. on the general population in the early period of the pandemic in December 2019, the number of smokers was 1271 and 48% of them stated that there was no change in their smoking, 15% increased their smoking and 37% reduced or quit smoking.[12] In the study of Klemperer et al. on the general population in the United States, it was observed that 28% of tobacco users reduced their tobacco use, 30% increased their tobacco use, and 42% did not change the amount of tobacco use during the COVID-19 period.[13] Similarly, in our study on healthcare professionals, it was determined that the number of cigarettes smoked by 28% of current smokers increased, the amount of smoking remained unchanged for 52%, and the number of cigarettes smoked by 20% declined. However, there are similarities when the studies are compared, both the population group in which the studies were conducted and the different pandemic periods in which the studies were carried out limit reliable comparisons. The tendency to quit or reduce smoking was found to be at a higher rate in the study conducted in the early period of the pandemic, which made us think that the tobacco use habits of people may have returned to the pre-pandemic situation after long-term quarantine and pandemic conditions, and there may be desensitization against the COVID-19 pandemic.

In a study conducted in our country during the COVID-19 pandemic and examining the psychological state of healthcare professionals, it was found that female healthcare professionals had higher anxiety and depression

scores than men.[14] In a study conducted in a tertiary pandemic hospital in China, the incidence of anxiety among female healthcare professionals and anxiety and stress disorder scores of females were found to be higher than male healthcare professionals.[15] In the literature, it was stated that four independent variables were found to be associated with the risk of anxiety among healthcare professionals, including living in rural areas, being at risk of contact with COVID-19 patients in hospitals, organic diseases, and being a woman.[16,17] In our study, anxiety was found to be higher in women, which supports the literature.

In a study by Stanton et al. in Australian adults during COVID-19, the average anxiety of single people was found to be significantly higher than those of married and divorced.[18] In a study conducted with healthcare professionals in our country, it was stated that the Health Anxiety Inventory scores of married healthcare professionals were lower than non-married ones.[14] In our study, the anxiety level of single healthcare professionals was, however, lower than the other two groups; but this difference was not statistically significant. The difference we observed in our study compared to the literature may be explained by the concern of healthcare professionals living with their families to transmit the disease from the work environment to the people they live with.

The anxiety levels of doctors and allied health professionals were found to be higher than other healthcare professionals in our study, but it did not make a significant difference. In a study conducted among healthcare professionals in a tertiary COVID-19 pandemic hospital in China, a higher incidence of anxiety and stress disorder was noted among healthcare professionals who were in direct contact with patients, and it was stated that the incidence of anxiety in nurses was higher than that of doctors.[1] In the literature, this has been attributed to the fact that the treatments are carried out by nurses, that nurses work longer hours than doctors in isolated wards, and that they have closer contact with patients. This situation made us think that high-risk contact with COVID-19 disease may be an important factor in the level of anxiety.

In the literature, it has been mentioned that healthcare professionals are afraid of carrying the disease home and transmitting it to their loved ones and family members, elderly parents, newborns and immunocompromised relatives.[19] In the study of Nguyen et al. on healthcare professionals in Vietnam; it was observed that the stress levels of those living with vulnerable groups were higher than the other group, and in two similar studies, it was reported that excessive workload, contact with heavy COVID-19 patients, infection and fear of infecting relatives caused stress in this group.[20-22] In our study, in accordance with the literature, the level of anxiety was found to be higher in healthcare professionals living with their families compared to those living alone, but it did not constitute a significant difference. This situation made us think that the thoughts of healthcare professionals to carry infection to their families during the COVID-19 period increased the level of anxiety.

Stress and boredom are known emotional triggers for smoking. Unexpected stress and increased stress at unusual times may be a significant risk for smoking. Especially the psychological effects of social isolation and increased stress may explain the increase in smoking rates.[12] In our study, the anxiety levels of the participants who stated that the amount of smoking decreased during the pandemic period were found to be significantly higher than the other two groups.

In a study conducted in Holland, a third of smokers were more willing to quit because of the coronavirus. Motivation to quit due to coronavirus was positively associated with beliefs that coronavirus is a serious threat, higher risk of being infected by the coronavirus and developing a serious illness, smokers being at a higher risk than non-smokers, and quitting smoking to reduce symptoms.[11] In a study on the general population among current and former smokers in Israel; it was stated that 66% of the participants were still smoking, 7% quit smoking in the first period of the restriction, and 44% of the smokers increased the amount of smoking while 16% tried to quit smoking.[23] 181 (64%) of the healthcare professionals who participated in our study stated that they were considering quitting smoking and 24 (8%) participants stated that they stopped smoking during the pandemic period. It was understood that the data of our study has similar smoking cessation data with the study conducted in Israel. Again, similar to the literature, it has been observed that those who have thoughts about the negative effects of smoking on COVID-19 infection (smoking increases the risk of COVID-19 infection and smoking increases death rates due to COVID-19 infection) are more inclined to reduce the amount of smoking.

The COVID-19 pandemic has made individuals much more open to smoking cessation advice. Thus, in our study, 64% of healthcare professionals stated that they wanted to quit smoking and 8% of healthcare professionals stated that they quit smoking during the pandemic period. There were significant differences in the amount of smoking among the participants with high levels of anxiety. As the level of anxiety increased, smoking decreased. In conclusion, the importance of combating smoking during the COVID-19 pandemic period has been understood once again. Support can be provided to healthcare professionals who can be seen as role models in society and who work in risky environments due to working conditions.

Ethical Considerations: Before initiating the study, approval was obtained from the Clinical Research Ethics Committee of Ankara Training and Research Hospital, University of Health Sciences by decision numbered 614/2021 and dated 24/02/2021.

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

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THE KNOWLEDGE ABOUT SEXUALITY AND SEXUALLY TRANSMITTED DISEASES OF SYRIAN WOMEN AND MEN IMMIGRATED TO HATAY-ANTAKYA: A QUALITATIVE STUDY

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Abstract

Objectives: The aim of this study is to comparatively present the knowledge and experiences about sexuality and the sexually transmitted infections in both the men and women migrating from Syria to the nearest province, Hatay-Antakya in Turkey, due to the ongoing internal conflicts in Syria.

Materials and Methods: The study consists of in-depth interviews with 12 female and 12 male participants who had to migrate from Syria. In the research, using the qualitative method, the findings were interpreted using the descriptive analysis technique.

Results: In consequence of the study, women and men were determined to have different knowledge levels on sexuality before marriage, especially women to have experienced it at first night after marriage and men to be more familiar with sexuality. To have a speech on sexuality and sex life before marriage is taboo, and it's keeping the "honor" under control for women. As they have not received sufficient education, they do not have enough information about sexually transmitted diseases (STD).

Conclusion: As a result, girls having been forced to get married at an early age have sexual experiences prematurely; their inadequate knowledge and experience about sexuality, belief and cultural truths cause certain traumatic processes. The education provided to men and women on sexuality and awareness about STD should be raised.

Keywords: Sexual health, sexually transmitted diseases, Syrian immigrants, primary health care, culture and disease, qualitative research.

Introduction

Having begun as a peaceful social movement in March 2011, the Syrian uprising turned into a war as a result of domestic clashes and exterior interventions.[1] According to United Nations Refugee Agency, the clashes in Syria have caused 6.2 million refugees to migrate to neighboring countries since 2011.[2,3] Turkey, located just by the Syrian border, has become nearly the most refugee receiving country.[4] While the number of Syrian immigrants under temporary protection status is 3,653,19 in Turkey; it is 437,095 in Hatay.[5] The immigrants' strong perception of human security in the country to immigrate increases the migration rate to that country.[6] Because of the security perception created by unending chaos, the migration still keeps going.

Even if migration has affected the neighboring countries, most Syrian immigrants have affected the world globally. Sexually Transmitted Diseases (STD) are one of these effects, and since these illnesses are carried through immigration, this issue is a global health problem.[7] Moreover, insufficient education about sexuality is also effective in STD contagion. Refugees have higher risks of getting STDs because of the factors related to displacement as a result of war and conflicts, including poor socio-economic situation and insecurity.[8] While socio-economic reasons lead people to migrate, they also obstruct these people from reaching the health system. Sexuality may constitute the most confidential side of the individuals, especially in traditional and patriarchal societies. Therefore, they may remain incapable of sexual knowledge and experiences, and some have limited or incorrect knowledge about STDs while others have no information. Hatay is one of the places where Syrians densely live in Turkey. Knowledge levels and attitudes about sexual knowledge and experiences and STDs of Syrian women and Syrian men who immigrated to Hatay-Antakya were discussed in this study with a qualitative approach.

Materials and Methods

A qualitative research method was used in this study. The qualitative study presents daily life practices and moods of the individuals, especially in migration-themed studies. In this way, accurate representations of human life can be introduced.[9] The discussed case in the qualitative study has a representation power whether it is singular or biographical, and the extent of sample discussed in a qualitative study is not supposed to be as in the quantitative study, because the significance of qualitative study results is their covering the empirical varieties and differences more than the extent of the sample.[10] The aim of the interview technique in qualitative studies is to determine the implications, silences, stresses and mimics of the interviewed person more than the determination of cold facts, and thus the findings are determined more effectively and thoroughly.[11] Semi-structured questions, snowball sampling and narrative techniques were used in the study. Narratives provide potential ways for revealing the comprehension of health and illness processes, how the subjective human experiences are shared and how the behavior is organized.[12] Medical anthropology and family medicine

specialists researched this topic together. Medical anthropology studies focus on the relationship between culture and health with qualitative studies. Health perceptions and practices are mostly affected by beliefs and traditions. Family Medicine discipline deals with biopsychosocial and cultural values with a holistic approach. Therefore, the togetherness of these disciplines and qualitative research techniques were preferred for this research. In this study, a total of 24 people, 12 women and 12 men, were interviewed. The age range of the women was 18-55 and 23-55 for men. The education levels of the participants are heterogenic, covering all steps (Table-1). One of the interview places is Immigrant Primary Health Center in Hatay-Antakya. 6 women and six men, 12 people in total, were interviewed in this center. They were interviewed in a special room for convenience in the company with an interpreter. The second interview place includes home or public areas. Interviewing with men was more difficult than with women. Some part of men put forwarded some reasons such as: not missing doctor row, going back to work as soon as it finishes or not making their wives wait. While women were more in comfort than men, some were tried to be interviewed with their kids in their lap. Participants from Hama, Homs, Idlib, Latakia and Aleppo were interviewed through 2 Syrian interpreters, one female and one male. Before starting the study, the participants were informed about the study and a pilot study was conducted with them. Privacy was tried to be provided by interviewing female participants with a female interpreter and men with a male. Voluntary Participant Form (VPF) was used in the research. VPF in Arabic and Turkish were used in the study, which was conducted in September and October 2019.

Table 1. General information for participants

Number	Sex	Age	Level of education	Marital status	City migrated from Syria	Year immigrated from Syria
P1	Female	35	High school	Widow	Idlib	2017
P2	Female	54	Secondary school	Widow	Humus	2015
P3	Female	31	Secondary school	Married	Idlib	2015
P4	Female	25	Diploma	Single	Latakia	2011
P5	Female	28	Diploma	Married	Idlib	2016
P6	Female	22	High school	Married	Latakia	2012
P7	Female	51	Secondary school	Married	Aleppo	2014
P8	Female	55	Elementary school	Married	Hama	2013
P9	Female	26	Secondary school	Married	Aleppo	2011
P10	Female	39	High school	Married	Latakia	2011
P11	Female	54	Secondary school	Widow	Humus	2015
P12	Female	43	Secondary school	Married	Idlib	2015
P13	Male	37	Diploma	Married	Hama	2013
P14	Male	50	Diploma	Married	Idlib	2018
P15	Male	55	College	Married	Idlib	2011
P16	Male	39	Diploma	Married	Hama	2016
P17	Male	33	College	Married	Latakia	2012
P18	Male	27	Diploma	Married	Latakia	2012
P19	Male	31	Diploma	Married	Latakia	2017
P20	Male	34	Diploma	Married	Latakia	2013
P21	Male	23	High school	Single	Latakia	2012
P22	Male	38	High school	Married	Hama	2017
P23	Male	31	Elementary school	Married	Aleppo	2013
P24	Male	28	Academic	Married	Aleppo	2015

Results

Sexuality as a taboo area: "shame" and "confidential"

The participants indicated sexuality as shame, it is not appropriate to talk about it clearly, and it should be a secret issue. Although high school and college students remarked that they learned from course books at school or from the internet, sexuality is not a freely spoken issue by women and men. Moreover, they remarked that their teachers did not cover this and similar issues in detail, and they wanted to skip another subject. The way to learn about first sexual experience differentiates between women and men. Most of the interviewed women got married at a young age, and they experienced the first experience without completing their developments. The sexual experience starting with marriage focuses on the child during the marriage. In addition, the sensations of women and men about the sexual experience throughout the marriage are different. *My husband told me that it is something nice, he is nice to me. Child strengthens the bond of love between spouses. It did not*

*affect our sexual life (*Participant, 15, P15). *We used to talk about sex more before having our children, but child necessarily affects. Now we talk about it less* (P10). In fact, the participant expresses that she/he experiences sexuality less. *You experience something more when you have no kids, but when you have kids, you fall into trouble. It doesn't come to your mind to talk about sexuality much* (P14). Sexuality is generally waved aside after having children (Table 2).

Table 2. Interview Quotes and Themes

Themes	**Interview Quotes**	
	Syrian Women	**Syrian Man**
Sexuality	Shame, Secret	Shame, Secret
First sexual experience knowledge	I learned at the night that I got married I learned from my husband. I learned from my fiancée. My mother never talks about it. It is a shame. I learned from a sibling or a friend. I learned from the ones who got married before me. I learned from school. My brother's wife expressed My paternal aunt expressed My mother-in-law expressed My maternal aunt expressed I learned from the internet	I learned with my wife when I married No one taught. It is not spoken with relatives, shame. Experienced friends expressed. It is not spoken with a brother or father. I learned from the internet I learned from school.
Perception of sexual life in marriage	We do not talk about sexuality. Children strengthen the bond of love. Children do not affect sexual life	We used to talk about it when we didn't have children Children affect the sexual life We used to talk about more at first. Child does not affect it, it is already standard. We had sexuality when we have no kids.
STD knowledge	I don't know STD I heard about STD but I do not know exactly. I heard about AIDS in Syria I heard about cervical cancer in Turkey.	AIDS Gonorrhea Penis's catching infection Developing a verruca on sexual organ I heard about cervical cancer in Turkey.

Sexual Knowledge and Experiences in Syrian Women

Sexuality, forming a taboo area, even sexual knowledge acquisition, is directly related to kinship relationships, especially in women. The participants generally express that they sometimes or never talk about sexuality besides not experiencing sexuality or, aunt or mother-in-law from family elders inform them about what will happen the night before the wedding when they get married. *I learned about it on my wedding day. My mother*

told me. However, it is a shame to talk about this with other people in our culture (P10). There are also women who learned from friends or siblings apart from the family elders. It also points out that they can share knowledge about sexuality with people they feel close to rather than elders. *I learned about it from my sisters and friends. They got married before me. They were experienced. The elders wouldn't talk with us about it. They would tell it on the wedding day before marriage. We did not have knowledge before it. The girls generally would be informed by their mothers or mother-in-law on the wedding day* (P2). Some of the participants indicated that they had no information about sexuality when they got married, and they couldn't have sexual relations in the first months of the marriage and learned about it in time. *I did not know about it; they did not even tell me about it when I got married; we did nothing in the first seven months, we slept just like siblings, something started to happen by learning something from someone as time went by* (P4). Knowledge about hymen together with first sexual experienced could be learned by women after they get married. As it is understood from the participant's statement below, the husband of the woman is seen to inspect whether she is a virgin or not, which is regarded as an "honor" symbol. *No one said anything. I found myself in bed after getting married. I bled when I was married for two months. I went to the doctor. It was my hymen's blood. Nevertheless, my husband had a try with me and then he had sex with me* (P8). Women's not having S turns their first sexual experiences into a fearful situation. *I did not have any education on it; even I was scared on the day I got married, I did not know what to do; nothing happened between us in the first six months, then he told me about it* (P2). *My mother told me about it. She told me just before the wedding, but I was scared a lot; there is no one who is not afraid of sexuality, everyone is frightened* (P6). *They told me about it when I wore my wedding costume. I did not know at all. I was deeply embarrassed, terrified. I did not know anything at all till I got married. Mostly paternal or maternal aunt expresses the sexual relation* (P9). *They explained too little. However, I got frightened. My husband behaved so nicely, he told me not to be afraid, and nothing will happen, but I was still frightened* (P5). Information about sexuality is obtained from the internet among youngsters. *No, I did not have any education, but I had searched on the net wonderingly* (P6).

Sexual Knowledge and Experiences in Syrian Men

Education on sexual knowledge hadn't been provided in men as in women. Mostly, they remarked to have learned about sexual knowledge and experiences and experienced sexuality when they got married. *We hadn't talked about these issues at all before getting married; we learned with my wife when we got married. We talked with friends after marriage. Indeed we got the education, too* (P15). *No one taught it; such issues are not spoken with relatives; you learn when you get married, you experience* (P13). Sexual knowledge is sometimes shared with friends by talking without getting married. Apart from that, mass media and wide-spreading internet networks led Syrian men to have more information about sexuality. *Some issues are expressed by experienced friends. It wasn't expressed at school, but they already learn most of them from the internet. This issue is not talked about with a relative, brother or father because it is a shame. It is talked about with friends* (P16). Although he

learns sexuality by reading, there also exist some people who say sexuality already inheres in humans, and it consists of a set of impulses appearing automatically when it is experienced. *I learned by reading. Sexuality already exists in human natality. It shows up when it finds a backcloth; we haven't talked about this issue with the others* (P14). The pulse in men is to learn sexuality by living instead of talking about sexuality with others. *I got married to my wife at the age of 16. She was 16. She fell pregnant after two months. I taught her* (P15).

STD Knowledge in Women and Men

Lack of sexual knowledge and experiences in women and men also caused them to have deficient knowledge of STDs. STD knowledge of women is much more limited compared to men. Yet already the most heard illness by two groups is AIDS. *I have no knowledge of sexually transmitted diseases. I am single now* (P4). *I just heard about AIDS disease; it is transmitted blood-borne or with sexuality* (P11). A Syrian woman summarizes the current situation with limited precautions taken: *My cousin was a health care worker; he used to tell about these diseases. For instance, he would say not to use others' razors; blood is contaminated. Male kids would be taught at mosques; we were informed not to go to women we do not know. For this reason, this disease would not be seen much in Syria* (P1). Syrian woman indicated as: *Yes, I heard about STD. It results from polygamy (*P3). Man can get married to four women in Syria. There also exist perceptions that this situation increases STD. *I was informed at high school in Syria. It occurs when men go to prostitutes. It occurs at women you do not know without taking precautions, not using preservatives. The ones having AIDS do not tell anyone. People look differently at patients with AIDS. They do not draw near to* (P10). The reality that AIDS disease in the expressions of the participants is especially hidden indicates that this disease is more common than we think. STD knowledge of men is a little bit more than women. *I have heard about AIDS and gonorrhea. I know they are transmitted sexually or blood-borne* (P13). Although they do not know the whole names of some diseases, they can describe their symptoms*. Yes, I heard about it. I also heard of AIDS disease. There is an illness like erupting acne around the organ. I do not know its name now, but it is also a venereal illness* (P10). There are also illnesses whose names are forgotten. *There may occur AIDS or maturation on the penis. I forgot the names of the illnesses* (P15). In addition, one said there is a relation between STD and religious beliefs. Based upon this belief, there also exists a notion that STDs won't be common in Islamic countries. *"I heard about venereal diseases. For instance, I heard about AIDS, acne erupts at the sexual organ, but actually, there aren't many venereal diseases in Islamic countries. The sexual act is not free insomuch in Islamic countries. It is a sin religiously. Everyone's peer is definite, there is no reason to get the disease, but we used to hear about it."* (P14). In conclusion, while women say they heard about AIDS in Syria, they do not know about STDs. They heard about STDs but did not know at all; men sort the diseases as AIDS, gonorrhea, penis's catching an infection, developing a verruca on a sexual organ.

Discussion

Culturally, the Middle East is a conservative society where sexuality or sexual violence issues are social taboos or personal matters.[13,14] Cultural and religious beliefs about sexuality may prevent refugees from openly discussing issues related to sexual health, such as sex before marriage or birth control.[14,15,16] In Arabic countries and Iran (except for some exceptions in Iran, Algeria, Djibouti, Sudan and Tunisia), the sexual and reproductive health of youngsters proceed to be discussed because of the taboos and religious sanctions against sexual relations before or outside marriage.[17] Talking about sexuality and STDs for Syrians is one of the sensitive subjects.[18] Women learn about sexuality by experiencing it with their husbands. It is expressed by first-degree relatives from school or the internet. Men learn about sexuality when they get married, from friends, school or the internet. While first-degree relatives give women little information, this is out of the question for men. Since sexuality is already seen as taboo, talking about sexuality with a relative reveals layered privacy. Since sexuality is approved as it can be experienced after marriage and it is not appropriate to talk about sex before marriage, the perception that sex is an issue to be ashamed of is understood to be common in our study. Whole participants being Muslim, emphasize that it is forbidden to have sexual relations outside marriage by their belief. Early marriage or traditions and beliefs specific to their country may result in deficiency of education on social gender roles, sexual knowledge, common public policies and STD. Besides, the migration factor is a reason in itself. Refugees' being separated from their regular sexual partners their problems in achieving health and social services increase their risk to catch STDs. [19] In addition to this, refugees' limited knowledge on STIs or their concealing/neglecting the disease is a risk threat both for the places they came from or they settled in. Most of the refugees in Malta did not use preservatives during sexual relations, their education/knowledge was detected to be low, and most of the research participants hadn't had AIDS tests in advance.[20] Hepatitis B-C and HIV/AIDS were seen to be more in refugees in New Zealand.[21] Male refugee laborers in Tanzania carry a higher risk of catching STIs relative to women.[22] While women, gonorrhea, infection on sexual organ or verruca know only HIV/AIDS are sorted as STD by men. STIs symptoms were detected in %50,2 of Syrian women in Şanlıurfa.[23] As to the findings obtained in the study, a preservative is not a commonly preferred preservation method. One of the reasons that Syrian men are not using preservatives for protection is their thought that "a human-made" thing is an obstacle for given fertility. Moreover, since women and men get married at early ages not have sufficient education on sexuality and STDs, they are at risk of STDs. Having deficient sexual and reproductive health knowledge, Syrian refugee mothers in Jordan perceived STD treatment as "not effective". They have a fear of embarrassment and breach of confidentiality.[24] Both female and male participants mostly know about HIV/AIDS. Knowledge on contamination of HIV/AIDS in the Middle East and North Africa is limited. [25] 5000 HIV/AIDS infection is estimated to be in Iran in 2016.[26] There is a relation between the spreading of the HIV/AIDS virus and poverty. Inadequate economic conditions, treatment, not having necessary medicines cause AIDS to spread.[27] WHO reported annual HIV infections to decrease in some regions while they increase

in the East Mediterranean region. Estimated infection number has the highest rate of increase by rising from 29.000 infections in 2010 to 36.000 in 2017.[28] The effect of Syrian immigrants should not be neglected in the aforesaid region between the years 2010-2017. The rate of HPV in Syrian patients was similar to women in our country, and the most common are other types of high-risk HPV.[29] Finally, some of both female and male participants indicated to have learned about cervical cancer after coming to Turkey.

The findings obtained in this study indicate the sexual knowledge and experiences and STD knowledge of Syrian immigrants to be insufficient. With the Syrian immigrants turned into a problem of the global world, insufficient information has spread to the whole world. When the massive extent of migration is considered, this situation may be reviewed to be a threat risk for public health. Training activities need to be conducted against this threat risk. In patriarchal tradition, knowledge on sexuality and sexually transmitted diseases that are related to this is gained in line with social norms' expectations. Thusly, the content of the training should be formed on eliminating common misconceptions about sexually transmitted diseases and social gender inequality.

Ethical Considerations: Ethical approval of this study was given by Hatay Mustafa Kemal University Social Sciences Ethics Committee with the decision dated 07.03.2019 and numbered 07.

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

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THE RELATIONSHIP BETWEEN CHILDREN WITH PSYCHIATRIC DISORDER AND PERSONALITY TRAITS OF THEIR MOTHERS

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Abstract

Objectives: The aim of our study was to determine whether there is a relationship between maternal personality traits and the child's psychiatric disorder.

Materials and Methods: The data for this cross-sectional case-control study were collected from mothers of 134 children with a psychiatric disorder who applied to the child psychiatry department of a university hospital between February and June 2021 and the mothers of 92 children without any psychiatric disorders. Participants were evaluated by using Eysenck Personality Questionnaire Revised-Short Form.

Results: A total of 226 mothers participated in our study, 59.29% (134) of whom were the mothers of a child diagnosed with a psychiatric disorder, and 40.71% (92) were the mothers of a healthy child. The neuroticism and psychoticism scores were significantly higher in the mothers of the patient group, and the extraversion score was significantly higher in the mothers of the control group. ($p<0.001$). There was no significant difference between the two groups in terms of lie traits scores ($p=0.309$). While the highest maternal extraversion scores were seen in the group with skin picking disorder followed by attention deficit and hyperactivity disorder (ADHD), the highest lie traits score was found in the mothers of children with ADHD. Neuroticism and psychoticism scores were the highest, while extraversion scores were the lowest in mothers of children with intellectual disabilities.

Conclusion: We determined that there was a significant relationship between the presence of psychiatric disorders in children and the personality traits of the mothers.

Keywords: Maternal personality, psychiatric disorder, child, adolescent.

Introduction

Personality is the sum of innate and acquired characteristics that distinguishes an individual from others and is the process of an individual exhibiting his/her mental, emotional, physical and social aspects in a consistent manner.[1] Both environmental and genetic factors play a role in the development of personality. While the intelligence levels, personality traits and skills of the parents constitute the genetic aspect of the child's personality development, environmental factors are the child's family characteristics, nutrition, and experiences with her/his five senses.[2] Along with the personality development of the child, adaptation to the environment and behavior style are also affected by the personality traits of the parents. The most important identification object since the birth of the child is the mother. For this reason, it is inevitable that the behavioral characteristics of the child and the ability to cope with stressful life events are affected by the personality trait of the mother.[3] The relationship between the diagnosis of the child's psychiatric disorder and the personality traits of the mothers were investigated in the context of various disorders. In one study, mothers of children with obsessive-compulsive disorder (OCD) were found to have high novelty seeking and low self-directedness and cooperative attitudes.[4] Mothers of children with encopresis have been shown to be intrusive, neat, meticulous, strict, and overly anxious.[5] Therefore, a mother with maladaptive personality traits can negatively affect the child's upbringing behavior and the child's mental health.[6]

There are a limited number of studies investigating the relationship between the mother's personality trait and the child's susceptibility to psychiatric disorders and which psychiatric disorder is associated with which trait of the mother's personality. In this study, we aimed to compare and evaluate the personality traits of mothers of children and adolescents aged 3-18 years who were followed up and treated with any psychiatric disorder in the child psychiatry outpatient clinic with the personality traits of mothers of the children without any psychiatric disorders.

Materials and Methods

Study Design

This cross-sectional case-control study was conducted in Yozgat Bozok University Child and Adolescent Psychiatry Outpatient Clinic. Data were collected between February and June 2021. Psychiatric diagnoses of children and adolescents were made according to the criteria of the diagnostic and statistical manual of mental disorders (DSM-5) and affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL), which is based on DSM-IV. Mothers of children and adolescents who applied to our outpatient clinic were informed about the study, and verbal consents were obtained from those who agreed to participate in the study. They filled out the data collection forms in approximately 10 minutes. Data were

privately collected in an isolated room. The control group consisted of mothers of children and adolescents who had never been diagnosed with a psychiatric disorder, did not apply to the child psychiatry department, and were not followed up and treated. These children and adolescents were the participants who applied to the general pediatric outpatient clinic for a routine check-up. These children and their mothers were also evaluated with the same procedure applied to the patient group.

Sampling

The study consisted of mothers of children and adolescents who applied to the Child and Adolescent Psychiatry outpatient clinic and the mothers of children and adolescents who did not have any psychiatric disorder diagnosis. When the value for type error (alpha) was 0.05, the power of the test (1-beta) was 0.8, the effect size was 0.42, and the alternative hypothesis (H1) was one-sided the minimum sample size required to find a significant difference using this test was determined as 85 in each group and 170 in total. We included 180 mothers by considering the possibility of losing some of the cases, and to increase the power of the study. However, 12 illiterate mothers and 34 mothers who did not want to fill in the questionnaires were not included in the study. Thus, the data from 134 mothers were included in the statistical analysis. The mothers of 92 children and adolescents without any psychiatric disorder diagnoses were classified as the control group. The inclusion criteria for the study group were being literate, having the ability to communicate (no mental problems, no visual/hearing impairment), having a child diagnosed with a psychiatric disorder by a child psychiatrist, and willingness to participate in the study voluntarily. Meanwhile, the exclusion criteria for the study group were being illiterate, having an intellectual disability, having a visual, speech and hearing disability, having a child without a diagnosed psychiatric disorder, and refusing to participate in the study.

Assessments

The psychiatric disorder diagnoses of children and adolescents were reviewed using the criteria of the diagnostic and statistical manual of mental disorders (DSM-5) and affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL). The personality traits of mothers were evaluated with the Eysenck Personality Questionnaire Revised-Short Form (EPQR-S).

K-SADS-PL (Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime version)

The K-SADS-PL is a widely used semi-structured diagnostic interview tool used to assess current and past episodes of child and adolescent psychiatric disorders. The Turkish version of the K-SADS-PL has good test-retest and inter-rater reliability.[7,8] In this study, K-SADS-PL was used together with DSM-5 diagnostic criteria to determine psychiatric diagnoses.

Eysenck Personality Questionnaire Revised-Short Form (EPQR-S)

Francis et al. (1992) reviewed the Eysenck Personality Questionnaire[9] and its short form (48 items)[10] and created the EPQR-S. The validity and reliability study of the scale for the Turkish population was conducted by Karancı et al. (2007).[11] The questionnaire consists of 24 items and evaluates personality in 3 main factors: extraversion, neuroticism, and psychoticism. The lie subscale aims to prevent bias during the application of the questionnaire and to control its validity. In this questionnaire, in which each factor is evaluated with six items, the participant is asked to answer 24 questions in the format of Yes (1)-No (0). The score that can be obtained for each personality trait varies between 0 and 6. Internal consistency values of the scale for its subscales are 0.78 for extraversion, 0.65 for neuroticism, 0.42 for psychoticism, and 0.64 for the lie.

Statistical Analysis

All statistical analyses were performed using SPSS v.20.0 (IBM Corp., Armonk, NY, USA) software. The results were stated in the tables as number and percentage (%), median, and interquartile range (25-75 p) values. The Kolmogorov-Smirnov test was used to assess the normal distribution of the variables. For continuous variables, the statistical difference between the two groups was calculated using the Mann-Whitney U test. Non-normally distributed data were compared using the Kruskal-Wallis test. Correlations between subscales in the groups were analyzed using Spearman's correlation test. A value of $p<0.05$ was accepted as statistically significant.

Results

Among 226 mothers that participated in the study, 59.29% (n=134) were mothers of children and adolescents with a psychiatric disorder diagnosis according to K-SADS-PL and DSM-5, and 40.71% (n=92) were mothers of children and adolescents without any psychiatric disorder diagnoses. The distribution of psychiatric diagnoses of children is shown in Table 1. The neuroticism and psychoticism scores of the mothers in the psychiatric disorder group were significantly higher than those of the mothers in the control group ($p <0.001$). The extraversion score was significantly higher in the control group ($p <0.001$). There was no significant difference between the two groups for lie traits scores ($p = 0.309$) (Table 2). When we examined the psychiatric disorders in children one by one, children whose mothers had the highest extraversion score had skin picking disorder followed by ADHD. Mothers of children with intellectual disabilities had the lowest extraversion score. Mothers of children with ADHD and tic disorders had the highest lie traits score, while the lowest lie traits scores were seen in mothers of children with trichotillomania. The highest neuroticism score was observed in mothers of children with intellectual disability, while the lowest was detected in mothers of children with trichotillomania

and stuttering. The maternal psychoticism score was the highest for children with intellectual disabilities (Table 3). When we examined the psychiatric disorders one by one, we found that the extraversion score was significantly lower than the control group in all psychiatric disorders except tic disorders, skin picking disorder, trichotillomania and stuttering. The Lie traits score was significantly higher only in the mothers of children with ADHD compared to the control group (p=0.010). The neuroticism score was significantly higher in mothers of children with panic disorder, intellectual disability, autism spectrum disorders, obsessive-compulsive disorder, tic disorders and anorexia nervosa compared to the control group. The psychoticism score was significantly higher in mothers of children with ADHD, major depressive disorder, intellectual disability, autism spectrum disorders and skin picking disorder compared to the healthy mothers (Table 3). When we analyzed the subscale scores of the patient and control groups with Spearman's correlation analysis, only a negative significant correlation was observed between extraversion and neuroticism in the mothers of the patient group (r=-0.248, p=0.004). In the control group mothers, there was a negative correlation between extraversion and neuroticism (r=-0.246, p=0.031) and a positive correlation with lie traits (r=0.373, p=<0.001). When we evaluated psychiatric disorders categorically based on the dimensional classification in DSM-5 instead of individually, no significant relationship was found between maternal personality scale scores and children's psychiatric disorders (Table 4).

Table 1. Psychiatric diagnosis distribution of the participants' children (n=226)

Psychiatric disorders	**n (226)**	**%**
Absent	92	40.71
ADHD	39	17.25
MDD	19	8.40
GAD	9	3.98
Panic disorder	8	3.53
ASD	11	4.86
ID	10	4.42
Tic disorders	9	3.98
Anorexia nervosa	6	2.65
OCD	10	4.42
SPD	4	1.76
Trichotillomania	4	1.76
Stuttering	5	2.21

ADHD: Attention deficit and hyperactivity disorder, MDD: Major depressive disorder, GAD: Generalized anxiety disorder, ASD: Autism spectrum disorders, ID: Intellectual disability, OCD: Obsessive-compulsive disorder, SPD: Skin picking disorder.

Table 2. Mean EPQR-S subscale scores of mothers of children with and without a psychiatric diagnosis (n=226)

EPQR-S subscales	Psychiatric disorder		P*
	Present (134)	Absent (92)	
Extraversion	4 (3-5)	5 (4-6)	<0.001
Lie traits	5 (5-6)	5 (4-6)	0.309
Neuroticism	4 (3-5)	3 (2-4)	<0.001
Psychoticism	1 (0-2)	0 (0-1)	<0.001

*Mann Whitney U Test, All data presented as median (percentile 25-75)

Table 3. The relationship between the mean EPQR-S subscales of the mothers of the patient and control groups and psychiatric disorders in children

Psychiatric disorders (n)	Extraversion*	p#	Lie traits¥	p#	Neuroticism*	p#	Psychoticism*	p#
Absent (92)	5 (4-6)		5 (4-6)		3 (2-4)		0 (0-1)	
ADHD (39)	5 (3-5)	**0.019**	6 (5-6)	**0.010**	3 (3-5)	0.184	1 (0-1)	**0.005**
MDD (19)	4 (3-5)	**0.009**	5 (4-6)	0.712	3 (2-5)	0.712	1 (0-2)	**0.004**
GAD (9)	3 (2-4)	**0.001**	5 (4-6)	0.681	3 (2-5)	0.750	0 (0-1)	0.732
Panic disorder (8)	4 (2.5-4.5)	**0.005**	5 (4-5)	0.282	4.5 (3.5-5)	**0.045**	0 (0-1)	0.982
ASD (11)	4 (2-5)	**0.005**	5 (5-6)	0.707	5 (5-6)	**<0.001**	1 (1-2)	**0.001**
ID (10)	2 (2-3)	**<0.001**	5 (5-5)	0.914	5.5 (5-6)	**<0.001**	2 (2-3)	**<0.001**
Tic disorders (9)	4 (3-5)	0.092	6 (5-6)	0.053	5 (5-6)	**<0.001**	0 (0-1)	0.789
Anorexia nervosa (6)	2.5 (2-5)	**0.007**	5 (5-5)	0.918	5 (5-6)	**0.007**	1 (0-1)	0.213
OCD (10)	3.5 (2-5)	**0.015**	5.5 (5-6)	0.145	4 (3-5)	**0.031**	1 (0-1)	0.396
SPD (4)	5.5 (4.5-6)	0.609	5 (4.5-5)	0.475	3.5 (3-4)	0.704	2 (1.5-2.5)	**0.002**
Trichotillomania (4)	4 (3-4.5)	0.053	2.5 (2-3)	0.001	2 (1.5-2.5)	**0.032**	0 (0-0.5)	0.510
Stuttering (5)	6 (5-6)	0.339	5 (5-6)	0.312	2 (2-2)	**0.015**	0 (0-1)	0.858

ADHD, Attention deficit and hyperactivity disorder; MDD, Major depressive disorder; GAD, Generalized anxiety disorder; ASD, Autism spectrum disorders; ID, Intellectual disability; OCD, Obsessive-compulsive disorder; SPD, Skin picking disorder.

¥p=0.006, *p<0.001; Kruskal-Wallis H test. p#: according to the Absent group (Mann–Whitney U test was used for comparison of the absent control group and the psychiatric disorders groups).

All data presented as median (percentile 25-75). Bold values indicate statistical significance.

Table 4. Comparison of maternal EPQR-S subscales scores when psychiatric diagnoses in children were categorized according to DSM-5

Psychiatric disorders (n)	Extraversion	p *	Lie traits	p *	Neuroticism	P *	Psychoticism	p *
Neurodevelopmental disorders	4 (3-5)		5 (5-6)		5 (3-6)		1 (0-2)	
Depression disorders	4 (3-5)		5 (4-6)		3 (2-5)		1 (0-2)	
Anxiety disorders	4 (2-4)	0.347	5 (4-5)	0.051	4 (3-5)	0.059	0 (0-1)	0.247
Obsessive-compulsive and related disorders	4 (3-5)		5 (4-6)		4 (3-4)		1 (0-1)	
Eating disorders	3 (2-5)		5 (5-5)		5 (5-6)		1 (0-1)	

*Kruskal-Wallis H test, All data presented as median (percentile 25-75)

Discussion

The aim of our study was to determine whether there is a relationship between the maternal personality traits and the child's psychiatric disorder and to determine which pediatric psychiatric diagnoses are associated with which maternal personality trait. The results of our study indicated that the presence of any psychiatric disorder in the child was associated with a high level of maternal neuroticism and psychoticism scores. The extraversion scores were higher in the mothers of the control group. When psychiatric disorders were categorized according to DSM-5, there was no significant relationship between maternal personality traits and psychiatric groups, but when disorders were evaluated individually, maternal personality traits were found to be associated with specific psychiatric disorders. Extraversion and lie traits scores of mothers of children with ADHD were higher than those of mothers of children with other diagnoses. At the same time, when compared with the control group, the lying traits scores of mothers of only ADHD children were significantly higher. Neuroticism and psychoticism scores were highest, while the extraversion scores were the lowest in mothers of children with intellectual disabilities. Extraversion and neuroticism personality traits were inversely correlated in both the patient and control groups. In addition, extraversion and lie traits were significantly correlated in the same direction in the control group.

Studies have suggested that when examining children's psychiatric problems and their loss of function, it is necessary to evaluate family relationships and personality traits of parents[12]. In particular, it is inevitable that the personality traits of the mother, who has a long-term relationship with her child from birth, affect the child's emotions, attitudes and behaviors. The child identifies his/her mother as a model and is directly affected by her attitudes and behaviors, and has a genetic connection[3]. In our study, we found that the presence of psychiatric disorders in the child and some specific diagnoses were associated with the personality traits of the

mother. It is argued that the extraversion subscale, which is one of the personality dimensions categorized by Eysenck, is associated with warmth, thrill-seeking, sociability, impulsivity, and uncontrolled emotions. It was also stated that neuroticism is associated with fear, anxiety, depression, and low self-esteem, while psychoticism is associated with anger, aggression, insensitivity to other people, lack of empathy, and antisocial behaviors. The lie subscale is used to check the validity of the scale and to measure bias.[9] In one study, more psychiatric disorders were found in the children of neurotic mothers.[13] Similarly, we found the neuroticism scores of the mothers of children with panic disorder, intellectual disability, autism spectrum disorders, obsessive-compulsive disorder, tic disorders and anorexia nervosa to be higher than the mothers of the control group. In a study conducted in Turkey, an increase in maternal neuroticism, psychoticism, and lie subscales was associated with an increase in attention problems, destructive behaviors, depression and anxiety symptoms in adolescents.[14] In a study using different personality scales, mothers of children with OCD were reported to have low self-directedness and cooperation, while mothers of children with encopresis had authoritarian, meticulous, spiteful, and normative personality traits[4,5]. In a study on children with separation anxiety disorder in which the temperament rating scale was used, the mothers of these children were found to have high irritability, depressive, cyclothymic, and anxious personality scores.[15] The extraversion subscale was found to be significantly higher in the control group. This sub-dimension includes impulsivity and uncontrolled behaviors, as well as positive features such as sociability, warmth and love.[9] In a study by Aksoy et al., as the extraverted personality traits of mothers with daughters increased, it was determined that social anxiety in children decreased and children's adaptation to life increased.[16] In our study, we found the extraversion and lie subscales of mothers of children with ADHD to be high. Similarly, one study found that the extraversion score of parents of children with ADHD was correlated with the child's behavioral problems.[17] Because extroversion is associated with positive traits such as warmth and sociability, as well as negative traits such as impulsivity, uncontrolled behaviors, and exaggerated emotions..[9] Although the etiology of ADHD is heterogeneous, the presence of ADHD in the parent increases the risk of ADHD in the child 2-8 times.[18] In a study, high extraversion, low agreeableness, and low reactive control were associated with specific hyperactivity-impulsivity and general ADHD.[19] For this reason, high extraversion scores in mothers may be expected in ADHD, where the genetic load is evident. Therefore, it is thought that the extraversion sub-dimension may have good and bad aspects depending on the situation. As a matter of fact, there are also studies stating that each of the personality traits has strengths and weaknesses and that no personality type is better than the other.[20] Also, mothers of children with ADHD had higher lie traits scores as well as extraversion scores. Prior literature has documented high neuroticism and low conscientiousness in mothers of children with ADHD.[21]People with a low conscience are defined as those who do not trust their words and do not recognize the rules, only success-oriented.[22] As much as an extroverted person is cheerful and loves to laugh, it has also been stated that people who have difficulty in controlling their emotions often get into trouble, are reactive and unreliable in their speech and behavior.[23] Already in the correlation analysis, we found a significant positive relationship between extraversion and lie traits in the control group. In our study, the highest neuroticism and

psychoticism and the lowest extraversion subscale scores were seen in mothers of children with intellectual disabilities. Shame, guilt, pity for both themselves and their children, social isolation, hopelessness, depression, and anxiety are common in families with mentally disabled children.[24] In a study, it was shown that mothers of children with mental retardation with Down syndrome were more introverted, depressed, anxious, and psychotic personality traits were dominant.[25] In the same study, fathers of children with Down syndrome also scored significantly higher in neurotic personality traits, somatization, and hostility than fathers with healthy children.[25] Neuroticism sub-dimension with anxiety, fear, depression; It is known that the psychoticism sub-dimension is characterized by being distant from other people and feeling guilty, while the extraversion sub-dimension is characterized by liking to enter social circles. Therefore, it is not surprising that we detected these findings in this group.[9] We found a negative correlation between extraversion and neuroticism, which are already considered two different extremes, in both the patient and control groups. We found the highest psychoticism subscale scores in mothers of children with intellectual disabilities. Having a mentally handicapped child, meeting the needs of such a child, and having to cope with the attitudes and behaviors of society towards their children may cause the emergence of anger in parents.[26] Therefore, it is not surprising that the psychoticism subscale, which is characterized by anger and aggression, is high in these mothers. In a study, when the personality traits of mothers of children with mental retardation with Down syndrome were examined, psychoticism scores were found to be higher than those of control mothers.[25] At the same time, the psychoticism score was significantly higher in mothers of children with ADHD, major depressive disorder, autism spectrum disorders and skin picking disorder, as well as an intellectual disability when compared with the control group. In our study, there was no difference between the two groups in terms of lie traits scores. The lie sub-dimension shows how honestly the questions in the scale were answered. However, this sub-dimension also includes behaviors that are assumed to be wrong by society but that everyone can exhibit from time to time.[11] For this reason, when it is considered for the general society, it is thought that wrong behaviors can be seen in every person from time to time and can be socially accepted. The lack of difference between the two groups can be associated with this situation.

We found that the mothers of children with a psychiatric disorder had higher neuroticism and psychoticism scores and lower extraversion scores than the control group and that there was a relationship between maternal personality traits and the psychiatric disorders of the children. Identification and control of risk factors that play a role in psychiatric disorders that impair the functionality of children and may require long-term psychiatric treatment are of great importance in terms of preventive mental health treatments. In this context, we think that mothers' personality traits and the quality of their relationship with their children should be evaluated. However, in order to generalize our study's findings, the relationship between maternal personality and a child's mental health should be investigated in large-scale community setting studies.

Limitations

Research findings are limited to the sample group and cannot be generalized to the population. Homogeneous distribution of psychiatric diagnoses in terms of number could not be achieved. Although mothers were questioned whether they had applied to psychiatry before and whether they received any treatment, a structured assessment tool was not applied to make a psychiatric diagnosis. This deficiency eliminated our chance to evaluate the interaction between psychiatric disorders and personality. This can be considered as a limitation of our study.

Ethical Considerations: Local ethics committee approval was obtained before the initiation of the study (Date; 10.02.2021 / Decision No; 2017-KAEK-189_2021.02.10_06). All children and mothers participating in the study were informed about the study, and their consent was obtained.

Conflict of Interest: The author declares no conflict of interest. This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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EFFECTS OF ACTIVE/PASSIVE SMOKING EXPOSURE IN PATIENTS WITH COPD

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Abstract

Objectives: Smoke exposure of COPD (Chronic Obstructive Pulmonary Disease) patients increases the frequency of exacerbations and affects the quality of life. However, most patients still continue to active/passive smoking exposure after being diagnosed with COPD. In this study, the effects of active/passive smoking exposure on symptoms exacerbation/pulmonary functions in COPD patients were investigated.

Materials and Methods: Totally 151 COPD patients were included in the study. Patient data on active/passive smoking exposure and exacerbation frequency, and COPD Assessment Test (CAT), modified Medical Research Council dyspnea scale (m-MRC), and pulmonary function tests (PFT) were recorded. As well as active smoking exposure, these parameters were especially evaluated in ex-smoker COPD patients according to passive smoking exposure. The data were evaluated in SPSS 22.0 program; X^2 and student t-tests were applied.

Results: Active/passive exposure was determined (26.49% and 43.05%, respectively). Total cigarette consumption was 1.5 times higher in men, and passive smoking exposure (69.56%) was higher in women. In addition, it was determined that the m-MRC score increased statistically significantly as exposure to passive cigarettes increased. It was observed that the number of exacerbations increased in ex-smoker COPD patients with passive exposure. Another finding in the study; was determined that the increase in each standard deviation in cigarette consumption caused a 19% decrease in pulmonary function capacity and an increase in m-MRC, CAT scores.

Conclusion: Active/passive smoking exposure was detected in most COPD patients. It was determined that continuous smoking exposure in patients caused an increase in the number of exacerbations and a deterioration in the quality of life. Therefore, it is necessary to increase awareness of passive smoking exposure in the management of COPD patients.

Keywords: COPD, smoking exposure, exacerbations.

Introduction

COPD is a common, persistent, and preventable dysfunction of the lung associated with limitation in airflow. COPD is a complex disease associated with abnormalities of the airway, which is predominantly caused by exposure to noxious gases and particulates over a long period.[1] The global prevalence of COPD was 251 million cases in 2016, and the death rate was 5% (3.17 million) alone in 2015. Until 2060, it has been reported that deaths annually from COPD and related conditions may be over 5.4 million by GOLD2020(Global Initiative for Chronic Obstructive Lung Disease).[2] COPD is ranked by the WHO as the third leading cause of death, especially with a particular burden in low and middle-income countries.[2,3] This burden is predicted to grow due mainly to increased global exposure to tobacco due to poor awareness.[4] It is known that the main factor for COPD is smoking. However, active/passive smoking exposure continues even after being diagnosed with COPD is a reality for many patients. This exposure hinders the treatment and control of exacerbation and affects the quality of life.[5] It is important to reduce exacerbations in COPD, and the most important cause of exacerbation is exposure to cigarette smoke. Passive smoking exposure, as well as active exposure to cigarette smoke, causes exacerbation.[6,7] However, the harmful effect of passive exposure in COPD and the level of the health results are not fully known. It has not been shown whether passive smoking exposure is an additional risk in active smokers COPD patients.[8] Although the possible contribution to the incidence of COPD is stated, the lack of evidence in passive exposure has been noted in the GOLD report.[2] There are limited studies that passive exposure adversely affects the quality of life, shortness of breath, and COPD exacerbation.[8] There is also a growing awareness of the adverse health consequences of passive smoking exposure in COPD.[9-13] In addition, it has also been reported that chemicals in passive exposure may differ from primary smoke, even for active smokers.[8] The effects of active smoking in COPD are investigated and shown in many studies.[8] However, studies investigating the effects of passive exposure are limited.

In this study, the level of active/passive smoking exposure, and its effects on symptoms, exacerbation/pulmonary functions were investigated in COPD patients.

Materials and Methods

This study was carried out in COPD patients between November-2019/March-2020. A total of 151 volunteer COPD patients diagnosed in the COPD clinic according to the GOLD-2020 criteria were included in the study and followed up within the scope of the Akdeniz University COPD Monitoring Project.[1]

Patients who refused to participate in the study and to follow-up were excluded. In addition, COPD patients were excluded if they have not the according to the GOLD criteria [Forced Expiratory Volume in one second/Forced Expiratory Volume (FEV_1/FVC) > 70%].[1]

Data on socio-demographic characteristics, active-passive smoking exposure, total cigarette consumption, complaints, exacerbation frequency (emergency admission, hospitalization, etc.) were collected. Total cigarette consumption was calculated as "pack/year" .[14] Pulmonary function test (PFT) measurements of the patients were made with the spirometer device. In addition, COPD Assessment Test (CAT) and modified Medical Research Council dyspnea scale (m-MRC)[15] score were applied for the severity of the disease and GOLD classification.

The study was designed to investigate the relationship between total cigarette exposure, active/passive smoking and pulmonary functions, complaints, acute exacerbations (defined as the number of hospital admission and emergency applications) in the last year in COPD patients. Firstly, active and passive smoking exposure rates of COPD patients were determined in the study. Furthermore, m-MRC and CAT scores were compared in current smokers or ex-smokers with COPD patients. In addition, these scores were compared in ex-smoker COPD patients with or without passive exposure.

Exacerbations, defined as the number of hospital admission and emergency applications in the last year, were recorded. It was compared in ex-smokers COPD patients with or without passive exposure. In addition, FEV_1, FVC and Peak End Expiratuar Flow(PEEF) values were compared in ex-smoker COPD patients with or without passive smoking exposure.

Statistical Analysis

The data were evaluated in SPSS 22.0 program. Normal distribution of study data was tested for compliance. In order to describe the qualitative variables, absolute frequencies and percentages were used. The description of quantitative variables was performed using the mean, standard deviation (SD), median. The chi-squared test was used to compare the numerical data, and the Student t-test was used for the comparison of the measurement data with exposure group and without. The results were described with p-values.

Results

Totally 151 COPD patients, 128 men and 23 women were included in the study. The mean age of the patients was 66.15±9.51, and the mean duration passed after COPD diagnosis was seven years. Active smoking was found on average 20 years, and a total cigarette consumption was found as 40.25 packs/year in patients. While total cigarette consumption was 38.71 packs/year in ex-smokers, it was approximately 10% higher in the current smokers (44.35 packs/year). While there was no never-smoker in men, this rate was 21.74% in women patients. The rate of ex-smokers was 75.00% in men, and this rate was 43.48% in women. The rate of current

smokers was higher in women than men (34.78%, 25.00%, respectively). The passive smoking exposure was higher in ex-smokers than current smokers (70.19% and 26.49%, respectively).

While the rate of active smoking exposure of COPD patients was 26.49%, the passive exposure rate was 43.05%. In addition, passive smoking exposure was 38.28% in men; this rate was approximately twice high in women (69.56%, p=0.005) (Figure 1).

Figure 1. Smoking status in patients with COPD by gender

Passive smoking exposure was relatively low (36.79%) in the ex-smokers, but it was observed in more than half of the current smokers (57.50%). So current smokers were more exposed to passive cigarette smoke. The rate of passive smoking exposure at home was 78.26%. It was 4.35% at work and 17.39% both at home and at work.

Table 1. Active/passive smoking status and total cigarette consumption in patients with COPD

			All patients		Passive smoking exposure		p
		Age*	n	%	n	%	
Gender	Women	63.22±8.41	23	15.23	16	69.56	0.005
	Men	66.68±9.63	128	84.76	49	38.28	
	Total	66.15±9.51	151	100	65	43.04	
Smoking status	Current Smokers	61.63±9.35	40	26.49	23	57.50	0.031
	Ex and never smokers	67.78±9.07	111	73.51	42	37.83	

Data are given as mean ± std. deviation.

The passive exposure of current smokers in the study group was 57.50%. Hospital admissions in the last year were higher (26.08%) among current smokers with passive exposure. In the study, the GOLD D class patients rate was 47.82%. (Figure 2).

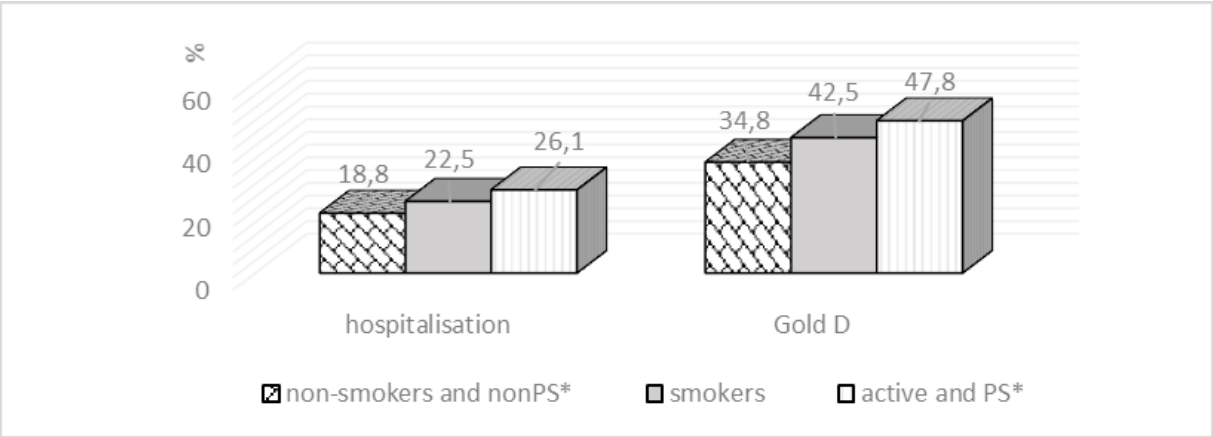

Figure 2. Active and passive smoking exposure rates in hospital admissions and GOLD D COPD patients

In current smokers, the passive smoking exposure rate was 43.05% in the study, and this rate was higher in women than men (69.56% and 38.28%, respectively). Passive smoking exposure of the patients was mostly at home (89.23%). The rate of those who received long-term oxygen therapy was 10.59% in the study. In this group, the passive smoking exposure rate was 43.75%. It was remarkable that the passive smoking exposure rate was 46.42%, even in group D patients.

The effects of passive smoking exposure were investigated among the ex-smokers, which constitutes the largest group, and the results were given in Table 2. Passive exposure was 36.79% in the ex-smokers. That is, one in three COPD patients there was passive smoking exposure even though they were smoking cessation.

The m-MRC CAT scores were evaluated in ex-smoker patients with passive smoking exposed. The m-MRC score was statistically significantly higher in ex-smoker patients with passive smoking than without passive smoking (1.69 and 1.25 respectively, p=0.016), (Table 2). Although those with passive smoking exposure were approximately four years younger, it was noteworthy that the m-MRC score of this group was significantly higher than without exposure group. This data shows that passive smoking exposure affects the dyspnea score. An increase of CAT score was also observed in the presence of passive smoking exposure, but this increase was not statistically significant (12.82 and 10.83 respectively), (p=0.199). In addition, the m-MRC and CAT scores were investigated in current smoker COPD patients. The CAT score was 12,87, and the m-MRC score was 1.67 in this group. These data showed that m-MRC and CAT scores of ex-smoker COPD patients with passive smoking exposure were close to the values of current smokers.

The number of exacerbations was compared in this group. While the number of exacerbations in the last year was 1.21 in the without passive smoking exposure group, it increased to 2.64 in patients with passive smoking exposure group (p=0.021), (Table2). Although those with passive smoking exposure were approximately four years younger, it was noteworthy that the number of exacerbations in the last year was twice as higher than without the passive smoking exposure group. PFT values of ex-smoker COPD patients were compared according to the presence of passive smoking exposure (Table 2). FEV_1 and PEEF values were found to be relatively lower in patients with passive exposure than without passive exposure, but there was no statistical difference (p= 0.574, p=0.103).

Table 2. Effects of the presence of passive smoking exposure in ex-smokers

Ex-smokers (n=106)		**Passive smoking exposure***		p
		No (n=67)	**Yes**(n=39)	
Age		69.13±8.34	65.36±10.28	**0.042**
FEV_1%		53.13± 15.91	51.37±14.69	0.574
FVC%		61.91± 14.43	61.92±15.13	0.998
FEV_1/FVC		61.68± 8.65	60.77±12.29	0.656
PEEF%		56.73± 16.38	51.16±17.55	0.103
m-MRC score		1.25± 0.82	1.69±1.00	**0.016**
CAT score		10.83± 7.12	12.82±8.41	0.199
At last year	Number of hospitalization	0,33± 0.93	0.64±1.32	0.158
	Number of emergency admissions	0.88± 1.93	2.00±3.00	**0.021**
	Number of exacerbations	1.21± 2.54	2.64±3.71	**0.021**

Data are given as mean ± std. deviation.

Discussion

Smoking is known to cause COPD. However, a significant portion of COPD patients continues exposure to smoke. While the rate of patients with COPD who continue exposure to smoke is reported to be 31-49% worldwide, this rate is higher (26% -58%) in developing countries.[16,17] In our study, it was found that one of four COPD patients (26.49%) were current smokers. This rate was lower compared to previous studies, and it was thought to be associated with the success of smoking cessation efforts. When our data was evaluated, it was seen that current smokers in COPD patients were higher in women patients than in men (34.78%, 25.00%, respectively). In other words, one in four men patients and one in three women patients were current smokers after being diagnosed with COPD. Patients receiving long-term oxygen therapy were "heavier" patients, however the rate of current smokers was 25.00% in this group. In other words, tough they were heavier patients could not quit smoking. In studies, it was reported that smoking addiction was higher and smoking cessation success was lower in COPD patients.[18-20] Therefore, specific strategies for smoking cessation should be developed for every current smoker patient after being diagnosed with COPD. One of the main goals of the

AKIZ project was to help COPD patients with smoking cessation. In the initial three-month period, approximately 10% of the smoker COPD patients were smoking cessation.

Although ex-smoker were six years older than current smokers, pulmonary functions (FEV_1% and PEEF%) were higher in ex-smokers. According to the guidelines, "smoking cessation" may equate the rate of decline in respiratory function in COPD patients to physiologically expected levels in non-smokers. Turan et al. reported that a decrease in FEV1 level could be prevented by quitting smoking.[21] In another study, it has been reported that the FEV_1 level increases by 29 ml in the first year after smoking cessation, whereas it decreases by 25 ml in current smokers.[22] In summary, respiratory functions of COPD patients, improve after smoking cessation. Our findings were compatible with the literature.

It has been reported that complaints are decreasing with smoking cessation in COPD patients.[23-25] In one study, it has been reported in current smoker COPD patients that CAT scores decreased from 18.9 to 8.1 six months after smoking cessation.[26] Similarly, m-MRC and CAT scores were lower in ex-smokers than smokers COPD patients in our study (0.26 and 1.31, respectively). The findings in our study were also compatible with the literature.

In the studies carried out, it has been reported that especially severe cases admitted to the hospital for an average of 1.5–2.5 times in last year for COPD attacks.[27] In our study, the annual number of exacerbations was found to be approximately two, and it was consistent with the literature. It has been reported in many studies that smoking is one of the most important factors causing acute exacerbation in patients with COPD. In addition, in the same studies, it has been reported that exacerbations could be prevented by smoking cessation.[22,28] In our study, the number of exacerbations was reduced by half in ex-smokers who did not smoke passively.

In our study, the passive smoking exposure rate was found to be 43.05% in COPD patients. This rate was higher in the women patients (69.56%). In a study conducted in Turkey, passive smoking was reported at a high rate in women with COPD.[29] It was remarkable that the passive smoking exposure was quite high in both current smokers and ex-smokers (57.50% and 37.83%, respectively). It was noteworthy that one out of three ex-smoker COPD patients was exposed to passive cigarette smoke indoors. It has been reported that passive smoking increases the risk of developing COPD.[13] In a comprehensive study, it has been reported that approximately 20% of COPD patients live with a smoker, and living with a smoker negatively affects SGRQ, SF12, CAT scores, and symptoms.[7] In our study, the m-MRC score was statistically significantly higher in ex-smoker COPD patients with passive smoking exposure than without exposure. In addition, the number of emergency/hospital admissions in ex-smoker COPD patients with passive smoking exposure was approximately two times higher than without exposure. These data clearly showed that passive smoking exposure should be prevented as well as smoking cessation to control COPD exacerbations. It is known that

exacerbations of COPD negatively affect both the quality of life and the prognosis of the disease. In our study, data showed that both active and passive smoking exposure should be prevented to control the symptoms exacerbations and to improve the quality of life in COPD patients.

Passive smoking exposure was particularly higher in women COPD patients (69.56%), and 18.75% of these patients had never smoked. In previous studies has been reported that women are more sensitive to cigarette smoke and may develop COPD even at lower exposures.[8,30] These findings demonstrated the importance of passive smoking exposure. Therefore, social awareness should be created, and new strategies should be developed to prevent passive smoking exposure, especially in indoor environments in COPD patients.

Although it was observed that passive smoking exposure negatively affected respiratory functions, it was not statistically significant as in the active exposure in our study. FEV_1 levels of ex-smoker COPD patients with passive smoking exposure were lower than those without smoking exposure, but the difference was not statistically significant. However, the quality of life of those with COPD who had active/passive exposure to smoking was declined. Further studies are needed in this area

Active/passive smoking exposure was observed in most COPD patients. Passive smoking exposure was very high, especially in women with COPD patients. According to our data, our main goal in the follow-up of COPD patients should be the prevention of active/passive smoking exposure, which decreases respiratory functions, increases complaints, increases the number of exacerbations, and causes deterioration in the quality of life. Hence social awareness should be created in terms of passive smoking exposure, especially in women COPD patients, and strategies to prevent passive smoking exposure should be developed.

Limitations

Our study is important in terms of the limited number of studies in the literature regarding the effect of passive cigarette exposure on exacerbation and quality of life in COPD. Although the data of our study showed the effect of passive cigarette exposure in COPD exacerbations and quality of life, more comprehensive studies were needed to be statistically significant. With the increase in the number of cases followed in the AKIZ project, the effects of passive cigarette exposure on exacerbation and quality of life in COPD will be more clearly evaluated in larger study groups.

Ethical Considerations: The necessary approval for the study was obtained from the Akdeniz University's Clinical Research Ethics Committee (Decision number: 2019/1109), and the Declaration of Helsinki and ethical principles were applied. The voluntary consent of the patients was obtained.

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

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Research Article

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AN EXAMINATION OF THE EFFECTIVENESS OF DIGITAL APPLICATIONS FOR OBESE PATIENTS WHOSE FOLLOW-UP AND TREATMENT WERE DISRUPTED DUE TO THE COVID-19 PANDEMIC

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Abstract

Objectives: This study aimed to investigate the effectiveness of digital technologies in the follow-up and treatment of obesity patients during the COVID-19 pandemic.

Materials and Methods: Prospective case-control study was carried out at the Obesity Centre of Antalya Training & Research Hospital. While 30 obese patients in the project group were followed and guided 7/24 for three months with smartphones/smart wristbands, 27 control patients were followed up with face-to-face meetings every two weeks as standard. Project group patients were evaluated in terms of calorie consumption, conditions regarding exercises, sleep and stress, and laboratory data in addition to anthropometric measurements at the beginning and end of the project, while control group patients were evaluated only in terms of anthropometric measurements.

Results: Mean age of patients in the project group was 42.57 ± 7.57 years, and the control group was 54.63 ± 6.20 years. Of all the patients, 94.74% of them were female, while 5.26% were male. At the end of the project, the weight of the project group patients dropped from 92.25 kg to 89.70 kg, and their BMI from 35.60 kg/m2 to 34.80 kg/m2 ($p<0.001$). In addition, a statistically significant decrease was found in laboratory parameters such as HbA1c and triglyceride levels, as well as systolic and diastolic blood pressures. There was a minimal decline in weight and BMI of the control group, which was not statistically significant.

Conclusion: Online and/or smartphone/smart wristband-based follow-up and guidance can be used as an effective method in the treatment of patients with obesity who do not tend to go to the hospital due to pandemics.

Keywords: Smart wristbands, smartphones, digital apps, obesity treatment, COVID-19 pandemic.

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Introduction

Obesity and overweight are important public health challenges that concern not only in developed countries but also developing countries in the 21st century, becoming pandemic day by day and causing the death of more than 4 million people every year.[1]

One of the most important systems affected by obesity is the respiratory system. In this regard, obesity is one of the major risk factors for diseases such as asthma, chronic obstructive pulmonary disease, pneumonia, obesity-hypoventilation syndrome, obstructive sleep apnea syndrome, pulmonary hypertension, and acute respiratory distress syndrome.[2,3] Weight gain and increased body mass index (BMI) have been regarded to be associated with a decrease in lung volumes shown by a more restrictive ventilation pattern in spirometry.[4,5] Fat accumulation in the abdominal and thoracic cavity and the mediastinal area directly affects the mechanical properties of the lung and chest wall. It also causes the diaphragm to remain upward, thus restricting its downward movement, increasing pleural pressure, and decreasing functional residual capacity.[6,7] As a result, it can be assumed that the COVID-19-related lung involvement increases in obese patients due to certain reasons such as airway resistance, ventilation-perfusion inequality,[8] decreased diaphragm movement and lung capacity, as well as increased inflammatory cytokines associated with obesity and that obesity, leads to a growing need for intensive care in COVID-19 patients.

As shown in many clinical studies, obesity increases lung involvement, intensive care need, morbidity and mortality in COVID-19 patients, which is why the fight against obesity has once again gained importance during the pandemic.[9-12]

Obesity Centers play an important role in the fight against obesity in Turkey.[13] In addition to individual training, interviews and therapies, interactive training that aim to develop necessary behavior in groups of 12 - 20 people towards healthy nutrition and regular physical activity, that is, lifestyle change, constitute the basis of the service offered in Obesity Centers. In our Obesity Centre, where we achieved successful results with high motivation, online applications via remote access were required for the patients' follow-up to prevent them from losing their motivation and returning to their previous weight during the pandemic. A special project call, namely "COVID-19 and Society: Social, Human and Economic Effects of the Pandemic, Problems and Solutions" opened within the scope of TUBITAK 1001 - Scientific and Technological Research Projects Support Program was applied for this study.

The present study aimed to research the effectiveness of digital applications (smartphone apps and smart wristbands) in the follow-up of patients with obesity who had already been followed up in an Obesity Centre and whose follow-up and treatment process had been disrupted due to the COVID-19 pandemic and to enable

the patients to continue losing weight by minimizing their visits to the Centre during that time in the light of the data to be obtained.

Materials and Methods

Sample groups

The population of this prospective clinical study consisted of 118 patients who were followed up and treated in the Obesity Centre of University of Health Sciences, Antalya Training and Research Hospital between 01.09.2019 and 15.03.2020. The patients whose follow-up and treatment were interrupted due to the COVID-19 pandemic were evaluated by the project team according to the inclusion criteria (patients between the ages of 18 - 50, patients BMI ≥ 30, patients who have completed the 3rd module training in the obesity center, patients at least had primary care education, patients who had smartphones and have the ability to use smartphone apps, patients who agreed to participate in the project) in the study, which then identified 43 patients who were between the ages of 18 - 50 with the BMI ≥ 30, and who had already completed the 3rd module training,[13] at least had primary care education and who had smartphones besides the ability to use smartphone apps. Subsequently, the patients were invited to the Centre and were informed about the project, the phone application, and wristbands. Thirty patients who volunteered to participate in the project were included in the study upon their signed informed consent forms.

Following the completion of equipment and service procurement, the first anthropometric measurements of 30 patients, physician examinations, necessary interviews with dieticians, psychologists, and physiotherapists were conducted as of September 21, 2020. During those first meetings, a special diet-calorie program was prepared for each patient, workout plans were made, and the necessary motivation was provided for changing appropriate behavior and raising consciousness. In addition, the software developed by the technical team was downloaded to the patients' smartphones, phone-wristband synchronization was ensured, and wristbands were delivered to the patients. The patients' blood pressure measurements and laboratory tests were also performed in the same interview. Then, 30 project patients recorded their calorie intake, water consumption and mood via smartphones and their exercise status, calorie expenditure, sleep patterns, and durations via smart wristbands. All data were monitored 24/7 online. The patients were given instant feedback, warnings and suggestions. And also participated in face-to-face interviews at the center every two weeks, and anthropometric measurements were made. Of all the patients, 27 control patients who were followed up in the Obesity Centre and had clinically similar characteristics were interviewed face-to-face with a dietician, a psychologist and a physiotherapist by taking their anthropometric measurements every two weeks without using any digital applications. However, since the laboratory measurements of the control group patients were

not performed, only the anthropometric measurements of the project group and control group patients were compared at the end of the 3 -month follow-up. The algorithm of the research is presented in Figure 1.

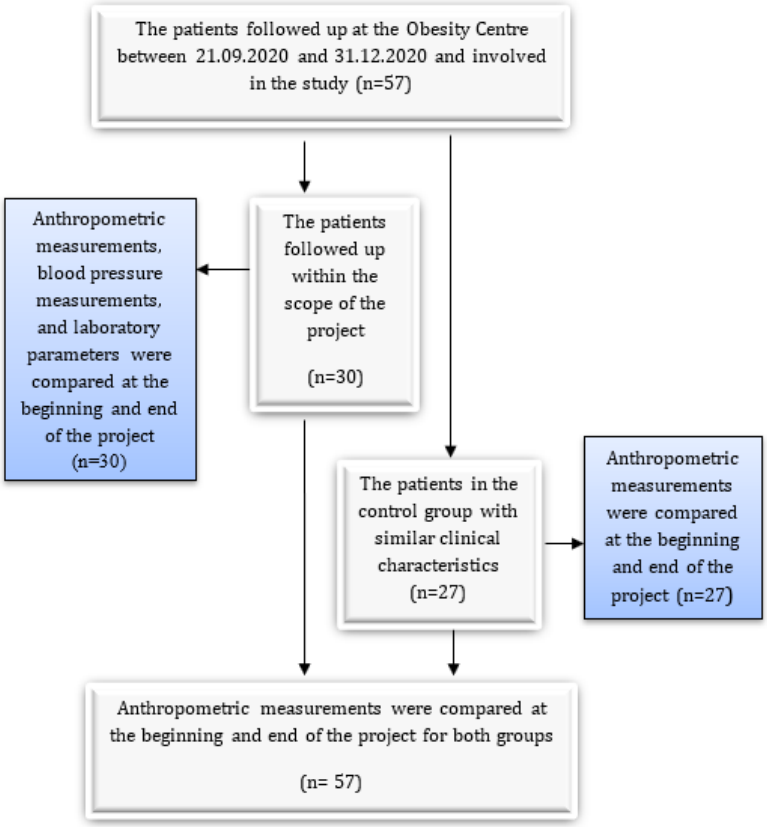

Figure 1. The algorithm of the research

Data collection and procedure

The blood pressure measurements of the patients at the beginning of the project were made in the sitting position after at least 5 minutes of rest, with the arm placed at the heart level, using a sphygmomanometer (Gez G-life Perfect Mechanic) and a stethoscope (3M Littman Classic II) from the cubital fossa and taken as the average of two measurements. The patients' heights were measured when the heels were together, the body was upright, without shoes, by taking the distance between the vertex point and the floor on the TESS brand height and weight scale. Bioelectrical impedance analysis (TANITA MC 580) was used to calculate body weights and body mass index (BMI). The measurement was made by placing the patient on the scale so that s/he could step on the appropriate parts of the analyzer with bare feet. Waist circumference measurements were made by placing the tape measure through the umbilicus level and hip circumference measurements by placing the tape

measure through the widest part of the hips by the same assistant personnel. Fasting blood glucose (FBG), glycosylated hemoglobin (HbA1c), fasting insulin, insulin resistance, total cholesterol (total-C), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglyceride (TG) were analyzed in blood samples taken after 12 hours of fasting. FBG, total - C, triglyceride and HDL - C levels were evaluated using a spectrophotometric method using Beckman Coulter commercial kits in a Beckman Coulter AU5800 (Beckman Coulter Inc., CA, USA) autoanalyzer. HbA1c levels were measured by a commercially available high-performance liquid chromatography method (Tosoh HLC 723 G8; Tosoh Bioscience, Japan). The Homeostasis Model Assessment (HOMA-IR) formula [FBG (mg/dL) x fasting insulin (μU/mL) / 405][14] was used in the estimation of insulin resistance, whereas the formula developed by Friedewald et al. was used to calculate the LDL-C level.[15] Prediabetes was diagnosed in accordance with TEMD recommendations in patients with FPG = 100 - 125 mg/dL and/or HbA1c = 5.7% - 6.4% who did not receive antidiabetic therapy. Based on the hospital laboratory classification, those with HOMA-IR > 2.5 were diagnosed with insulin resistance.

Statistical analysis

The data analyses were conducted with IBM SPSS 23.0 package software (IBM Corp., Armonk, NY). Descriptive statistics were presented with n (%), mean±standard deviation, and median (min-max) values. Categorical data were analyzed by Pearson chi-square or Fisher's Exact test. Mann–Whitney U test and Student's t-test were used for the analyses of non-normally and normally distributed numerical data, respectively. The McNemar-Bowker test was used to evaluate the changes in the patients' emotional states before and after the project, and only the McNemar test was used to evaluate the changes in chronic diseases. The difference between the measurement values of the patients before and after the project was analyzed with the Wilcoxon Signed Rank test when the assumption of normal distribution was not provided and with the Paired Samples t-test when provided. Multiple linear regression analysis was used to identify the factors independently associated with patients' post-project weight loss. As a result of the post hoc power analysis performed to compare the BMI percentage change of the patients in the project patients and the control group, statistical power was calculated as 99.3% for 0.05 margin of error and d=1.188 effect size. And for the weight percentage change, statistical power was calculated as 99.5% for 0.05 margin of error and d=1.224 effect size. The p values less than 0.05 were considered statistically significant.

Results

A total of 57 patients with obesity, 30 of whom were digitally monitored, and 27 of them were control patients, were included in the study. The mean age of the project patients was calculated as 42.57 ± 7.57 years, while it was 54.63 ± 6.20 years for the control group. Of all the patients, 94.74% were female, and 84.21% of them were

married. Divorced patients were included in the single group. Table 1 presents the detailed demographic data and clinical characteristics of the control group and the project patients.

Table 1. Comparison of the demographic and clinical characteristics of the project patients and the control group

Variables	Project patients (n=30)	Control group (n=27)	p-value
Age (years)	42.57±7.57	54.63±6.20	**<0.001**
Gender			
Women	29(96.67)	25(92.59)	0.599
Men	1(3.33)	2(7.41)	
Marital status			
Single	3(10.00)	6(22.22)	0.283
Married	27(90.00)	21(77.78)	
Educational background			
Primary school	9(30.00)	14(51.85)	0.119
High school	10(33.33)	9(33.33)	
University	11(36.67)	4(14.82)	
Chronic diseases			
Diabetes mellitus	8(26.67)	9(33.33)	0.583
Prediabetes	7(23.33)	2(7.41)	0.149
Insulin resistance	5(16.67)	2(7.41)	0.427
Hypertension	6(20.00)	17(62.96)	**0.001**
Hyperlipidemia	15(50.00)	4(14.81)	**0.005**
Hypothyroidism	6(20.00)	3(11.11)	0.476
Chronic pulmonary disease	2(6.67)	1(3.70)	0.999
Anxiety disorder	3(10.00)	3(11.11)	0.999

Findings are shown as mean ± SD or n (%). Column percentages are given. Student's t-test, Pearson chi-square test, Fisher's Exact test are used.

There was a statistically significant decrease in the project patients' final control weight and BMI. They were followed up for three months by instant digital means and met face-to-face every two weeks, in comparison to the baseline values. In contrast, the decline in the weight and BMI of the control group, who were followed up face-to-face only once every two weeks within the same period, was not statistically significant (Table 2).

When the weight changes of the project patients and control group patients at the beginning and end of the process were evaluated as percentage values, the declines in weight and BMI in the project patients were statistically significant compared to those of the control group (Table 3).

Table 2. The change in anthropometric measurements of all patients at the beginning and end of the project

	Project patients (n=30)			**Control group (n=27)**		
	Project beginning	**Project end**	**p**	**Project beginning**	**Project end**	**p**
Weight (kg)	92.25 (73.50-138.20)	89.70 (71.80-136.60)	**<0.001**	87.80 (65.10-183.40)	87.70 (66.30-191.60)	0.614
BMI (kg/m²)	35.60 (31.50-50.20)	34.80 (30.50-49.60)	**<0.001**	35.20 (30.10-56.00)	34.90 (29.70-58.50)	0.764
Waist circ. (cm)	105 (87-159)	105 (90-158)	0.730	104(86-201)	107 (81-209)	0.457
Hip circ. (cm)	116.50 (104-159)	113 (102-158)	0.089	113 (104-201)	115 (100-209)	0.646

Findings are shown as median (min-max). Wilcoxon Signed Ranks test.
BMI: Body mass index.

Table 3. The comparison of percentage changes in anthropometric measurements of project patients and control group during the follow-up

	Project patients (n=30)	**Control group (n=27)**	**p**
Weight change (%)	-2.06(-8.41-0.62)	-0.11(-4.12-7.39)	**<0.001**
BMI change (%)	-2.04(-8.49-0.84)	-0.28(-3.84-7.29)	**<0.001**
Waist circumference change (%)	-0.31(-7.14-5.75)	-1.79(-6.11-6.86)	0.467
Hip circumference change (%)	-0.88(-8.94-4.27)	-0.9(-6.11-6.96)	0.637

Findings are shown as median (min-max). Mann-Whitney U test was used.
BMI: Body mass index.

At the end of the project, there was a statistically significant decrease observed in HbA1c, triglyceride, systolic blood pressure (SBP) and diastolic blood pressure (DBP) values. In contrast, the decline in fasting blood glucose (FBG) and insulin resistance was not statistically significant. On the other hand, an increase was found in the high-density lipoprotein-cholesterol (HDL-C) level, though not statistically significant (Table 4).

At the end of the project, it was also observed that there was a non-significant decline in the amount of calories consumed by the patients and a significant increase in the length of jogging and sleeping. A statistically significant change was found in the emotional states of the patients towards developing anxiety-stress and feeling empty (Table 5).

The changes in weight percentage of the patients at the end of the project was found to have a statistically significant weak negative correlation (r = -0.371; p = 0.044) with the length of jogging, a moderate positive

correlation with fasting insulin values (r = 0.408; p = 0.034), and a weak positive correlation (r = 0.374; p = 0.043) with HOMA-IR values at the end of the project. It was observed that the increase in the length of jogging at the end of the project increased the weight loss, while the increase in fasting insulin and HOMA-IR values decreased the amount of weight loss (Table 6).

The examination of the effect of the change in the amount of calories consumed by patients on blood pressure and laboratory parameters indicated a statistically significant moderate positive correlation between the changes in the amount of calories consumed and fasting insulin (r = 0.403; p = 0.041), HOMA-IR (r = 0.466; p = 0.016), and triglyceride values (r = 0.453; p = 0.020) (Table 7).

Table 4. The changes in laboratory data of project patients at the beginning and end of the project

Variables	Project start (n=30)	Project end (n=30)	p-value
FBG (mg/dL)	94.50(77.00-157.00)	93(78.00-242.00)	0.597
HbA1c (%)	5.50(4.40-7.70)	5.30(4.60-8.20)	***0.009***
Fasting insulin (mIU/mL)	7.55(2.12-16.64)	5.74(1.89-16.54)	0.055
HOMA-IR	1.87(0.44-3.74)	1.32(0.41-5.16)	0.118
Total-C (mg/dL)	210.50(134.00-387.00)	216.00(149.00-325.00)	0.614
LDL-C (mg/dL)	130.50(65.00-278.00)	132.00(89.00-221.00)	0.324
HDL-C (mg/dL)	53.60±15.22	56.48±9.08	0.310
Triglyceride (mg/dL)	125.50(38.00-365.00)	111.00(35.00-265.00)	***0.036***
SBP (mmHg)	120(110-140)	110(90-145)	***<0.001***
DBP (mmHg)	80(70-90)	70(60-90)	***<0.001***

Findings are shown as mean ± SD or median (min-max). Paired Samples t-test, Wilcoxon Signed Ranks test.
FBG: Fasting blood glucose, HbA1c: Glycosylated hemoglobin, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, SBP: Systolic blood pressure, DBB: Diastolic blood pressure

Table 5. The changes in the amount of calories taken, lengths of exercises and sleep, and their emotional states at the beginning and at the end of the project in project patients

Variables	Project start (n=30)	Project end (n=30)	P
The amount of calories patients consumed (kcal)	1271(984-2596)	1257(932-1810)	0.222
The length of exercises performed by the patients (minutes)			
Jogging	45(30-105)	47.50(23-116)	***0.029***
Home workout	30(0-120)	30(0-120)	0.388
Total	70(30-180)	82.50(28-180)	0.087
The length of sleep (hours)	07h58m±01h05m	08h34m±01h03m	***0.004***
Emotional states			
Feeling empty	4(13.33)	6(20)	***0.020***
Anxious and Stressful	9(30)	19(63.33)	
Happy	17(56.67)	5(16.67)	

Findings are shown as mean ± SD, median (min-max), or n (%). Paired Samples t-test, Wilcoxon Signed Ranks test, McNemar-Bowker Test, h: hours, m: minutes.

Table 6. The relationship between the changes in weight percentage and demographic features, laboratory parameters in project patients

Values	Changes in weight percentage	
	r*	p*
Age (years)	-0,132	0,486
Metabolic age (years)	0,062	0,744
The amount of calories taken (kcal)	-0,258	0,177
The length of exercises (minutes)		
Jogging	-0.371	***0.044***
Home workout	-0.170	0.370
Total	-0.313	0.092
The length of sleep (hours)	-0.080	0.702
Fasting insulin (uIU/mL)	0.408	***0.034***
HOMA-IR	0.374	***0.043***

*Spearman correlation test

Table 7. The relationship between the changes in the amount of calories consumed by patients and the change in blood pressure and laboratory parameters

Variables	Change in the amount of calories consumed	
	r*	p*
FBG (mg/dL)	0.235	0.248
HbA1c (%)	0.059	0.775
Fasting insulin (mIU/mL)	0.403	***0.041***
HOMA-IR	0.466	***0.016***
Total-C (mg/dL)	-0.128	0.532
LDL-C (mg/dL)	-0.121	0.557
HDL-C (mg/dL)	-0.166	0.417
Triglyceride (mg/dL)	0.453	***0.020***
SBP (mmHg)	0.035	0.859
DBP (mmHg)	0.235	0.229

*Spearman correlation test.
FBG: Fasting blood glucose, HbA1c: Glycosylated hemoglobin, HOMA-IR: Homeostatic model assessment insulin resistance, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol,
SBP: Systolic blood pressure, DBB: Diastolic blood pressure

Discussion

In this study, 30 patients who had been followed up at the Obesity Centre of University of Health Sciences, Antalya Training and Research Hospital, but whose therapy was disrupted due to the COVID-19 pandemic, were followed up for three months by instant digital means as well as meeting face-to-face every two weeks. As a result, a statistically significant decrease was found in weight and BMI from anthropometric measurements and in HbA1c and triglyceride levels from laboratory parameters as well as in systolic and diastolic blood pressures (during the project period, no changes were made in the antidiabetic, antihypertensive and antihyperlipidemic treatment of any patient. Therefore, the results obtained were only the changes obtained by losing weight). In the same process, a non-significant decline was detected in weight and BMI of the control group patients who were followed up face to face only once every two weeks.

Although there are various studies in the literature investigating the effectiveness of digital technologies (web-based, internet, e-mail, smartphone applications, etc.) in obesity treatment and weight control, the amount of studies examining the follow-up and treatment of patients with obesity via digital technologies and online methods during the pandemic is limited.

Numerous studies have been published showing that weight gain has increased in the general population and particularly in obese patients since the beginning of the COVID-19 pandemic. In a study investigating the effect of "stay-home" days due to the COVID-19 on weight-related behaviors, 123 obese patients who were followed up in an obesity clinic were evaluated. It was determined that 69.6% of the patients had difficulty losing weight during the period, 11.1% did not exercise at all, 47.9% reduced the length of their exercise, and 61.2% tended to eat more because of stress.[16] A study conducted by Pellegrini et al. in Italy with 150 obese patients, who were followed up in an obesity center affiliated to a Diabetes and Metabolic Diseases Clinic and went through a "mandatory quarantine" period for a month, found that males gained an average of 1.3 kg, whereas females gained 1.57 kg during the period. In the same study, eating more, doing less exercise, feeling boredom/loneliness, experiencing anxiety/depression, and increasing consumption of snacks/unhealthy foods/cereals/sweets were associated with greater weight gain.[17]

Examining the relevant data obtained from the studies (web-based, over the internet, as well as e-mails or smartphone apps, etc.) investigating whether weight control can be achieved through digital applications in the pre-pandemic period is of great value in terms of shedding light on the treatment of patients with obesity who tend to avoid going to health institutions and whose comorbidity is likely to aggravate the course of the COVID-19 disease, as is widely expressed in every circumstance. Before writing our project, we reviewed the literature regarding the issue and included a new perspective of remote follow-up treatment into our existing program in our Obesity Centre. We developed a model with smartphones, smart wristband applications, and

only 2-weekly planned visits to our Centre. Conducting a study to evaluate online weight control and weight change along with the related factors, Pappa et al. reported that female participants as well as those with higher BMI, those who were using the program more actively, and those who were taking part more in discussions that could provide online activity and social support ended up losing more weight.[18] In the light of such research, we observed that the patients who were more successful in losing weight in our program appeared to be those who went jogging more, those who entered their data more regularly via the smartphone application, those who used their smart wristbands more efficiently, and those who attended the face-to-face meetings held once every two weeks more regularly. In another study conducted before the pandemic, 91 patients with BMI = 25 - 40 kg / m^2 were randomly divided into two treatment groups, one of which was determined as the intervention group and the other as the late intervention group. The study in the intervention group involved using smart Bluetooth-connected scales for daily weighing, web-based graphs of weight changes, checking the frequency of self-weighing, and weekly special feedback on weight loss progress via e-mails, besides further e-mails consisting of 22 lessons on behavioral weight control. In the controls in the third month, an average weight loss of 4.41% was observed in the intervention group, while an average weight loss of 0.37% was observed in the delayed intervention control group.[19] In our study, an average of 2.76% weight loss was observed in the Project patients during the 3 -month follow-up period. However, the study by Steinberg et al. excluded those who participated in a structured weight loss program in the last six months and lost 10 lbs (1 lb = 453.5924 gram), those with HT, those with unstable thyroid disease, those with psychiatric disorders other than depression, and those who were pregnant or planning to get pregnant. In our study, all of our patients had been treated in the structured weight loss program in our Centre in the last six months (the patients included in our study had completed at least Module 3 training in our Obesity Centre, and even the one who achieved the least weight lost, successfully lost 5.21 kg during that period). Meanwhile, six patients were being followed up and treated with HT diagnosis, six patients with hypothyroidism, and three patients with anxiety disorder. On the other hand, one patient informed us that she was pregnant in the last three weeks of the project. Factors such as lifestyle changes during the pandemic and weekend lockdowns that started to be implemented in the last four weeks of the project can be considered important obstacles for our patients to lose more weight.

In the study, which can be considered the closest study to our project because it was planned with people who participated in a web-based weight loss program during the COVID-19 pandemic, Pellegrini et al. investigated the relationship between stress and weight management in 99 participants. They reported a clear association between more stress and higher BMI, higher education level, more working hours, and having a school-age child at home. In the same study, more stress was also associated with higher levels of worry and anxiety related to the COVID-19 and less time spent on weight loss efforts.[20] In our study, it was observed that at the end of the project, the emotional states of our patients changed at a statistically significant level in the direction

of being anxious and stressed. Despite this, a significant decrease in the weight and BMI of our patients were performed.

As a result, it has been determined that online or smartphone/smart wristband-based follow-up and guidance can be used as an effective method to maintain the treatment of patients with obesity who do not prefer to go to the hospital due to the pandemic. In addition, appropriately adapting and expanding the system, which we apply, is considered beneficial in public and private obesity centers, in obesity units affiliated to Endocrinology and Metabolism Clinics, and in centers where obesity surgery is performed. This system is also believed to provide convenience both for the treatment provider and the patient receiving treatment in the instant evaluation of the data in the follow-up of chronic diseases such as diabetes mellitus and hypertension, and to be effective in solving the problem of malnutrition, which is a common and considerable health concern, especially in patients receiving home health care.

Ethical Considerations: The Antalya TRH Clinical Research Ethics Committee approved the study before its implementation (approval no; 7/18, date; June 03, 2020), and the study was performed in compliance with the Declaration of Helsinki.

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

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Research Article

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EVALUATION OF THE RELATIONSHIP BETWEEN HIGH-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS AND COMMUNITY-ACQUIRED PNEUMONIA SEVERITY IN ADULT PATIENTS

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Abstract

Objectives: Inflammation and acute phase reactions lead to altered high-density lipoprotein cholesterol (HDL-C) concentrations. This study aimed to evaluate HDL-C levels in community-acquired pneumonia (CAP) and to determine the predictive value of disease severity in CAP.

Materials and Methods: This prospective study was conducted in the Department of Pulmonary Diseases. One hundred twenty-five adult patients with CAP were included in the study. Patients were classified into three groups as follows: Group 1; outpatients, Group 2; hospitalized patients and Group 3; patients admitted to the intensive care unit. C-reactive protein (CRP), procalcitonin (PCT) and HDL-C levels were evaluated at baseline, 7th and 30th days in all CAP patients. The relationship between CRP, PCT and HDL-C levels was investigated. Diagnostic performance of baseline HDL-C levels was assessed using receiver-operating characteristic (ROC) curve analyses.

Results: HDL-C levels were found to be decreased in all groups compared to their normal ranges. There was a significantly negative correlation between HDL-C and CRP and PCT (Spearman's r=-0.557, r=-0.841, respectively; p< 0.001). The sensitivity and specificity of HDL-C cut-off value were 0.738 (95% CI=0.580-0.861) and 0.875 (95% CI=0.732-0.958), with an overall accuracy of 0.861 (95% CI=0.728-0.935).

Conclusion: HDL-C levels can be used as an acute phase reactant in patients with CAP.

Keywords: Community-acquired pneumonia, high-density lipoprotein cholesterol, biomarker.

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Introduction

Community-acquired pneumonia (CAP) represents a major infectious cause of mortality that is associated with significant utilization of healthcare resources all over the world. Almost 40% of the patients with CAP require hospitalization, with a further 10% requiring admission to intensive care unit (ICU).[1] Determinant of mortality in CAP patients includes the severity of the disease, treatment regimens and admission status (i.e., admission to hospital and/or ICU). Therefore, scoring systems have been developed to assist physicians in defining the disease severity and predicting possible clinical outcomes. As, CURB-65 (confusion, blood urea nitrogen >20 mg/dL (>7 mmol/L), respiratory rate ≥30 breaths per minute, systolic blood pressure <90 mmHg or diastolic blood pressure ≤60 mmHg, and age ≥65 years), and Pneumonia Severity Index (PSI) represent two scoring systems to predict the clinical response and long-term outcomes in CAP patients.[2] In recent years, various biomarkers have been extensively studied in CAP for diagnosis, disease severity, and treatment monitoring. C-reactive protein (CRP) and procalcitonin (PCT) are the most commonly used biomarkers in CAP.[3] In recent years, several studies have been published investigating the relationship between CAP and serum lipoproteins.[4,5]

High-density lipoprotein cholesterol (HDL-C) and other plasma lipoproteins act as neutralizing agents against endotoxins, inactivating the bacterial endotoxins and leading to anti-inflammatory effects.[6,7] Patients with sepsis and multi-organ dysfunction have significant reductions in total cholesterol and HDL-C concentrations that correlate with the severity of inflammation and poor outcomes.[8,9] It was also shown that HDL-C concentration decreases in septic patients, and the low level of HDL-C is associated with a poor prognosis.[11]

There are few studies that have examined the role of HDL-C levels in CAP patients. Thus, in this study, we aimed to evaluate HDL-C levels in CAP and to determine the predictive value of disease severity in CAP.

Materials and Methods

Study Design and Patient Selection

This single-center, prospective study was conducted in the Department of Chest Diseases in September 2017 and September 2018. The study was approved by the local ethical committee. Informed consent was obtained from all participants.

One hundred twenty-five newly diagnosed adult patients with CAP were included in the study. CAP was defined as an acute condition characterized by at least one respiratory symptom together with two or more of the following clinical signs: fever, chills, cough, sputum production, shortness of breath, pleuritic chest pain, and

one auscultation sign in conjunction with newly developing infiltration in chest X-ray.[12] The patients with CAP were assigned into three groups as follows: Group 1; outpatients, Group 2; hospitalized patients and Group 3; patients requiring intensive care unit. CRP, PCT and HDL-C levels were evaluated at baseline, 7th and 30th days in all CAP patients. The relationship between CRP, PCT and HDL-C levels was investigated. Demographic data, clinical and laboratory parameters of all CAP patients were recorded.

Exclusion criteria were age under 18 years, presence of mental disability, pregnancy, hyperlipidemia and use of anti-lipid drugs, end-stage cancer, those receiving parenteral nutritional support and unwillingness to participate in the study.

CRP (Siemens BN II System, Munich, Germany), HDL-C (Roche Cobas 8000, Mannheim, Germany) and PCT levels (Roche Cobas 6000, Tokyo, Japan) were measured using commercial kits. Normal levels based on the kit used were: CRP 0-5 mg/L, HDL-C in male > 40 mg/dL, in female > 50 mg/dL, PCT < 0.01 ng/mL.

Statistical analysis

The distribution of the continuous variables was examined by both Shapiro-Wilk's test and normality plots. Normally distributed variables were expressed by the mean and standard deviation (mean ± SD), while other continuous and discrete variables were summarized by median (minimum-maximum). Frequency (%) was given for categorical variables. Three patient groups were compared in terms of demographic characteristics by one-way analysis of variance (ANOVA), Kruskal-Wallis test or Chi-square tests. Bonferroni correction and Bonferroni-Dun correction were performed as posthoc tests for ANOVA and Kruskal-Wallis test, respectively. Column proportions were compared by z test in the case chi-square test resulted significantly.

The interaction effect of group and time on serum CRP, PCT, and HDL-C levels was examined with the F1-LD-F1 design for nonparametric analysis of longitudinal data since the two-way mixed ANOVA assumptions were not met. P values of ANOVA-type statistics were given for group-time interaction effect and time effect in each group. LD-F1 design and Bonferroni correction were applied to obtain pairwise comparisons within each group. The diagnostic performances of baseline HDL-C levels discriminating Group 3 from Group 2 and Group 2 from Group 1 were examined by ROC curve analysis. The area under the curve (AUC) and its standard error (SE) were given. The optimal cut-off point was determined by Youden's index. 95% "exact" Clopper-Pearson confidence interval (CI) were calculated for sensitivity, specificity and accuracy, as 95% CI of the predictive values were the standard logit confidence intervals given by Mercaldo et al.[13]

F1-LD-F1 design and LD-F1 design were performed by nparLD package in RStudio (Version 1.1.456). All other analyses were performed via IBM SPSS Statistics 21.0 (IBM, Armonk, NY, USA). A p-value < 0.05 was accepted as statistically significant.

Results

A total of 125 subjects with CAP were included in the study. There were 40 patients in Group 1, 42 in Group 2, and 43 in Group 3. The mean age in these three groups was 42.31 ± 16.78 years (min-max: 18-86), 63.14 ± 14.83 years (30-85), and 70 ± 17.86 years (19-93), respectively. There were significant age differences between in three groups (p< 0.001). In Group 1, 45.20% of the patients (n= 17) were male, and the proportion of male patients in Group 1 was smaller as compared to the other two groups (p= 0.004). The demographic data general clinical manifestations are shown in Table 1.

Table 1. Demographic data and clinical characteristics in patients with community-acquired pneumonia

Variables	Group 1 (n=40)	Group 2 (n=42)	Group 3 (n=43)	p
Age (mean ± SD)	42.31 ± 16.78	63.14 ± 14.83	70 ± 17.86	< 0.001*
Gender (n, %)				
Male	17 (42.50)[1,2]	30 (71.41)[1]	32 (74.43)[2]	0.004
Female	23 (50)[1,2]	12 (26.12)[1]	11 (23.91)[1]	
BMI (normal< 25 kg/m²) (n, %)	25 (62.50)	20 (47.64)	21 (48.82)	0.327
Smoking status (n, %)	18 (45)	26 (61.95)	24 (55.81)	0.299
SpO_2 (mean ± SD)	95.69 ± 2.61	91.28 ± 4.21	88.11 ± 4.14	< 0.001*
Systolic blood pressure mmHg (mean ± SD)	112.16 ± 11.57	116.51 ± 14.89	115.91 ± 14.50	0.341
Bilateral lung infiltration on chest X-ray (n, %)	7 (17.50)[1]	15 (35.71)[2]	32 (74.41)[1,2]	< 0.001
Comorbidities (n, %)				
Diabetes mellitus	4 (10)[1]	14 (33.33)[1]	11 (25.58)	0.039
Chronic heart disease	5 (12.50)	19 (45.24)	35 (81.39)	< 0.001*
Chronic lung disease	4 (1)[1]	11 (26.19)	17 (39.53)[1]	0.009
Chronic liver disease	0 (0)	3 (7.14)	1 (2.32)	–
Cerebrovascular disease	0 (0)	1 (2.38)	3 (6.98)	–

*All groups were significantly different from each other.
[1,2]: Corresponding groups were significantly different.
BMI: Body mass index, SpO_2: Oxygen saturation.

Table 2 shows the serial CRP, PCT, and HDL-C results measured at baseline and at days 7 and 30 of the study. There was a significant decline in CRP and PCT from baseline to day 30 in all groups (p< 0.001), while HDL-C levels increased significantly from baseline to day 30 (p< 0.001). However, the difference between HDL-C at

baseline and HDL-C at day 7 were not significantly different in Group 1. HDL-C levels were significantly higher in Group 1 patients compared to Group 2 and 3 patients at baseline, 7th and 30th days.

A strong positive and linear correlation between baseline PCT and CRP levels was found (Spearmen's r= 0.722, p< 0.001). A moderately strong, negative linear correlation between HDL-C and CRP (Figure 1) and PCT (Figure 2) was found (Spearman's r= -0.557, r= -0.841, p< 0.001). A significant change was observed in serial CRP, PCT, and HDL-C levels in all groups. The extent of change was similar in Groups 2 and 3 (p> 0.05), while it was significantly different as compared to Group 1 (Table 3, Figure 3).

Baseline HDL-C was able to differentiate Group 2 from Group 1, with a cut-off of 21.35 mg/dl. HDL-C levels did not provide statistical significance for differentiating Group 3 from Group 2. The sensitivity and specificity of HDL-C cut-off value were 0.738 (95% CI: 0.580-0.861) and 0.875 (95% CI: 0.732-0.958), with an overall accuracy of 0.861 (95% CI: 0.728-0.935) (Figure 4).

Table 2. Serial CRP, PCT and plasma HDL-C measurements in study groups

Variables	**Group 1**	**Group 2**	**Group 3**	
	Median (min-max)	**Median (min-max)**	**Median (min-max)**	**p***
CRP (mg/L)				
CRP1	77.10 (7.50-343)	192 (44.57-51)	226 (47.11-17)	**< 0.001†**
CRP7	7.50 (3-110)	24 (4.33-104)	38.12 (3.27-139)	**< 0.001†**
CRP30	3.50 (3-27)	5.90 (3-24)	7.51 (3.13-47)	**< 0.001†**
p-value**	**< 0.001‡**	**< 0.001‡**	**< 0.001‡**	
PCT (ng/mL)				
PCT1	0.09 (0.02-25)	0.76 (0.04-39)	1.58 (0.09-89)	**< 0.001†**
PCT7	0.05 (0.01-0.85)	0.11 (0.03-2.94)	0.12 (0.03-1.92)	**< 0.001†**
PCT30	0.03 (0.01-1)	0.04 (0.03-0.23)	0.04 (0.01-2.11)	0.162
p-value**	**< 0.001‡**	**< 0.001‡**	**< 0.001‡**	
HDL-C (mg/dL)				
HDL-C1	34 (4.21-72)[1]	16 (2.82-56)	14.89 (2.91-52)	**< 0.001†**
HDL-C7	34.37 (12-70)[2]	25.71 (10.36-56)	28 (9-54)	**< 0.001†**
HDL-C30	47 (25-82)[1,2]	40.28 (26-68)	42 (27-73)	**0.043§**
p-value**	**< 0.001**	**< 0.001‡**	**< 0.001‡**	

* Between-group comparison result, ** Within-group comparison result
† Group1 was significantly different compared to the other two groups
‡ All time points were significantly different from each other
§ Group1 was significantly different compared to Group3
[1,2] p< 0.05
CRP: C-Reactive protein, PCT: Procalcitonin, HDL-C: High-density lipoprotein cholesterol.

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Table 3. Group-time interaction for PCT, CRP, and HDL-C

	Group-time interaction			
	All Groups	**Group 1-Group 2**	**Group 1-Group 3**	**Group 2-Group 3**
	p	**p**	**p**	**p**
CRP	0.005	0.006	0.012	0.299
PCT	< 0.001	0.007	< 0.001	0.243
HDL-C	< 0.001	< 0.001	< 0.001	0.780

CRP: C-Reactive protein, PCT: Procalcitonin, HDL-C: High-density lipoprotein cholesterol

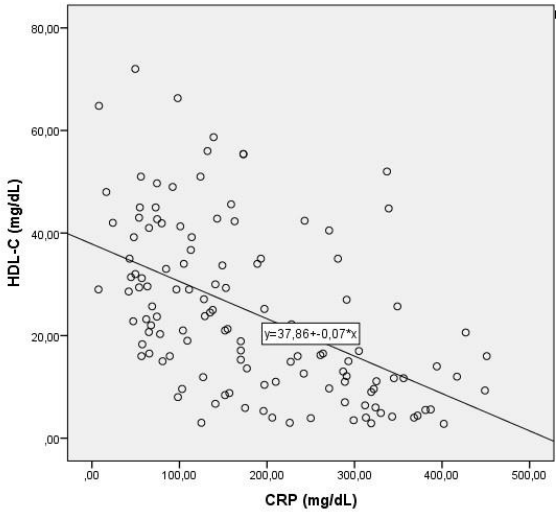

Figure 1. The relationship between HDL-C (mg/dL) and the CRP (mg/L) (r=-0.557, p<0.001). (CRP: C-Reactive protein, HDL-C: High-density lipoprotein cholesterol.)

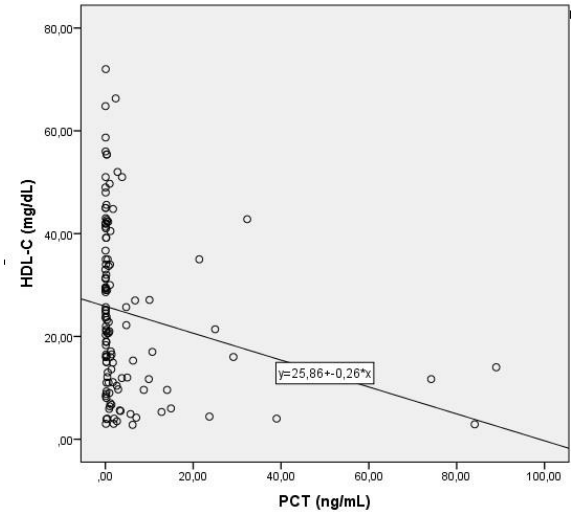

Figure 2. The relationship between HDL-C (mg/dL) and the PCT (ng/mL) (r=-0.841, p<0.001). (PCT: Procalcitonin, HDL-C: High-density lipoprotein cholesterol.)

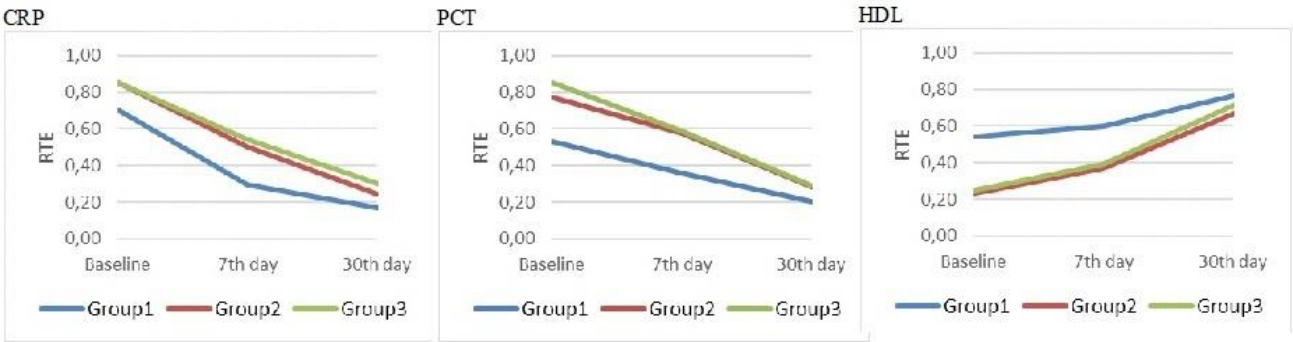

Figure 3. Change in serum CRP, PCT and HDL-C over time in study groups.
(CRP: C-Reactive protein, PCT: Procalcitonin, HDL-C: High-density lipoprotein cholesterol.)

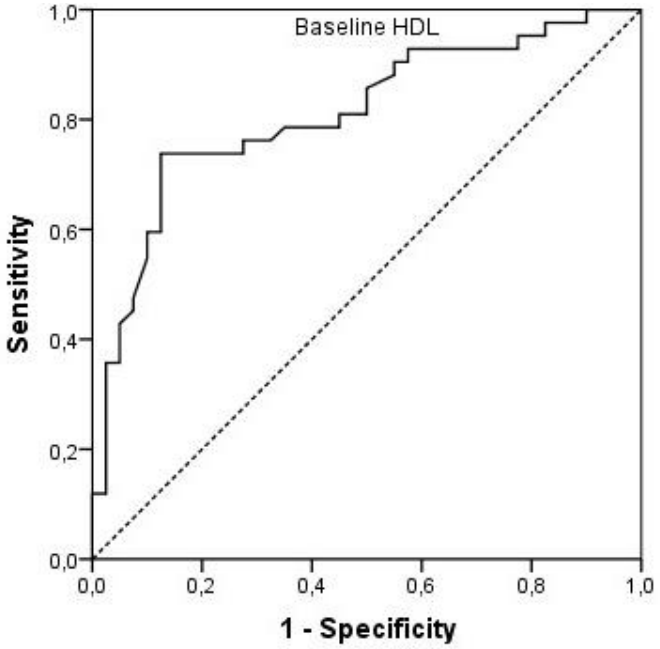

Figure 4. The discriminative power of ROC curves for baseline PCT and HDL-C in Groups 2 and 1. (HDL-C: High-density lipoprotein cholesterol.)

Discussion

In this study, we found a significant reduction in HDL-C during the acute course of CAP. Also, HDL-C levels were found to be significantly lower in more severe patients such as Groups 2 and 3 than outpatients in Group 1. In the follow-up of the patients, it increased compared to the baseline on the 7th and 30th days. HDL-C cut-off value was 73% sensitive and 87% specific in distinguishing cases requiring outpatient treatment and hospitalization. There were significant negative correlations between HDL-C levels and PCT, CRP levels.

Biomarkers are any substances, structures, or processes that can be measured within the body and that can impact or predict the incidence or outcome of a disease.[14] In pneumonia, biomarkers are utilized to assist in diagnosis to determine the disease severity, risk category, triage, administering antibiotherapy, and predicting the prognosis. Several studies have examined potential biomarkers with high sensitivity and specificity as well as high with positive and negative predictive values that can be measured simply and reliably in pneumonia patients.[15]

In recent years, HDL-C particles have been reported to possess anti-inflammatory, antioxidant, and immunomodulatory properties. HDL-C has significant functions in normal lung physiology and plays a role in triggering a pulmonary immune response against lung injury and infections.[16] During the acute phase response in humans, HDL-C and its parent apolipoprotein (ApoA-I) levels decrease with changes in the protein content of HDL-C associated proteins. Ultimately, this leads to a decline in serum paraoxonase levels and in the antioxidant properties of HDL-C.[17] In adult lungs, ApoA-I is released from the alveolar epithelial cells and

alveolar macrophages. It is neutralized by binding to lipopolysaccharides produced by the cell wall of gram-negative bacteria and to lipoteichoic acid, which is a component of the cell wall of gram-positive bacteria. Also, HDL-C modulates innate cellular immunity and prevents the release of inflammatory cytokines. In sepsis, it transports cholesterol to adrenal glands for steroid synthesis.[17,18] On the other hand, HDL-C is oxidized during acute or chronic inflammation, becoming dysfunctional and pro-inflammatory. Dysfunctional HDL is not only devoid of its protective properties but also may be associated with the spread of tissue injury and infection.[19,20] HDL-C and ApoA-I also affect the pathogenesis of influenza A infections. HDL-C derived from mice infected with influenza A virus exhibit reduced anti-inflammatory, antioxidant, paraoxonase and platelet-activating capacity.[21]

Changes in lipid metabolism have been studied in only a few studies in patients with CAP. Rodriguez Reguero et al. found a significant reduction in total cholesterol, HDL-C, apolipoproteins A1 and B during the acute phase of CAP. They only reported a significant increase in HDL-C levels after 15 days of follow-up.[22] Deniz et al. observed a significant negative correlation between HDL-C levels and the radiological extent of the disease in 97 patients. Also, a similar correlation was reported for erythrocyte sedimentation rate, while other biomarkers such as CRP and PCT have not been investigated.[23] In another study in patients with lower respiratory tract infections, a reduction in serum total cholesterol, LDL cholesterol, and HDL-C was observed among those diagnosed with CAP.[24] Our findings confirm the data of the authors who reported a decrease in HDL-C levels in the acute process in CAP. In this present study, a decrease was observed in the acute process in cases with high baseline HDL-C values. In Group 2 and Group 3 patients, HDL-C levels were observed to be lower than the Group 1 patients. Since Group 3 patients are the patients who absolutely need to be hospitalized, it may be useful to evaluate HDL-C levels to make the decision for hospitalization among Group 1 and 2 patients.

In a study by Chien et al., the prognostic value of serum lipid levels was examined in severe CAP patients requiring ICU. The CRP, LDL, and HDL cholesterol levels at admission did not differ significantly between those who did and did not survive, although a significant decline in HDL-C at day seven was observed among those who subsequently died. Accordingly, HDL-C levels of ≥ 17 mg/dL and an LDL cholesterol level of ≤ 21 mg/dL were reported to be predictors of in-hospital mortality.[5] In a retrospective study by Sabalis et al., mean HDL-C levels in patients developing shock was 16.25 mg/dL, while it was 23.66 mg/dL in those admitted to intensive care.[4] In the current study, the cut-off value for HDL-C to differentiate outpatients from those requiring hospitalization was 21.35 mg/dL. Serial measurements (i.e., baseline, day 7, and day 30) showed a trend toward decline in CRP and PCT in Groups 1, 2, and 3, while HDL cholesterol levels increased in response to treatment. These observations are in line with previous studies, supporting the inverse association between HDL-C and inflammatory serum markers such as CRP and PCT. HDL-C serves as an effective inflammatory modulator during infection. In another study with sepsis patients, baseline HDL-C was found to be correlated with albumin and CRP, suggesting that HDL-C serves as an acute phase reactant.[25]

The present study had certain limitations. One of the limitations of our study is that the lipid profiles of most of the participants were not known before they became ill. The duration and change of antibiotic treatments during this study were not recorded. Also, the association between HDL-C levels and mortality was not explored, and the duration of ICU stay in patients in Group 3 was not assessed. Another limitation of our study relates to the fact that due to the low number of patients in whom a causative organism could be identified, the association between HDL-C and possible pathogens was not assessed.

In conclusion, HDL-C levels can be used to identify acute phase reactions in patients with CAP and to evaluate disease severity. In this study, HDL-C was found to be particularly useful in distinguishing outpatients from those requiring hospitalization. Low HDL-C levels may be a warning to healthcare professionals for closer follow-up in outpatient cases. Also, we believe that HDL-C levels in CAP patients may be a useful marker for monitoring response to therapy, such as CRP and PCT.

Ethical Considerations: The study procedure was established in compliance with the basis of the Helsinki Declaration and confirmed by the local ethics board (Decision number: 115, Date: 13.04.2016)

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

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Research Article

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THE EFFECT OF BARIATRIC SURGERY ON CALCIUM METABOLISM

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Abstract

Objectives: Obesity is one of the most important chronic metabolic diseases that includes many comorbidities. Lifestyle changes play the most important role in the treatment of obesity. Despite this, medical treatment and bariatric surgery procedures gain importance in patients whose weight control can not be achieved. In recent years, sleeve gastrectomy (SG) has become very popular. Nevertheless, its effects on gastrointestinal system physiology and bone metabolism are still not known properly.

Materials and Methods: Fifty-two patients who underwent SG between 2018 and 2019 were included in our observational study. Calcium, albumin, albumin-adjusted calcium (AAC), phosphorus (P), 25-hydroxyvitamin D [25(OH)D], alkaline phosphatase (ALP), parathyroid hormone (PTH), creatinine, glomerular filtration rate (GFR) and body mass index (BMI) of the patients were recorded both in the pre-operative period and three months postoperatively. Patients were grouped as patients with low calcium (10.2mg/dL) according to pre-operative and post-operative calcium levels.

Results: The mean age of the patients was 38.96±8.93 years. 1 (8.33%) out of 12 patients with high serum calcium levels in the pre-operative period had low serum calcium levels in the post-operative period, eight patients (66.67%) had normal reference values, three patients (25%) had high serum calcium levels, the difference was significant. Based on ACC, eight patients (15.38%) had high calcium levels postoperatively.

Conclusion: Hypocalcemia, normocalcemia, and hypercalcemia may be observed during the follow-up after bariatric surgery. Although PTH and 25(OH)D play the most important roles in calcium metabolism, the interaction of bone- gut hormones are still unclear and complicated.

Keywords: Sleeve gastrectomy, hypercalcemia, bone, gastric hormones.

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Introduction

Obesity is a serious yet preventable health problem all over the world.[1] Hypertension, cardiovascular diseases (CVDs), Type 2 Diabetes Mellitus, non-alcoholic fatty liver disease (NAFLD/ steatohepatitis), obstructive sleep apnea, cancer, impaired quality of life, depression are the comorbid conditions associated with obesity.[2] Bariatric surgery options could be considered in patients who do not respond to diet, sports or medical treatment. Vitamin D deficiency is common in the obese population. Calcium deficiency may be detected in obese individuals in the pre-operative period.[3] Ionized calcium (Ca^{+2}) is the key to ensuring cell membrane stability, so its level in circulation is tightly maintained. Important changes are present in mineral metabolism in obese patients; firstly, adipose tissue accumulates vitamin D and reduces its use for a substrate of 25(OH)D synthesis. Vitamin D provides intestinal calcium and phosphorus absorption, stimulates bone regeneration, and plays a key role in mineral homeostasis by regulating PTH and Fibroblast Growth Factors-23 (FGF-23) synthesis.[4] It is thought that leptin is the adipokine secreted from adipose tissue that provides the relationship between adipose tissue and the skeletal system. The presence of leptin receptors in osteoblasts and the determination of the effects of leptin on bone suggest that leptin works together with PTH, $1,25(OH)_2D_3$, FGF-23. Leptin, PTH, FGF-23 and bone alkaline phosphatase were found in higher levels in a study on female patients having undergone bariatric surgery.[5] As the frequency of bariatric surgery has increased, publications on its effects on bone health also increase. In our study, we detected patients who developed hypercalcemia after sleeve gastrectomy (SG) and examined the effects of SG on calcium metabolism from a detailed perspective.

Materials and Methods

Fifty-two patients having undergone sleeve gastrectomy (SG) between 2018- 2019 were included in our observational study. All the patients had to meet the criteria for bariatric surgery bearing a BMI of ≥40 kg/m^2 or a BMI of ≥35 kg/m^2 with obesity-related complications such as poorly controlled Type 2 Diabetes Mellitus and hypertension. Exclusion criteria included that chronic kidney disease, solid and hematological malignancies, thyroid dysfunctions, thiazide diuretics medications. Calcium, albumin, albumin-corrected calcium (ACC), phosphorus (P), 25(OH)D, alkaline phosphatase (ALP), parathyroid hormone (PTH), creatinine, glomerular filtration rate (GFR) and body mass index (BMI, kg/m^2) of the patients were recorded in the pre-operative period and three months postoperatively. ACC was calculated with the formula [(4- serum albumin concentration in g/dl) * 0.8) + total serum calcium (mg/dl)].

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and categorical data as numbers and percentages. In the intergroup analysis of continuous variables, normality analyzes were performed with the Kolmogorov-Smirnov Goodness of Fit Test. Preoperative-postoperative analyses of continuous variables with normal distribution were performed with the Paired Samples T-test and those that did not fit with the Wilcoxon Signed Ranks Test. The McNemar test was used for preoperative-postoperative comparison of categorical data. Data were analyzed using IBM SPSS Statistics 22.0 (IBM Corporation, Armonk, NY, USA) packaged software. The value of $P < 0.05$ was considered statistically significant.

Results

The mean age of the patients was 38.96±8.93 years, 92.30% of whom were female. 10 patients (100%) with a low (<8.4 mg/dL) preoperative serum calcium level reached normal reference values (8.4-10.2 mg/dL) in the postoperative period. 23 of them (76.7%) had normal and 6 (20%) had high (>10.2 mg/dL) serum calcium levels. 1 (8.3%) out of 12 patients with high serum calcium levels in the pre-operative period had low serum calcium levels in the post-operative period, eight patients (66.70%) had normal reference values, three patients (25.00%) had high serum calcium levels, the difference was significant (Table 1).

Based on corrected calcium level (ACC); it was determined that 11 patients with high ACC levels in the post-operative period. Among them, while eight patients (15.40%) had normal ACC levels preoperatively, two patients (18.20%) were found to have high serum calcium levels preoperatively and postoperatively (Table 2).

In the post-operative period, the mean BMI (34.36±6.28) decreased statistically ($p<0.05$) compared to the pre-operative period (47.36±6.38), on the other hand, serum P, 25(OH)D, ALP, albumin, PTH, creatinine and GFR levels were not found to be statistically significant ($p>0.05$) (Table 3).

Evaluation of pre-operative and post-operative values of 8 patients with high post-operative ACC is shown in Figure 1.

Table 1. Calcium levels three months after bariatric surgery

		Pre-operative serum calcium			Total	*P*
		<8.4 mg/dL	**8.4-10.2 mg/dL**	**>10.2 mg/dL**		
Post-operative serum calcium	**<8.4mg/dL**	0 (0%)	1 (3.33%)	1 (8.33%)	2 (3.85%)	**0.034***
	8.4-10.2 mg/dL	10 (100%)	23 (76.67%)	8 (66.67%)	41 (78.85%)	
	>10.2mg/dL	0 (0%)	6 (20.00%)	3 (25.00%)	9 (17.31%)	
Total		10 (100%)	30 (100%)	12 (100%)	52 (100%)	

* McNemar Test (Column percentages are shown)

Table 2. ACC levels before and three months after bariatric surgery

		Pre-operative ACC			Total	*P*
		<8.4mg/dL	**8.4-10.2mg/dL**	**>10.2mg/dL**		
Post-operative ACC	**<8.4mg/dL**	1 (7.69%)	1 (3.57%)	1 (9.09%)	3 (5.77%)	**0.014***
	8.4-10.2mg/dL	12 (92.31%)	21 (75.00%)	8 (72.72%)	41 (78.85%)	
	>10.2mg/dL	0 (0%)	6 (21.43%)	2 (18.18%)	8 (15.38%)	
Total		13 (100%)	28 (100%)	11 (100%)	52 (100%)	

* McNemar Test, ACC: albumin-corrected calcium (Column percentages are shown)

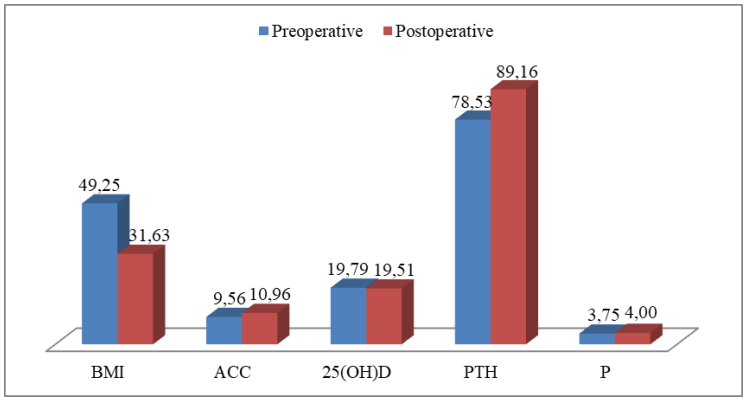

Figure 1. Evaluation of pre-operative and post-operative values of 8 patients with post-operative high ACC (>10.2 mg/dL)

(BMI: body mass index, ACC: albumin-corrected calcium, PTH: parathyroid hormone, P: phosphorus)

Table 3. Biochemical parameters before and three months after bariatric surgery

	Pre-operative	Post-operative	*P*
BMI (kg/m²) (mean±SD)	47,36±6,38	34,36±6,28	**<0.001***
Calcium((mg/dL) (mean±SD)	9,41±1,08	9,47±0,89	0.711*
ACC (mg/dL) (mean±SD)	9,28±1,13	9,40±0,86	0.470*
P (mg/dL) (mean±SD)	3,92±0,39	3,92±0,33	1.000*
25(OH)D (ng/mL) (mean±SD)	20,62±10,64	21,35±8,05	0.610*
ALP (U/L) (mean±SD)	63,40±28,08	59,98±20,31	0.329*
Albumin (g/dL) (mean±SD)	4,16±0,36	4,08±0,29	0.160*
PTH (pg/mL) (mean±SD)	73,15±24,72	67,03±30,28	0.196*
Creatinine(mg/dL) [median (min-max)]	0.70 (0.50-6.00)	0.75 (0.50-1.10)	0.460**
GFR (ml/dk) [median (min-max)]	97.0 (49.0-121.0)	97.0 (83.9-120.2)	0.926**

* Paired Samples T Test
** Wilcoxon Signed Ranks Test
(BMI: body mass index, ACC: albumin-corrected calcium, P: phosphorus, ALP: alkaline phosphatase, PTH: parathyroid hormone, GFR: glomerular filtration rate)

Discussion

We analyzed the calcium levels of 52 patients who had undergone SG operation due to obesity in the pre-operative period and at the third month postoperatively. The prevalence of post-operative hypercalcemia was calculated as 15.40%. When we evaluated the pre-operative and post-operative values of 8 patients, we saw that the vitamin D levels remained the same despite the elevation of calcium (Figure 1). We aimed to examine the effects of SG on calcium and bone metabolism and the mechanism of hypercalcemia occurrence. As to our knowledge, it is the first publication in the literature on hypercalcemia without parathyroid adenoma after bariatric surgery; we hope that our paper can help in lightening these complex mechanisms like part of the puzzle.

The metabolic effects of bariatric surgery and especially its effects on bone have been examined in recent years. Bariatric surgery is a metabolic procedure that includes both malabsorptive and complex physiological changes.[6] Vitamin D deficiency which is especially common in obese individuals because of accumulation in adipose tissue, may increase further in the post-operative period. Pre-operative PTH elevation is possible and similar to primary hyperparathyroidism. The catabolic effect of parathormone on cortical bone has also been demonstrated in obese individuals by quantitative CT (pQCT).[7] In our study, the mean 25(OH)D level of the patients was 20.62±10.64ng/mL, PTH levels were 73.15±24.72pg/mL. In order to decide whether secondary hyperparathyroidism has developed or the patient has primary hyperparathyroidism, it is important to measure calcium, albumin and PTH in the pre-operative period. For musculoskeletal health, reduction of

fracture risk, preservation of bone mineral density, and prevention of secondary hyperparathyroidism after SG, 25OHD levels are recommended to be above 75nmol/L, 2000-4000 IU/day (at least 3000IU/day) vitamin D3, 1200-1500 mg/daily calcium treatment is recommended.[8,] Vitamin D supplementation was performed at their commended doses in the pre-operative and post-operative periods for the patients enrolled in the study. Bariatric surgery procedures involve both malabsorption and dietary restrictions. Among the causes of vitamin D deficiency in patients after bariatric surgery are; vitamin D deficiency before surgical procedure, insufficient vitamin D support during rapid weight loss after bariatric surgery, bile salt deficiency associated with bariatric surgical procedures, vitamin D malabsorption due to intestinal bacterial overgrowth.[9] Osteomalacia cases with severe bone pain secondary to calcium and vitamin D deficiency after bariatric surgery are also encountered. Calcium and 25(OH)D levels should also be measured during replacement. Suthakaran et al. found increased calcium values within the normal reference range 24 months after RYGB and SG. They thought that it was associated with post-operative temporary 25(OH)D elevation and vitamin supplementation.[10] No significant changes in post-operative 25(OH)D levels were observed in our study. There was a significant decrease in BMI of the patients in the pre-operative (47.36±6.38) and post-operative period (34.36±6.28). Hormonal change that causes bone loss due to calorie restriction involves cortisol, adiponectin, 25(OH)D, ghrelin increases, Insulin-like Growth Factor-1 (IGF-1), estrogen, leptin, glucagon-like peptide-1 (GLP-1), GLP-2, Gastric inhibitory polypeptide (GİP), IL-6, and tumor necrosis factor (TNF) alpha decreases.[11] Studies show increased leptin and IGF-1 levels after bariatric surgery.[12] After SG, ghrelin and leptin decreases, adiponectin, GLP-1 and PYY levels also increase. GH response improves after bariatric surgery.[13] Negative regulatory effects on osteoblastic bone formation PYY and the anabolic effect of ghrelin have been shown in studies.[14,15]

Calcium absorption is expected to be better in the duodenum and jejunum due to the low pH, while it is absorbed in greater amounts due to a longer stay in the ileum. As a result, 65% of calcium absorption is achieved. There are two epithelial calcium channels that support the passive transport of Ca^{+2} from the apical membrane to the enterocyte cytoplasm; transient receptor potential vanilloid 5 (TRPV5) and TRPV6. The largest store of calcium in the body is bone. Therefore, it is important in bone calcium homeostasis. Normal serum calcium levels can be maintained by increased levels of $1,25(OH)_2D_3$ and PTH. While vitamin D receptor (VDR) signaling in osteoprogenitors increases Receptor Activator of Nuclear Factor κB (RANKL) expression, VDR signaling in mature osteoblasts has anabolic effects by reducing RANKL expression. The main effect of $1,25(OH)_2D_3$ and VDR is calcium absorption in the intestine. Only 8-10% of calcium absorption takes place in the duodenum.

In a study designed with three groups of patients, i.e., who underwent Roux-en-Y gastric bypass (RYGB) and SG or obese but non-operated patients had been followed up in terms of fracture risk for three years. They found that the fracture risk of those who had RYGP was similar to obese patients who were not operated and that there was a decrease in fracture risk in patients who had SG.[16] In a retrospective cohort analysis of 49113

bariatric surgery patients (16371 having undergone RYGB, 16371 having undergone SG a significantly reduced risk of humeral fracture and the overall fracture was found in those who had undergone SG.[17] In the first study comparing the bone mineral density (BMD) of adolescent and young adults having undergone SG with patients who were followed-up without surgery, a decrease in the femoral neck and total hip BMD and an increase in cortical volumetric BMD in both regions were found after surgery.[18] Stemmer et al. revealed a tendency for higher bone resorption and lower bone formation in rats administered RYGB in their animal study. IGF-1 was found to be low in rats treated with SG, but it was much lower in those treated with RYGB. In their study, they found that RYGB, but not SG, caused a significant trabecular bone loss that could not be corrected by dietary supplementation. In this study, similar weight loss in both sex groups includes the effect of mechanical factors and highlights the effect of endocrine and hormonal factors. A similar decrease in leptin insulin levels, a similar increase in postprandial GIP levels, and gastric pHs were detected. Low albumin level, decreased lipid absorption, and mild decrease in calcium was detected only after RYGB.[19] Saif et al. did not detect changes in calcium, magnesium and phosphorus levels in the first, third and fifth years of follow-up after SG in their studies, but it was observed that the magnesium level increased significantly from baseline. In the first year follow-up of the patients, PTH and 25(OH)D levels returned to normal levels with replacement therapy. However, despite vitamin D replacement, the level remained low in 33% of patients. PTH levels were elevated at five years, although there was no change in 25(OH)D levels.[20]

After SG, ghrelin levels decrease by removing the gastric fundus where ghrelin is most abundant, GLP-1, GLP-2, peptide YY (PYY), cholecystokinin levels increase, thus increasing the feeling of satiety. In malabsorptive procedures such as RYGB, they found an increase in the risk of fracture in osteoporotic regions that occur 2-5 years after the operation, but no such result with SG was achieved. In some studies, it has been thought that bone marrow adipose tissue (BMAT) may contribute to the negative effects on the skeletal system after bariatric surgery.[21,22] BMAT is an endocrine organ that accounts for 70% of the bone marrow volume and 10% of the total fat mass in healthy adults. As a defense mechanism in starvation states, the bone marrow can accumulate adipose tissue or secrete adipokines such as adiponectin, which can increase insulin sensitivity and increase appetite. The relationship between bone marrow adipose tissue and BMD is still unclear.[23,24] Cawthorn et al. showed that BMAT expansion in caloric restriction is an endocrine organ with systemic effects with increased circulating serum adiponectin level.[25] We think that the effects of BMAT on calcium and bone metabolism secondary to weight loss after bariatric surgery are subjects that need to be investigated.

There are publications mentioning that leptin increases the level of osteocalcin, a hormone produced by osteoblasts and known to play a role in bone growth and glucose-insulin homeostasis recently. Studies have shown that leptin stimulates osteocalcin release through its receptors in the hypothalamus. Thus, leptin has beneficial effects on the skeletal system and energy homeostasis.[26] Osteoblasts and adipocytes are cells originating from the same mesenchymal progenitor that play an important role in bone remodeling. 25(OH)D

is a key molecule in mineral homeostasis in bone remodeling due to its main effect on increasing intestinal calcium and phosphorus absorption and regulating PTH and FGF-23 synthesis. Leptin is the molecule that transmits signals from adipose tissue to bone, and osteocalcin is just the opposite. Adipose tissue stores cholecalciferol, which can affect calcium balance and energy expenditure.[4,27] FGF-19 level, which is low in obese patients, has been shown to increase after bariatric surgery. On the contrary, FGF-21 level is high in obese patients; it has been shown to decrease after SG, but not after RYGB.[28] Arhire et al. found an increase in adiponectin and a decrease in leptin after SG. Although there was no decrease in BMD, they detected an increase in bone mineral content (BMC) one year after the operation.[29] It should be kept in mind that parathyroid adenoma may develop secondary to hypocalcemia after bariatric surgery.[30] Parathyroid adenoma was not clinically considered and detected in our patients with hypercalcemia.

The limitation of our study is the lack of long-term calcium follow-up. However, this is the first article in the literature on this subject. With the rapid increase in obesity worldwide, the increase in the frequency of bariatric surgery and the mechanisms of osteoporosis after bariatric surgery are still being investigated. Based on the fact that SG does not increase the risk of fracture and on the findings of post-operative hypercalcemia in our study, issues such as the effects of bone marrow adipose tissue the interaction of hormones secreted from the intestine with the bone should be clarified and further studies are needed.

Ethical Considerations: The protocol was conducted in agreement with the Helsinki Declaration. We obtained informed consent from all participants before their participation. The ethics committee approval was obtained from the Keçiören Training and Research Hospital Observational Research Ethics Committee (Ethics Committee Approval No:2012-KAEK-15/2484).

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

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EFFECTS OF RECONSTRUCTION OF HEALTH CARE ON SERVICE DELIVERY PERFORMANCE IN TURKEY: THE PUBLIC HOSPITAL UNIONS

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Abstract

Objectives: In this study, the performance of 555 public hospitals was evaluated to research the impact of the Public Hospital Unions (PHU) practice applied in Turkey.

Materials and Methods: Performance has two dimensions: efficiency and effectiveness. The scores obtained as a result of Data Envelopment Analysis (DEA) and Malmquist Index (MI) methods were taken as efficiency indicators. The degree of achievement of the targets was taken as effectiveness indicators, and the evaluation of effectiveness was performed by examining to what extent it has gotten closer to the targeted values on the Strategic Plans prepared by Turkey Public Hospitals Authority (TPHA).

Results: According to the results of the DEA-VRS model, the percentage of efficient hospitals; was 69% in 2012, 74% in 2013, 70% in 2014, 70% in 2015, and 71% in 2016. According to the results of the DEA-CRS model, the percentage of efficient hospitals; was 55% in 2012, 60% in 2013, 56% in 2014, 55% in 2015, and 53% in 2016. The efficiency changes of all hospitals between the period of 2012-2016 were analyzed by the MI method, and the Technical Efficiency Change (TEC), Technological Change (TC), and Total Factor Productivity (TFP) values of the hospitals were found to decrease by 45%, 87%, and 72%, respectively.

Conclusion: The public hospital unions (PHU) model, which was created to use resources effectively and efficiently in the field of health, did not significantly enhance hospitals' performance.

Keywords: Public hospitals, performance, data envelopment analysis, Malmquist index.

Introduction

Turkey launched a program known as the "Health Transition Program" (HTP) in 2003. With this program, there have been important developments in hospital services and have made radical changes in the health care system in Turkey.[1] 663 numbered Decree-Law published on November 2, 2011, dated Official Gazette as by central and provincial organizations of Ministry of Health (MoH) restructured and Turkey Public Hospitals Authority (TPHA) were established.[2] Turkey Public Hospitals Authority, which is responsible for the service delivery of secondary and tertiary health care services, consists of central and provincial organizations. As the projection of this restructuring, an important step was reorganized in the MoH and rural hospital structure by uniting 843 MoH hospitals into 87 Public Hospital Unions (PHUs) and devolving important tasks to these PHUs in 2012.[3] The TPHA was delegated the authority of establishing financial and administrative regulations for public hospitals and carrying out annual monitoring and assessment of public hospitals and PHUs for improving effectiveness, quality, and efficiency.[2,3]

Public hospitals have an important role in the delivery of health services in the Turkish health system, as the number of these hospitals is more than the sum of private hospitals and university hospitals. There are three main types of providers of the hospital in Turkey, with public hospitals being the most common ones (62.5% of hospital beds), followed by private hospitals (20.8%) and university hospitals (16.7%). In addition, 63.2% of the health care professionals are employed in public hospitals.[4]

The distribution of budget differs for public hospitals, university hospitals, and private hospitals. Public hospitals are mainly financed from two sources. The general budget financial system is the part of the MoH and affiliated health institutions financed by the Ministry of Treasury and Finance.[5] Staff salaries, and investment expenditures are mostly covered by the appropriation item allocated from the general budget. Public hospitals also have an additional budget from their revolving funds from which they generate income from reimbursement agencies and households for services provided.

World Health Organization assessed comparative efficiency of national health systems;[6] Sahin et al. and Kacak et al. analyzed the technical efficiency of public hospitals under the health transformation project.[7,8] Besides, PHU technical efficiency was assessed with Constant Return to Scale (CRS) and Variable Return to Scale (VRS) model of Data Envelopment Analysis (DEA) by Yiğit.[9] Similarly, Yildirim et al. analyzed the efficiency of the pre and post PHU period with Malmquist Index (MI).[10] Kucuk et al. analyzed the efficiency of the public hospitals in Turkey and evaluated their efficiency at provincial and regional levels output-oriented model of VRS.[11]

According to Sherman and Zou, two key performance concepts are defined. Efficiency is the ability to reach outputs using the least amount of inputs; effectiveness is the ability of an enterprise to achieve its

predetermined goals and objectives.[12] In this study, the information had been obtained regarding the efficiencies of public hospitals through analyzing to what extent had the public hospitals actualized their objectives announced by the MoH. Thus, public hospitals have been evaluated in terms of efficiency and effectiveness. This feature makes up the unique aspect and the distinctive part of this study.

Materials and Methods

When the methods that can be used in health institutions for performance evaluation are examined, it is observed that these methods are divided into three main methods as ratio analyses, parametric methods, and non-parametric methods. Least squares regression and stochastic frontier analysis constitute the parametric methods, while DEA and MI are the non-parametric methods.[7-9] It is recommended to use DEA and MI when conducting performance evaluations for health institutions since they have complex inputs and outputs.[13-17]

Within the framework of the study, the relative efficiency scores of each hospital in the years 2012, 2013, 2014, 2015, and 2016 were measured via DEA.

Both the change in their efficiency score had been revealed year by year and their time-dependent change between 2012-2016 had been presented by using MI. Total Factor Productivity (TFP) scores had originated been determined by obtaining the scores for Technical Efficiency Change (TEC) and Technological Change (TC) constituting the TFP separately.[18]

As a result of DEA and MI analyses, recommendations have been proposed regarding optimal resource utilization and providing efficiency changes correspondingly.

In this study, firstly, efficiency scores and changes in efficiency scores were measured via DEA and MI. After that, the effectiveness of the study hospitals was examined. The realization degree of the objectives desired to be accomplished through the strategic plan TPHA's performance indicators has been used as the effectiveness degree. Thus, this study handled the performance holistically.

Research methods

DEA is a non-parametric analysis used to measure efficiency in decision-making units in various industries.[12,19-22] DEA can be benefited as input or output-oriented.[19-22] In this study, input-oriented DEA was selected because it was recommended to use input-oriented models in health care.[13-17] In addition, DEA can be benefited from the CRS or the VRS. In this study, both of them were used.

CRS model is presented below:[20]

$$E^k = max \sum_{r=1}^{s} u_r\, y_{rk}$$

$Constraints$;

$$\sum_{i=1}^{m} v_i x_{ik} = 1$$

$$\sum_{r=1}^{s} u_r y_{rj} \leq \sum_{i=1}^{m} v_i x_{ik} = 1$$

$$v_i, u_r \geq \varepsilon;\ r = 1,2, \ldots . . \text{s}; i = 1,2, \ldots . . \text{m}; j = 1,2, \ldots . . \text{n}$$

VRS model is presented below:[21]

$$E^k = max \sum_{r=1}^{s} u_r\, y_{rk} - U_0$$

$Constraints$;

$$\sum_{i=1}^{m} v_i x_{ik} = 1$$

$$\sum_{r=1}^{s} u_r y_{rj} - U_0 \leq \sum_{i=1}^{m} v_i x_{ij}$$

$$v_i, u_r \geq \varepsilon;\ r = 1,2, \ldots . . \text{s}; i = 1,2, \ldots . . \text{m}; j = 1,2, \ldots . . \text{n}$$

E^k: efficiency value of the decision-making unit k,
u_r: The weight given to the output of r by the decision-making unit k,
y_r: output of r produced by the decision-making unit k,
v_i: The weight given to the i input by the decision-making unit k,
x_{ik}: the input of i used by the decision-making unit k,
y_{rj}: the output of r produced by the decision-making unit j,
x_{ij}: the input of i used by the decision-making unit j,
ε: a sufficiently small positive number.

MI is a dynamic analysis based on DEA and shows the efficiency changes of decision-making units over time.[23,24] As in DEA, MI can also be benefited as input or output-oriented.[18] In this study, input-oriented MI benefited for the same reason as in the DEA.

The following formulas present TEC, TC, and MI:[23,24]

$$TEC = \left[\frac{d^{t+\iota}(y^{t+\iota}, x^{t+\iota})}{d^{t}(y^{t}, x^{t})}\right]$$

$$TC = \left[\frac{d^{t}(y^{t+\iota}, x^{t+\iota})}{d^{t+\iota}(y^{t+\iota}, x^{t+\iota})} \times \frac{d^{t}(y^{t}, x^{t})}{d^{t+\iota}(y^{t}, x^{t})}\right]^{1/2}$$

$$MI = TEC \times TC = \left[\frac{d^{t+\iota}(y^{t+\iota}, x^{t+\iota})}{d^{t}(y^{t}, x^{t})}\right] \times \left[\frac{d^{t}(y^{t+\iota}, x^{t+\iota})}{d^{t+\iota}(y^{t+\iota}, x^{t+\iota})} \times \frac{d^{t}(y^{t}, x^{t})}{d^{t+\iota}(y^{t}, x^{t})}\right]^{1/2}$$

D is the distant function. *t* and *t+ı* on *x* and *y* present the time period for the efficiency and represent the outputs and inputs. $D^{t}(x^{t}, y^{t})$ and $D^{t+\iota}(x^{t+\iota}, y^{t+\iota})$ are within-period distance functions.

Research variables

In the studies regarding the efficiency and effectiveness of the health care systems, there is a tendency to use activity-based measurements instead of health outcomes since the result indicators of health institutions such as health status cannot be measured directly.

While creating the model, the functional indicators and financial indicators of the public hospitals were used together as input and output variables (Table 1). In DEA and MI, as input variables; first material and material expense, staff fees and expenses, other service costs, general and administrative expenses, the total number of beds, number of specialist physicians, number of assistant physicians, number of general practitioners, number of nurses and midwives and number of other health personnel and as output variables; revolving fund sales, number of inpatients, number of outpatients, and number of A, B and C group surgeries were used. The variables used in this study are compatible with the relevant studies.[7-11]

Table 1. Input and output variables

	Variables	Definition
Input variables	The first material and material expense	First material and material
	Staff fees and expenses	Salaries of Civil Servants,
		Wage Expenses of Workers and Contracted Employees,
		Additional Payment
	Other service costs	Benefits and Services Provided From Outside,
		Other Miscellaneous Expenses, Taxes, Duties, and Fees
	General and administrative expenses	General Administrative Expenses Account
	Total number of beds	Intensive Care Beds Included
	Number of specialist physicians	
	Number of assistant physicians	Used only in A-I Group Hospitals
	Number of general practitioners	
	Number of nurses and midwives	
	Number of other health personnel	Including health officers
Output variables	Revolving fund sales,	Domestic Sales Account
		Overseas Sales Account
		Other Income Account
	Number of inpatients	Including Intensive Care
	Number of outpatients	Including the number of emergency department visits
	Number of A group surgeries	Excluded E group hospitals
	Number of B group surgeries	
	Number of C group surgeries	

Results

The aim of this study put forward to the performance of the public hospitals in Turkey between 2012-2016 period. Performance has two dimensions: effectiveness and efficiency. The purpose is to enhance the performance by achieving the desired scores both in terms of efficiency and effectiveness.[12] Therefore, scores obtained from DEA and MI have been regarded as an efficiency indicator; and the achievement level of the objectives is considered as an effectiveness indicator.

Evaluating efficiency

In this study, the efficiencies of public hospitals grouped as hospitals Group A-I, A-II, B, C, D, and E by the MoH have been evaluated. Within this context, each hospital's efficiency has been evaluated within its group, and a general result has been reached by combining the DEA and MI scores obtained afterward. Combined efficiency

scores of all the hospitals within the framework of this study are provided on the chart and the graphs below and a general evaluation of the efficiency of the public hospitals in Turkey have been performed.

Combined DEA scores of the public hospitals in Turkey between the years 2012-2013-2014-2015-2016 are shown in Table 2. Accordingly, the ratio of efficient hospitals among all hospitals on the CRS Model; is 55 % in 2012, 60 % in 2013, 56 % in 2014, 55 % in 2015, and 53 % in 2016. In the VRS Model, on the other hand, the ratio of efficient hospitals among all hospitals has been calculated as; 69 % in 2012, 74 % in 2013, 70 % in 2014, 70 % in 2015, and 71 % in 2016.

Table 2. DEA scores of all the hospitals

Total Hospital (n=555)	VRS					CRS				
	2012	**2013**	**2014**	**2015**	**2016**	**2012**	**2013**	**2014**	**2015**	**2016**
The number of efficienct hospital	384	413	390	387	393	308	331	309	306	292
The number of inefficienct hospital	171	142	165	168	162	247	224	246	249	263
Efficient hospital (%)	69	74	70	70	71	55	60	56	55	53
Inefficient Hospital (0,91-0,99)%	21	17	18	19	17	24	22	19	20	19
Inefficient Hospital (0,81-0,90)%	9	7	10	10	10	15	13	18	17	14
Average efficiency	**0.98**	**0.98**	**0.98**	**0.98**	**0.98**	**0.96**	**0.97**	**0.96**	**0.96**	**0.94**
Standard deviation	**0.04**	**0.04**	**0.04**	**0.04**	**0.04**	**0.05**	**0.05**	**0.06**	**0.06**	**0.07**

In the CRS Model, the ratio of inefficient public hospitals among all the hospitals was; 45 % in 2012, 40 % in 2013, 44 % in 2014, 45 % in 2015, and 47 % in 2016. In the VRS Model, on the other hand, the ratio of inefficient public hospitals among all the hospitals was; 31 % in 2012, 26 % in 2013, 30 % in 2014, 30 % in 2015, and 29 % in 2016 (Figure 1).

The efficiency scores of all the hospitals whose efficiency changes were evaluated in groups by the MI method, calculated by years between periods 2012-2013**,** 2013-2014**,** 2014-2015, and 2015-2016 have been compared with the previous year's scores and the scores that were obtained were combined and the ratio of hospitals which are progressing to TFP level, remaining stable and degrading has been presented in percentages (Figure 2). According to MI, the ratio of progressing hospitals between periods 2012=>2013 in terms of TFP among all the hospitals is 36 %, while this ratio was 39 % in the 2013=>2014 period, 32 % in 2014=>2015 period, and 42 % in 2015=>2016 period.

Figure 1. All the efficient-inefficient hospitals in DEA, (%) (All periods between 2012-2016)

All the hospital's efficiency changes have been evaluated by the MI method between the periods 2012=>2016, and the scores obtained were combined and their TEC, TF, and TFP values were presented in percentages. According to Graph 2, 49 % of all the hospitals examined within this study between periods 2012=>2016 have shown progress in TEC values, 11 % in TC values, and 24 % in TFP. While the hospitals showing the decrease in TEC values make up 45% of all the hospitals, hospitals showing the decrease in TC values make up 87%, and, showing the decrease in TFP values make up 72 %.

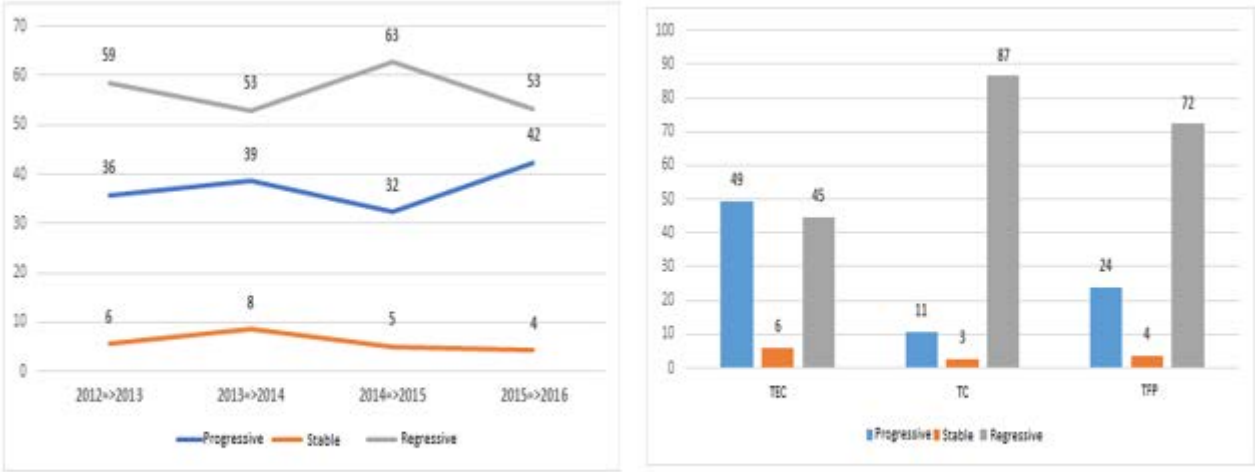

Figure 2. All the progressing/stable/degrading hospitals according to Malmquist TFP Index and Sub-indexes (%) (All periods between 2012-2016)

To prevent this inefficiency arising from technological change, health care service delivery must be featured toward adopting new technologies through identifying the direction and the size of the change in treatment technologies and the expectations in demands for services. It does not seem possible to achieve this technological change with the hospital's facilities. MoH needs to make strategic decisions in resource allocation, and within this context, it is recommended that the technologically insufficient hospitals must apply prioritization in centralized resource allocation in such a way as to prevent these kinds of deficiencies.

Evaluation of effectiveness

Measuring the outcomes and quality is more problematic than efficiency measures.[22] Effectiveness is an indication as to what extent has the realized values come close to the pre-set objectives, in this section, the evaluation of effectiveness was performed by examining to what extent has it gotten closer to the targeted values on the Strategic Plans prepared by TPHA.[25]

According to the strategic plan prepared by TPHA, although the measurable performance indicators of the presented objectives are revealed, some performance indicators have not been assessed since the current situation analysis cannot be performed, or it is in the preparation phase.

Operating results regarding objectives and indicators of the public hospitals in Turkey are included in the Strategic Plan and Performance Program prepared by TPHA for the 2014-2018 period.[25] Performance indicators monitored within this period were evaluated by the accomplishment level in respect to the objectives, and the result has been provided below (Table 3).

In the strategic plan prepared by TPHA for the 2014-2018 period, 53 performance indicators were determined, 10 out of 49 singularly specified indicators were not included since the current state was not clarified, and 3 of them were not included because they were on the preparation phase while 19 indicators which are on the tables above were included in the evaluation.[25] Among these indicators included in the evaluation, 6 of them were deemed to be successful, and 13 of them were found unsuccessful; it is observed that the ratio of indicators that are found successful is 31.5 %.

Table 3. Effectiveness Evaluation based on the operating results of the Strategic Plan prepared by TPHA for the 2014-2018 period[25,26,30]

Performance Target	Performance Indicator	The situation in 2012-2013	Level of Realization 2016-2017	Targeted Indicator	Realization Status
Target 1.1. Target 2.2. Target 2.4.	Overall satisfaction with health care	75.7	71.7	85	Unsuccessful
Target 1.2.	Total number of physicians per 100,000 people in MoH hospitals	50	59	56	Successful
Target 1.2.	Number of dentists per 100,000 people in MoH hospitals	9	12	12	Successful
Target 1.2.	Number of nurses, midwives per 100,000 people in MoH hospitals	133	147	163	Unsuccessful
Target 1.3.	Number of medical specialty students per instructor in health facilities	3	3,1	20% increase	Unsuccessful
Target 2.1.	Number of intensive care beds in MoH hospitals	10,728	14,996	16,979	Unsuccessful
Target 2.1.	Rate of qualified beds in MoH hospitals (%)	36	60,3	92	Unsuccessful
Target 2.1.	Number of beds per 10,000 people (All Sectors)	26	27,9	30	Unsuccessful
Target 2.1.	Number of MRI devices per 1,000,000 people in MoH hospitals	4.1	3.9	5.45	Unsuccessful
Target 2.1.	Number of BT devices per 1,000,000 people in MoH hospitals	5.9	6.6	7.4	Unsuccessful
Target 2.2.	The bed occupancy rate in MoH hospitals	66.4	69	80	Unsuccessful
Target 2.2.	The average number of days of stay in MoH hospitals	4.3	4.5	3	Unsuccessful
Target 2.5.	Number of active patients receiving home health care	105,588	301,863	160,000	Successful
Target 2.7.	Number of patients in health tourism	14,000	153,063	100,000	Successful
Target 2.7.	Income from health tourism (TL)	6 million	48 million	300 million	Unsuccessful
Target 3.1.	Increase Rate of Revenues	10%	10%	10%	Successful
Target 3.1.	Revenue coverage ratio, %	102	87.3	100	Unsuccessful
Target 3.1.	Inventory turnover	5.2	28.5	5.8	Successful
Target 3.1.	Total debt to total assets ratio	0.84	2.5	0.5	Unsuccessful

Administrative activity reports explaining public hospitals' activities conducted according to their strategic plans and performance programs, determined performance indicators and causes of deviations associated with objectives and their accomplishment status, and containing general and financial information regarding the administration as well as TPHA financial performance indicators by their strategic plans are provided on Table 4.

Table 4. Public Hospitals Administration of Turkey financial performance indicators 2012-2016[25,26,30]

Million TL	Total Revenue	Total Expense	Revenue Growth Rate (%)	Income Coverage Rate	Inventory Turnover	Total of Foreign Resources / Total Assets
2012	18,079	17,907		100.96	11.85	0.84
2013	20,535	18,944	13.58	108.40	26.55	1.1
2014	22,524	21,752	9..69	103.55	32.60	1.25
2015	23,903	24,035	6.12	99.45	35.31	1.80
2016	27,192	31,164	13.76	87.25	28.25	2.50

According to the 2014-2018 TPHA strategic plan, among the performance indicators on Objective 3.1, an annual increase of 10 % has been projected for **the increase in income**. When we examine the realizations regarding these performance indicators, it is observed that the objectives have been achieved to a great extent. As follows, the increase in the income rate had become 10 % for the year 2014 and this increased rate decreased to 6 % in 2015. The negative realization difference in the rate of increase in the income for 2015 was recovered in 2016 with an increased rate of 14 %.

According to the 2014-2018 strategic plan of public hospitals, an objective of 100 % accomplishment rate has been set for the **expense coverage ratio of the incomes,** which were among the performance indicators on Objective 3.1. When we look at the realizations regarding the aforementioned performance indicators, it is observed that the objective was achieved in 2014 (103.5 %) but could not be accomplished in 2015 (99.5 %). Especially in 2016 (87.3 %), there has been a realization far below the aforementioned objective.

Under the 2014-2018 strategic plan of public hospitals, an objective of 5.8 % accomplishment rate has been set for the **inventory turnover,** which was among the performance indicators on Objective 3.1. When we look at the realizations regarding the aforementioned performance indicators, it is observed that while the inventory turnover was 26.55 in 2013, it had been 32.6 in 2014, 35.31 in 2015, and 28.25 in 2016.[26] There has been a realization far above the objective of 5.8 determined for the inventory turnover.

By the 2014-2018 strategic plan of public hospitals, an objective of 50 % accomplishment rate has been set for the ratio of the **total debt to total assets,** which were among the performance indicators on Objective 3.1.

When we look at the realizations regarding the performance indicators mentioned above, it is observed that the ratio of total debt to total assets increased 1.25 times in 2014, 1.8 times in 2015, and 2.5 times in 2016.[26]

While the **objective of the ratio of decrease in the expenses** as a performance indicator in providing efficient and effective usage of the resources in public hospitals had been determined as 7 % (growth and inflation-

adjusted expenses), the realization for the end of 2016 has been 0 %, the efficient and effective usage of the resources in health care service delivery has resulted in failure.[26]

When the Malmquist Index TFP scores for the 2012- 2016 period are taken into account, it is observed that the ratio of public hospitals making progress in this period in terms of TFP is 24 % (Graph 2). When it is considered that the two main determinants of performance are efficiency and effectiveness, it can be stated that the public hospitals in Turkey had not measured up to the desired level for the 2012=>2016 period both in terms of efficiency and effectiveness. Public hospitals in Turkey must make progress in efficiency and effectiveness to display high performance.

Discussion

The HTP aimed to improve the overall performance of the hospital system by providing efficient, quality healthcare due to more horizontally organized hospitals with administrative and financial autonomy. However, structural and functional problems arising after the implementation of the union model could not be solved.[27] In this period, four ministers in MoH and seven Chairperson in TPHA have been replaced. Nearly all of the senior management positions have been reassigned in the headquarters based on these replacements in the institution and the province; both the secretary-general position in PHU have encountered reassignments, and significant rotations in the hospitals affiliated to TPHA have taken place in the management systems and managers.[28]

Turkey requires a certain change of approach to enable the realization of the TPHA organization and PHU, which are among the reconstruction practices for the health care services in Turkey. However, this change could not be adequately managed since the legislative changes were not supported by mental change. In this period, the demands on changing the organizational structure aimed at decree-law no. 663 have outweighed without actually being realized, and TPHA had been shut down upon the decree-law no. 694 introduced on August 25, 2017, TPHA has been transferred to MoH and some of the changes made had been withdrawn.[2,29]

In the TPHA Reports of the Court of Accounts, it is recommended to define the activities related to the performance targets of the hospitals at regular intervals with scientific evaluations and to reach the performance targets completely and accurately by establishing a relationship between the resources allocated from the budget and the performance target.[30] More objective performance criteria and evaluation could not be created, and accountability along with administrative effectiveness could not also be provided since holistic analysis had not been performed to the scores obtained from the Efficiency Scorecard Evaluation.

The reorganization in the health care system must be designated to produce high-quality health outputs, and health managers should focus on ways to find practices that will improve quality and use the current resources efficiently. One of these policies is putting the Turkish health care system into service in other countries; neighboring countries are first. Thus, both the capacity usage problem of large-scaled hospitals can be solved, and contributions can be made to the financial sustainability of the hospitals. Practices and applications to be made both by the public and the private sector would feature Turkey in the health care field.

As a limitation of this study, general budget subsidies, which have an important place in the budget of hospitals, were not included in the financial data.

The results of the PHU Productivity Scorecard Evaluation application were used to evaluate the associations and hospitals affiliated to the TPHA in terms of the determined criteria and quality objectives. It is known that effectiveness also naturally includes quality objectives.[12,22] Since the results of the Productivity Scorecard Evaluation could not be accessed; the inability to assess in terms of quality objectives constitutes the limitation of this study.

Ethical Considerations: The data used in this study were obtained with the permission of the TR Ministry of Health, Department of Strategy Development, dated 17.11.2017 and numbered 15722817/841.99.

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

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ANKARA MEDICAL JOURNAL

Research Article

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HOW DOES A WOMAN'S REPRODUCTIVE AND BREAST-FEEDING HISTORY, WEIGHT, HEIGHT, BODY MASS INDEX, BREAST SIZE AND BREAST DENSITY AFFECT THE RADIATION DOSE SHE TAKES DURING MAMMOGRAPHY?

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Abstract

Objectives: Mammography is the screening test for breast carcinoma. The radiation dose received during this imaging has always been a point of consideration. The aim of this study is to search the relation of radiation dose received during mammographic imaging and the patient's age, menarche age, menopause age, childbirth history, total time of breastfeeding, height, weight, body mass index, mammographic breast density pattern and breast size.

Materials and Methods: Patients applying for mammography imaging were questioned about their menarche age, menopause status and age and their weight, height, and breast upper and inferior mammary fold sizes were measured. Their mammographic breast density and radiation doses were recorded. Statistical analysis was made with ANOVA and Pearson correlation.

Results: Breast size, weight, body mass index are found to be related to the radiation dose received during mammography. Age, number of given births, weight, body mass index and breast size have an effect on the mammographic breast density, which is a factor in both developing and diagnosing breast carcinoma.

Conclusion: Breast density on mammography can show differences according to the patient's reproductive history and body stature. Radiation dose taken during a mammography is found to be affected by body mass index and breast size. Breast tissue with increased adipose tissue is suitable for mammographic imaging in the aspect of radiation exposure.

Keywords: Breast density, mammographic density, radiation, weight, height, menarche, menopause, breast.

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Introduction

Breast cancer is the most common malignancy and the leading cause of death from malignancy among women.[1] It affects 1.5 million women each year, and in 2015, 570,000 women lost their lives because of this cancer. It is 15% of all women's cancer deaths. Due to its high incidence and mortality rates, it is tried to be diagnosed early with screening programs all around the world.[1] On the other hand, it has various morbidity effects on the survivor, mostly about the upper limb. Edema and decreased range of motion are the main morbidities after the treatment of breast cancer.[2]

Mammography is the screening tool for breast cancer. The World Health Organization (WHO) declared the principles of effective breast screening in 1968, and the WHO screening guidelines mentions five key points, each of which applies to breast cancer and mammography: Breast cancer, being screened is serious and prevalent, the test-mammography is sensitive and specific, the test is well tolerated, the test is inexpensive, and the test changes therapy or outcome.[3]

The radiation dose received during mammography imaging has always been a point of consideration.[4] Radiation doses received at this procedure change from person to person; even changes from year to year in the same woman.[5]

X-ray is electromagnetic radiation energy that can cause ionization at the tissue.[6]

In order to produce x-ray suitable for soft tissue composition, breast mammography devices eradiate low kilovoltage x-rays.

The interaction of the x-ray with the tissue is affected by the composition of the tissue.[7]

The breast is composed of fibroglandular tissue and adipose tissue. Fibroglandular tissue is affected by hormonal changes both during menstrual cycles and during the lifetime. Adipose tissue can change with the weight of the woman. Also, personal and familial properties have an effect on the composition of the breast tissue.

The relation of dens breast structure and breast cancer development risk has been studied for a long time.[4, 8-11] The aim of the study is to find the effects of patient's age; hormonal history as menarche age, menopause age, menopause status; reproductive history as the number of births, total time of breastfeeding; body stature as weight, height, body mass index, and breast size and mammographic breast density on radiation dose received during mammography. Also, the effects of these variables on breast density are searched.

Materials and Methods

Patients and Image collection

After the approval of the institutional ethical review board, all patients applied to our conventional mammography (Giotto IMS, Bologna; Italy) unit in June 2015 (179 women) formed the study group. Informed consent was obtained from all participants.

Patients were questioned for their age, menarche age, menopause status and age, number of births, total time of breastfeeding as a summation of breastfeeding periods of all children. The menopause situation and age were questioned and noted. Menopause ages were also grouped in 5 years intervals

Their weight and height were measured. Breast size was found with the measurements of the breast's maximum size over areola (breast upper size) and the chest size from the infra-mammary fold (breast lower size). The cup size was calculated by subtracting inferior mammary fold measurement from maximum breast size.

Each patient had two mammograms (RCC: right craniocaudal, LCC: left craniocaudal, RMLO: right mediolateral oblique, LMLO: left mediolateral oblique) for each breast.

Image evaluation

Breast density was codded according to the BIRADS (Breast Imaging Reporting and Data Systems) density categories as; Type A (less than 25% of the mammogram is fibroglandular tissue), Type B (25-50% of the film is fibroglandular tissue), Type C (50-75% fibroglandular tissue), Type D (dense breast-more than 75% is fibroglandular tissue).[12]

The radiation doses during each of these films, average radiation doses, and total radiation doses were recorded. For the patients with unilateral mammography, total doses were calculated with twice the unilateral doses for correction.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007&PASS (Power Analysis and Sample Size) 2008 Statistical Software (Utah, USA) were used for all statistical analysis, including descriptive statistics. The normal distribution was searched with histograms. The parametric values were analyzed with the ANOVA test, and correlation analysis was made with Pearson correlation. The significance was accepted at %95 confidence

interval. Weight's contribution to breast size's relation with radiation dose is searched with a multiple linear regression test.

Results

There were 179 patients between 19 and 77 years old with a mean of 51.57 years.

The age of the patients and menarche age, menopause age, reproductive years, breast upper size, breast fold size, breast cup size, height, weight, body mass index, number of births, total breastfeeding duration (in months) and radiation doses of each projection images are summarized at Table 1.

Table 1. The descriptive statistics of the variables

	Minimum	Maximum	Mean	Std. Deviation
Age	19	77	51.57	8.35
Menarche age	11	21	13.52	1.55
Menopause age	24	58	46.33	5.12
Reproductive years	12	47	33.22	5.48
Breast upper size	77	133	99.26	10.93
Breast fold size	65	118	89.05	9.14
Breast cup size	-3	23	10.20	4.32
Height	145	173	159.56	6.11
Weight	41	116	74.64	13.49
Body mass index	18	48.3	29.41	5.41
Birth	0	10	2.50	1.50
Breast feeding (in months)	0	144	30.6	29.2
RCC dose	0.30	0.90	0.43	0.09
RMLO dose	0.30	1.10	0.39	0.10
LCC dose	0.30	0.90	0.43	0.08
LMLO dose	0.30	1.10	0.39	0.10
Average dose	0.30	1.00	0.41	0.08
Total dose	1.20	4.00	1.66	0.34

RCC: Right craniocaudal graph, RMLO: Right mediolateral oblique graph, LCC: Left mediolateral oblique graph, LMLO: Left mediolateral oblique graph.

Age of the woman, her upper and lower breast sizes and cup size, her weight, body mass index and her fertility are found to be correlated with her breast density type in the analysis of One-way ANOVA (Table 2).

The total radiation dose was found to be related to breast upper size, breast fold(lower) size, weight, and BMI (Table 3).

Table 2. Breast density types according to patients' age, reproductive properties and body stature in the analysis of One-way ANOVA.

Breast density type	P
Age	0.002
Menarche age	0.463
Reproductive period	0.229
Menopause age	0.151
Breast upper size	<0.001
Breast lower size	<0.001
Cup size	0.023
Height	0.138
Weight	0.001
Body mass index	<0.001
Birth	<0.001
Breast feeding period	0.318

In order to search the effect of the weight on breast size and eventually in the radiation dose, a multiple-linear regression test was performed. It is seen that BMI was the factor affecting mainly the dose (R:0.4 $p<0.001$ for BMI and $p=0.512$ for breast cup size), not the breast size.

Radiation dose and breast density type relation are demonstrated in Table 4. It is seen that both total and average breast doses and mediolateral oblique projection doses are affected by breast density, but craniocaudal projection radiation doses were not significantly affected by breast density.

Older age, being in menopause, having larger breasts, increased weight and BMI, being more parous have a negative relation with breast density (Figure 1a, 1b and 2a, 2b).

Only body mass index and weight, and- with their effect- breast upper and lower sizes had a negative relation with the total and average radiation doses taken during mammography as well as lower breast density (Figure 1a, 1b and 2a, 2b).

Table 3. Results of Pearson Correlations of variables with total radiation dose. ** points significance.
BMI- Body Mass Index

		Total dose
Age	Correlation	-0.063
	P	0.402
Menarche age	Correlation	0.010
	P	0.895
Reproductive period	Correlation	0.107
	P	0.306
Menopause age	Correlation	0.177
	P	0.082
Breast upper size	Correlation	-0.300**
	P	<0.001
Breast fold	Correlation	-0.332**
	P	<0.001
Cup size	Correlation	-0.056
	P	0.460
Height	Correlation	0.043
	P	0.571
Weight	Correlation	-0.407**
	P	<0.001
BMI	Correlation	-0.401**
	P	<0.001
Birth number	Correlation	-0.048
	P	0.527
Breast feeding	Correlation	-0.023
	P	0.762

** points significance. BMI: Body Mass Index

Table 4. Breast density and radiation doses of 4 projections of mammography, average and total doses.

	RCC	RMLO	LCC	LMLO	AVARAGE DOSE	TOTAL DOSE
P	0.482	0.003	0.200	0.001	0.020	0.035

RCC: Right craniocaudal graph, RMLO: Right mediolateral oblique graph, LCC: Left mediolateral oblique graph, LMLO: Left mediolateral oblique graph. One-way ANOVA test was used.

Discussion

As a cancer screening tool, the radiation dose of mammography has always been a matter of interest for both radiologists and clinicians. As the technology develops in the path of mammography with a better resolution by using lower radiation doses, the subjective factors depending on the patient still remain as a factor in the dose absorbed.[13]

Mean glandular dose is the main measure for quantifying mammographic radiation dose absorbed. But in this equation, half-value layer of aluminum, milliampere second values, breast thickness and patient's age are also included in the equation to obtain the mean glandular radiation dose.[14] Since this equation includes breast thickness as a multiplier, and our study also aims to search the effect of breast size in radiation, the row radiation dose value was used for each mammography.

This study revealed a negative correlation between weight and BMI and the total radiation dose. As the weight increased, the total dose and breast density decreased consecutively. If the breast is composed of more adipose tissue, an X-ray can penetrate it more easily, and the required radiation dose will be lower.[15]

Upper and lower breast sizes (transverse measurement of the chest passing from the nipple and inframammary fold levels) were related to the radiation dose in contrast to cup size. But all three of these measurements were in relation to breast density. In order to search the effect of the weight on breast size and eventually in the radiation dose, a multiple-linear regression test was performed. It's seen that BMI was the factor affecting mainly the dose (R:0.4 $P<0.001$ for BMI and $p=0.512$ for breast cup size), not the breast size. This is an important finding because if we would use only the breast size passing over the nipple, we could find a relation between breast size and radiation dose. But cup size did not show this relationship, and in addition, even the upper breast size passing through the nipple did not confirm a relationship with radiation dose with multiple regression study. Only one measurement of a breast is not trusty in assessing a relationship between breast size and radiation dose.

It is understood that; despite both breast size, BMI and weight have a relation with the total radiation dose; the BMI is the factor that has also affected the breast size and eventually in the radiation dose (Figure 1 and 2). Height revealed a relationship with neither breast density nor radiation dose. So, the main factor in BMI and radiation dose interaction is due to weight.

Although we were expecting a decrease in the radiation dose with increased fertility, we could not see that relation, but breast density was seen to be affected(decreased) from the birth number. Having more children resulted in more lipomatous breast tissue and decreased breast density. Similarly, Nakajima et al. also show that having children was related to having less mammographic breast densities.[16] In our study17/179 patients were nulliparous. Lifetime breastfeeding period in months had a non-significant tendency of negative relation with breast density ($p=0.063$) and did not lead to a decreased radiation.

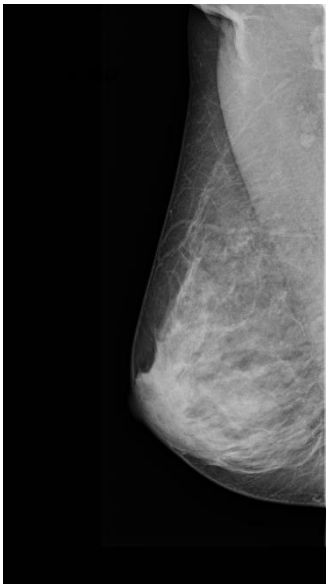

Figure 1a. Right mediolateral oblique mammogram of a 51 years old female. [BIRADS category D, dens breast. She has one child. Her BMI is 22.6. Total radiation dose is 2.8 mGy. Her upper breast size is 86, lower breast size is 79 cm (cup size 7cm)]

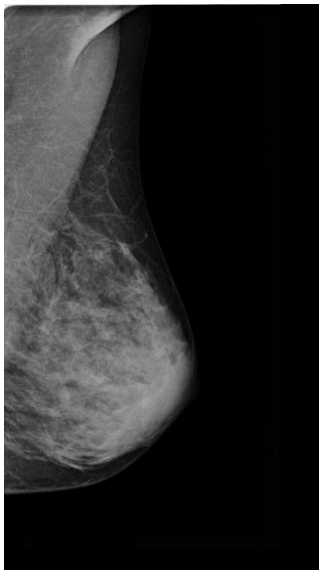

Figure 1b. Left mediolateral oblique mammogram of a 51 years old female. [BIRADS category D, dens breast. She has one child. Her BMI is 22.6. Total radiation dose is 2.8 mGy. Her upper breast size is 86, lower breast size is 79 cm (cup size 7cm)]

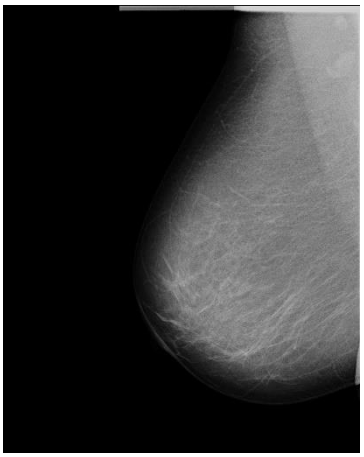

Figure 2a. Right mediolateral oblique mammogram of a 46 years old woman with 3 children, who has breast measurements of 108 and 98 cm (cup size10) with a BMI of 35.9. She has BIRADS type A breast pattern. Her total radiation dose was 1.2 mGy.

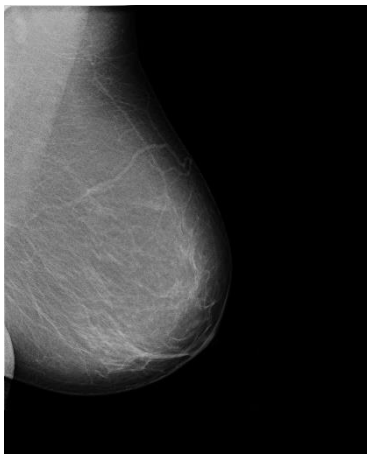

Figure2b. Left mediolateral oblique mammogram of a 46 years old woman with 3 children, who has breast measurements of 108 and 98 cm (cup size10) with a BMI of 35.9. She has BIRADS type A breast pattern. Her total radiation dose was 1.2 mGy.

There was not a relation between being in menopause and the radiation dose. But it was related to the mammographic breast density. Post-menopausal women had lower breast density as it is expected that they are losing the effect of sex hormones on fibroglandular tissue.

Age of menarche or menopause, total reproductive years did not reveal a correlation with radiation dose. These factors have been related to breast carcinoma.[4,17] Alexeeff et al. showed a negative relation between the menarche age and breast density, pointing out late menarche as a factor for dense breast pattern in their very large numbered patient study with digital breast density measurement application.[4] In our study, menarche age was not found as a factor influencing the breast density either but the breast density evaluation techniques were different between these two studies. In our study, the BIRADS mammographic visual categorization is used.

Older age, being in menopause, larger cup size and higher number of births given were only related to lower mammographic breast density. Higher breast density is a known risk for breast carcinoma and a reason for lower sensitivity in mammographic screening. Younger, premenopausal patients with small breast sizes and fewer children will form the dense breast group, which will be the difficult ones to diagnose and have increased risk due to density.

Mammographic breast density showed a correlation with the radiation dose (Table 4). It was prominent on MLO projections. It can be a result that, on MLO projections, imaged volume is larger since the axillary tail is also included in the evaluation.[18] Another property of MLO projections is the compression is less than the CC projections, and evaluated breast thickness is more.[18] On the contrary, on CC image compression is stronger, and as a result, glandular tissue is more dispersed and less dense, resulting in less radiation.[19]

Breast density as a risk factor for breast cancer seems to be a problem for breast health in another aspect.[20] Women with dense breasts are recently accepted as a group of people that should be informed about their increased risk.[20] And due to this increased risk, a more serious screening should be issued for this group of people. But it is seen that this group is also having higher amounts of radiation during screening mammography, which will result in a dilemma.

The main limitation of this study is the scarcity of the patient number. Also, the breast density was not obtained with computerized mammographic programs.[21]

In conclusion, women in older age, in menopause, having larger breasts, with increased weight and BMI and women who are more parous had lower density breasts. It is concluded that lower body mass index, as well as the higher mammographic breast density pattern, is the main factor affecting the increased radiation during mammography.[9-10] Despite obesity being a risk factor for breast cancer, it is seen that slim body feature results

in more radiation intake during mammography. Similarly, dens breast, as a known risk factor of breast cancer, also appears to be a risk factor for increased radiation dose during screening mammography in this study. But still, studies with larger patient numbers are required. Evaluation of each patient should be planned according to patient-based medicine properties.

Ethical Considerations: The ethical approval of the institutional ethical review board (AYBU No: 26379996/103) was obtained for this study. Informed consent was obtained from all participants.

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

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Case Report

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PARA-INFECTIOUS GUILLAIN BARRE SYNDROME IN A PATIENT DIAGNOSED WITH COVID-19

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Abstract

Accumulating evidence suggests the neurotropic characteristics of the SARS-CoV-2. Although the pathogenesis is unclear, the relationship between COVID-19 and Guillain Barre Syndrome (GBS) has been described previously. In this report, a 66-year-old male with para-infectious COVID-19-related GBS admitted with bilateral weakness in distal lower limbs was presented. Five days ago, since he had a risky contact with the COVID-19 patient, the SARS-CoV-2 PCR test was performed and resulted in positive. Favipiravir treatment was given as outpatient therapy. On the fifth day of antiviral treatment, he had applied to Emergency Department with two days of muscle weakness of lower extremities consistent with GBS; hence lumbar punction was performed. The cerebrospinal fluid examination revealed albumin-cytological dissociation. Despite the administration of immunoglobulin infusions, neurological findings worsened, dysphagia, and facial paralysis occurred. Although he was stable for COVID, he was followed up in the intensive care unit for plasmapheresis and then intubated for the respiratory involvement of GBS. Early diagnosis and treatment are critical in GBS related to COVID-19. Since para-infectious COVID-19-related GBS has poor outcomes, clinicians should be aware of this kind of complication to manage patients as it's supposed to be.

Keywords: COVID-19, para-infectious GBS, SARS CoV-2, Guillain Barre Syndrome.

Introduction

SARS-CoV-2 causes a wide range of clinical symptoms since it uses angiotensin-converting enzyme-2 (ACE2), which presents in various organs and systems. The evaluation of neurological manifestations of 214 patients with COVID-19 revealed that dizziness, headache, taste disturbance, and hyposmia were the main findings.[1] The COVID-19 related Guillain-Barre Syndrome(GBS) cases have rarely been reported.[2] Parainfectious GBS is a newly defined rare form of COVID-19 related GBS and has poorer outcomes. Clinicians should be aware of this syndrome to define and manage cases properly.

Case Report

A 66-year-old male patient was admitted to another hospital with the complaint of diarrhea and tested for SARS-CoV-2 PCR since he had a high-risk contact history with his wife, who had a diagnosis of laboratory-confirmed COVID-19. The oropharyngeal swab sample tested for SARS-CoV-2 PCR was positive. On the fifth day of favipiravir treatment, he was admitted to the emergency department(ED) with a 2-day acute symmetric weakness in distal lower limbs. He had no respiratory symptoms. On physical examination, muscle strength was found as 2/5 on lower extremities and 4/5 and 5/5 on the upper right and left extremity, respectively. Deep tendon reflexes of the lower limbs were absent. The blood oxygen saturation level was 97%. Brain magnetic resonance imaging was normal, and there was no diffusion restriction. Chest Computed-Tomography showed typical early findings of COVID pneumonia. Oxygen support was not needed on the follow-up. A lumbar puncture was performed with the suspicion and clinical diagnosis of GBS. Cerebrospinal fluid(CSF) analysis revealed albumin-cytological dissociation: protein 2335.13 mg/L (normal range: 150-400), albumin 1393mg/L (normal range: 100-300), no white blood cell. SARS-CoV-2 PCR was negative.

Intravenous immunoglobulin(IVIG) 0.4g/kg per day (35 g/day) treatment was planned for five days. On the third day of hospitalization, the patient's muscle weakness progressed. Bilateral hypoesthesia was also determined in the lower extremities. Plasmapheresis therapy was suggested due to the clinical progression of IVIG treatment, and it was given seven times every other day. The patient was admitted to the Intensive Care Unit(ICU) to implement plasmapheresis. He developed dysphagia and facial paralysis on the eighth day of symptoms onset for COVID-19. He was intubated due to respiratory muscle involvement on the 11thday of admission. Although he was given plasmapheresis and IVIG therapies, neurological findings worsened progressively, and he became quadriplegic. He had secondary infections (ventilator-associated pneumonia and candidemia) on the ICU follow-up and died on the 48thday of ICU admission, although he had been given effective antimicrobial therapy. The timeline for the progress of findings of GBS and implementations of therapies are summarized in Figure 1. Informed consent was obtained from the patient for publication at the time of diagnosis.

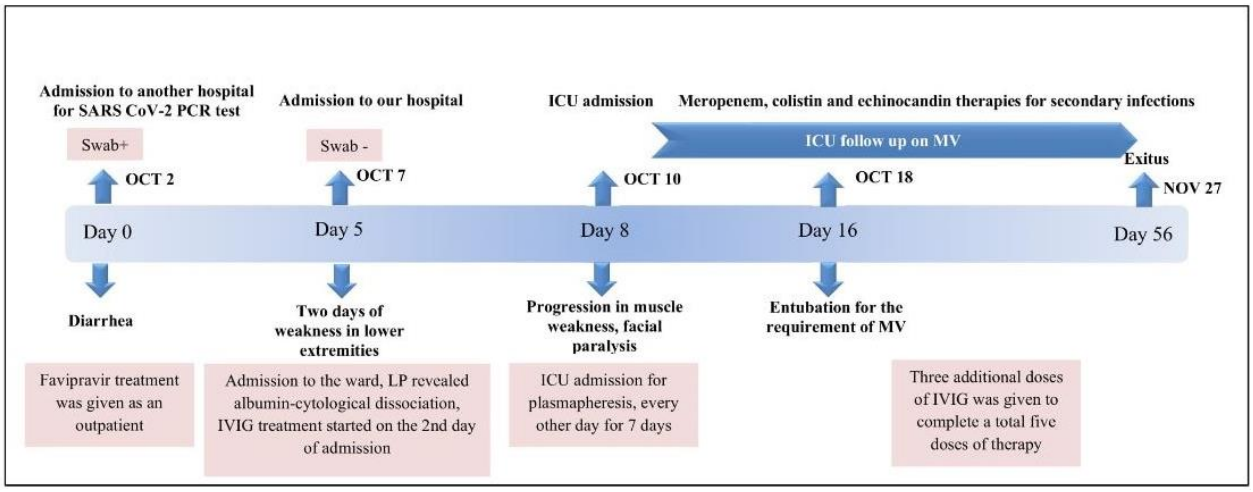

Figure 1. Timeline of the clinical progress of the patient diagnosed with COVID-19 related parainfectious GBS (ICU: Intensive Care Unit, LP: Lumbar Puncture, MV: Mechanical Ventilation)

Discussion

Neurological manifestations were reported in 36.4% of COVID-19 patients.[1] GBS is a typical post-infectious disease that generally occurs within four weeks of disease onset.[3] However, para-infectious GBS related to SARS CoV-2 was reported previously.[4] Neuro-invasion or autoimmune response of the virus via ACE2 receptors in neuronal tissues is thought to play a role in the etiology.[4] GBS mainly progresses with limb weakness and areflexia development.[3] This is how it developed in our case, as well. He had rapid progressive neurological findings resulting in quadriplegia, facial paralysis, and dysphagia. Cranial neuropathies, including facial paralysis, consist of a rare form of GBS.[5] The diagnostic criteria for GBS can be evaluated with the Brighton Criteria, and our patients had all the defined criteria.[6] CSF examination revealed no pleocytosis, but increased protein levels and albumin-cytological dissociation were identified consistent with GBS.[5] In addition, the test for SARS CoV-2 PCR in CSF was negative. Published reports of GBS in the literature have indicated negative results in all tested 32 patients with COVID-related GBS.[5] Nerve conduction studies are the main tool to determine the subtype of GBS. Electromyography(EMG) was performed after his admission to ICU, and prolonged distal latencies, conductions block, slowing of conduction velocities, and low action potentials were identified. F waves were absent, as were all sensory nerves, except the sural nerve, which has been typically reported in patients with GBS. Overall, electrical abnormalities were consistent with the demyelinating form of GBS with secondary sensory-motor axonal degeneration. The review of published 37 COVID-19 cases with GBS revealed that the mean-time between COVID-19 symptoms onset and GBS symptoms onset was 11±6.5 days.[2] Another review of 51 COVID-19-related GBS cases reported that 70.5% of the patients were post-infectious whilst 24.5% were para- infectious.[5] Respiratory failure via GBS and the requirement of mechanical ventilation were reported as 17%-30%.[7] Besides, para- infectious COVID-19-related GBS cases were found riskier for

ventilator requirement.[5] In the present case, GBS symptoms developed on the third day of COVID-19. Although IVIG treatment was given on the second day of admission, limb weakness progressed, and bilateral facial paralysis developed. Hence, plasmapheresis was started. Although the recommended treatment regimens were implemented, rapid progression to quadriplegia developed. He needed intubation via respiratory muscle involvement and needed ICU follow-up, similar to %20-%30 of non-COVID GBS patients.[6] The severity of clinical progress is highly variable in patients with GBS, ranging from the mild weakness of muscles to serious weakness resulting in quadriplegia and the need for ventilator support.[3] IVIG and plasmapheresis were accepted as efficient treatment modalities.[3,8] Either of them should be implemented as soon as possible after disease onset to prevent the occurrence of permanent nerve damage.[3,9,10] IVIG (0.4 g/kg per day) or plasma exchange for five days constitute effective treatment alternatives. However, a combination of them was not reported as more beneficial compared to the use alone.[3] There is a clear need for more effective treatment agents since many of the patients have developed progressive weakness despite using IVIG or plasmapheresis.[3] GBS is a life-threatening disease with a mortality rate of 3%-7%.[3] The development of respiratory insufficiency via respiratory muscle involvement constitutes one of the most probable causes of death in patients with GBS.[3] Early diagnosis and treatment are critical in GBS related to COVID-19. Moreover, since parainfectious COVID-19-related GBS has poor outcomes, the probability of this syndrome should be kept in mind in patients with neurological findings of COVID-19 to manage cases properly without delay. Comprehensive studies are needed to find out the different patterns of COVID-19 related GBS.

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Conflict of Interest: None to declare

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