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RESEARCH ARTICLE

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Evaluation of Tetanus Immunoglobulin G Levels According to Age and Sociodemographic Characteristics: A Community-Based Study

ABSTRACT

Objective: In the present study, it was aimed to determine the serum tetanus antibody levels in individuals aged 18 and over and examine whether the antibody levels have changed with advancing age.

Methods: This descriptive research was carried out on 916 adults aged 18 years and over in Konya. A survey containing sociodemographic features was filled and tetanus IgG levels was measured.

Results: In this study, 916 suitable people in total who consisted of 68.4% (n=627) female and 31.6% (n=289) male were included. Of the participants, 756 (82.5%) had protective tetanus antibody levels (≥0.1 IU/mL), and 160 (17.5%) had unreliable protective antibody levels (<0.1 IU/mL). No significant difference was found between male and female gender (p=0.225). Antibody levels of those who had secondary and higher education were found significantly higher than those with primary education or less. Antibody levels decrease significantly with increasing age (p<0.001). Antibody levels were significantly found higher the employees than the unemployed (p<0.001), the unmarried than the married (p=0.004), and the people with high income than those with low income (p<0.001) statistically. Antibody levels of those who were vaccinated earlier were found significantly higher (p<0.001).

Conclusions: In this study, it was determined that tetanus antibody levels of the people at old age, with low educational level and without vaccine were lower. Tetanus is a life-threatening public health problem, so new health policies should be developed in this regard.

Keywords: Tetanus Antibody, Vaccine, Adult, Seroprevalence.

Tetanoz İmmünoglobulin G Düzeylerinin Yaş Ve Sosyodemografik Özelliklere Göre Değerlendirilmesi: Toplum Temelli Bir Çalışma

ÖZET

Amaç: Sunulan çalışmada serum tetanoz antikor seviyelerinin 18 yaş ve üzeri bireylerde belirlenmesi ve ilerleyen yaş ile birlikte antikor düzeylerinin değişip değişmediğinin incelemesi amaçlanmıştır.

Gereç ve Yöntem: Bu tanımlayıcı araştırma Konya'da 18 yaş ve üstü 916 yetişkin üzerinde yapılmıştır. Sosyodemografik özellikler içeren bir anket dolduruldu ve tetanoz IgG düzeyleri ölçüldü.

Bulgular: Çalışmaya % 68,4 (n = 627) kadın, % 31,6 (n = 289) erkek toplam 916 uygun kişi alındı. Katılımcıların 756'sında (%82,5) koruyucu tetanoz antikor düzeyi (≥0,1 IU / mL) ve 160'ında (%17,5) güvenilir olmayan koruyucu antikor düzeyi (<0,1 IU / mL) vardı. Erkek ve kadın cinsiyet arasında anlamlı bir fark bulunmadı (p=0.225). Ortaokul ve daha üstü eğitimlilerde antikor düzeyleri, ilkokul ve daha az eğitim almış olanlara göre anlamlı olarak yüksek bulunmuştur. Antikor seviyeleri yaş arttıkça önemli ölçüde azalıyordu (p<0,001). Antikor düzeyleri, çalışanlarda işsizlere göre (p<0,001), bekarlarda evli olanlara göre (p=0,004) ve gelir seviyesi yüksek olanlarda düşük geliri olanlara göre (p<0,001) istatistiksel olarak anlamlı derecede yüksek bulundu. Daha önce aşılananların antikor düzeyleri anlamlı olarak yüksekti (p<0,001).

Sonuç: Bu çalışmada, ileri yaşta olanlarda, eğitim düzeyi düşük ve aşılanmamış kişilerde tetanoz antikor düzeylerinin düşük olduğu belirlenmiştir. Tetanoz hayatı tehdit eden bir halk sağlığı sorunudur, bu nedenle bu konuda yeni sağlık politikaları geliştirilmelidir.

Anahtar Kelimeler: Tetanoz Antikoru, Aşı, Yetişkin, Seroprevalans.

INTRODUCTION

Tetanus is an acute disease characterised by the action of a highly potent neurotoxin, tetanospasmin, and generalized rigidity in skeletal muscle caused by *Clostridium tetani*, which is an anaerobic bacillus (1). The notification is a mandatory disease and it has high mortality rates, it can be prevented by adequate immunization (1,2). It is estimated that the incidence rate of tetanus is 18 per one hundred thousand. Mortality rate is between 30% and 50% around the world and it is thought that more than one million cases occur. At least half of the deaths occur among newborn infants (1-5).

According to the national immunization program applied in Turkey, primary vaccination starts in the second month of life with DaBT-IPA-Hib vaccine (Diphtheria, acellular Pertussis and Tetanus- inactive Polio – *Haemophilus influenzae* type B vaccine) and the application of three dose vaccine continues at 8 week intervals. Booster dose is performed at 18 months old. In the first class of primary school, DaBT-IPA (Diphtheria, acellular Pertussis and Tetanus, Inactive Polio Vaccine) and in the eighth year Td (Adult type tetanus and Diphtheria) are applied as single booster dose. Besides, women have two doses of tetanus vaccine in pregnancy and men have single dose of tetanus vaccine in the military service (4). However, loss of immunity with increasing age increases the risk to have tetanus. In a multicenter study conducted in the United States (USA), the immunization frequency of 6 years and over was found 72.3% and this frequency was determined as 31% at the age of 70 and over (5). In a study conducted in Turkey, 68% of the individuals >18 years of age showed protective levels (>0.01 IU:ml) of antitetanus antibodies (6).

In the presented study, it was aimed to determine the antibody levels of the individuals aged 18 years and over against tetanus in Konya city center. In addition, it was aimed to examine the relationship between serum antibody levels and age and sociodemographic characteristics and to vaccinate individuals who do not contain sufficient antibodies.

MATERIAL AND METHODS

The Type and the Place of the Study: This descriptive research was carried out on 916 adults over 18 years old. The universe of the study was composed of individuals aged 18 and over who lived in the center of Konya. The presented study was carried out in Family Health Centers number 40, 48 and 72 randomly selected in Meram, Selçuklu and Karatay regions in Konya city center.

Sampling of the Research*:* According to TUIK data, the proportion of population aged 18 and over (70.1%) was 942431 in the center of Konya province for 2017. As it is known that the number of people in the population was known, it was planned to include 888 people in the study using "$n=N.t^2.p.q/d^2(N-1)+t^2.p.q$" formula. Tetanus seroprevalence was found as 68% from previous study in Turkey (6), sample size was calculated as 95% confidence interval and 3% deviation. This study was carried out with 916 adults.

Ethical Authorisation of the Study: Before the study was started, an ethical approval was received from Necmettin Erbakan University, Meram Medical Faculty, Ethic Committee (Number: 2017/1002). Later, necessary permissions were obtained from Konya Governorship and Konya Provincial Public Health Directorate for the study. Participants were initially informed about the study and their written and verbal consents were obtained according to the principles of the Helsinki Declaration.

Collecting the Data: The questionnaire prepared by the researcher was filled in through face to face interview technique. The age, gender, occupation, educational status, and level of income of the patients and whether they had a disease affecting their immunity were recorded in the questionnaire form. Their situation of vaccination against tetanus, how many doses of vaccines they had, when and why they had last tetanus vaccine, whether they had accidents/ injuries or not, whether they were vaccinated or given serum after the accident or not, whether the women had tetanus vaccine in their last pregnancy or not and whether the men were vaccinated in the military service were all questioned. In this study, the housewives, the retired and the students were categorised in the group of the unemployed; and the officials, the tradesmen and the workers were categorised in the group of the employed. The net amount of minimum wage earned in 2017 was 1404 TL. Accordingly, the monthly income level was evaluated as below 1500TL and above 1500 TL.

Laboratory Analysis: Nearly 7-8 mL venous blood sample was taken from the participants. The samples which were put into non-aerating vacutainer tubes without anticoagulants by means of special needles were centrifuged for 8 minutes in 4000 rpm. Serum samples were sent to Necmettin Erbakan University, Meram Medical Faculty Microbiology Laboratory and they were kept in -80°C after they were put into eppendorf tubes. After the kits were provided, they were kept in 2-8 ºC until they were used according to the instructions of the producer. Tetanus IgG antibodies were tested by using ELISA kits (DRG Instruments GmbH, Germany) according to the information in the manual of the producing company.

Evaluating of the Vaccine Protection Levels: According to the current categorisation in the manual of tetanus antibody ELISA kit that we

used, vaccine protection level and suggested vaccination situations were shown at Table 1 (7). According to the kit results we used, values of <0.1Iu/mL were non-protective against the disease, values of >0.1 Iu/mL were evaluated as protective tetanus antibody (7,8). In this presented study, tetanus antibody titers were evaluated in 3 groups. For tetanus antibody levels less than 0.1 IU/mL indicated susceptibility to tetanus, antibody levels between 0.1-1.0 IU/mL were protective and levels in excess of 1.1 IU/mL were considered long-term protection.

Table 1. According to tetanus antibody concentration values, levels of protection and recommended vaccine situations (7)

Tetanus IgG **Level**	**Protection status**	**Recommended Vaccination**	**n**	**%**
<0,1 IU/mL	Unreliable protection	Booster dose	160	17.5
0,1-0,5 IU/mL	Reliable protection	Booster dose	98	10.7
>0,5-1,1 IU/mL	Reliable protection	Booster dose in 2-5 years	83	9.1
>1,1-5,0 IU/mL	Reliable protection	Booster dose in 5-10 years	552	60.3
>5,0 IU/mL	Reliable protection	Booster dose every 10 years	23	2.5

Statistical Analysis: While evaluating the findings obtained in the study, SPSS (Statistical Package for Social Sciences) for Windows 20.00 program was used for statistical analyses. Descriptive statistics belonging to continuous variables were summarized with standard deviation and descriptive statistics belonging to categorical data were summarised in frequency and percentage at a table. While comparing the categorical data, Chi-Square test was used. Correlation between the parameters was made by Pearson correlation analysis. Correlation coefficient (r) was evaluated as weak between 0.00–0.24, moderate between 0.25–0.49, strong between 0.50–0.74 and very strong relationship between 0.75–1.00. The results were evaluated at 95% confidence interval and significancy was evaluated at $p<0.05$ level.

RESULTS

In this study, 916 suitable people in total who consisted of 68.4% (n=627) female and 31.6% (n=289) male were included. The mean age of the participants was 36.9±14.6 years (min: 18, max: 91). When looking into their educational status, it was seen that 41.5% (n=380) of them had primary and pre-school education and 58.5% (n=536) of them had secondary and higher education. Of the participants, 31.3% (n=287) were employed and 70.4% (n=645) were married.

The mean level of tetanus antibody in the participants was 2.0±1.6 IU/mL. According to tetanus IgG test kit used in the research, the ones whose antibody levels are >0.1 IU/mL are regarded as protective against the disease. Accordingly, when studying the antibody levels of the participants in this study, it was determined that 17.5% (n=160) of them was below the protective level, 82.5% (n=756) of them were at protective level. According to tetanus antibody concentration values, levels of protection and recommended vaccine situations were shown in Table1.

Protective tetanus antibody titers were quite high in the 18-27 age group (47.4%), whereas the protection rate was very low in the over 58 years of age (2.6%). Distribution of tetanus antibody titers according to age groups was shown in Figure 1. It was determined that the median values of tetanus antibody were decreasing with advancing age. This difference was found statistically significant **($p<0.001$)**.

In Turkey, according to the national vaccination program; routinely immunization against diphtheria–pertussis–tetanus (DPT) vaccine has been applied since 1968. It appears that many elderly people are unvaccinated, and have no protective immunity against tetanus. Distribution of tetanus antibody levels in the individuals born before and after 1968 was shown in Figure 2.

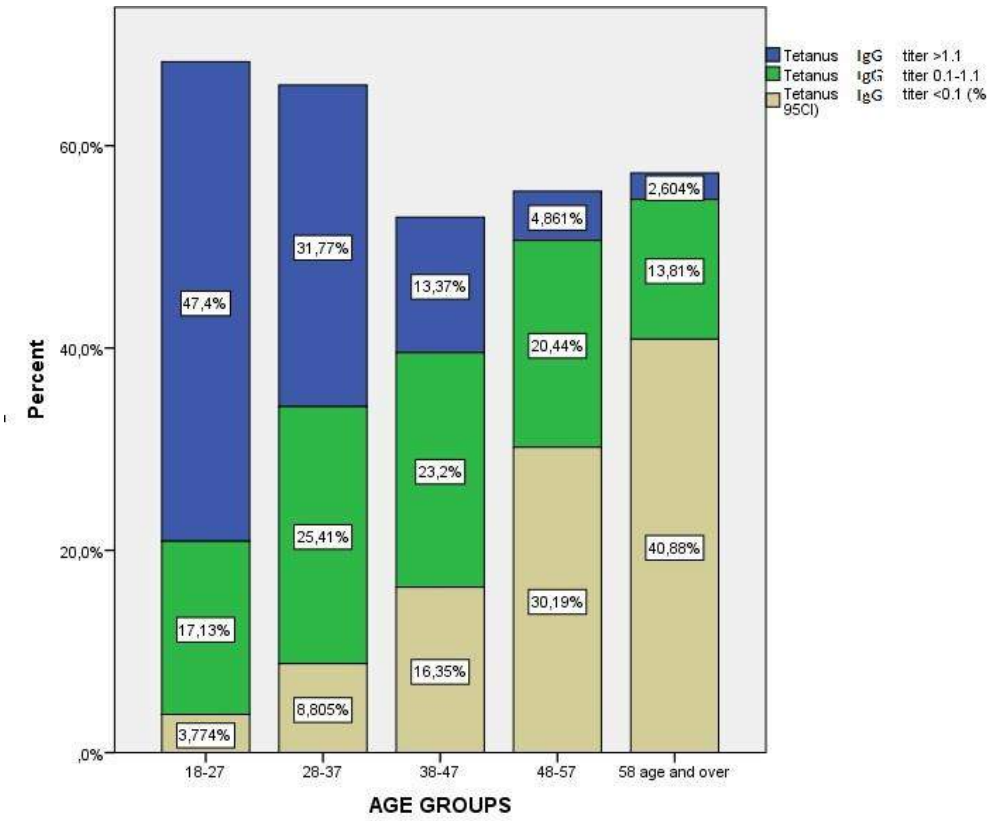

Figure 1. Distribution of tetanus antibody titers according to age groups.

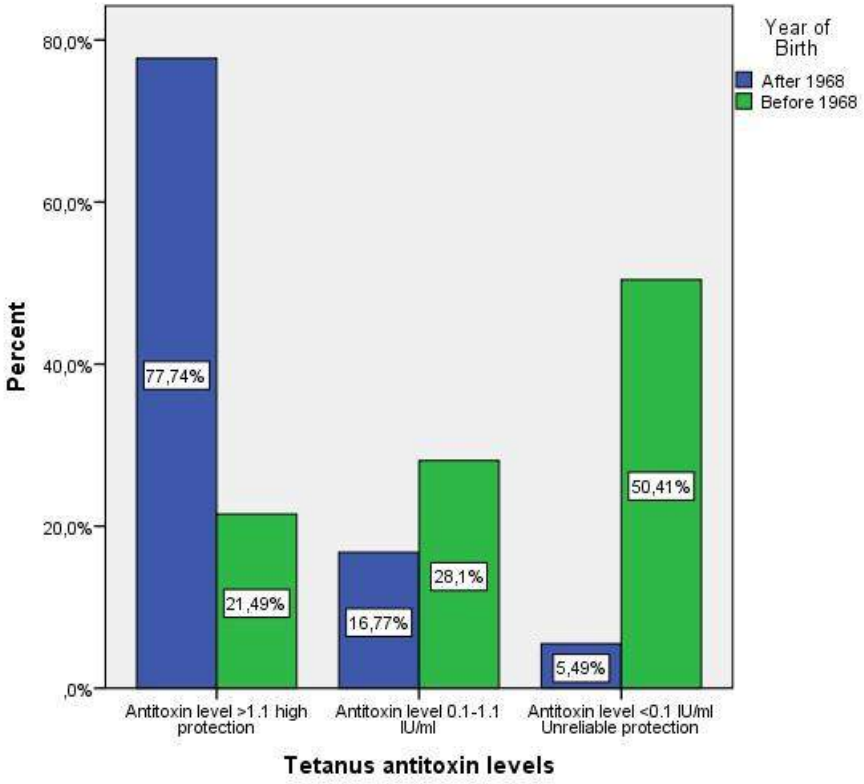

Figure 2. Distribution of tetanus antibody levels in the individuals born before and after 1968.

While examining the vaccination in the last pregnancy, 41.6% (n=193) of 464 women who have been pregnancy story had tetanus vaccine, 28.2% of them (n=131) were not vaccinated and 30.2% of them (n=140) didn't remember if they were vaccinated or not. When the genders and protective

antibody values were compared in our study, no significant difference was found between the groups **(**p=0,225). When the marital status and protective antibody values of the participants were compared, the antibody values of the single individuals were significantly higher than the married (**p<0.001).** Sociodemographic features and protective tetanus antibody was shown in Table 2.

Table 2. Sociodemographic features and protective tetanus antibody

Variables	Protective tetanus antibody (+) n (%)	Protective tetanus antibody (-) n (%)	Total (n)	*p value*
Age (Year)				
18-27	303 (97.7)	7 (2.3)	310	**<0.001**
28-37	229 (94.2)	14 (5.8)	243	
38-47	119 (82.1)	26 (17.9)	145	
48-57	65 (57.5)	48 (42.5)	113	
≥ 58	40 (38.1)	65 (61.9)	105	
Gender				
Female	511 (81.5)	116 (18.5)	627	0.225
Male	245 (84.8)	44 (15.2)	289	
History of vaccination				
Positive	449 (93.7)	30 (6.3)	479	**<0.001**
Negative	88 (66.2)	45 (33.8)	133	
Unknown	219 (72.0)	85 (28.0)	304	
Working Status				
Employed	259 (90.2)	28 (9.8)	287	**<0.001**
Unemployed	497 (79.0)	132 (21.0)	629	
Marital status				
Married	512 (79.4)	133 (20.6)	645	**<0.001**
Single	244 (90.0)	27 (10.0)	271	
Education				
< Primary school graduated	276 (70.3)	113 (29.7)	380	**<0.001**
≥Secondary school graduated	489 (91.2)	47 (8.8)	536	
Monthly income				
<1500 TL	279 (75.0)	93 (25.0)	372	**<0.001**
≥ 1500 TL	477 (87.7)	67 (12.3)	544	

Tetanus antibody levels were compared in terms of some variables, except for non-pregnant women and men who did not do military service in Table 3. Of 221 men who did military service, 25.8% (n=57) stated that they were vaccinated in the military; 19.4% (n=43) of them said they did not have vaccine and 54.8% (n=121) of them did not remember if they were vaccinated or not.

Table 3. Comparison of tetanus antibody levels in gender in terms of some variables.

Variables	FEMALE			MALE		
	Titers of antibody (IU/mL)			Titers of antibody (IU/mL)		
	≥1.1 n (%)	**0.1-1.1 n(%)**	**<0.1 n(%)**	**≥1.1 n(%)**	**0.1-1.1 n(%)**	**<0.1 n(%)**
Age (Year)						
18-27	189(85.1)	28(12.6)	5(2.3)	84(95.5)	3(3.4)	1(1.1)
28-37	128(72.7)	37(21.0)	11(6.3)	55(82.1)	9(13.4)	3(4.5)
38-47	45(51.1)	26(29.5)	17(19.4)	32(56.1)	16(28.1)	9(15.8)
48-57	14(17.5)	27(33.8)	39(48.7)	14(42.4)	10(30.3)	9(27.3)
≥ 58	6(9.8)	12(19.7)	43(70.5)	9(20.5)	13(29.5)	22(50.0)
	(p<0.001)			**(p<0.001)**		
Did you have an accident?						
No	312(61.1)	101(19.8)	98(19.1)	99(65.1)	27(17.8)	26(17.1)
Yes	70(60.3)	29(25.0)	17(14.7)	95(69.3)	24(17.5)	18(13.2)
	(p=0.315)			(p=0.624)		
***Vaccination in the pregnancy (n=464)**						
No	53(40.5)	34(26.0)	44(33.5)			
Yes	150(77.7)	34(17.6)	9(4.7)	------		
Unknown	51(36.4)	37(26.4)	52(37.2)			
	(p<0.001)					
****Vaccination in military service (n=221)**						
No						
Yes	-------			22(51.2)	9(20.9)	12(27.9)
Unknown				44(77.2)	10(17.5)	3(5.3)
				67(55.4)	27(22.3)	27(22.3)
				(p=0.007)		
*****Year of birth**						
Before 1968	25(16.2)	44(28.6)	85(55.2)	27(30.7)	24(27.3)	37(42.0)
After 1968	357(75.5)	86(18.2)	30(6.3)	167(83.1)	27(13.4)	7(3.5)
	(p<0.001)			**(p<0.001)**		

* Women who were not pregnant were not evaluated.

****** Men who did not do military service were not evaluated.

****In Turkey, immunization against diphtheria, tetanus and pertussis has been applied since 1968.

When comparing accident situations and the genders of the participants, it was seen that those who have not had accidents consist of 77.1% (n=511) women and 22.9% (n=152) men. There was a statistically significant difference between them (χ^2=82.669, **p<0.001**).

The participants were divided into three groups according to their vaccination situations: those who had vaccines 52.3% (n=479), those who didn't vaccines 14.5% (n=133) and those who didn't remember being vaccinated 33.2% (n=304). When comparing the participants'vaccination situations and their genders, the ratio of both vaccination and not remembering being vaccinated was higher in women than men. A statistically significant difference was found between them (χ^2=13.229, **p<0.001**).

The participants' reasons for vaccination were divided into three groups as pregnancy 40.5% (n=194), trauma/cuts 26.5% (n=127) and protection 33.0% (n=158). When comparing the reasons of vaccinating and the genders of the participants, a statistically significant difference was found between them (χ^2=229.421, **p<0.001**). A majority of those who were vaccinated due to trauma/cuts consisted of men (Table 4).

Table 4. Relationship between gender and accident/vaccination status

PARAMETERS	Gender						χ^2	p
	Female		Male		Total			
	n	%	n	%	n	%		
Did she/he have an accident?								
No	511	77.1	152	22.9	663	100.0	82.669	**<0.001**
Yes	116	45.8	137	54.2	253	100.0		
Vaccination Status								
No	109	82.0	24	18.0	133	100.0	13.229	**0.001**
Yes	315	65.8	164	34.2	479	100.0		
I do not remember	203	66.8	101	33.2	304	100.0		
Reason of being a vaccine								
Pregnancy	194	100.0	-	-	194	100.0	229.421	**<0.001**
Trauma / injury	49	38.9	78	66.1	127	100.0		
To be protected	72	45.6	86	54.4	158	100.0		

The protective antibody values of the women vaccinated in their last pregnancy were significantly higher than of those who did not have vaccine **(p<0.001).**

When the vaccination situation and the protective antibody levels of the participants were compared, the protective antibody values of those who were vaccinated were significantly higher than of those who did not have vaccine **(p<0.001).** When examining the correlation between age and serum tetanus IgG values, it was found out that there was a powerful relationship in negative direction between them (r= -0.521, **p<0.001**). 27.1% of the decrease in the tetanus antibody level was attributed to advanced age (R^2=0.271, **p<0.001**) Linear regression analysis between age and tetanus antibody levels was shown in Figure 3.

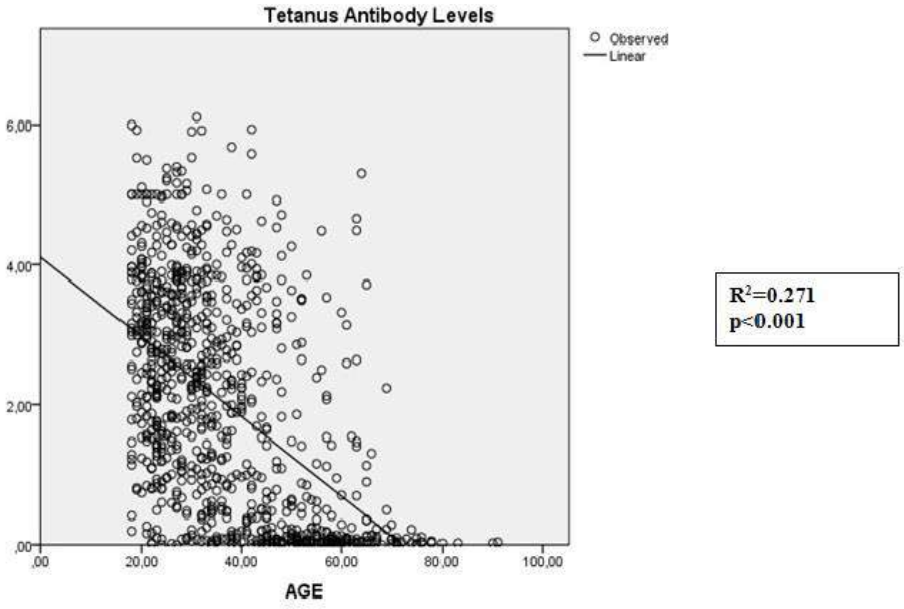

Figure-3. Linear regression analysis between age and tetanus antibody levels

DISCUSSION

Tetanus is a fatal disease that can be prevented with vaccine and that has high mortality rates. It continues to be an important health problem in the world. For this reason, it is vitally important to conduct vaccination programs (1-3). The protectiveness rate against tetanus varies by the development level and vaccination programs of the countries. There are many researches about this matter in the literature (1-10). In the presented study, the frequency of protectiveness against tetanus in Konya city center was determined to be 82.5% in adults at the age of 18 and over. In a study performed on 255 people in India, showed that 47.0% of the participants were unprotected against to tetanus (11). Domínguez et al. (12) performed a study on 1296 people in Spain and they stated that the protectiveness rate was 68.3%. In a study performed on 295 people in Edirne, Tansel et al. (13) determined that the protectiveness rate of the participants was 98.6%.

In this study, the relationship between tetanus antibody level and sociodemographic features was searched. The tetanus antibody levels of those with secondary and higher education were found significantly higher than of those with primary and pre-primary education. In some several studies, it was shown that the protective antibody levels of well educated participants were higher. In a study performed in the U.S.A., McQuillan et al. reported that as the educational status increases, the protectiveness rate against tetanus increases as well (5). In a study carried out in Edirne, Tansel et al. (13) determined that the protectiveness rate of those with primary and pre-primary education was lower than of those who had secondary and higher education. As it is understood from this study, the knowledge obtained through education shows us how important vaccination is to prevent a deadly disease such as tetanus.

It was determined that tetanus IgG values had decreased significantly with increasing age. In the studies performed in Germany by Aue et al. (2003); in Greece by Symeonidis et al. (2003); in Australia by Gidding et al. (2005); it was found out that the protective antibody level against tetanus was significantly lower with increasing age (14-16). The reason why tetanus antibody levels are lower in advanced age may be because the necessary booster dose vaccine is not applied decennialy and immune response decreases with increasing age.

Tetanus IgG values of the participants with high income were found significantly higher. As the level of income increased, their antibody levels increased as well. Likewise, in a study performed in the U.S.A., McQuillan et al. (5) stated that when level of income goes up, the protectiveness level against tetanus rises, too. In a different study performed on 10618 people by Gergen et al. in the U.S.A., it was reported that protectiveness rate against tetanus went up with increasing level of income (3). The fact that the individuals with high income can get better medical services and their vaccination rates are higher may be effective on having higher protective antibody levels against tetanus in U.S.A. Differently from this, Dundar et al. could not find a significant relationship between socioeconomic status and immunity in a study they performed in Kocaeli (17). This may be due to the fact that tetanus vaccine is free of charge in all health institutions in our country.

In this study, the significant difference was not found in tetanus IgG values between male and female gender. Similar to our study, Wu et al. (2009) stated in a study performed in Taiwan that there was not a significant difference between men and women in terms of protective antibody levels (10). In a study performed in Spain, Domínguez et al. (12) and in the Netherlands, Melker et al. (18), it was shown that the antibody levels were higher in men. In a study performed by Afzali et al. (19), they stated that there was no statistically significant difference in the tetanus antibody levels between both sexes. Tetanus vaccination due to the military service in men and due to pregnancy in women is an opportunity for adult vaccine. The fact that a majority of the participants leave pregnancy and military service behind may affect their protectiveness rates against tetanus positively.

Tetanus IgG values of the employed individuals were found significantly higher than of the unemployed. In a study in the U.S.A. Hayney et al. determined that the antibody levels of the farmers were higher than the ones who were not farmers (20). In a study performed in Kocaeli, Dundar et al. (17) showed that the antibody levels of the employed were significantly higher than of the unemployed. Ozturk et al. stated in a study they performed in Kayseri that the occupations did not create a significant difference in protective antibody levels (21). The employees have more risk to get injured and they are vaccinated due to the injuries, so this may be related to the high tetanus antibody levels. Besides, the fact that the educational status of the employed is higher than the unemployed may cause higher vaccination percentage and tetanus antibody levels.

In this study, tetanus IgG values of those who were vaccinated were found significantly higher than of those who were not. In a study performed in Canada, Yuan et al. (22) determined that the tetanus antibody values of those who did not remember whether they were vaccinated or not were significantly lower. In a study carried out in Kocaeli, Dundar et al. stated that the tetanus antibody levels of those with vaccination history were significantly higher. The studies show the importance of vaccination to have high tetanus antibody level (17).

Tetanus antibody levels of those who were vaccinated more recently were found significantly

higher than of those who were vaccinated a long time ago. Coplu et al. (23) researched the effects of the length of vaccination on tetanus antibody levels in the studies they carried out in Antalya, Samsun and Diyarbakır. They stated that the protectiveness rates start to decrease as the time passes after the last vaccination. The studies reveal that vaccination should be performed regularly every 10 years in order to maintain adequate antibody values against tetanus.

Tetanus antibody values of single people were found significantly higher than of the married. The reason why the antibody levels of the single are higher may be because they are younger than the others. In our study, the relationship between having accident and tetanus IgG values was searched. There was not a significant difference in tetanus antibody values between the ones who had accidents and those who didn't. In their study conducted in Kocaeli, Dundar et al. stated that they could not find a relationship between immunization and injury history (17). This may be due to the fact that the the participants did not show the sensitivity required for tetanus vaccination although they have accidents. It was determined that while the history of the vaccination and the injury was being questioned, most of the individuals had difficulty in remembering it or they were indecisive about it. Memory was an important factor in their statements and failure rate on remembering was quite high, so this was an important limit in our study.

In this presented study, tetanus antibody levels were significantly higher in those who were vaccinated in the military than those who were not vaccinated. Similar to this study, McQuillan et al. (5) found that the protective antibody levels of those vaccinated in the military were significantly higher than those who were not vaccinated in the USA. In a study performed in Kocaeli by Dundar et al, the significant difference was not found in tetanus antibody levels between those who did their military service and those who did not (17). The fact that the participants can't remember being vaccinated in the military or that they remember it wrong can clarify this situation.

In this study, the relationship between vaccination in the last pregnancy and tetanus IgG values was studied. Tetanus IgG values of those who were vaccinated in their last pregnancy were found significantly higher than of those who were not vaccinated. In a study performed in Ankara, Maral et al. (24) examined the immunity of 493 pregnant women against tetanus and they found that the protectiveness rate of those who had two doses of vaccine was 95.6%. In women who had single dose of vaccine it was 93.5% and for those who never had vaccine this rate was 46.4%. In a study performed by Aboud et al. (2002) in Tanzania, it was determined that the protectiveness level against tetanus was 94.5% in pregnants (25).

In conclusion, in this study conducted in Konya city center on 916 people at the age of 18 and more, seropositivity of serum tetanus IgG was determined as 82.5%. It was determined that tetanus IgG values decreased significantly with increasing age. There was a strong relationship between age and tetanus IgG in a negative direction. 27.1% of the decrease in antibody level was attributed to increasing age. Tetanus IgG values were found significantly higher in people with high income, those with secondary and higher educated, the single and working group. Tetanus IgG values of those who were vaccinated were found significantly higher than of those who were not vaccinated. No significant difference was found between men and women in tetanus IgG values.

Although tetanus is a disease with high mortality rates and it can be prevented by vaccine, it still appears. The primary objectives of health policies are the existence of a healthy community with healthy individuals. To maintain long-term protective immunity against tetanus, booster immunization is essential for adolescents and adults. After routine vaccination in childhood, during military service for men, and pregnant women during pregnancy, booster dose is recommended in Turkey. Tetanus vaccine has been recommended to be administered once every 10 years, especially to people aged 20 and over. It may be beneficial that society must be informed about tetanus disease and the individuals unvaccinated or with incomplete vaccined must be vaccinated.

Conflict of interest: The authors declare that they have no conflict of interest.

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RESEARCH ARTICLE

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Evaluation of Accordance to Guidelines on the Management of Chronic Obstructive Pulmonary Diseases in Family Medicine

ABSTRACT

Objective: Chronic Obstructive Pulmonary Disease (COPD) has become increasingly important in recent years. The CAT (COPD Assessment Test) and mMRC (Modified British Medical Research Council) scales can be used in the clinical evaluation of the patients according to GOLD the COPD Protection Diagnosis and Treatment Guideline guideline. Patients were divided into groups A, B, C and D using the scales with the combined assessment scheme proposed by GOLD, and recommended treatment scheme for each step is determined. In this study, it is planned to investigate whether COPD patients getting the optimal treatment according to GOLD guideline.

Methods: This is a descriptive, cross-sectional study. 218 patients were included in the study. The questionnaire form of the study was applied to the patients and the patients were evaluated and scored with the help of these scales. Statistical analysis of the data obtained in this way was done by the SPSS program.

Results: According to the CAT result, guideline compliance was 9.8% in group A, 22.3% in group B, 5.8% in group C and 77.7% in group D. According to the mMRC result, guideline compliance was 12.5%, 24.4%, 14.2%, 80.8% in the group A,B,C,D respectively. It was determined that 40.8% of patients according to mMRC and 33% according to CAT were receiving the optimal treatment.

Conclusions: Patients with stable COPD had significantly higher use of bronchodilator drugs than recommended. The use of this scale by Family Doctors, will be important in determining the needs for treatment and COPD patients follow-up.

Keywords: Family Practise, Pulmonary Disease, Chronic Obstructive, Primary Health Care

Kronik Obstuktif Akciğer Hastalığı Tedavisinde Rehberlere Uyumun Aile Hekimliğinde Değerlendirilmesi

ÖZET

Amaç: Kronik Obstrüktif Akciğer Hastalığı (KOAH) solunum yollarının kısıtlamasıyla karakterize bir hastalık olup son yıllarda hasta sayısının ve hastalığın morbidite-mortalitesinin artması sebebiyle önemi giderek artmaktadır. KOAH rehberlerine göre ilgili hastaların klinik değerlendirmesinde CAT (COPD Assessment Test) ve mMRC (Modified British Medical Research Council) ölçekleri kullanılabilmektedir. GOLD (Global Initiative for Chronic Obstructive Lung Disease) KOAH Koruma Tanı ve Tedavi Kılavuzunun önerdiği birleşik değerlendirme şemasıyla hastalar bahsedilen ölçekler kullanılarak A, B, C ve D gruplarına ayrılmıştır ve her basamak için önerilen tedavi belirlenmiştir. Bu çalışmada inhaler tedavi kullanan KOAH hastalarının GOLD önerilerine göre optimum tedaviyi alıp almadığının araştırılması amaçlanmıştır.

Gereç ve Yöntem: Araştırma tanımlayıcı, kesitsel tipte bir araştırmadır. Hastalığının son üç ayında tedavi değişikliği yapılmamış ve aktif yakınması olmayan KOAH hastalarından araştırmamıza katılmayı kabul edenler çalışmaya dahil edilmiştir. Çalışmanın anket formu hastalara uygulanmış ve bu ölçekler yardımı ile hastalar değerlendirilmiştir. Hastanın aldığı tedavinin rehberlerle uyumlu olup olmadığı araştırılmıştır. Bu şekilde elde edilen verilerin istatiksel analizi SPSS programı ile yapılmıştır.

Bulgular: CAT sonucuna göre yapılan değerlendirmede tedavide kılavuza uyum A grubunda %9,8, B grubunda %22,3, C grubunda %5,8, D grubunda %77,7 bulundu. mMRC sonucuna göre yapılan değerlendirmede tedavide kılavuza uyum A, B, C, D gruplarında sırasıyla %12,5, %24,4, %14,2, %80,8 bulundu. Sonuçlar değerlendirildiğinde mMRC'ye göre hastaların %40,8'i, CAT'e göre ise %33'ü gruplarına tam olarak uygun olan tedaviyi almaktadır.

Sonuç: Stabil dönem KOAH hastalarında azımsanmayacak bir oranda önerilenden daha yüksek grup bronkodilatör ilaç kullanımı olduğu saptanmıştır. Bu ölçeklerin aile hekimleri tarafından kullanılmasının, stabil dönem KOAH hastalarının takibi ve tedavi ihtiyaçlarının belirlenmesinde önemli olacağı düşünülmüştür.

Anahtar Kelimeler: Aile Hekimliği, Akciğer Hastalığı, Kronik Obstrüktif; Temel Sağlık Hizmeti.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a disease characterized by severe restriction of the airways, especially in expiratory flow (1). There is a rising significance of COPD in recent years as the number of patients and morbidity-mortality rates of the disease increase (2). The most effective treatment of COPD is inhaler therapies. Current COPD diagnosis and treatment guidelines offer practical advice on how to optimize these therapies (3). GOLD (Global Initiative for Obstructive Lung Disease) guide is one of the main guidelines used by the Department of Chest Diseases. In the GOLD 2018 guideline, a scheme for COPD patients has been established and patients are divided into groups A, B, C, D. These groups are assigned considering symptom scoring CAT (COPD Assessment Test and mMRC (Modified British Medical Research Council), number of emergency visits and number of hospital admissions in the last year. The recommended treatments for each group are detailed as in Figure 1(1).

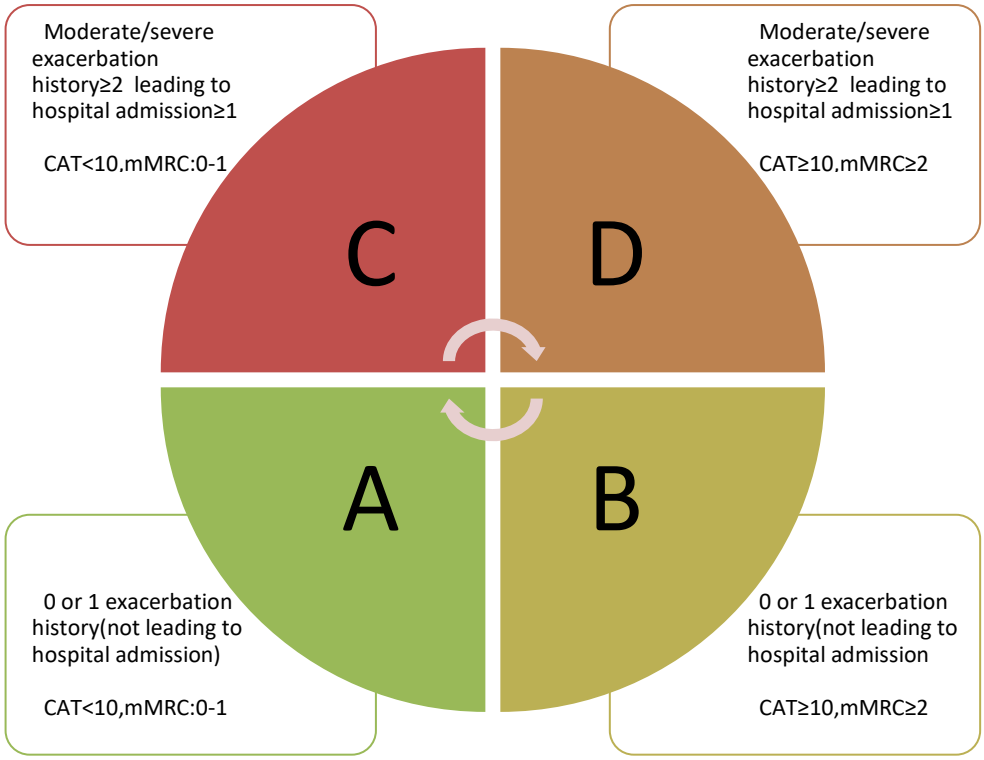

Figure 1. GOLD ABCD assessment tool(1)
*This table is taken from the GOLD guideline and arranged.

COPD patients are receiving more intensive treatments than the recommended treatments in the guidelines (4-7). This overtreatment comes with an excessive medical cost and burden (4). We have noticed the same overtreatment in our clinical experience. In order to emphasize this situation, we found it necessary to carry out this study.

In this study, we tried to understand whether the treatments that patients receive are compatible with the recommended treatments. Also it was aimed to introduce and remind the CAT and mMRC scales to the Family Medicine clinic, which are frequently used in Chest Diseases practice. In addition, it has been intended to contribute to the relatively few studies and related literature of Family Medicine and Primary Health Care.

MATERIAL AND METHODS

Participants and Study Design: Our study was an observational cross-sectional study. Universe is chosen by stable COPD patients admitted to Ankara Numune Research and Application Center of Family Medicine and Chest Diseases Clinic. A sample was calculated according to 600 COPD patients who were admitted to these two outpatient clinics in January, February and March 2018. It is calculated with %95 confidence interval and %5 share of error, a sampling of 235 people was aimed to be achieved. The questionnaire was prepared by the researchers. Clinical questions recommended in the guidelines were asked to patients. The treatment of each patient was recorded. Symptom categories and the treatment categories were compared, thus, the level of compliance with international guidelines was observed in the treatment of COPD patients. The number of patients was reached in consecutive

order in June - August 2018 and the patient collection phase was completed.

Patients who had been diagnosed with COPD for at least 5 years, who were in the stable period of the disease, who received the same treatment for the last 3 months and who accepted to participate in the study were included in the study. Pulmonary Function Test values were not requested from each patient. Patients with COPD during acute exacerbation and cognitive impairment and dementia were excluded from the study.

Instruments: Socio-demographic characteristics such as age, gender, smoking status, additional diseases and the treatments they used were recorded with the relevant questionnaire. mMRC and CAT scales were administered to all patients. In addition, the patient's urgent applications within the last year, hospitalizations due to COPD and bronchodilator therapies used in the last 3 months were recorded. Patients were divided into groups A, B, C and D using the combined assessment scheme proposed by GOLD according to their severity (according to their symptoms) and the treatment they used.

To use the combined assessment scheme, symptoms are first assessed and scored with CAT or mMRC. Patient if CAT score <10 or mMRC level 0-1 is in the low-symptom groups. Low symptom groups are A and C. If the CAT score is ≥10 or the mMRC level is ≥2, the patient has located in high symptom groups. High symptom groups are B and D. If the number of exacerbations in the last year is 0 or 1, it is in the low-risk group A or B, and if it is 2 or more, it is in the high-risk group C or D. If there is one or more hospitalizations due to exacerbation in the last year, then it is again in the high-risk group (C-D group). Thus, according to the combined evaluation, A,B,C,D groups are determined.

According to the treatments they were divided into groups;

Group A: short-acting bronchodilator drugs,

Group B: Those who use a long-acting bronchodilator drug (LABA or LAMA),

Group C: Two long-acting bronchodilator drugs (LABA + LAMA),

D group: LABA + LAMA + IKS / Theophylline, Macrolide group antibiotic, Roflumilast users were grouped.

Statistical Analysis: Microsoft Office Excel 2016 program was used for initial data entry. At the end of the study, SPSS for Mac Version 20.00 (SPSS Inc., Chicago, IL., USA) was used for statistical analysis. Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were expressed as number and percentage (%). The Kolmogorov-Smirnov test was used to determine whether the continuous variables were normal distribution. Chi-square test for discrete variables and Mann Whitney U test and Student-t tests for continuous variables were used for comparison of groups. Statistical significance was taken as $p < 0.05$.

Ethics Approval: This paper got ethics approval with 2043/2018 decision number at 07/06/2018 date, from Health Science University Ankara Health Practice Research Center Clinic researchers ethics committee.

RESULTS

A total of 250 patients who met the inclusion criteria of our study were included in the study. A total of 32 patients were excluded from the study, 18 of which were due to irregular drug use, 8 of whom were diagnosed with an acute attack period after the examination, and 4 of them refused to be included in the study. The data of a total of 218 patients were used for the study. The mean age of the patients was 62.5 ± 10.7 years, the mean body mass index (BMI) was 26.7 ± 5.3 years with a minimum 16.1, maximum 44.1kg/m2. The median smoking rate was 18% (n = 84), 41.1 ± 34.2 packs / year with a minimum of 0 and a maximum of 165 packs / year. 22.9%(n=50) of patients with COPD were found to have never smoked before (Table1).

Table 1. Age, BMI and smoking characteristics of the patients

Categories	Mean±SD	Min	Max
Age(year)	62.5±10.7	41	86
BMI(kg/m^2)	26.7±5.3	16.1	44.1
Cigarette(package/year)	41.1±34.2	0	165

Around half of the patients (48.2%, n=105) had no comorbidities. The most common comorbidities were hypertension (30.7%) and followed by diabetes mellitus (16.5%) and coronary artery diseases (13.7%) (Table2)

Table 2. Comorbidities of patients

Comorbidities	**n (%)**
Hypertension	67 (30.7)
Diabetes Mellitus	36(16.5)
Coronary Artery Disease	30(13.7)
Benign Prostatic Hypertrophy	9(4.1)
Bonchial Asthma	7(3.2)
Bronchiectasis	6(2.7)
Rheumatic Disease	5(2.2)
Heart failure	5(2.2)
Malignancy	5(2.2)
Chronic renal failure	3(1.3)
Hyperthyroidism	3(1.3)
Other	5(2.2)
None	105 (48.1)

Patients who were categorized according to the mMRC scale by questioning the symptom;18.3% of patients (n = 40) were in group A, 45% of patients (n = 98) were in group B, 3.2% patients (n = 7) were in group C and 33.5% (n = 73) were in group D. In patients whose symptoms were questioned and categorized according to CAT scale; 32.6% of patients (n = 71) were in group A, 30.7% of patients (n = 67) were in group B, 7.8% (n = 17) were in group C and 28.9% (n = 63) were in group D (Table3).

According to mMRC, 12.5% of patients with group A, 24.4% of patients with group B, 14.2% of patients with group C, 80.8% of patients with group D received treatment proper to their group (Table4). According to CAT, 9.8% of those with A group, 22.3% of those with B group, 5.8% of those with C group and 77.7% of those with D group were treated properly (Table5).

Table 3. Treatment-Symptom categories and percentages of patients and their categories

Groups	According to the treatment, n(%)	According to mMRC scale n (%)	According to CAT scale n (%)
A	28 (12.8)	40 (18.3)	71 (32.6)
B	36 (16.5)	98 (45)	67 (30.7)
C	34 (15,6)	7 (3.2)	17 (7.8)
D	120 (55)	73 (33.5)	63 (28.9)

Table 4. Comparison of the groups of patients determined according to mMRC with the treatment group and percentage of patients has proper treatment

			mMRC				TOTAL
			A	B	C	D	
TREATMENT GROUP	A	n	5 (12.5%)	10	0	13	28
	B	n	12	24 (24.4%)	0	0	36
	C	n	9	23	1 (14.2%)	1	34
	D	n	14	41	6	59 (80.8%)	120
TOTAL		n	40	98	7	73	218

Table 5. Comparison of the groups of patients determined according to CAT with the treatment group and percentage of patients has proper treatment

			CAT				TOTAL
			A	B	C	D	
TREATMENT GROUP	A	n	7 (9.8%)	8	0	13	28
	B	n	21	15 (22.3%)	0	0	36
	C	n	14	18	1 (5.8%)	1	34
	D	n	29	26	16	49 (77.7%)	120
TOTAL		n	71	67	17	63	218

When the results were evaluated, it was determined that 40.8%(n=89) of patients according to mMRC and 33%(n=72) according to CAT were receiving the optimal treatment that was completely suitable for their groups (Table 4,5).

DISCUSSION

Generally, as in our study, the mean age of the patients with COPD patients is above 60 years and the ratio of male patients is higher(8-11). We found that the smoking rate was 18%. In the literature smoking rate changes between %31-%52(8,12,13). Ratio of active smoking patients and the duration of use in our patient population is lower than the literature.

Of the 218 COPD patients in our study, 22.9% of patients (n=50) had no history of smoking. In literature non-smokers rate of COPD patient rates changes between %15-%52(2,14-17). The burden of COPD in never smokers is higher than previously believed (14). Tobacco use in the etiology of COPD is the most important risk factor, and there is a considerable proportion of patients who do not have smoking.

COPD is more common in patients aged 60 years and older (1). In this age group, the presence of additional diseases is also common. 51.8% (n = 113) of our study population had at least one comorbidity. The most common comorbidities were hypertension (%30.7) in accordance with the literature (8,9).

We applied both mMRC and CAT scales to patients and evaluated the results separately and compared the treatment group. When mMRC scale used 18.3%, 45%, 3.2%, 33.5% of patients, when CAT scale used 32.6%, 30.7%, 7.8%, 28.9% was in the A, B, C, D group respectively. In the Han et al.'s study, mMRC and SCRQ scales were used, 33.5%, 20.5%, 9%, 38% of the patients in the A, B, C, and D groups (18). In another similar study, Jones and his colleagues used CAT and found rates of A, B, C, D as 9.3%, 48.5%, 0.7% and 41.5%, respectively (19). While there is more similarity in categorization according to CAT, the lowest number of C group patients in all studies. Group C patients symptoms tests are low scores but hospital admissions or emergency referral is high and that is a rare situation. While the number of patients in the

C group was low, the rates of evaluations according to CAT were more similar to the literature.

When we have compared the scales among themselves according to the COPD severity levels as A + B (mild symptom) and C + D (severe symptom) by using GOLD suggestion; both CAT and mMRC, the ratio of patients in A + B group was 63.3%, C + D group was 35.7%. This suggests that the CAT and mMRC scales do not always give the same category, but are quite consistent in distinguishing between severe symptoms and mild symptoms.When we examine the group determined according to the patient's symptoms, rates of group A patients were 18.3% and 32.6% according to mMRC and CAT questionnaires respectively. When the treatment of the patients was examined, it was seen that the treatment of 18% of the patients was compatible with the treatment recommended for group A. In this case, group A patients who expressed the low symptom and low risk category were receiving the recommended treatment for the higher groups.

The rates of group B patients were, 45%, 30.7% according to mMRC and CAT questionnaires respectively, and 16.5% of patients were receiving the recommended treatment for group B. The rates of group C patients were 3.2%, 7.8% according to mMRC and CAT questionnaires respectively, and those who received the recommended treatment for this group were 15.6%. The rates of group D patients were 33.5% and 28.9% according to mMRC and CAT questionnaires respectively, 55% of patients received intensive therapy recommended to group D.

This situation shows that there is a shift towards C and D in the treatment categories and the highest rate of drug use in the D group, whereas the symptom categories are mostly in the A and B bands. This makes us think that many COPD patients are taking too much bronchodilator medication. It is a situation that should be considered in terms of both cost increase and drug side effects. There is no other study in the literature on the subject of treatment categorization A, B, C, D. In the ALPHABET study, based on all patients, the most preferred treatment regimen is a triple treatment regimen consisting of long-acting beta 2 agonist (LABA), inhaled corticosteroid (ICS) and long-acting anticholinergic (LAMA), recommended for each group according to the guidelines for pharmacological treatment. When the treatments were considered as equal priority, 7.3% of the patients should use this triple treatment regimen while 62% of the patients were using LABA + ICS + LAMA. The guideline compliance in the treatment was as low as in our study (8). Similar to our study, in a study conducted by Safka et al. In Canada, symptom categories were found to be intense in groups A and B, and treatment was found to be higher in the triple treatment regimen, LABA + LAMA + IKS, in the higher group compared to the new treatment categorization (20). In the new classification, when LABA + LAMA + IKS treatment is considered to be the D group, it is interpreted as this group is the most widely used treatment.

As far as the literature on this subject can be scanned, evaluating CAT and mMRC scales separately and while comparing treatment compliance, no other study grouping the recommended treatments in the GOLD 2018 guideline as A, B, C, D was found. When the results were evaluated, it was determined that 40.8% (n=89) of patients according to mMRC and 33% (n=72) according to CAT were receiving the optimal treatment that was completely suitable for their groups. Even if the patient was less symptomatic and included in the low symptom category, he was receiving the recommended triple treatment regimen for more severe symptoms and was exposed to overtreatment.

CONCLUSION

We concluded that usage of overdose bronchodilators in stable COPD patients has a significant rate. In order to prevent this, we found that CAT and mMRC scoring systems and CAT and mMRC symptom tests with GOLD guide suggestions can be easily applied by a family physician. We think that these scales can be easily performed in the primary care system. Early determination of the optimum treatment needs of patients with stable COPD, will have an important place in terms of diagnosis and disease management.This study was one of the rare studies in which both treatment groups and grouping of disease severity were evaluated together (considering GOLD 2018 Guidelines update).

Limitations: Our study has some limitations witch a single-center study with a limited number of patients. Patients with COPD diagnosis and active drug use were accepted as COPD patients, and Pulmonary Function Test values were not requested from each patient. We think that this study will be more meaningful if the diagnosis of COPD is confirmed by Pulmonary Function Test and this study is performed with a larger population. Symptom tests are based on patient statements, thus there may be error factors here as well.

Suggestions: COPD patients are an important part of the chronic disease follow-up in family medicine. Knowledge and experience about inhaler therapies should be increased in order to better manage the treatment and follow-up of COPD patients in Family Medicine practice. CAT and mMRC scales should be used in the clinical follow-up of COPD patients. The clinical condition of the patient should be understood better by using the scales recommended by the guides and the correct use of the treatment should be reminded to the patient at each Family Medicine visit..

Supplementary Materials:

Supp 1. CAT (COPD Assessment Test)(1)

I never cough	**1 / 2 / 3 / 4 / 5**	I cough all the time
I have no phlegm (mucus) in my chest at all	**1 / 2 / 3 / 4 / 5**	My chest is completely full of phlegm (mucus)
My chest does not feel tight at all	**1 / 2 / 3 / 4 / 5**	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	**1 / 2 / 3 / 4 / 5**	When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	**1 / 2 / 3 / 4 / 5**	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	**1 / 2 / 3 / 4 / 5**	I am not at all confident leaving my home because of my lung condition
I sleep soundly	**1 / 2 / 3 / 4 / 5**	I don't sleep soundly because of my lung condition
I have lots of energy	**1 / 2 / 3 / 4 / 5**	I have no energy at all

*This table is taken from the GOLD guideline

Supp 2. mMRC (Modified Medical Research Council) (1)

Grade 1	Not troubled by breathless except on strenuous exercise
Grade 2	Short of breath when hurrying on a level or when walking up a slight hill
Grade 3	Walks slower than most people on the level, stops after a mile or so, or stops after 15 min walking at own pace
Grade 4	Stops for breath after walking 100 yards, or after a few minutes on level ground
Grade 5	Too breathless to leave the house, or breathless when dressing/undressing

*This table is taken from the GOLD guideline.

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RESEARCH ARTICLE

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Evaluation of the Effect of Physical Activity on Sleep Quality and Cardiovascular Disease Risk in Women in the Postmenoposal Period in Turkey

ABSTRACT

Objective: Menopause is a period of life in which women are at increased risk of cardiovascular diseases and sleep problems. In this study, we aimed to determine the effect of physical activity on CVR and sleep quality in women in this period.

Methods: The study was conducted with 342 postmenopausal women (PMW) who met the inclusion and exclusion criteria who applied to the outpatient clinic between August and December 2018 at Health Sciences University Dışkapı Yıldırım Beyazıt Training and Research Hospital. Women were given sociodemographic data form, International Physical Activity Questionnaire short form(IPAQ-SF), Pittsburgh Sleep Quality Index (PSQI) , calculated CVR estimation with Framingham formulation. The data were evaluated with SPSS 23 program.

Results: In our study the mean age of women was 60.77 ± 9.2 years. The rate of patients with a 10-year CVR was 66.1%. The Pittsburgh Sleep Quality (PSQI) scorewas 9.05 ± 4.33 and the rate of good sleep quality (PSQI ≤5) was 24.6%. Physical activity (PA) level was found to be 848.68 ± 1213.08 MET-min /week. It was observed that the state of being physically inactive was associated with the presence of a diagnosis of hypertension (p = 0.026). It was observed that those with severe PA levels in women had low body mass index (BMI) (p = 0.035), and increased CVD as the BMI and daytime dysfunction increased. Cardiovascular risk (CVR), sleep quality score and subparameters did not change according to physical activity. While there was a significant difference between the severity of PA level and Framingham risk score (FRS) (p = 0.032), those with high PA levels had the lowest FRS. Sleep quality and subparameters did not change according to PA level. In the presence of obesity, CVR, habitual sleep afficiency and sleep disorder component scores were shown to increase.

Conclusions: From the pre-menopausal period, women should be directed to perform appropriate PA to reduce obesity and prevent the onset or progression of CVD. Sleep hygiene trainings can be given to improve sleep quality in the postmenopausal period.

Keywords: Cardiovascular Diseases, Exercise, Postmenopause, Sleep.

Postmenopozal Dönemdeki Kadınlarda Fiziksel Aktivitenin Uyku Kalitesi ve Kardiyovasküler Hastalık Riskine Etkisinin Değerlendirilmesi

ÖZET

Amaç: Menopoz dönemi kadınların kardiyovaskülerhastalık(KVH) riskinin ve uyku sorunlarının arttığı yaşam dönemidir. Çalışmada bu dönemdeki kadınlarda fiziksel aktivitenin kardiyovasküler riskve uyku kalitesine etkisini saptamayı amaçladık.

Gereç ve Yöntem: Çalışma, Sağlık Bilimleri Üniversitesi Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi'nde 2018 yılı Ağustos-Aralıkayları arasında polikliniğe başvuran dahil olma ve dışlanma kriterleri karşılayan 342 postmenopozal kadın ile yapılmıştır. Kadınlara sosyodemografik veri formu, Uluslararası Fiziksel Aktivite Anketi kısa form, Pittsburgh Uyku Kalite İndeksi uygulanmış, Framingham formülasyonu ile kardiyovasküler risktahmini hesaplanmıştır. Alınan veriler SPSS 23. programı ile değerlendirilmiş, Pearson korelasyon, ANOVA ve Ki-kare test teknikleri kullanılmıştır.

Bulgular: Çalışmamızda kadınların yaş ortalaması 60,77±9,2 yıl idi. 10 yıllık KVR yüksek olanların oranı %66,1 idi. Pittsburgh Uyku Kalitesi (PUKİ) Skoru 9,05±4,33 ve iyi uyku kalitesine (PUKİ ≤5) sahip olanların oranı %24,6 idi. Fiziksel aktivite düzeyi 848,68±1213,08 MET-dk/hafta olarak saptandı. Fiziksel olarak aktif olmama durumunun hipertansiyon tanısı varlığı ile ilişkili olduğu görülmüştür. (p=0,026). Kadınlarda fiziksel aktivite düzeyi şiddetli olanların beden kitle indeksinin(BKİ) düşük olduğu (p = 0,035) , beden kitle indeksi ve gündüz işlev bozukluğu arttıkça KVR'ninarttığı görüldü. Kardiyovasküler riskile uyku kalite skoru ve alt parametreleri fiziksel aktiviteye göre değişmedi. Fiziksel aktivite düzeyinin şiddeti ile Framingham risk skoru(FRS) arasında anlamlı fark olduğu (p=0,032) , fiziksel aktivite düzeyi yüksek olanların FRS en yüksek iken fiziksel aktivite düzeyi düşük olanların FRS en düşüktü. Uyku kalitesi ve alt parametreleri fiziksel aktivite düzeyine göre değişmedi. Obezite varlığında kardiyovasküler risk, alışılmış uyku etkinliği ve uyku bozukluğu komponent skorunun arttığı gösterildi.

Sonuç: Menopoz öncesi dönemden itibarenobeziteyi azaltıp KVH'ınbaşlamasını veya ilerlemesini önlemek için kadınlar uygun fiziksel aktivite yapmaya yönlendirilmelidir. Postmenopozal dönemde uyku kalitesini arttırmak amacıyla uyku hijyeni eğitimleri verilebilir.

Anahtar Kelimeler: Egzersiz, Kardiyovasküler Hastalık, Postmenopoz, Uyku.

INTRODUCTION

Menopausal and postmenopausal period make up about one third of women's life, and it is estimated that there will be 1.1 billion post-menopausal women in the world by 2025 (1).

It has been shown that during the normal physiological process of menopause, it can contribute to a number of cardiometabolic risks such as central obesity, reduced glucose tolerance, increased blood pressure, abnormal levels of plasma lipids, and vascular inflammation with decreased ovarian follicle function (1). As a result of the decrease in estrogen in the postmenopausal period, the risk of developing cardiovascular diseases (CVD), osteoporosis, visceral obesity and type II diabetes is higher (2,3). As there is no longer any estrogen protection, it can lead to an increased prevalence of diabetes, atherosclerosis, and CVD (4,5).

The risk of developing depression, stress, anxiety and emotional distress increases in women during the menopause transition, and sleep disorder is higher in postmenopausal and menopausal transition compared to women in premenopause (6,7) It is known that irregular sleep duration and timing may be novel risk factors for CVD, regardless of traditional CVD factors and sleep amount or quality (11). Decreased physical activity has been shown to be strongly associated with cardiovascular risk profiles in the postmenopausal women population (8). Women who are physically active have been found to have better body composition and lower cardiovascular risk profiles (8,9) .Physical exercise in postmenopausal women significantly contributes to metabolic fitness and decreased cardiovascular risk, additionally (12). Physical activity and exercise have been shown to increase sleep time and provide significant improvements in sleep quality and delay in falling asleep (13,14).

It is important to know for physicians working with this age group that appropriate physical exercise has an impact on the risk of CVD and sleep problems, and it may be a helpful CVD preventive intervention. Physical exersize is strongly recommended for women in the postmenopausal period, regardless of their form. Beneficial physical activity includes exercise that will promote cardiovascular fitness (aerobic), muscle strength (resistance), flexibility (stretching), and balance (many of the preceding, and additional activities such as yoga) (15).

In the limited studies on postmenauposal women (PMW) and physical activity are mostly conducted by sports medicine, special techniques and special tests made in the laboratory environment were used. We think that more suitable and clear physical activity index/ questionnaires which will provide comfortable and quick evaluation should be used in primary care, but there are few studies with validity and reliability in Turkish (16,17). In this study we aimed to examine the relationship between sleep quality, physical activity and risk of cardiovascular disease using a comprehensive and valid tool in women in the postmenopausal period, practically.

MATERIAL AND METHODS

Study Population: It is a cross-sectional and descriptive study conducted in a University Hospital Family Medicine Clinic between August 31 and December 1,2018.

As the universe of the study, the number of women over the age of 50 who applied to the family medicine outpatient clinic for a period of 3 months was found to be 6426. CVD prevalence in post-menopausal women is evaluated as 30%, we plan to include 383 patients in our study in order to ensure 95% confidence interval and 5% margin of error in the Statcalc program. Women in the menopausal period who agreed to participate in the study were included; those who have malignancy who are not actively receiving chemotherapy treatment, those who have been diagnosed with obstructive sleep apnea, urinary incontinence and psychiatric illness (depression, bipolar disorder, schizophrenia, anxiety disorder, posttraumatic stres disorder, etc.) Patients with a problem and mental illnesfs were excluded from the study.

Data Collection Tools

Sociodemographic Data: A questionnaire consisting of questions about age, marital status, level of education, occupation, accompanying chronic diseases, medications, smoking status, use of tea, coffee or energy drinks after 7 pm, last menstruation, uterineorovarian surgery were applied to the patients in the postmenopausal period. There are a total of 11 questions evaluating the usage of hormone replacement therapy after menopause.

Anthropometric and Blood Pressure Measurements: Body Mass Index (BMI) and Systolic (SBP) and diastolic (DBP) blood pressures were measured and recorded of women's included to the study.

Physicial Activity(PA) Measures: The Turkish version of the International Physical Activity Assessment Questionnaire (IPAQ)-Short form was used to evaluate PA intensities (16). The amount of PA (vigorous, moderate, walking and sitting) of the participants during the last week was questioned. The term MET (Metabolic Equivalent of Task) is used to refer to the amount of oxygen consumed at the time of physical activity. A score as MET-min day is obtained by multiplying the minutes, days and MET values (16). In this study, inactive PA level was defined as <600 MET- minute/week; low intensity(minimal active) PA level was defined as 600-3000 MET-minute/week and sufficient PA level for health (high intensity) was defined as >3000 MET- minute/week (17).

Sleep Measures: In our study, PSQI, which gives a quantitative measurement of sleep quality, was used to define good and bad sleep. It contains a total of 24 questions. In scoring the PSQI, seven

component scores are derived, each scored 0 to 3. This questionnaire addresses seven self reported components of sleep including, sleep quality, sleep duration, sleep latency, sleep disturbance, use of sleep medication, day time dysfunction, and habitual sleep efficiency. The component scores are summed to produce a global score (range 0 to 21). Higher scores score indicates worse sleep quality, with a score ≥ 5 (18).

CVR Factors Measurement: Framingham Risk Score (FRS) is used to assess the 10-year CVD risk. Age, systolic blood pressure, using antihypertensive, history of diabetes, current smoking status, total cholesterol and HDL cholesterol values are used (1).

Statistical Methods: For analyzing the data collected, descriptive and inferential statistics were performed with SPSS® IBM 23.0 software in 95% confidence level. In the study, One Way ANOVA, and chi-squared tests were used. In determining the relationship between the two groups, the relationship with Pearson correlation Analysis was determined. Statistical significance level was accepted as <0.05 in all analyzes.

RESULTS

The mean age of the women included in the study was 60.77 ± 9.2 years and 39.2% (n = 134) were 50-59 years old, 69.3% (n = 237) were married, 56.4% (n = 193) primary school graduates, 84.5% (n = 289) were unemployed. Mean height was 155.48 ± 8.01 cm, and weight was 79.75 ± 15.39 kg, and BMI mean was 32.88 ± 6.22 kg / m2. 67.3% of the women were obese and 9.1% of the participants were smoking. Tea, coffee, and energy drinks consume rate after e was 71.6%.

It was found a statistically significant relationship between the presence of hypertension, education level and BMI and physical activity levels, it was observed that being physically inactive was associated with the presence of a diagnosis of hypertension, being illiterate, and obesity decreased by performing severe physical activity (Table 1).

Table 1. Cardiovascular and menopause features and lifestyle habits of women according to their physical activity levels (*Chi-Squared Test)

		Physical activity level				
		inactive n (%)	Low intensity n (%)	High intensity n (%)	X^2	p
Age(years)	Under 50 age	15 (42.9)	19 (54.3)	1 (2.9)	4.669	0.587
	50-59 age	68 (50.7)	59 (44)	7 (5.2)		
	60-69 age	57 (51.4)	46 (41.4)	8 (7.2)		
	70 age and older	37 (59.7)	21 (33.9)	4 (6.5)		
Marital Status	Married	125 (52.7)	98 (41.4)	14 (5.9)	0.350	0.839
	Single	52 (49.5)	47 (44.8)	6 (5.7)		
Education Level	Uneducated	71 (59.2)	38 (31.7)	11 (9.2)	10,465	0,005*
	Educated	106 (47.7)	107(48.2)	9(4.1)		
Employmentstatus	Retired	15 (38.5)	22 (56.4)	2 (5.1)	8.034	0.090
	Employed	4 (28.6)	8 (57.1)	2 (14.3)		
	Unemployed	158 (54.7)	115 (39.8)	16 (5.5)		
Hypertension	No	68 (47.6)	69 (48.3)	6 (4.2)	11.053	0.026*
	Yes	109 (54.8)	76 (38.6)	14 (6.6)		
Diabetes	No	115 (50.7)	101 (44.5)	11 (4.8)	2.015	0.365
	Yes	62 (53.9)	44 (38.3)	9 (7.8)		
Hypercholesterolemia	No	134 (52.8)	107 (42.1)	13 (5.1)	1.108	0.575
	Yes	43 (48.9)	38 (43.2)	7 (8)		
Coronary Artery Disease	No	156 (52.3)	125 (41.9)	17 (5.7)	0.351	0.839
	Yes	21 (47.7)	20 (45.5)	3 (6.8)		
Hypothyroidism	No	156 (52.7)	122 (41.2)	18 (6.1)	1.311	0.519
	Yes	21 (45.7)	23 (50)	2 (4.3)		
The presence of other diseases	No	112 (50.7)	93 (42.1)	16 (7.2)	2.224	0.329
	Yes	65 (53.7)	52 (43)	4 (3.3)		
Diabetes medication use	No	122 (51.9)	102 (43.4)	11 (4.7)	1.933	0.380
	Yes	55 (51.4)	43 (40.2)	9 (8.4)		
Use of anti-hypertensive medications	No	75 (49)	71 (46.4)	7 (4.6)	2.216	0.330
	Yes	102 (54)	74 (39.2)	13 (6.9)		
Cholesterol medication use	No	151 (53)	121 (42.5)	13 (4.6)	5.340	0.069
	Yes	26 (45.6)	24 (42.1)	7 (12.3)		
Thyroid replacement therapy	No	157 (52.9)	122 (41.1)	18 (6.1)	1.637	0.441
	Yes	20 (44.4)	23 (51.1)	2 (4.4)		
Allergy medication use	No	175 (51.8)	143 (42.3)	20 (5.9)	0.294	0.863
	Yes	2 (50)	2 (50)	0 (0)		
Use of other drugs	No	110 (49.3)	98 (43.9)	15 (6.7)	1.938	0.380
	Yes	67 (56.3)	47 (39.5)	5 (4.2)		
BMI(kg / m^2)	NormalRange	12 (41.4)	14 (48.3)	3 (10.3)	11.019	0.026*
	Overweight	47 (57.3)	26 (31.7)	9 (11)		
	Obese	117 (50.9)	105 (45.7)	8 (3.5)		
Current smoker	Yes	15 (48.4)	15 (48.4)	1 (3.2)	0.764	0.683
	No	162 (52.1)	130 (41.8)	19 (6.1)		
Drinking tea. coffee. energy drinks after 7 pm	Yes	122 (49.8)	110 (44.9)	13 (5.3)	2.348	0.309
	No	55 (56.7)	35 (36.1)	7 (7.2)		

In the analyzes, it was observed that the PSQI score was 9.05 ± 4.33 and 24.6% of the women had good sleep quality. Lipid profiles, blood pressures and sleep quality characteristics were compared according to PA levels, but no statistically significant difference was found (Table 2).

Table 2. Blood pressure. serum lipid values and sleep quality characteristics by physical activity levels.

	Physical activity level			F	*p* value
	Inactive Mean ± SD.	Low intensity Mean ± SD	High intensity Mean ± SD		
Systolic blood pressure (mmHg)	131.95±21.46	128.89±17.54	136.7±20.78	1.845	0.160
Diastolic blood pressure(mmHg)	81.49±13.02	81.12±11.02	83.15±14.25	0.243	0.784
Total cholesterol(mg/dl)	206.83±42.43	211.36±82.77	209±36.49	0.208	0.812
LDL cholesterol (mg/dl)	145.42±31.68	144.03±31.85	143.05±29.11	0.106	0.900
HDL cholesterol (mg/dl)	48.67±9.95	49.04±12.07	53.2±12.21	1.521	0.220
Triglycerides (mg/dl)	176.66±95.28	205.35±545.31	143.45±45.79	0.403	0.669
Subjective sleep quality	1.59±0.94	1.41±1.05	1.15±0.93	2.668	0.071
Sleep latency	1.91±1.08	1.93±1.1	1.8±1.2	0.127	0.881
Sleep duration	1.1±1.22	1.22±1.2	1.05±1.23	0.455	0.635
Habitual sleep efficiency	1.29±1.13	1.37±1.17	1.3±1.08	0.187	0.830
Sleep disturbance	1.82±0.54	1.68±0.57	1.8±0.77	2.520	0.082
Use of sleep medication	0.19±0.69	0.26±0.82	0.35±0.93	0.603	0.548
Dysfunction of daytime	1.29±1.01	1.17±0.99	1.05±1.05	0.908	0.404

* One-way ANOVA test; HDL. high density lipoprotein; LDL. low-density lipoprotein.

Relationship Between PA, FRS and Sleep Quality Parameters: There was a weak negative relationship between women's PA score and BMI (r = -0,201) (Table 3). There was no statistically significant relationship between women's PA score and FRS, and between PA score, sleep score and sleep parameters, but there was weak positive correalation between FRS and BMI of women (p=0,013, r = 0,135), and FRS dysfunction during daytime score (p=0,002, r = 0.171)(Table 3).

Table 3. Relationship Between Physical Activity Score and BMI, FRS, Sleep Quality Parameters.

	Physical activity score		**Framingham Risk Score**	
	r	*p-value*	***r***	***p*-value**
BMI	**-0.201***	0.002*	**0.135***	0.013*
PSQI score	0.017	0.757	0.091	0.093
Subjective sleep quality	-0.006	0.919	0.077	0.153
Sleep latency	-0.082	0.128	0.007	0.897
Sleep duration	-0.020	0.713	-0.003	0.959
Habitual sleep efficiency	0.006	0.916	-0.002	0.972
Sleep disturbance	0.043	0.425	0.090	0.095
Use of sleep medication	-0.024	0.653	0.063	0.242
Dysfunction of daytime	0.079	0.145	**0.171***	0.002*

*p < 0.05 pearson correlation r:correlation coefficient

But there was a statistically significant difference in FRS, habitual sleep efficacy component score, sleep disorder score among different BMI women. In another way, in terms of BMI and FRS there was a significant difference between women with inactive, low and very active PA levels (p <0.05), but there's not statistically significant difference in terms of PSQI score (Table 4). There was a statistically significant difference in FRS, habitual sleep efficacy component score, sleep disorder score among women with different BMI (p=0,035). According to the level of physical

activity, BMI and FRS were associated but PSQI was not related (See in table 4). Those with higher BMI were more inactive, and women with the highest FRS were the most active. There were similarities between physical activity groups in terms of PSQI scores.

Table 4. Comparison of BMI. FRS. PSQI score in terms of Physical Activity Level.

	Physical activity level			
	inactive n=177	Low intensity n=145	High intensity n=20	p
	Mean ± SD.	Mean ± SD.	Mean ± SD.	
BMI	33.58±6.88	32.39±5.31	30.28± 5.22	0.035*
FRS	14.54±7.91	12.61±7.78	16.35±8.25	0.032*
PSQI score	9.19 ±4.22	8.99±4.37	8.45±5.07	0.745

BMI. body mass index;FRS.framingham risk score;PSQI.Pittsburgh sleep quality index
*p<0.05.ANOVA

DISCUSSION

It is well-known that the prevalence of CVD in PMW is higher than that of premenopausal women and men of the same age, because estrogen deficiency is considered an important factor leading to cardiovascular diseases (19). Nevertheless, physical activity, sleep quality in menopausal women, and their effects on CVD risk, there is a few study that evaluates all aspects (20,21). Our study aims should be evaluated as a whole these problems and CVR factors were evaluated by FRS. Scheltens T, et al. Also evaluated the risk of cardiovascular disease under the age of 60 with both FRS and SCORE and found to be similar (21.) In our study, the rate of those with a high risk of CVD was found to be 66.1% of PMW over 50 ages by FRS. In an another large population-based study it was found higher total and low-density lipoprotein cholesterol levels, SBP and BMI as CVR factors in PMW over 50 ages than premenauposal ones (22).These show that even over the age of 50 or in the postmenopausal period increases the risk.

Long-term sitting time is a common feature of modern society that includes television viewing, screen time, computer use, desk work sedentary behaviors at home (23).In this study, the PA levels of the participants that were 51.75% were inactive and 42.4% were low-active, and sitting time of women was 525.32 minutes per day. In addition to the high rate of chronic diseases, low educated and unemployed in this age group, we think that the elderly in our country generally prefer home activities such as watching TV to outdoor activities such as sports and walking. In already overweight and obese PMW, a strong positive correlationbetween sitting time and CVD markers has been demonstrated like our participants (24).Postmenopausal women often complain of disturbed and unsatisfactory sleep. According to a study 46.7% of participants scoring over 5 on the PSQI (25). This common health problem has some long-term consequences of sleep disruption in otherwise healthy individuals include hypertension, dyslipidemia, CVD, weight-related issues, metabolic syndrome, and T2DM. (26). In this study population mostly have at least one chronic disease like diabetes, hypertension but we excluded initially those with psychiatric, neurological or obstructive pulmonary disease, medical problems were not associated with sleep quality consequently.

Most studies have reported that PA affects sleep quality positively like the study conducted by Wu et al., low PA level was associated with poor sleep quality (27), and the study by Magee et al. they found an association between low PA with poor sleep quality and high BMI (28). Although the relationship has not been detected with sleep quality and PA levels in our study, the subgroup score of daytime dysfunction was associated with CVR in terms of FRS.

The total PSQI score, especially sleep latency, habitual sleep efficiency, and sleep disturbance scores were significantly increased in postmenopausal women. In addition to BMI, hypertension, diabetes, smoking, marital status, PA showed a positive correlation with high PSQI score and menopausal symptoms (29). Similarly, in our study, it was found that in women with different BMI, the usual sleep efficiency and sleep disorders core increased. In our study, CVD does not change according to the sleep score. There is a weak positive correlation between the FRS daytime dysfunction score. As daytime dysfunction increases, CVD increases. In another study conducted by Zhou et al., it was found that subjects with sleep disorders had older, obese, menopause and had higher blood pressure and an increased waist-to-hip ratio. In addition, hyperlipidemia and glucose disorders were observed in the group with sleep disorders. It has been shown that there is an increasing tendency to sleep prevalence during menopause (30). In a study by Cappuccio et al., people who reported that they slept 5 hours or less at night were considered to be a higher risk group for cardiovascular morbidity and mortality, and long sleep duration was associated with more CVD (31). This may be one of there as ons why we found the CVR score too high. In a prospective study

involving 66 postmenopausal women, a diet and exercise program was applied to patients, and FRS decreased by 3% after 3 months (32). Unlike our study, a significant relationship was found between PA and FRS. The absence of such a relation in our study can be explained by not having sufficient sample size.

Strengths and Limitations of the Research: The strength of our research; data collection tools are applied by a single researcher, face to face with each patient. In addition, our study is a field work conducted by family physicians and it is important for preventive medicine. Our research was carried out in a single center, low sociocultural, immobile, obese and almost homogeneous sample. In order to generalize the results of there search to all PMW in the country, more detailed studies on the subject should be conducted in different groups in different areas in order to repeat the study with a larger sample group and to prevent problems of the menopausal period. There is a need for studies where sleep quality is evaluated with more objective methods such as polysomnography. Physicalactivity should be examined with a more comprehensive and specific tool. Because there are deficiencies in determining the characteristics of women's activities such as homestate and transportation.

CONCLUSION

Women should be given a lifestyletraining that includes variables such as nutrition and exercise, starting before the menopause period with appropriate methods that will create behavioral changes in adults. In order to reduce obesity, post-menopausal women should be encouraged and guided to practice physical activities suitable for their physical and financial conditions, away from conditions that limit the PA of the person such as computers and TV. Grading the risk of CVD with FRS plays an impressive role in implementing medical treatment and behavioral changes that can prevent the onset or progression of cardiovascular disease, and allows more patients to be noticed earlier. It is considered that this study is important in terms of showing the effect of PA on sleep quality and the risks of cardiovasculardisease in women of this age group in the current health agenda, where active aging comes to thefore, which will help other studies in the field. Sleep hygiene trainings can be given to increase sleep quality.

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RESEARCH ARTICLE

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Identification of the Gram Positive Bacterial Sepsis Agent with Rapid Genotype Test

ABSTRACT

Objective: An irreversible process begins when a systemic infection causes sepsis. Therefore, rapid identification of the agent bacteria in sepsis and its antibiotic resistance is crucially important. In this study, it was aimed to investigate the efficiency of rapid genotype test in detecting sepsis agent Gram positive bacteria and important antibiotic resistance.

Methods: 2132 blood culture samples sent to the laboratory were examined with an automatic blood culture system (BACTEC, BD, USA) between 2018-2019. Blood culture bottles sent to the laboratory were Growing bacteria was identificated by VİTEK (bioMérieux, France) automated bacteria identification / antibiotic susceptibility system. In addition, bacterial species and mecA, vanA, vanB, vanC1, vanC2 / C3 genes in blood cultures with Gram positive bacterial growth were also determined by the "Genotype® BC Gram-positive (Hain Lifesience, Germany)" test.

Results: 72 patients with gram-positive bacteria growth in two or more blood culture bottles were included in the study. In 44 of the samples (61%) the same bacterial species were detected with conventional method (bacteria culture) and BC Gram positive test. In 28 of the samples (39%) differences were detected between results of methods regarding bacterial species name or vancomycin/methicillin resistance rate. Although single agent was isolated with culture method in all of the samples, multiple agents were detected in eight samples with rapid genotype test. Also, it was found that in mecA positive samples, ciprofloxacin resistance was higher than mecA negative ones.

Conclusions: In the study, it was observed that BC Gram positive test could correctly identify sepsis agent bacteria and their resistance genes within 4-5 hours.

Keywords: Drug Resistance, PCR, Rapid test, Sepsis, Staphylococci.

Gram Pozitif Bakteriyel Sepsis Etkenlerinin Hızlı Genotip Test ile Tanımlanması

ÖZET

Amaç: Sistemik bir enfeksiyon sepsise neden olduğunda geri dönüşü olmayan bir süreç başlamaktadır. Bu nedenle sepsisteki etken bakterinin ve antibiyotik direncinin hızlı bir şekilde tanımlanması çok önemlidir. Bu çalışmada, sepsis etkeni Gram pozitif bakterileri ve önemli antibiyotik dirençlerini saptamada hızlı genotip testinin etkinliğinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Laboratuvara 2018-2019 yılları arasında gönderilen 2132 kan kültürü örneği otomatik kan kültürü sistemi (BACTEC, BD, ABD) ile incelenmiştir. Üreyen bakteriler VİTEK (bioMérieux,Fransa) otomatize bakteri identifikasyon/antibiyotik duyarlılık sistemi ile tanımlanmıştır. Ayrıca Gram pozitif bakteri üremesi olan kan kültürlerindeki bakteri türleri ve mecA, vanA, vanB, vanC1, vanC2 / C3 genleri "Genotype® BC Gram-pozitif (Hain Lifesience, Almanya)" testi ile de belirlenmiştir.

Bulgular: İki veya daha fazla kan kültürü şişesinde Gram pozitif bakteri üremesi saptanan 72 hasta çalışmaya dahil edildi. Örneklerin 44'ünde (% 61) konvansiyonel yöntemle (bakteri kültürü) ve BC Gram pozitif testi ile aynı bakteri türü tespit edildi. Örneklerin 28'inde (% 39) bakteri tür adı veya vankomisin / metisilin direnç oranı ile ilgili yöntemlerin sonuçları arasında farklılıklar tespit edildi. Tüm örneklerde kültür yöntemi ile tek etken izole edilmesine rağmen hızlı genotip testi ile sekiz örnekte birden fazla etken tespit edildi. Ayrıca mecA pozitif örneklerde siprofloksasin direncinin mecA negatiflere göre daha yüksek olduğu bulundu.

Sonuç: Çalışmada BC Gram pozitif testinin, sepsis etkeni bakterileri ve direnç genlerini 4-5 saat içinde doğru bir şekilde belirleyebildiği görülmüştür.

Anahtar Kelimeler: İlaç direnci, PCR, Hızlı test, Sepsis, Stafilokok.

INTRODUCTION

Rapid identification of bacterial pathogens and antibiotic resistance that grow in the blood cultures of patients with sepsis enables the selection of the most effective antibiotic for treatment. With early treatment, morbidity/mortality and hospitalization period decreases, unnecessary use of antibiotics is prevented and hospital costs are reduced. (1-4) Automatized blood culture systems used in clinical microbiology laboratories has significantly decreased the period of identification of bacterial pathogens. (1,2) However, the resulting takes a minimum of 2 days after receiving the positive signals. Faster identification systems are required to start treatment as early as possible. For this purpose, some laboratories use molecular methods to quickly identify the agent and resistance situation, such as DNA microarray, Nested polymerase chain reaction (PCR), multiplex PCR, in addition to non-molecular methods such as matrix-associated laser desorption ionization-time of flight (MALDI-TOF) MS , molecular methods, despite their high costs. (5,6)

In our study, rapid identification of bacterial species and mecA, vanA, vanB, vanC1, vanC2/C3 genes using "Genotype® BC Gram-positive (Hain Lifesience, Germany)" test in blood cultures with Gram positive bacteria growth was aimed.

MATERIAL AND METHODS

This cross sectional study aims identification and resistance detection with rapid genotype test in the patients of Duzce University Health Practice and Research Center who has a growth of gram positive bacteria in blood culture samples. Approval was obtained from Duzce University clinical research ethics committee, dated 21.09.2019 and numbered 2020/201.

Sampling: Among the 2132 blood cultures tested from 14.04.2018 to 26.01.2019, belonging to the patients of Duzce University Health Practice and Research Center. Seventy-two patients with Gram-positive bacteria growth in two or more blood culture bottles were included in the study.

Laboratory Analyses: When the growth signal was received from the automated blood culture system (BACTEC Blood Culture Test--BD, the USA) in our hospital's bacteriology laboratory, Gram staining from blood culture bottle and inoculation to blood agar (Oxoid, England) and eosine methylen blue agara (Oxoid, England) were performed.

Phenotypic Method: VITEK automated bacterial identification system (bioMérieux, France) and conventional methods were used in the phenotypical identification of the growing bacteria. In addition to the susceptibility of the bacteria to methicillin, vancomycin and teicoplanin, susceptibility to ciprofloxacin, gentamicin, trimethoprim / sulfamethoxazole (TMP-SXT) were also examined with VITEK automated system (bioMérieux, France) and with the method of disc diffusion. Antibiotic susceptibilities were evaluated according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria. (7)

Genotype Test: When gram positive bacteria is detected at least in two samples of the same patient according to the gram staining results, Genotype® BC Gram positive Ver.3.0 (Hain Lifescience Germany) assay kit that detects 17 different Gram positive types (*Streptococcus anginosus / constellatus / intermedius / mutans / sanguinis, Streptococcus mitis / oralis, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus dysgalactiae ssp. equisimilis, Streptococcus bovis, Streptococcus pneumoniae, Staphylococcus aureus, Staphylococcus haemolyticus, Staphylococcus epidermidis, Staphylococcus hominis, Staphylococcus warneri, Staphylococcus simulans, Enterococcus faecalis, Enterococcus faecium, Enterococcus gallinarum ve Enterococcus casseliflavus*) was used in this system, methicillin (mecA) and vancomycin (vanA , vanB, vanC1 and vanC2 / C3) resistance genes can be detected, too.

Genotype test results have not been confirmed by any other molecular method.

Statistical Analysis

Descriptive statistics of all data in the study were estimated. Chi-square and Fisher Exact tests were used in comparison among rates. The compatibility between the test results was examined by Mc Nemar test.

RESULTS

Seventy-two blood culture samples in Duzce University Health Practice and Research Center which were found to have gram positive bacteria growth two times consecutively between April 2018 and January 2019 were included to the study.

The median ages of the patients whose blood samples were taken were 72, (min: 1 max: 91). 36 of them were female (50%) and 36 of them were male (50%). All of the samples were sent from intensive care units.

A total of 45 Coagulase Negative *Staphylococcus* (CNS) (16 of which were *S. hominis*, 15 *S. haemolyticus*, 12 *S. epidermidis*, 2 *S. warneii*), 17 *S. aureus* [9 Methicillin Resistance *S. aureus* (MRSA), 8 Methicillin sensitive *S. aureus* (MSSA)], 9 *Enterococcus* (5 *E. faecalis*, 4 *E. faecium*) a *group D streptococcus* growth was detected with bacteria culture method. In 44 of the samples (61%) the same bacterial species were detected with both methods, while in 28 of the samples (39%) differences were detected regarding bacterial species name or vancomycin / methicillin resistance rate. In the statistical analysis, the results of rapid genotype test CNS, *S. aureus* and bacteria culture for enterococcus species were found to be significantly compatible (respectively p=0,375, p=0,999, p=0,999). However, vancomycin

susceptible *E. faecalis* and MR *S. hominis* species detected in a culture method sample, were found to be undetectable with rapid genotype test. In addition, *S. pneumoniae* species that were not detected in two blood culture samples, were detected with rapid genotype test. Moreover, while single agent was isolated in the samples, multiple agents were detected in 8 (11%) samples with rapid genotype test. In blood culture samples, the distribution of bacteria that were found to be similar or different with rapid genotype test and culture method is shown in Table 1 and Table 2. Results of rapid genotype test are shown in Figure 1.

Table 1. Distribution of bacteria that were found to be similar rapid genotype test and culture method

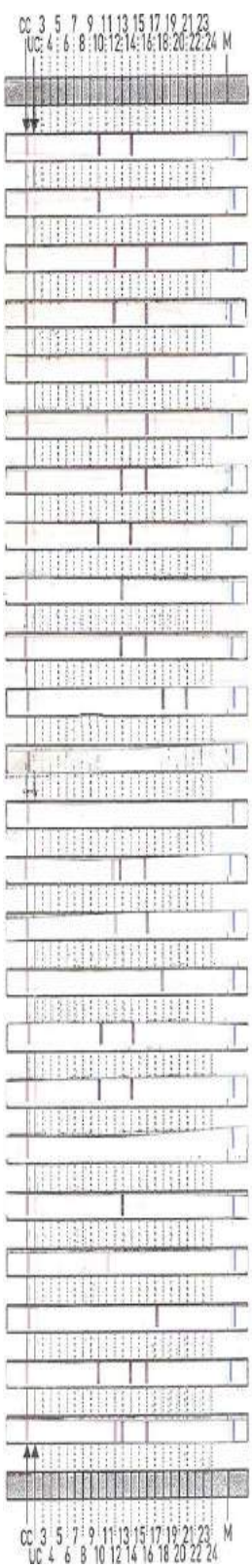
Number (Total=44)	Culture method	Rapid genotype test	
		Bacteria	Resistance gene
11	MR *S. epidermidis*	*S. epidermidis*	Mec A
9	MR *S. haemolyticus*	*S. haemolyticus*	Mec A
6	MR *S. aureus*	*S. aureus*	Mec A
6	MS *S. aureus*	*S. aureus*	-
5	MR *S. hominis*	*S. hominis*	Mec A
1	MS *S. hominis*	*S. hominis*	-
1	MS *S. haemolyticus*	*S. haemolyticus*	-
2	VR *E. faecium*	*E. faecium*	Van A
1	VS *E. faecium*	*E. faecium*	-
2	VS *E. faecalis*	*E. faecalis*	-

MR: Methicillin resistant, MS: Methicillin sensitive, VR: Vancomycin resistant, VS:Vancomycin sensitive

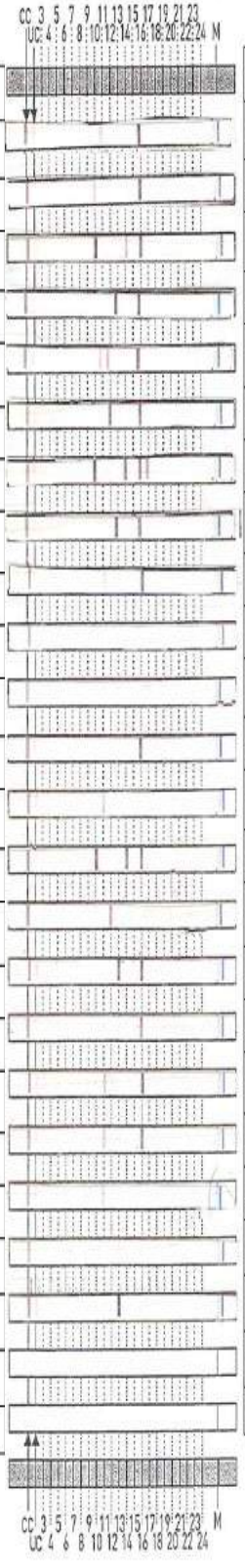
Table 2. Distribution of bacteria that were found to be different with rapid genotype test and culture method

Number (Total=28)	Culture method	Rapid genotype test	
		Bacteria	Resistance gene
3	MR *S. hominis*	*S. hominis*	-
2	MS *S. hominis*	*S. hominis*	Mec A
1	MS *S. hominis*	*S. aureus*	Mec A
1	MR *S. hominis*	*S. haemolyticus*	Mec A
1	MR *S. hominis*	*S. hominis, S. mitis/oralis, S. pneumoniae*	Mec A
1	MR *S. hominis*	-	-
1	MR *S. hominis*	*S. aureus*	-
3	MR *S. haemolyticus*	*S. haemolyticus*	-
1	MR *S. haemolyticus*	*S. haemolyticus, E. faecalis*	
1	MS *S. haemolyticus*	*S. haemolyticus , E. faecium*	Mec A, Van A
1	MR *S. epidermidis*	*S. epidermidis*	-
1	MS *S. aureus*	*S. aureus*	Mec A
1	MS *S. aureus*	*S. epidermidis, E.faecalis*	Mec A
1	MR *S. aureus*	*S. hominis*	Mec A
1	MR *S. aureus*	*S. aureus, E. faecalis*	Mec A
1	MR *S. aureus*	*S. aureus, S. hominis*	Mec A
2	MR *S. warneii*	*S. haemolyticus*	Mec A
1	VS *E. faecium*	*E. faecium, S. haemolyticus*	Mec A, Van A
1	VR *E. faecalis*	-	-
1	VS *E. faecalis*	*S. aureus*	-
1	VS *E. faecalis*	*S. hominis*	Mec A
1	Streptococcus grup D	*S. mitis/oralis, S. pneumoniae*	

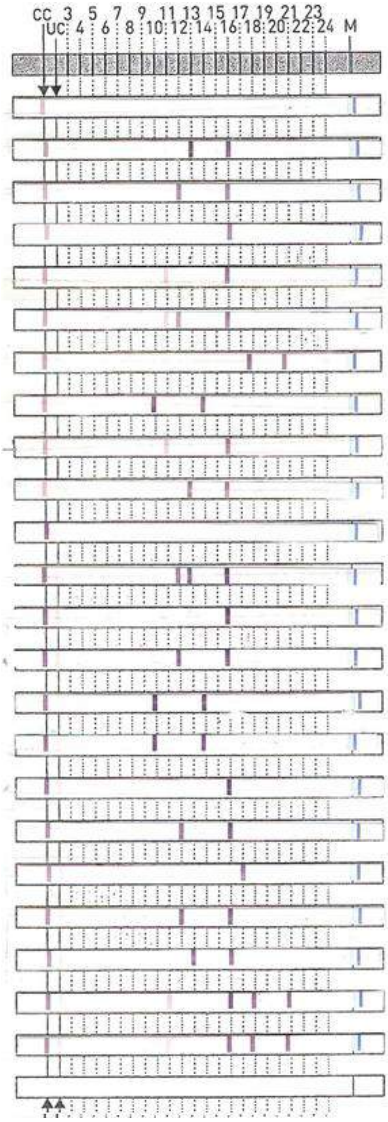
MR: Methicillin resistant, MS: Methicillin sensitive, VR: Vancomycin resitant, VS:Vancomycin sensitive



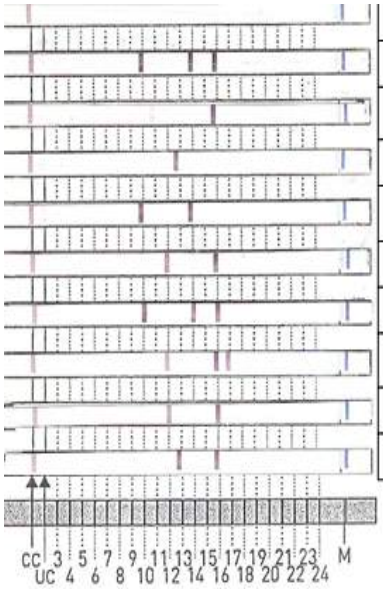
Species of bacteria	Resistance
S. aureus	
S. aureus	
S. epidermidis	Mec A
S. epidermidis	Mec A
S. haemolyticus	Mec A
S. haemolyticus + E. faecalis	
S. hominis	Mec A
S. aureus	MecA
S. hominis	
S. hominis	Mec A
E. faecium	Van A
Negative control	
Negative control	
S. epidermidis	Mec A
S. hominis	
E. faecium	
S. aureus	
S. aureus	
Negative control	
S. hominis	
S. haemolyticus	
E. feacalis	
S. aureus	Mec A
S.epidermidis + S. hominis	Mec A



Species of bacteria	Resistance
S. haemolyticus	Mec A
S. aureus	Mec A
S. aureus	Mec A
S. hominis	Mec A
S. epidermidis	Mec A
S. epidermidis	Mec A
S. aureus + E. faecalis	Mec A
S. hominis	Mec A
S. haemolyticus	Mec A
Negative control	
Negative control	
S. haemolyticus	Mec A
S. haemolyticus	
S. aureus, S. hominis	Mec A
S. epidermidis	
S. hominis	Mec A
S. haemolyticus	Mec A
S. haemolyticus	Mec A
S. haemolyticus	
S. haemolyticus	
non-working	
S.mitis/oralis+S.pneumoniae	
non-working	-
non-working	-



Species of bacteria	Resistance
Negative control	
S. hominis	Mec A
S. epidermidis	Mec A
S. haemolyticus	Mec A
S. haemolyticus	Mec A
S. epidermidis	Mec A
E. faecium	Van A
S. aureus	
S.haemolyticus	Mec A
S. aureus	Mec A
Negative control	
S.hominis+S.pneumoniaeS.mitis/oralis	Mec A
S. hominis	Mec A
S. epidermidis	Mec A
S. aureus	
S. aureus	
S. hominis	Mec A
S. epidermidis	Mec A
E. faecalis	
S.epidermidis	Mec A
S.haemolyticus	Mec A
S. aemolyticus + E. faecium	Mec A+VanA
S. haemolyticus + E. faecium	Mec A+VanA
Non-working	-



Negative control	
S. aureus	Mec A
S. haemolyticus	Mec A
S. hominis	
S. aureus	
S. epidermidis	Mec A
S. aureus	Mec A
S. epidermidis + E. faecalis	Mec A
S. epidermidis	Mec A
S. hominis	Mec A

Figure 1. Results of rapid genotype test

When the resistance rates of antibiotics other than beta lactam group in staphylococcus species were examined by VITEK automated system (bioMérieux, France) and disc diffusion method, it was found that the resistance rate of ciprofloxacin among the antibiotics included in the study was

higher than the mecA negative ones (p <0,001). Gentamicin and TMP-SXT were found to have similar susceptibility in mecA positive and negative samples (p = 0.447, 0.601, respectively). The susceptibility of staphylococcus species to ciprofloxacin, gentamicin and TMP-SXT is shown in Table 3.

Table 3. The susceptibility of staphylococcus species to ciprofloxacin, gentamicin and TMP-SXT (n/%)

	Ciprofloxacin,	TMP-SXT	Gentamicin
MecA positive staphylococci (n=44)	34 (77)	8 (18)	19 (43)
MecA negative staphylococci (n=18)	2 (11)	3 (17)	6 (33)
p değeri	<0,001	0,999	0,473

TMP-SXT: trimethoprim / sulfamethoxazole

DISCUSSION

Sepsis is a syndrome that is caused by uncontrollable inflammatory response against the infection in the host and organ failure as a result. The most common triggers in sepsis are bacterial infections. Early diagnosis of sepsis is crucially important in order for it to be treated before the patient's condition deteriorates and results in death. (8) Worldwide, 31 million cases of sepsis and 6 million deaths are reported regarding sepsis, each year. In one out of ten patients that has access to health services, an infection with sepsis characteristic develops. (9) When only culture-oriented microbiological analyzes are used in sepsis treatment, physicians do not have time to wait for microbiological bacteria culture results. (10) Time is crucially important in the treatment of sepsis and antimicrobial treatment is recommended to start in 60 minutes after the diagnosis. In the conducted studies, it is found that every hour of delay in antibiotic treatment after the diagnosis of sepsis, causes 8.4% mortality in patients. (11-13) Until the bacteria culture results of patients diagnosed with sepsis are received, physicians should empirically start the most extensive antimicrobial treatment which contains antibiotics that can affect all possible agent bacteria pathogens. As a result of this approach, not only costs increase but also antimicrobial resistance development is caused. (13)

Blood culture made in the diagnosis of sepsis is accepted as the "gold standard". (14-17) In the modern blood culture systems, positive signal can be received within few days after culturing in the bottles. It is necessary to wait a minimum of five days before the culture bottle can be detected to be negative. Microorganisms causing sepsis give a positive signal in automated blood culture systems in 90% of the cases within the first 48 hours. However, identifying microorganisms in blood culture that signals growth and making tests for their antibiotic susceptibility requires an additional few days. (16,17) Due to this crucial disadvantage in automatized blood culture systems, use of molecular diagnostic methods has become dominant on the agenda. The most practical and the most common of these is the PCR method. (18) There are studies indicating that mortality decreases and various molecular methods allow early antimicrobial treatment with rapid identification/antibiotic susceptibilities among microorganisms growing in blood cultures. (1,3,4,19-27)

One of the most common problems encountered in identification with molecular methods from blood cultures is PCR inhibition with inhibitors in the structure of the sample and blood culture bottles. (1,16,28-31)

In our study, the results of bacterial culture and genotyping tests were found to be compatible. However, it has been observed that streptococci and enterococci can be overlooked or misidentified in bacterial culture, especially in mixed infections. These factors can be important causes of mortality and morbidity. Correct identification of these overlooked bacteria and detection of resistance genes can allow early treatment and inhibit spreading in the hospital. Similar to our study, Gülhan et al. found in their study that the results found with the genotypic method were 83.6% compatible with phenotypic results. They also reported that mecA and vanA resistance genes can be detected with genotypic method and this method can be used practically in routine diagnosis for rapid diagnosis and treatment of sepsis caused by gram positive cocci. (1)

Moreover, while single agent was isolated in the samples, multiple agents were detected in 8 (11%) samples with rapid genotype test. Rapid genotype testing was found to be more susceptible in detecting mixed infections than bacteria culture methods with these results. Gülhan et al. found similar results in their study and stated that genotyping method is more susceptible in detecting mixed infections.

In our study, for staphylococci, which are considered causative agents since they are grown in both blood culture sets, methods of detecting methicillin resistance in culture and detecting presence of mecA with rapid genotype test methods were found compatible. However, incompatible results have been encountered in some samples. MecA gene detection is considered the gold standard in detecting methicillin resistance. (15-17) Rapid genotype testing is much faster than the culture method. Bacterial culture-antibiogram analysis is closely related to the personal experience

and attention of the laboratory worker. Therefore, it is thought that mecA detection can be used more frequently with rapid genotype testing to minimize errors. In similar studies, it is reported that the detection of the presence of the mecA gene with methicillin resistance and genotyping in culture in staphylococci has been found to be compatible and that mecA gene can be detected rapidly by the genotyping method. (1,3,27,31)

In our study, when glycopeptide resistance and van genes were examined in enterococci; the vanA gene was found positive in two species of *E. faecium* detected as susceptible to glycopeptides and culture antibiogram (Table 2). In two species of *E. faecium*, antibiotic susceptibility testing revealed glycopeptide resistance and vanA gene was detected positive (Table 1). In the rapid genotype test, glycopeptide resistance was not detected in two species in which the vanA gene was detected positive with VITEK2 and other conventional antibiogram methods. Considering that the presence of the vanA gene is the gold standard in the glycopeptide resistance, it was found that with genotyping method, resistance detection was easier and quicker than bacterial culture antibiogram methods and that major errors could be prevented. Since the glycopeptide resistance could be detected 4-5 hours after receiving a positive signal from the blood culture and making the gram staining, the empirical broad spectrum antibiotic treatment will be very short. In this case, unnecessary drug use and glycopeptide resistance can be prevented. This will decrease morbidity/mortality as well as patient care costs. In the conducted studies, compatibility was detected in enterococci with genotypic and phenotypic analyzes. It was reported that genotyping method can be used in the detection of van genes. (1,3,27,31)

In recent years, there has been an increase in staphylococcus bacteremia. With this increase, CNS and *S. aureus* species are isolated more than the blood cultures. Increasing rate of methicillin resistance in staphylococci causes major problems in treatment. (21) Therefore, resistance of antibiotics other than beta lactam group has been gaining importance. In our study, the resistance rates of staphylococci to antibiotics other than the beta lactam group were examined, and the resistance to ciprofloxacin was significantly higher in those with positive mecA gene than negative ones (Table 3).

CONCLUSION

Genotyping method can accurately and rapidly identify the infection agents in sepsis, which can be overlooked by the bacterial culture method. Early treatment is provided with rapid detection of the agent and resistance genes. Thus, the success of treatment increases and morbidity/mortality, the empirical treatment period, patient hospitalization time and the cost decreases. Since the treatment does not start until the suscepibility pattern is provided, meticillin and glycopeptide resistances will be prevented as unnecessary antibiotic treatment is not performed. In addition, patients with positive mecA appear to have a high resistance to ciprofloxacin. Therefore, use of this antibiotic in the empirical treatment for patients who are mecA positive is not advisable. In addition to these advantages of genotype tests, it should be used with bacterial culture methods.

Conflict of interest None to declare.

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RESEARCH ARTICLE

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Surveillance Analysis and Microbiological Profiles of Nosocomial Infections in A Palliative Care Center

ABSTRACT

Objective: Despite the wide availability of palliative care units in several countries, they have been founded in our country recently. This study aimed to contribute to the development of appropriate treatment protocols by determining the causes of hospitalizations, comorbidities, infection rates, and causative microorganisms in a palliative care center.

Methods: Blood cultures were taken from the patients suspected to have developed nosocomial infections. Samples for cultures were taken from the foci that were thought to be the origin of infection. Identification of isolates was performed using automated systems and conventional methods. The numbers of patients and patient days, and the numbers and rates of nosocomial infections were retrieved from the infection control unit data records and were analyzed. The rates and incidences of nosocomial infections in our hospital and the palliative care unit were calculated.

Results: Of the patients, 51% were men and 49% were women. The mean age was 72±12.6 years. Nosocomial infection rates were 6.3% in 2019, 9.1% in 2020, and 3.3% in the first six months of 2021. Urinary system infections ranked first with a rate of 58.6%. The most common cause of hospital admissions was malignancy with a rate of 25.9%. The most commonly isolated microorganism was *Klebsiella* spp with a rate of 27.5%.

Conclusions: Palliative care aims to improve symptoms and the quality of life of patients. Our study has contributed to developing practical solutions by documenting prognostic factors, infections, causative microorganisms, and issues experienced in palliative care patients.

Keywords: Palliative Care, Infection, Surveillance, Microbiological Profile.

Palyatif Bir Bakım Merkezinde Hastane Enfeksiyonlarının Sürveyans Analizi Ve Mikrobiyolojik Profilleri

ÖZET

Amaç: Global olarak yaşlı nüfustaki ve kronik hastalıklardaki artış, palyatif bakım ihtiyacını artırmaktadır. Dünyada Palyatif bakım birimleri yaygın olmakla birlikte ülkemizde birçok hastanede yeni açılmaktadır. Bunun için bu merkezlerde takip edilen hastaların, yatış sebepleri, komorbiditeler, enfeksiyon hızları ve etken mikroorganizmalar belirlenerek uygun tedavi protokollerinin oluşturulmasına katkı sağlanması amaçlandı.

Gereç ve Yöntem: Palyatif bakım ünitesinde yatan 457 hasta değerlendirildi. Hastane enfeksiyonu geliştiği düşünülen hastalardan kan kültürü ile birlikte enfeksiyon olduğu düşünülen odaklardan kültürler alındı. İzolatların tanımlanması otomatize sistemler ve conventional yöntemler kullanılarak yapıldı. Enfeksiyon kontrol birimi kayıtlarından hasta sayısı, hasta günü sayıları, hastane enfeksiyonu sayısı, hastane enfeksiyonu hızı verileri incelendi. Hastanemizdeki ve palyatif bakım ünitesindeki hastane enfeksiyon oranları ve insidansları hesaplandı.

Bulgular: Hastaların %51'i erkek, %49'u kadın, yaş ortalaması 72±12,6 olarak bulundu. Hastane enfeksiyonu hızı 2019 yılında % 6,3, 2020 yılında %9,1 ve 2021 yılının ilk altı ayında %3,3 olarak hesaplandı. Üriner sistem enfeksiyonları %58,6 ilk sırayı alırken, en sık görülen yatış tanısı %25,9 oanı ile malignite idi. En çok izole edilen mikroorganizma ise %27,5 oranı ile *Klebsiella* spp idi.

Sonuç: Palyatif bakım, güçlü koordinasyon ve işbirliği gerektiren multidisipliner uygulamaları içerir. Palyatif bakım, hastaların semptomlarını iyileştirmeyi ve hayat kalitelerini artırmayı amaçlamaktadır. Çalışmamız, palyatif bakım hastalarının problemlerini, prognostik faktörleri, enfeksiyonları ve etken mikroorganizmaları dokümente ederek, bu hastalar için pratik çözümler geliştirilmesine katkı sağlamıştır.

Anahtar Kelimeler: Palyatif Bakım, Enfeksiyon, Sürveyans, Mikrobiyolojik Profil.

INTRODUCTION

The World Health Organization describes palliative care as a comprehensive approach to improve the quality of life for patients and their families when they face a terminal disease. The primary goal of palliative care is to provide a multidisciplinary approach that focuses on providing the best possible quality of life through early diagnosis, assessment, and treatment for physical, mental, psychological, and social problems experienced by patients and their families. Palliative care aims to relieve distress in all stages of the disease. Palliative care can be provided simultaneously along with curative or life-prolonging treatments (1,2). The need for palliative care is increasing in parallel to the aging population in our country and in the world. Diseases treated in palliative care include cancers, central and peripheral neuronal diseases, muscle diseases, organ failures, and irreversible trauma damage (2,3). Palliative care patients are highly susceptible to infections. Infection increases the symptom burden and further reduces the quality of life. The diagnosis of infection is difficult in palliative care patients because of multiple comorbidities, the absence of clinical signs, or the presence of symptoms too vague to be recognized (3). Nosocomial infections (NIs), also called hospital-acquired infections, are not present at the time of admission but develop while the patient receives healthcare services. Invasive procedures and surgery or the placement of permanent medical or prosthetic devices are associated with NIs in the era of modern healthcare. NIs constitute a major health issue worldwide as they do in our country, increasing morbidity and mortality rates, treatment costs, and the length of hospital stay (4). Antibiotic-resistant microorganisms constitute a major problem in the fight against NIs. Options for antibiotherapy are limited to treat infections caused by antibiotic-resistant microorganisms. It is of great importance that relevant staff in a healthcare center should be aware of microorganisms, which are isolated as the causative agents of infections in that specific health center (4,5).

Our aim in this study is to contribute to the establishment of appropriate treatment protocols by determining the causes of hospitalizations, comorbidities, infection rates, causative microorganisms, and the distribution of hospital infections according to the body systems in patients treated in an adult palliative care center.

MATERIAL AND METHODS

A total of 457 patients; who were treated in Ankara Pursaklar Public Hospital's palliative care unit in the period between January 2019 and June 2021, were reviewed for the occurrence of NIs and the retrieved information was analyzed. The study was commenced after obtaining approval from Ankara Numune Training and Research Hospital's Ethics Committee (23.08.2021-E-41303261-799). Samples for blood culture tests and samples for relevant culture tests from suspected foci of infections were obtained from patients; who were suspected to have developed NIs. The identification of isolates was performed using Phoenix (Becton Dickinson, ABD) automated systems and conventional methods. Patients meeting the criteria for the diagnosis of NIs were enrolled. The diagnosis of NIs was made based on the diagnostic criteria published by the "Centers for Disease Control and Prevention" (CDC) (6). The numbers of patients, patient days, and the number and rate of NIs were retrieved from the infection control unit data records and analyzed. The rates and incidences of NIs in our hospital and palliative care unit were calculated. Incidences of NIs were calculated by the formula below:

NI incidence (%) = (Number of NI diagnosed in a specified period / Number of inpatients in the same specified period) x 100 (7). Data were analyzed using SPSS 18.0 version software (SPSS Inc, Chicago, USA). Categorical variables and frequency distributions were summarized as numbers and percentages. Nominal variables were summarized as mean±standard deviation.

RESULTS

In the years 2019 - 2021, a total of 7.795 patients were hospitalized. NI rates were 2.63% in 2019, 1.22% in 2020, and 0.67% in the first six months of 2021. The distribution of NIs by years is presented in Table 1.

Table 1. Distribution of Nosocomial Infections by Years

Year	Number of Patients	Number of Patient Days	Number of Infections	NI Rate (%)	Incidence Density of NI (‰)
2019	2.742	27.749	72	2.63	2.91
2020	3.119	33.248	38	1.22	1.14
2021 (first 6 months)	1.934	14.697	13	0.67	0.88

Of the 457 patients treated in the palliative care unit, 174 (51%) were men and 145 (49%) were women. The mean age was 72±12.6 years. The NI rates in the palliative care unit were calculated as 6.34% for the year 2019, 9.16% for 2020, and 3.31% for the first six months of 2021. The distribution of NIs in the palliative care center by years is presented in Table 2.

Table 2. Distribution of nosocomial infections in the palliative care center by years

Year	Number of Patients	Number of Patient Days	Number of Infections	NI Rate (%)	Incidence Density of NI (‰)
2019	205	5.344	13	6.34	2.43
2020	131	4.956	12	9.16	2.42
2021 (first 6 months)	121	1.928	4	3.31	2.07

The most common NIs in the three-year study period were urinary system infections (58.6%, n=17), circulatory system infections (37.9%, n=11), and skin and soft tissue infections (3.4%, n=1) in decreasing order of frequency. The most common three diagnoses and comorbidities were malignancies with a rate of 25.9% (n=66), respiratory system diseases with a rate of 18.8% (n=48), and cardiovascular system diseases with a rate of 12.9% (n=33). The causes of admission to palliative care are shown in Table 3.

Table 3. Causes of hospitalization in patients admitted to the palliative care unit.

Cause of hospitalization	n	%
Malignancy	66	25.9
Respiratory system disease	48	18.8
Cardiovascular system disease	33	12.9
Cerebrovascular disease	28	11.0
Neurodegenerative diseases (dementia and/or Parkinson's disease)	19	7.4
Nutritional disorders	17	6.6
Diabetes and associated complications	13	5.1
Miscellaneous	30	11.8
Total	254	100

Twenty-nine microorganism species were isolated from patients diagnosed with NIs in the palliative care center. The most commonly isolated microorganism was *Klebsiella* spp with a rate of 27.5%. *Acinetobacter* spp and *Escherichia coli* were the second and third most common species isolated with rates of 20.6% and 13.7%, respectively (Table-4).

Table 4. Distribution of microorganisms as causative agents of nosocomial infections in the palliative care

Microorganism	(n)	%
Klebsiella spp.	8	27.5
Acinetobacter spp	6	20.6
Escherichia coli	4	13.7
Pseudomonas spp.	4	13.7
Pseudomonas aeruginosa	3	10.3
Proteus spp.	2	6.8
Staphylococcus aureus	1	3.4
Streptococcus pneumoniae	1	3.4
Total	29	100

DISCUSSION

Palliative care is a multidisciplinary system that aims to improve the quality of life in progressive, incurable, and fatal diseases. Advances in modern medicine have offered many improvements in living conditions and increased the life expectancy of persons with chronic and fatal diseases (1,8). However; interventions for diagnosis and treatment, comorbidities, and treatment protocols for comorbid diseases weaken the immune system and increase the risk of NIs. Surveillance of causative infectious agents should be performed, necessary measures should be implemented, and infection control plans should be developed accordingly in order to control NIs (9). Although NI rates in our country vary from 1.0% to 8.6%, NIs usually occur in 5-10% of hospitalized patients (9,10,11). In our study, this rate was found in the range between 1.2% and 2.6%. In a study conducted on adult patients admitted to a palliative care center (12), this rate was 10.8%. Another study (9) reported rates varying from 6.6% to 4.7% in palliative care patients. In our study, NI rates in the palliative care unit were in the range between 6.34% and 9.16%, which were higher than the overall NI rates in the hospital similar to the reports in previous studies (Table-1, Table-2). We think that treatment interventions, comorbidities, and a compromised immune system increase the patients' risk of developing NIs.

The evaluation of demographic data showed that 51% of our palliative care patients were men and 49% were women, with a mean age of 72±12.6 years. In the study performed by Dinçer et al., 59% of the patients were men and 41% were women, with a mean age of 70.6±17.2 years (12). In the study performed by Yürüyen et al., 55% of the patients were men and 45% women, with a mean age of 71±15.8 years (13). Thus, our study was compatible with the literature in terms of demographic findings.

In our study, it was determined that the most common reason for hospitalization was malignancy. Respiratory system diseases were the second and cardiovascular system diseases were the third most common causes of hospital admissions (Table-3). In the study conducted by Komaç et al., patients received treatment for malignancy, followed up for the completion of long-term antibiotic therapy, and given treatment for diabetes and complications at rates of 33%, 17%, and 17% respectively (14). The study performed by Turgut et al. reported that patients were followed up for malignancy, cerebrovascular diseases, and cognitive disorders at rates of 28.5%, 25.5%, and 17.6%, respectively (15). In the study by Yürüyen et al., the three most common causes for treatment were malnutrition, malignancy, and infections at rates of 59%, 44%,

and 33%, respectively (13). A study performed by Dinçer et al. reported that 52.2% of the patients were followed up for nutritional support, 40.5% for pressure sores, 42.3% for neurological disease, and 23.4% of the patients were followed up for cancer (12). Another study reported the most common causes for hospital admissions as cerebrovascular disease, malignancy, and cardiovascular disease at rates of 22.15%, 20.8%, and 15%, respectively (8).

When we examined the distribution of nosocomial infections by body systems in palliative care patients, urinary system infections were found to take the first rank with a rate of 58.6%. Blood circulation infections and skin and soft tissue infections took the second and third ranks with rates of 37.9% and 3.4%, respectively. Chun et al. found the following such rates as 51.4%, 21.4%, and 25.7% for infections of the respiratory, gastrointestinal, and urinary systems, respectively (16). In another study, microbial growth in culture tests was reported to have occurred in the samples collected from the urinary tract, the respiratory tract, the blood, and the skin and subcutaneous tissues at rates of 42.5%, 22.9%, 12.5%, and 12.5%, respectively (17). Dağlı et al. detected urinary tract infections, respiratory tract infections, and blood circulation infections at rates of 45.1%, 42.5%, and 16.8%, respectively (18). Akdoğan et al. found out that growth occurred in urine, blood, and wound culture tests at rates of 67.9%, 32.1%, and 30.2%, respectively (19). In this study, the most commonly isolated microorganisms from patients diagnosed with NIs in the palliative care unit were *Klebsiella spp*. with a rate of 27.5%, *Acinetobacter spp*. with a rate of 20.6%, and *E.coli* with a rate of 13.7% (Table-4). Pereira J et al. isolated *E. coli*, *Staphylococcus aureus*, and *Enterococcus spp* at rates of 22.9%, 20.0%, and 11.4%, respectively (17). Another study reported the isolated microorganisms as *Klebsiella spp*, *Pseudomonas spp, and Staphylococcus spp* at rates of 28.3%, 27.4%, and 22.1%, respectively (18). Another study reported *E. coli* as the most commonly isolated microorganism (20).

In conclusion, patients followed in the adult palliative care center were mostly geriatric cancer patients. Urinary system infections ranked first among all NIs. NIs constitute a major problem in our hospital similar to the worldwide data. NIs are critically important quality indicators of healthcare. Rates of NIs vary across countries, regions, and hospitals. Hospital administrators should identify causative microorganisms and determine the distribution of infections in the respective hospital so that antibiotics are used appropriately and NIs can be kept under control. The Infection Control Committee in our hospital monitors and analyzes infection rates. Using the results, infection rates specific to our hospital are found and the clinical units at high risk are identified. Subsequently, infection control measures are revised and implemented accordingly. Surveillance studies are essential to keep NIs under control. Surveillance studies guide the identification of actual problems and the evaluation of the success of implemented policies. Besides the surveillance studies for NIs in palliative care, in this study, we have contributed to the development of practical solutions for the wellbeing of patients by documenting prognostic factors, infection types, causative microorganisms, and problems experienced in our patients.

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RESEARCH ARTICLE

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Histopathological Comparison of Biopsy and Resection Materials in Bone and Soft Tissue Tumors: The Experience of a Tertiary Oncology Referral Center "Istanbul Medeniyet University Prof.Dr. Süleyman Yalçın City Hospital"

ABSTRACT

Objective: To evaluate the consistency of pathology results in biopsy and resection materials of bone and soft tissue tumors referred to a tertiarry referral center.

Methods: 270 patients who were admitted to the Department of Orthopedics and Traumatology of Istanbul Prof. Dr. Suleyman Yalcin City Hospital between January 2015 and March 2021, were retrospectively reviewed. Collected data included demographic data, type of biopsy technique, the pathology report of biopsy and resection.

Results: Bone tumors had been detected in 125 patients (mean age: 38.3 years, 58 female, 67 male). Tumor localizations were most common in the lower extremity (53.6%) and upper extremity (28%), followed by clavicle, rib, hip, and vertebra. Core needle (n=109) or incisional biopsy (n=16) was performed. The rate of biopsy material that deemed adequate in core needle and incisional biopsies was 89.91% and 93.75%, respectively. Biopsy was done in 145 patients due to soft tissue tumors. (mean age: 38.8 years, 75 female, 70 male). Tumor localizations were most common in the lower extremity (64.1 %) and upper extremity (22%), followed by neck, hip, retroperitoneal, and scapula. For diagnosis, core needle (n=136), incisional biopsy (n=7) or fine needle aspiration (n=2) was performed. In 94.78% of soft tissue tumors with adequate first biopsy material, the biopsy and resected material pathology was found to be consistent.

Conclusions: A multidisciplinary approach plays an important role in increasing the diagnostic accuracy after biopsy in bone and soft tissue tumors. In patients with inconsistent clinical and radiological findings, repeat biopsy is mandatory in order to plan the correct treatment approach..

Keywords: Biopsy, Bone Tissue Neoplasms, Soft Tissue Neoplasms.

Kemik Ve Yumuşak Doku Tümörlerinde Biyopsi Ve Rezeksiyon Materyallerinin Histopatolojik Karşılaştırılması: Üçüncü Basamak Onkoloji Referans Merkezi Deneyimi "İstanbul Medeniyet Üniversitesi Prof.Dr. Süleyman Yalçın Şehir Hastanesi"

ÖZET

Amaç: Üçüncü basamak bir sevk merkezine sevk edilen kemik ve yumuşak doku tümörlerinin biyopsi ve rezeksiyon materyallerinde patoloji sonuçlarının tutarlılığını değerlendirmek.

Gereç ve Yöntem: Ocak 2015-Mart 2021 tarihleri arasında İstanbul Prof.Dr. Süleyman Yalçın Şehir Hastanesi Ortopedi ve Travmatoloji Anabilim Dalı'na başvuran 270 hasta retrospektif olarak incelendi. Toplanan veriler, demografik verileri, biyopsi tipini, biyopsi ve rezeksiyonun patoloji raporunu içeriyordu.

Bulgular: 125 hastada kemik tümörü saptandı (ortalama yaş: 38.3 yıl, 58 kadın, 67 erkek). Tümör lokalizasyonları en sık alt ekstremitede (%53,6) ve üst ekstremitede (%28), ardından klavikula, kaburga, kalça ve omurgadaydı. Hastalara core needle (n=109) veya insizyonel biyopsi (n=16) yapıldı. Çalışmamızda, core needle ve insizyonel biyopsilerde yeterli biyopsi materyali oranı sırasıyla %89.91 ve %93.75 idi. 145 hastamıza yumuşak doku tümörü nedeniyle biyopsi uygulandı (ortalama yaş: 38.8 yıl, 75 kadın, 70 erkek). Tümör lokalizasyonları en sık alt (%64.1) ve üst ekstremitede (%22) görülmekle birlikte daha az sıklıkta sırasıyla boyun, kalça, retroperitoneal ve skapula bölgelerinde yerleşim göstermekteydi. Tanı amacıyla tru-cut biyopsi (n=136), insizyonel biyopsi (n=7), veya ince iğne aspirasyonu (n=2) yapıldı. İlk biyopsi materyali yeterli olan yumuşak doku tümörlerinin %94,78'inde biyopsi ve rezeksiyon patolojisinin uyumlu olduğu saptandı.

Sonuç: Biyopsi sonrası tanısal doğruluğu arttırmak amacıyla çok disiplinli yaklaşım önemli rol oynamaktadır. Uyumsuz klinik ve radyolojik bulgular görülen hastalarda tedavi yaklaşımının doğru planlanabilmesi için biyopsinin tekrar edilmesi gereklidir.

Anahtar Kelimeler: Biyopsi, Tümörler, Kemik Doku, Yumuşak Doku Neoplazileri.

INTRODUCTION

Bone and soft tissue tumors are rare neoplasms and pose a diagnostic challenge due to the high differentiation capacity of mesenchymal tissue. Reactive and tumor-like lesions may morphologically overlap with benign or malignant tumors (1). In addition to specialized knowledge and experience, a multidisciplinary perspective is important (2).

As clinical, laboratory, radiological, and pathological data are evaluated with a multidisciplinary approach, it is possible to diagnose and plan the appropriate treatment in most of the bone and soft tissue lesions. As a result of the clinical and radiological evaluation, a biopsy should be performed to reach a definitive diagnosis in aggressive looking and behaving lesions. In majority of bone and soft tissue tumors, histopathological evaluation forms the basis of diagnosis and treatment.

Due to the heterogeneity of bone and soft tissue tumors, different areas of the tumor may show different tissue characteristics, and the histological grade of the cells may not reflect the whole lesion. Considering this situation, clinicians should take tissue from the area that can reflect the aggressive nature of the lesion as much as possible in cooperation with radiologic findings. An accurate biopsy result would avoid unplanned resections in malign bone and soft tissue tumors.

Based on these, this study aims to compare the adequacy rates of the preoperative biopsies of the patients and the compatibility of biopsy results with final resection materials..

MATERIAL AND METHODS

270 patients who were admitted to the Department of Orthopedics and Traumatology of Istanbul Prof. Dr. Suleyman Yalcin City Hospital between January 2015 and March 2021, were retrospectively reviewed. Collected data included type of biopsy technique, the pathology report of biopsy and resection. The age and sex of the patients, the localization of the tumor, the biopsy method, histopathological diagnosis of biopsy, and resection materials were retrieved from the pathology archives of our hospital.

Exclusion criteria included absence of preoperative biopsy report, local recurrence of primary sarcoma or metastatic lesion of a previously diagnosed malignancy, having a biopsy report outside our institution. They were evaluated in two groups as bone and soft tissue tumors. Our study cohort consisted of 270 patients, 125 of them were diagnosed with bone tumors, and the remaining 145 patients had soft tissue tumors.

Biopsy materials with findings compatible with the neoplastic process were evaluated as adequate, and those without benign or malignant neoplastic processes were evaluated as inadequate. Biopsy materials that were evaluated as adequate were divided into three subgroups as "benign," "malignant," and "benign or malignant differentiation could not be made." Those in the group benign or malign differentiation could not be made were further subdivided into three groups as "descriptive benign," "descriptive malignant," and "unspecified."

RESULTS

Bone Tumors: Bone tumors had been detected in 125 patients (mean age: 38.3 years, 58 female, 67 male). Tumor localizations were most common in the lower extremity (53.6%) and upper extremity (28%), followed by clavicle, rib, hip, and vertebra. Core needle (n=109) or incisional biopsy (n=16) was performed.

Biopsy results were first divided into "adequate" or "inadequate" biopsy material. In adequate biopsies, samples were further subdivided into three groups as described above (Table 1-2).

Table 1. The adequacy of bone biopsy material according to biopsy technique

Biopsy technique	Adequate (no of patients)	Inadequate (no of patients)	Total (no of patients)
Incisional	15	1	16
Core needle	98	11	109
Total	**113**	**12**	**125**

Table 2. Biopsy results of all bone biopsies

Biopsy result	Number of patients
Adequate	113
benign or malignant differentiation could not be made	5
Descriptive- benign	3
Descriptive-malign	2
Benign	38
Malign	70
Inadequate	12
Total (number of patients)	**125**

The rate of biopsy material that deemed adequate in core needle and incisional biopsies was 89.91% and 93.75%, respectively. In all malignant bone tumors with a single biopsy, biopsy and resection results were found to be consistent.

The second biopsy was indicated in ten patients that were clinically and radiologically thought to be malignant; however, the first biopsy was reported as benign or inadequate with non-diagnostic features. The results were compared with the pathology results of the initial biopsies and resection materials. Cases that had been underwent second biopsy with adequate material for diagnosis, the result of biopsies and resection materials were consistent (Table 3).

Table 3. Details regarding patients with second bone biopsy

Cases	First biopsy result	Second biopsy result	Diagnosis of resection material
Case 1	Benign	Benign	Benign
Case 2	Benign	Benign	Benign
Case 3	Benign	Benign	Benign
Case 4	Benign	Benign	Benign
Case 5	Benign	Malign	Malign
Case 6	Benign	Malign	Malign
Case 7	Inadequate	Descriptive benign	Benign
Case 8	Inadequate	Benign	Benign
Case 9	Inadequate	Descriptive benign	Benign
Case 10	Inadequate	Malign	Malign

In patients with malignant tumours who underwent a single biopsy, the diagnostic accuracy of the biopsy was found to be 100% compared to histopathological findings of the resected specimen. Two cases of cartilage tumors, which were reported to be benign in their initial biopsies, were found to be malignant in the curettage material. In these two cases, the final pathology was reported as atypical cartilaginous tumor/Grade I chondrosarcoma (Table 4). Final pathology of bone tumors was shown in Table 5.

Table 4. Comparison of first biopsy results with the final resection diagnosis

	Diagnosis of resection material		
First biopsy diagnosis	**Benign**	**Malign**	**Total**
Benign or malign differentiation could not be made	**3**	**2**	**5**
Descriptive-benign	3		3
Descriptive-malign		2	2
Benign	**30**	**2**	**32**
Malign		**70**	**70**
Unspecified + inadequate	**7**	**1**	**8**
Total	**40**	**75**	**115**

Table 5. Final pathology of bone tumors according to WHO 2020 Classification

Undifferantiated round cell sarcoma	10
Chondrogenic tumors	22
Osteogenic tumors	18
Fibrogenic tumors	3
Vascular tumors of bone	2
Osteoclastic giant cell rich tumors	14
Notochordal tumors	5
Other mesencymal tumors of bone	16
Hematopoetic neoplasms of bone	9
Metastatic carcinoma	26
Overall	125

Soft Tissue Tumors: Among 145 patients with soft tissue tumors, the mean age was 38.8 years. (75 female, 70 male). Tumor localizations were most common in the lower extremity (64.1 %) and upper extremity (22%), followed by neck, hip, retroperitoneum, and scapula. A core needle biopsy was performed in 136 cases. Incisional biopsy was performed in 7 cases. Fine needle aspiration was done in 2 patients.

Biopsy materials with findings compatible with the neoplastic process were evaluated as adequate, and those without benign or malignant neoplastic processes were evaluated as inadequate. Biopsy materials that were evaluated as adequate were divided into three groups as "benign," "malignant," and "benign or malignant differentiation could not be made". Those in the group that could not be differentiated as benign or malignant differentiation could not be made were further divided into three subgroups "descriptive benign, "descriptive malignant," and "unspecified." (Table 6).

Table 6. Biopsy results of soft tissue tumors according to WHO 2020 Classification

Biopsy result	Number of patients
Adequate	139
Benign or malign could not be made (descriptive benign/ descriptive malign/unspecified)	23
Benign	68
Malign	48
Inadequate	6
Total	145

The biopsy material was sufficient in 100% of the patients who underwent incisional biopsy . In tru-cut biopsy, this rate declines to 95.59% of all patients. The diagnostic accuracy rate of the first biopsy in soft tissue tumors was 94.78%. Diagnostic error in soft tissue tumors was 5.22%.

The second biopsy was performed in 6 cases that were clinically and radiologically considered to be malignant, however, that came of to be inadequate or not diagnostic in the first biopsy. These were compared with the pathology results of the initial biopsies and resection materials. Diagnostic accuracy was determined in 4 (66.8%) patients. The biopsy technique in these cases was tru-cut biopsy. In patients with a second biopsy, insufficient biopsy material was obtained in one patient (16.6%). The accuracy of the diagnosis could not be determined in one patient (16.6%).

Three cases, whose diagnosis was descriptively interpreted as benign in the first biopsy, were reported as malignant in the resection material. In these cases, no findings in favor of malignancy were observed in the first biopsy materials. The pathological diagnoses in the resection materials were reported as cribriform carcinoma, atypical lipomatous tumor, and myxoid liposarcoma. The malignant potential could not be determined in the tru-cut biopsy material of the patient diagnosed with cribriform carcinoma. It was interpreted in favor of benign lesions since it did not contain significant atypia and necrosis. Lipoblast was not observed in the tru-cut biopsy material of the patient who was diagnosed with atypical lipomatous tumor, and since no staining with MDM2 and CDK4 was detected immunohistochemically, it was evaluated in favor of lipoma. Myxoid lipomatous tumor was considered in the tru-cut biopsy material of the patient who was diagnosed with myxoid liposarcoma, but it was evaluated in favor of lipoblastoma due to age of 15 years.

Of the 6 cases whose diagnosis was classified as unspecified in the first biopsy, 4 cases were evaluated as benign, and resection diagnoses were reported as benign peripheral nerve sheath tumor, inflammatory myofibroblastic tumor, solitary fibrous tumor and nodular fasciitis. Two cases were reported as atypical lipomatous tumor/well-differentiated liposarcoma in the final resection specimen.

Initial biopsies of 3 cases regarded as benign were hibernoma, papillary endothelial hyperplasia, and benign endothelial vascular proliferation/hemangioendothelioma. However, resection diagnoses were myxoid liposarcoma, myxoid liposarcoma, and angiosarcoma, respectively. In the case, which was initially reported as benign in the biopsy material but evaluated as angiosarcoma in the resection material, the tumor had a heterogeneous structure with well-differentiated angiosarcoma, papillary endothelial hyperplasia, and kaposiform hemangioendothelioma-like areas in the resection material. The diagnosis of the resection material was evaluated in favor of angiosarcoma since metastases were detected in the early postoperative period. The initial biopsy material consisted of papillary endothelial hyperplasia-like areas, resulting in inconsistent findings between the first biopsy result and the histopathological examination of the resection material. In another case whose initial biopsy result was reported as dermatofibrosarcoma protuberans, the final result in the resection material was nodular fasciitis. Final pathology of soft tissue tumors was shown in Table 7.

Table 7. Final pathology of soft tissue tumors

Fibroblastic and myofibroblastic tumors	38
Vascular tumors	6
Adipocytic tumors	39
Smooth muscle tumors	3
Skeletal muscle tumors	4
Peripheral nerve sheath tumors	13
Tumors of uncertain differentiation	32
Undifferantiated small round cell sarcomas	2
Nontumoral lesions	7
Chondroosseous tumors	1
Overall	145

DISCUSSION

Biopsy is essential to determine the diagnosis, the need for neoadjuvant chemo or radiotherapy, and determine the surgical treatment strategy in aggressive lesions that cannot be definitively diagnosed with clinical and radiological evaluation. In our series with bone and soft tissue tumors, the diagnostic yield was comparable to literature (3). The concordance between the preoperative malignant bone biopsy results and final resection material was 100%.

Morphological features of Grade 1 chondrosacomas in cartilage tumors were usually similar to enchondromas. Entrapment, permeative spread, cellularity and pleomorphism, which are signs of malignancy, may not be seen or detected in biopsy materials. In our study, 2 cases were diagnosed as cartilage tumors in the biopsy material, and no signs of malignancy were found. However, the final pathology was reported as Grade 1 chondrosarcoma/atypical cartilaginous tumor. Laitinen et al. found that the rate of consistency between the biopsy and final pathology in cartilaginous tumors was 43%. This finding confirms our two cases which were initially mistaken for benign cartilaginous tumor (4).

Since biopsy materials in atypical lipomatous tumors may represent lipoma-like areas, it is critical to interpret biopsy materials carefully. If malignancy is suspected in the clinical preliminary diagnosis, it should be considered that tru-cut biopsy material may not be sufficient for definitive diagnosis. Thavikulwat et al, reported lower accuracy of diagnosis in atypical lipomatous tumors/ well-differentiated lyposarcomas (5). Sung et al. (6) found that there is a low accuracy of biopsy results in heterogeneous soft tissue tumors which included angiosarcoma, liposarcoma, synovial sarcomas, and hemangiomas. In our series,

we encountered such heterogeneous tumors. Our discordant cases was performed non image-guided biopsies in early experience in our clinic.

It is known that papillary endothelial hyperplasia and angiosarcoma may have similar histomorphological features. It is not uncommon when a final diagnosis results in angiosarcoma after a biopsy report with papillary endothelial hyperplasia (7).

Nodular fasciitis (NF) which may also be referred as an infiltrative or pseudosarcomatous fasciitis, is a benign, self-limited fibroblastic and myofibroblastic proliferative process (8). Nodular fasciitis is usually misdiagnosed as a soft tissue sarcoma as reported by Plaza et al. (9). The histolopathological findings are usually similar to those found in sarcoma but most often differentiated by plump, immature looking fibroblasts, in short irregular bundles and fascicles with positive staining with alpha smooth muscle actin (SMA) (10). Hence, tumor heterogeneity is again an important point. Due to the heterogeneity of bone and soft tissue tumors, different areas of the tumor may show different characteristics. In this context, the histological grade in the biopsy sample may not represent the whole tumor. Although, the immunohistochemical Ki 67 proliferation index is often helpful in distinguishing benign or malignant bone tumors it may rarely be useless due to low grade thus proliferating capacity of the tumoral tissue (11,12). A high Ki-67 proliferation index in soft tissue tumors is also diagnostically significant for malignancy (13).

With the tumor growth, nutritive blood vessels may become insufficient. This will lead to necrotic areas within the lesion. Sampling from necrotic areas may result in non-diagnostic sampling. The optimal site for biopsy is the periphery of the tumor tissue. It is necessary to avoid core needle from central areas with dense necrotic tissue (14).

One important issue to consider is that there is a shift towards taking biopsy samples from bone and surrounding soft tissue in recent years. Moreover, open biopsy is replaced by imaging-guided biopsy, which is performed even by orthopedic surgeons in the outpatient setting. Also, image-guided bone biopsy is commonly performed in the operating room. All these facilities provide higher accuracy in a biopsy procedure (15).

Although literature is not enough to determine the best biopsy technique, we tend to prefer core needle biopsy instead of open biopsy due to low risk of contamination and no need of anesthesia (16). Intraoperative frozen biopsy is used in our center, but we didn't include those cases due to small number of patients which warrants further investigation (17).

CONCLUSION

A multidisciplinary team approach by an orthopedic oncologist, radiologist and pathologist is essential in the evaluation of patients whose clinical and radiological findings do not overlap with histopathological findings. If necessary, a repeat biopsy should be performed, and the treatment planning should be carried out according to the biopsy result.

It should be kept in mind that the biopsy material of cartilage tumors may not always reflect malignancy criteria. However, this does not rule out malignancy, especially radiological imaging findings should be taken into consideration.

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RESEARCH ARTICLE

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Evaluation of Vitamin D Levels in Home Care Patients

ABSTRACT

Objective: Vitamin D deficiency has become an epidemic for all age groups in the world. This research aims to evaluate the vitamin D deficiency in home care patients and related lifestyle reasons.

Methods: This research included Home Care patients registered to İstanbul Şişli Hamidiye Etfal Training and Research Hospital between January 2015 – February 2016. After getting the patients' vitamin D records retrospectively, we have inquired patients if they had regular exposure to sunlight, whether they had a history of fracture or osteoporosis, and other related lifestyle habits. D vitamin deficiency were grouped as normal (>30ng/ml), insufficiency (20-30ng/ml), deficiency (lower than 20ng/ml), and severe deficiency (lower than <10ng/ml). The data was evaluated with SPSS 20.0 program, using frequencies, chi-square, and T-tests.

Results: A total of 232 patients were included in this study. There were 160 (69%) women and 72 (31%) men. Vitamin D insufficiency was found in 11.2% (n=26), and vitamin D deficiency in 70.3% (n=163). 70.1% (n=96) of 137 patients who answered the questions were female and 29.9% (n=41) were male. 86.1% of them (n=118) did not benefit from sunlight, 63.5% (n=87) had not received vitamin D treatment before. Vitamin D deficiency was detected in 79.3% (n=69) of those who did not receive vitamin D treatment, and a significant relationship was found between them.

Conclusions: Our study found that most home care patients had low Vitamin D levels, did not have regular exposure to sunlight, and did not exercise regularly. Vitamin D replacement is vital in home-care patients as vitamin D deficiency increases the risk of osteoporosis, falls, and fractures.

Keywords: Vitamin D, Home Care, Home Health Care, 25(OH)D, Elderly.

Evde Bakım Hastalarında D Vitamini Düzeylerinin Değerlendirilmesi

ÖZET

Amaç: D vitamini eksikliği tüm dünyada bütün yaş grupları için bir salgın haline gelmiştir. Bu araştırmanın amacı evde bakım hastalarında D vitamini eksikliğini ve buna bağlı yaşam tarzı nedenlerini değerlendirmektir.

Gereç ve Yöntem: Bu araştırma, Ocak 2015 - Şubat 2016 tarihleri arasında İstanbul Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesine kayıtlı Evde Bakım hastalarında yapılmıştır. Hastaların D vitamini kayıtları retrospektif olarak toplandıktan sonra, hastalara düzenli güneş ışığına maruz kalıp kalmadıkları, kırık veya osteoporoz öyküsü olup olmadığı ve diğer ilgili yaşam tarzı özellikleri sorgulandı. D vitamini eksikliği şu şekilde gruplandırıldı; normal (> 30ng / ml), yetersizlik (20-30ng / ml), eksiklik (20ng / ml'den az) ve ciddi eksiklik (<10ng / ml'den az). Veriler SPSS 20.0 versiyonunda frekans, ki-kare ve T testi kullanılarak değerlendirildi.

Bulgular: Çalışmaya evde bakım hizmeti verilen 232 hasta dahil edildi. Hastaların %69'u (n=160) kadın; %31'i (n=72) erkekti. % 11.2'sinde (n=26) D vitamini yetersizliği; %70.3'ünde (n=163) D vitamini eksikliği saptandı. Soruları yanıtlayan 137 hastanın %70.1'i (n=96) kadın, %29.9'u (n=41) erkekti. Bunların %86.1'i (n=118) güneş ışığından faydalanmıyordu, %63.5'i (n=87) daha önce D vitamin tedavisi almamıştı. D vitamini tedavisi almayanların% 79,3'ünde (n = 69) D vitamini eksikliği tespit edildi ve aralarında anlamlı bir ilişki bulundu.

Sonuç: Çalışmamızda, evde bakım hastalarının çoğunun düşük D vitamini seviyelerine sahip olduğunu, düzenli olarak güneş ışığından faydalanmadıklarını, düzenli egzersiz yapmadıklarını bulduk. D vitamini eksikliği, osteoporoz, düşme ve kırık riskini arttırdığı için, evde bakım hastalarında D vitamininin replasmanı önemlidir.

Anahtar Kelimeler: D Vitamini, Evde Bakım, Evde Bakım Hizmetleri, 25(OH)D, Yaşlı.

INTRODUCTION

Home health service provides physical and laboratory examinations, treatment, medical care, and rehabilitation services at home and in the family environment of individuals who need care due to various diseases (1). The prolongation of the average life expectancy along with the increase in the elderly population and consequently the chronic diseases have necessitated the need for qualified long-term care services (2). With home care service, it is aimed to provide care and health services for the patients who are elderly, disabled, with chronic diseases, and who need long-term care so that they can continue their lives within the home environment. In addition, social and psychological support services are provided to these people and their family members as a whole (1). With the increasing need for home care, the Ministry of Health started to provide home health services within the scope of the social state policy with the directive published in 2010.

Patients receiving home care services are individuals with a high risk of vitamin D deficiency due to reasons such as immobilization, disability, and being bedridden. Vitamin D can be classified as a steroid hormone produced in human skin from 7-dehydrocholesterol due to exposure to ultraviolet B rays (UVB; 280–315 nm range) from sunlight (3). To assess a patient's vitamin D status, 25(OH)D is measured, which is the vitamin D metabolite (4). Until the 21st century, vitamin D was primarily recognized for its role in regulating calcium and bone health and preventing rickets (5). However, in the last 20 years, research has shown that vitamin D also profoundly influences immune cells and generally lowers inflammation (6,7). Vitamin D is a powerful epigenetic regulator, influencing more than 2500 genes (8) and impacting dozens of our most serious health challenges, including cancer (9,10), diabetes mellitus (11), acute respiratory tract infections (12), and autoimmune diseases such as multiple sclerosis (13).

Elderly residents in residential care homes/nursing homes, particularly those with limited mobility, are likely to spend more time indoors and have limited sun exposure. For nearly 30 years, they have been recognized in the UK as a group vulnerable to vitamin D deficiency and requiring routine supplementation without pre-screening (14,15,16). In 2016, recommendations for daily vitamin D supplements were extended to the entire population in the winter months and throughout the year for those living in care homes (17). National bodies from countries around the world have issued similar recommendations for care home residents, including Australia, Canada, France, Norway, New Zealand, and the USA (18 19). Although the elderly and insufficient exposure to the sun are considered high-risk groups for vitamin D deficiency (20), in our country, routine vitamin D supplementation without pre-screening is not recommended for home care patients yet.

Due to the high rates of vitamin D deficiency in home care patients, the importance of the subject was emphasized because of its complications and lack of studies in the literature. This study was performed to obtain information about the vitamin D levels, determine the related lifestyle reasons, and emphasize the importance of vitamin D replacement of the patients within the scope of home health services.

MATERIAL AND METHODS

Study Design: This study had a retrospective descriptive design.

Study Population and Design: This research was performed by evaluating the examination records of the patients registered in the Home Health Services Unit of Istanbul Şişli Hamidiye Etfal Training and Research Hospital for the past 14 months, between January 2015 and February 2016. No questionnaire was applied in the study. Instead, the patients were asked about benefiting from sunlight, using vitamin D supplements, history of active and passive exercises, history of fractures, whether they had a bone scan, and whether they were diagnosed with osteoporosis, by phone or during home visits. In addition, the patients' files were reviewed to record age, gender, medications used, comorbidities, and related to vitamin d deficiency complications. The research population consisted of home care patients registered in Şişli Hamidiye Etfal Training and Research Hospital Home Care services.

Home care patients whose previous examination results could be obtained, volunteer patients of both genders, who were contacted by telephone or visited at home, did not have any psychiatric disease, and did not have communication barriers, were included in the study. Those with communication barriers, those who did not agree to answer the questions, those diagnosed with any degree of active and/or chronic psychiatric disease, and those who had a history of psychiatric drug use at the time of admission were excluded from the study.

In order to determine the rates of vitamin D deficiency, the examination results of 232 patients registered in the home care unit were obtained. The causes of vitamin D deficiency were evaluated in 137 patients who could be contacted among the patients whose examination results were obtained.

Vitamin D deficiency and normal values were grouped based on the Osteoporosis and Metabolic Bone Diseases Diagnosis and Treatment Guidelines of the Turkish Society of Endocrinology and Metabolism (TEMD). Vitamin D deficiency were grouped as normal (>30ng/ml), insufficiency (20-30ng/ml), deficiency(lower than 20ng/ml) and severe deficiency (lower than <10ng/ml).

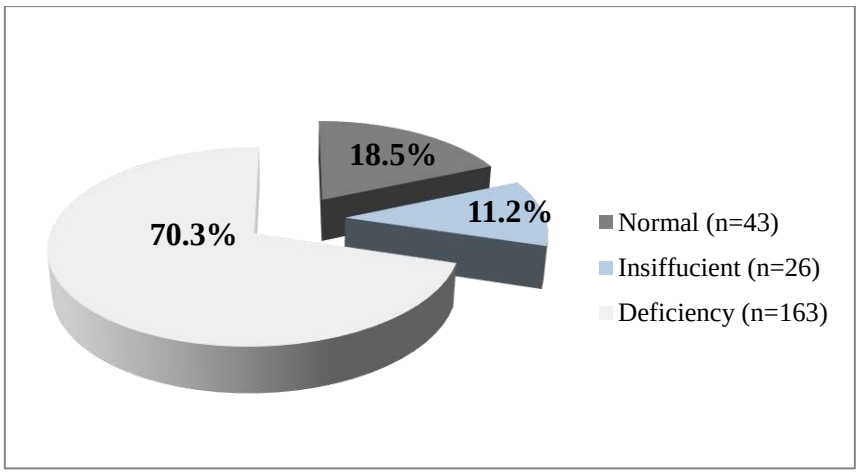
Research Approval: Sisli Hamidiye Etfal Training and Research Hospital Home Care Services Manager. 02.03.2016.

Statistical Analysis: The data were analyzed using a statistical package program (Statistical Package for the Social Sciences-SPSS for Windows, Version 20). The normality analysis of numerical values was performed using the Shapiro-Wilk test. The frequencies of the data were expressed as percentages (%) and n values. The Mann-Whitney U test compared numerical data that did not show normal distribution between two independent groups.

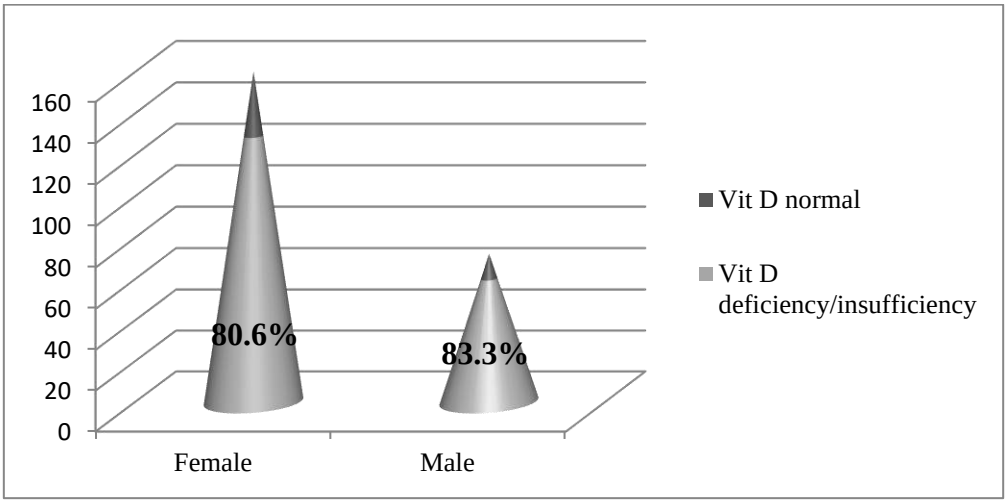
The chi-square test investigated the statistical difference between two variables with the nominal dichotomous distribution. The results were evaluated at the 95% confidence interval and a p-value of <0.05 was considered statistically significant.

RESULTS

Two hundred thirty-two patients who received home care services were included in the study. 69% of the patients (n=160) were female, and 31% (n=72) male. Vitamin D level was found to be normal in 18.5% (n=43) of home care patients. Vitamin D insufficiency was found in 11.2% (n=26), and vitamin D deficiency in 70.3% (n=163) (Graphic 1). When the vitamin D levels of patients were evaluated according to their genders, as shown in Graphic 2, 80.6% (n=129) of females and 83.3% of males (n=60) who received home care services had vitamin D deficiency or insufficiency. No significant relationship was found between gender and vitamin D deficiency (p=0.623).



Graphic 1. Vitamin D levels of patients



Graphic 2. Vitamin D levels by gender

137 of the 232 patients included in the study answered the questions. An additional evaluation was made between the vitamin D levels of 137 patients who answered the questions and criteria such as benefiting from sunlight, exercising, using vitamin D supplements, getting a diagnosis of osteoporosis. In this evaluation, no significant relationship was found between the vitamin D levels of the patients who answered the questions by gender; in both samples, it was found that p-values were close to each other (p=0.689 n=137/ p=0.623 n=232). 70.1% (n=96) of the patients who answered the questions were female, and 29.9% (n=41) were male. 86.1% of them (n=118) did not benefit from sunlight, 63.5% (n=87) had not received vitamin D treatment before.

Vitamin D deficiency was detected in 79.3% (n=69) of those who did not receive vitamin D treatment, and a significant relationship was found between them (p=0.005) (Table 1). Also 89.6% (n=86) of those with vitamin D deficiency did not benefit from sunlight (p=0.194) (Table 2).

Table 1. Vitamin D levels by vitamin D use status of patients

Vitamin D Level	Normal	Insufficiency	Deficiency	P
Those who use Vitamin D	61.5% (n=16)	46.7% (n=7)	28.1% (n=27)	0.005
Those who do not use Vitamin D	38.5% (n=10)	53.3% (n=8)	79.3% (n=69)	

Table 2. Status of benefiting sunlight by vitamin D levels of patients

Status of Benefiting Sunlight	Yes	No	P
Vitamin D Normal	23.1% (n=6)	76.9% (n=20)	0.194
Vitamin D Insufficiency	20% (n=3)	80% (n=12)	
Vitamin D Deficiency	10.4% (n=10)	89.6% (n=86)	

59.9% (n=82) of the patients did not exercise regularly, 13.1% (n=18) had active exercises, and 16.8% (n=23) had passive exercises.16.7% (n=3) of active exercisers, 13% (n=3) of passive exercisers, 33.8% (n=8) of both active and passive exercisers benefited from sunlight, and a significant relationship was found between them (p=0.014) (Table 3).

Table 3. Benefiting from sunlight rates by active/passive exercise status

Status of Benefiting Sunlight	Yes	No	P
Those who Exercise Actively	16.7% (n=3)	83.3% (n=15)	0.014
Those who Exercise Passively	13% (n=3)	87% (n=20)	
Those who Exercise Actively and Passively	6.9% (n=5)	93.1% (n=67)	
Those who do not Exercise	33.3% (n=8)	66.7% (n=16)	

The rate of those diagnosed with osteoporosis was 22.6% (n=31), and 69.3% (n = 95) did not know whether they had osteoporosis or not, as well as 21.9% (n=30) of the patients had a fracture history, while 75.2% (n=103) did not have a bone scan before (Table 4). 64.7% (n = 22) of those who had a bone scan did not have a history of fractures, and 17.5% (n=18) of those who did not have a bone scan had a history of fractures. A significant relationship was found between bone scan rates and fracture history (p=0.029).

Table 4. Fracture history, undergoing bone scanning and osteoporosis diagnosis rates of patients

	Yes	No	Unknown
Fracture History	21.9% (n=30)	% (n=107)	
Undergoing Bone Scanning Status	75.2% (n=103)	% (n=34)	
Osteoporosis Diagnosis	22.6% (n=31)	% (n=11)	69.3% (n=95)

18.8% (n=18) of those with vitamin D deficiency and 24.4% (n=20) of those who did not exercise regularly had a history of fracture (p=0.377 and 0.389, respectively). 20.7% (n=17) of those who did not exercise regularly were diagnosed with osteoporosis (p=0.087).

When the rates of undergoing a bone scan by gender were evaluated, 29.2% of females (n=28) and 14.6% of males (n=6) underwent a bone scan. No significant relationship was found between gender and undergoing a bone scan (p=0.071). Moreover, 85.3% (n =29) of those who had a bone scan were diagnosed with osteoporosis, and the relationship between them was considered significant (p=0.000). When the relationship between gender and the diagnosis of osteoporosis was evaluated, 26.0% of females (n=25) and 14.6% of males (n=6) were diagnosed with osteoporosis, and no significant relationship was found between gender and osteoporosis (p=0.181)

DISCUSSION

Vitamin D deficiency, which is considered a pandemic today, is observed at high rates in home-care patients as it is also common in society. In our study, approximately 4 out of 5 home care patients were found to have vitamin D deficiency or insufficiency. It was determined that the majority of home care patients with vitamin D deficiency did not benefit from sunlight and did not take vitamin D supplements before. The sunbathing opportunities of the elderly have decreased even more, especially in those who are home-dependent, which indicates the importance of oral vitamin D supplementation (21).

It is estimated that 200 million people in the world have osteoporosis, one of the complications of vitamin D deficiency. Moreover, every 1 in 3 women and 1 in 5 men are at risk for osteoporotic fractures (22). In this study, when the relationship between vitamin D deficiency was evaluated by gender of the patients, it was concluded that gender did not affect the vitamin D level. Similarly, no significant relationship was found between osteoporosis diagnosis and fracture history to gender. Supporting our study, Küçükardalı et al. and Erkin et al. stated that the bone fracture rate in geriatric patients in our country is between 7.3-14.3%, regardless of gender (23,24).

Our study revealed that there was a significant relationship between exercising and benefiting from sunlight. Supporting our study, Bischoff-Ferrari et al. found a positive relationship between 25(OH)D vitamin and lower extremity functions, proximal muscle strength, and physical activity (25,26). In line with our study results, we think that supporting home care patients in terms of active and passive exercise and increasing their benefit of sunlight will both increase the muscle strength of the patients and meet their vitamin D needs. In this way, complications that may develop will be prevented, and the quality of life of home care patients will be positively supported.

When the fracture rates, which is another complication of vitamin D deficiency, and bone scanning of the patients were evaluated, a significant relationship was found between them. In the study of Khaw et al. and Martinez et al., with vitamin D supplementation, they found a positive correlation between serum calcidiol levels and lumbar spine BMD in postmenopausal women and BMD of the femoral neck, thoracic, and Ward triangle in women over 60 years old (27,28). As per the Turkish Association of Endocrinology and Metabolism (TEMD), BMD is closely related to bone strength. Prospective studies have shown that the risk of fracture increases with the decrease in BMD. Therefore, BMD has been accepted as an excellent indicator of possible future fracture risk (20).

On the other hand, in the study of Bartl et al., it was emphasized that bone mineral density measurement is a valuable method to detect the presence of osteoporosis before a fracture occurs (29). Today, evaluation of BMD is considered the golden standard in diagnosing osteoporosis (22), and it is recommended that women aged 65 and over and men aged 70 and over should have a BMD measurement at least once in their lives (30). In our study, 85.3% of those who had a bone scan were diagnosed with osteoporosis, and their relationship was considered significant.

It was determined that approximately 2 out of 5 patients diagnosed with osteoporosis also had a fracture history. Also, Akpolat et al. emphasized that the most critical complication associated with osteoporosis is a fracture (31). Wacker et al. found that the risk of fracture was lower in patients with 25(OH)D vitamin levels of >30 ng/mL (32). Vitamin D deficiency is an identified risk factor for osteoporosis, falls, and fractures (33). In addition, muscle strength, postural and dynamic balance can be increased with vitamin D supplementation (25,26).

CONCLUSION

With the prolongation of human life, the number of patients receiving home care services has gradually increased. The lack of sunbathing opportunities in home-care patients brought vitamin D deficiency along with it, and vitamin D deficiency rates of home care patients were found to be high in our study.

Benefiting sunlight directly affects the synthesis of vitamin D. Active or passive exercise positively affects vitamin D metabolism. Measurement of bone mineral density enables osteoporosis diagnosis and determination of vitamin D deficiency, which is another etiological cause.

Vitamin D replacement is vital in home-care patients as vitamin D deficiency increases the risk of osteoporosis, falls, and fractures.

With the detection and treatment of vitamin D deficiency, the quality of life of home care patients should be increased, and mortality and morbidity rates should be reduced. Also, considering the examples in the world, studies should be increased to ensure that home care patients receive vitamin D replacement without routine screening.

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RESEARCH ARTICLE

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A Comparison of the Effectiveness of Hypnotherapy and Cognitive Behavioral Therapy in the Treatment of Primary Vaginismus

ABSTRACT

Objective: This study compared the therapeutic effectiveness of hypnotherapy and cognitive behavioral therapy in patients with primary vaginismus previously assessed by a psychiatrist and a gynecologist.

Methods: We performed as a single-center, cross-sectional study in 35 patients with primary vaginismus.

Results: Successful coitus was achieved by 19 (95%) individuals in the hypnotherapy group and by 14 (93.3%) members of the cognitive behavioral therapy group. These success rates were similar (p=0.681). The mean number of sessions until successful coitus was significantly lower in the hypnotherapy group (p=0.000).

Conclusions: Hypnotherapy and cognitive behavioral therapy can be applied with similar high success rates in the treatment of vaginismus. However, success may be achieved with fewer sessions with hypnotherapy.

Keywords: Vaginismus, Hypnotherapy, Cognitive Behavioral Therapy.

Vajinismus Tedavisinde Hipnoterapi ve Bilişsel Davranışçı Terapi Etkinliğinin Karşılaştırılması

ÖZET

Amaç: Bu çalışmanın amacı vajinismus tedavisinde hipnoterapi ve Bilişsel Davranışçı Terapi (BDT) etkinliklerinin karşılaştırılmasıdır.

Gereç ve Yöntem: Primer vajinismuslu 35 hastada tek merkezli, kesitsel bir çalışma olarak gerçekleştirdik.

Bulgular: Hipnoterapi grubundaki 19 (% 95) birey ve bilişsel davranışçı terapi grubundaki 14 (% 93,3) kişi tarafından başarılı bir ilişki sağlandı. Bu başarı oranları benzerdi (p = 0,681). Hipnoterapi grubunda başarılı birleşmeye kadar ortalama seans sayısı anlamlı olarak daha düşüktü (p = 0.000).

Sonuç: Hipnoterapi ve bilişsel davranışçı terapi vajinismus tedavisinde benzer yüksek başarı oranları ile uygulanabilir. Ancak hipnoterapi ile daha az seans ile başarı elde edilebilir.

Anahtar Kelimeler: Vajinismus, Hipnoterapi, Bilişsel Davranışçı Terapi.

INTRODUCTION

Vaginismus is a common, well-described, and important sexual function disorder widely reported in the sexology literature (1,2).

Vaginismus is defined as the penis, finger, or any other object being unable to enter the vagina, even though the woman actively wishes such penetration to occur. Varying levels of involuntary pelvic muscle contraction, (phobic) avoidance and anticipation or fear of pain may be observed (1,2). The condition may be primary or secondary in form. Primary or lifelong vaginismus is defined as permanent inability to experience penetrative intercourse due to involuntary pelvic muscle contractions. In contrast, secondary or acquired vaginismus refers to the loss of a previously existing ability to have intercourse following a non-symptomatic period. This form can also occur as a complication of female dyspareunia.

The most common form in the literature is primary vaginismus (3). This may cause significant anxiety, and is also an important source of intrafamilial problems. Concealment of the problem due to concerns over privacy leads to further worsening of outcomes. Various methods are applied in the treatment of vaginismus, and varying success rates have been reported (4,5). While several studies have investigated cognitive behavioral therapy (CBT) in the treatment of vaginismus (6-12), the number of studies involving hypnotherapy is very low, and with one exception these have all been in the form of case reports (13,14). Our research revealed only one study comparing hypnotherapy and CBT in the treatment of vaginismus (15). The present study compares our results in cases of vaginismus undergoing hypnotherapy and CBT.

MATERIAL AND METHODS

Study Design and Setting: Diagnosis of vaginismus was based on DSM-V diagnostic criteria (5). All our patients were primary vaginismus cases.

Interviews and hypnotherapy were formed by the same hypnotherapist (KT) in all sessions. Patients were first told about the therapeutic methods being considered for application. Participants determined the method to be applied, and informed consent forms were obtained accordingly. Coitus within the recommended process was adopted as a criterion of success. Treatment was concluded following two successful acts of coitus. Successful acts of coitus was accepted as the penis being able to enter the vagina without pain and discomfort.

In the hypnotherapy group (20 women) the patient and her partner were requested to attend the first session together. Both were given simultaneous information about hypnosis during the initial evaluation process. Any questions concerning hypnosis were answered. Information concerning male and female sexual anatomy and physiology was given to both partners in the first session. Sexual fears and inaccurate mental images were identified by means of a detailed sexual history.

The principal incorrect ideas identified were 1 – The penis will cause injury after entering the vagina, or injury involving severe pain, excessive bleeding, and irreparable damage to the hymen. 2 – The vagina being very small or very narrow. 3 – the penis being very large. 4 – Negative attitudes toward sexual relations: the idea that sexuality is something shameful or dirty. 5 – Negative attitudes toward male sexuality; the penis, testes and/or sperm being regarded as repulsive.

Negative thought patterns used by the subject were particularly investigated while sexual history was being taken, and mental visualizations and positive suggestion patterns were employed in correcting these during the therapeutic process. Particular care was taken during the initial evaluation process to use language patterns that would encourage the subject. Suggestions were made during almost all sessions concerning pleasurable images of sexual scenes and events in order to increase sexual stimulation. All hypnotherapy sessions were administered in the form of 60-min appointments. All hypnotherapy sessions were held at weekly intervals, and the subject was given positive ideation homework. Subjects were taught autohypnosis in order to perform this homework more comfortably. Subjects experiencing difficulty with autohypnosis were asked to perform sexual visualization. Attempted coitus in sexual relations was prohibited until the patient was able to imagine comfortable penile penetration of the vagina. However, individuals able to imagine such relations without anxiety and with pleasure were encouraged to attempt coitus. During this process, the male partner was asked to assist his partner and not to pressurize her into coitus without her being ready for relations.

Inclusion and Exclusion Criteria: Patients presenting to a physician for the first time are not included in treatment sessions in our clinic. For that reason, patients who had been treated by at least one psychiatrist, but in whom success had not been achieved, were enrolled. In order to rule out anatomical problems, all patients were examined by a gynecologist before treatment.

Intervention: The ‘visual fixation, verbal suggestion method was employed during hypnosis. This was followed by relaxation hypnosis. The subject was instructed to perform positive imagining. The reframing technique was applied in cases of history of sexual abuse or rape, or of first night fear. Posthypnotic suggestion was given before subjects were released from hypnosis to enable them to attend the next session in a greater state of relaxation and to enter deeper hypnosis within a shorter period of time.

Standard methods were applied in subsequent hypnosis sessions. Following relaxation hypnosis, subjects enrolled for hypnosis received suggestion concerning establishing sexual fantasies with their partners and being able to experience this comfortably in an environment of their choosing. In addition, all subjects were taught autohypnosis and given homework concerning the creation of these fantasies in their own homes. Subjects were advised not to attempt coitus with their partners so long as they were unable to perform these measures without anxiety and stress, and until they experienced pleasure from them.

Similarly to the hypnotherapy group, the cognitive behavioral group (15 women) were asked to attend the first session together with their partners. Both partners were given information, together, about the therapeutic process. During the first session, in order to determine the module at which treatment should commence, the patient was asked questions about her vaginismus (Module 1: Nothing can enter the vagina. Module 2: Nothing belonging to another person can enter the vagina. Module 3: The penis cannot enter the vagina). Each of these modules lasts approximately four sessions. If the individual is to start from the first module, the process is concluded after 11 sessions. Each session was applied for 60 min, on a once-weekly basis.

Once the patient's status had been determined, treatment was administered based on the relevant CBT module. Kegel exercises, breathing exercises, finger exercises, systematic desensitization, the parking technique, and limited penile penetration were generally employed in these modules. The patient was asked to employ the finger technique, first using her own fingers, and afterward to perform the exercises with her partners' fingers. Partners were advised not to attempt coitus during this process. However, they were informed that they could attempt coitus once they were able to perform these exercises comfortably, without anxiety and stress.

Statistical Tests: The research was performed as a single-center, cross-sectional study. Statistical analysis was performed on SPSS 20 software. Since the data were not normally distributed, numerical data were expressed as mean plus standard deviation (Mean±SD), and categorical data were expressed as number and percentage values. The t test (Mann-Whitney U test) was used to compare numerical data, and the chi-square test in the comparison of categorical data. p values ≤0.05 were regarded as statistically significant.

Ethical Approval: The records for vaginismus patients presenting to the Medical Faculty Traditional and Complementary Medicine Hypnosis Polyclinic between July 2013 and August 2018 were retrieved retrospectively, and patient characteristics and treatment outcomes were subjected to statistical analysis and comparison. Ethical approval for the study was granted by the faculty ethical committee (Date:30.05.2019, Number: B.30.2.ATA.0.01.00).

RESULTS

The study commenced with 42 patients with primary vaginismus, 24 in the hypnosis group and 18 in the CBT group. Four members of the hypnosis group discontinued treatment (two after the first session, one after the second session, and one after the fourth session), and three members of the CBT group also discontinued treatment (one after the first session, one after the second session, and one after the third). Data were evaluated for the remaining 35 patients (20 receiving hypnosis, 15 receiving CBT).

Patients' sociodemographic data and results are shown in Table 1.

Table 1. Patients' sociodemographic characteristics and results

	Hypnosis		**CBT**		**p**
Parameter	**n**	**%**	**N**	**%**	
Education					
Primary	0	-	1	6	
High school	7	35	8	53	0.165
University	13	65	6	40	
Occupation					
Housewife	9	45	7	46.6	
Civil servant	8	40	4	26.6	0.928
Self-employed	3	15	4	26.6	
Sexual history					
Presence of abuse	6	35.2	5	33.3	0.517
Presence of rape	1	5.8	0	-	0.571
Negative emotion burden concerning the first night	10	58.8	10	58.5	0.627
	Mean±SD		**Mean±SD**		
Age	30±5.9		31±6.8		0.299
Length of marriage	4±3.2		2.3±2.1		0.109
Number of sessions	4.2±1.9		10.7±1.6		<0.001
	n (%)		n (%)		
Discontinuation of treatment n (%)	4 (16.7)		3 (16.7)		0.665
Success rate n (%)	19 (95)		14 (93.3)		0.681

The groups were similar in terms of education level, occupation distributions, prevalence of factors related to sexual history, and length of marriage.

Treatment discontinuation rates were similar between the groups. At the end of the sessions, successful coitus was achieved by 19 (95%) individuals in the hypnotherapy group and by 14 (93.3%) members of the CBT group (Table 1). These success rates were similar (p=0.681). The mean number of sessions until successful coitus was significantly lower in the hypnotherapy group (p<0.001).

DISCUSSION

Research into women diagnosed with vaginismus have shown that have a fear of pain and extreme discomfort, excessive bleeding, tearing or rupture, fear of the penis remaining trapped inside them, fear of fainting or dying, and feelings of repulsion or disgust. [16-21] Since sexual behavior and beliefs are highly susceptible to societal factors, cultural influences may be clearly visible in sexual function disorders (22). Male-centered Eastern cultures in particular teach girls that sexuality is something to be performed only for reproduction, as an act very important to the spouse's pleasure and satisfaction, but not as a source of pleasure (23). Lack of sex education, women being unacquainted with their own sexual organs, exaggerated importance attached to virginity, sexual experience beginning with direct coitus rather than developing in stages, and taboos concerning the general conception of sexuality are all regarded as reasons why vaginismus is more prevalent in Eastern cultures (20,22).

Bridal virginity is of particular importance in traditional Turkish families, and the bride is obliged to prove her virginity to her husband and his family on the first night. Such a tradition exacerbates anxiety in sexual relations, particularly for couples with insufficient knowledge and no experience of sexuality. Traditionally, an older female member of the family describes her own first night experience to the bride to be (24). Clinical observations suggest that this transmitted information is both unrealistic and catastrophic, suggesting that sexual relations cause unbearable pain to the woman and discomfort lasting several days. It is thought that such misinformation can lead to sexual function disorders or exacerbate sexual problems (13,14).

The reported prevalence of vaginismus in sexual function disorder clinics is 5-17% (26,27). The global prevalence varies, but vaginismus represents 43-73% of all sexual function disorders presenting for treatment in Turkey, and is the most common such disorder (28-30).

Incidences of divorce, depressive emotions, and low self-esteem are also high in patients with vaginismus (15). It is therefore of great importance for treatment to be initiated immediately in these patients.

If somatic causes are eliminated, and if sufficient treatment is administered, then the prognosis in vaginismus is excellent. Studies have reported success rates of 78-100% (31,32). Studies have also reported acceptable and similar effectiveness for various therapeutic techniques (31,32). The treatments currently most commonly applied are; Kaplan's traditional, symptom-focused, and short term-therapies consisting of muscle relaxation techniques using systematic desensitization and relaxation (3). Methods such as sex therapy and CBT are widely employed in the treatment of vaginismus (3). However, a lengthy treatment period may be difficult for the patient and her spouse. The need for further studies in order to increase the success of treatment and reduce the duration thereof has been emphasized (33). Another modality successfully employed in vaginismus is hypnotherapy (15). Studies have reported that hypnotherapy can be applied with a high rate of success (13-15). Studies in the international literature have investigated the effectiveness of hypnotherapy in the treatment of vaginismus, but only one has compared the results of hypnotherapy with those of CBT (15). Our study compared the outcomes of hypnotherapy and CBT in the treatment of vaginismus, and elicited important results.

Success rates of 78-100% have been reported in previous studies (31,32). Sughayir reported 100% success in both hypnotherapy and CBT groups (15). We also achieved high and similar success rates in our hypnotherapy and CBT groups (Table 1). However, the number of sessions required until achievement of full coitus was significantly lower in the hypnotherapy group than in the CBT group (p<0.001). This finding indicates that hypnotherapy may be a more suitable option for patients without reservations concerning hypnosis and thought to be possibly non-compliant with treatment. It should also be remembered that a short duration of treatment will also reduce costs.

There is no doubt that sexual relations are not necessarily limited to successful coitus. Sexual satisfaction is important in terms of harmonious spousal relations. One study showed a significant increase in sexual satisfaction in patients receiving hypnotherapy and behavioral therapy, together with a decrease in spouses' anxieties concerning sexual relations, although no difference was observed between the groups (15). Sexual satisfaction analysis was not performed in the present study since the focus in therapy sessions was primarily on successful coitus.

One important problem in the treatment of vaginismus is the therapeutic process being discontinued halfway through. Kabakçı and Batur applied CBT to 28 women diagnosed with vaginismus, and their spouses, for a period of six months, and reported that 14 couples discontinued treatment in the first sessions (18). Other studies

have also reported that large numbers of patients discontinue treatment (15). Researchers have speculated that this early discontinuation may be due to very rapid treatment expectations and fears concerning the results of treatment (15). In addition, it has been suggested that levels of anxiety and perfectionism is patients may also be important factors in treatment not being completed, and that these factors may need to be considered in the therapeutic process (4). Discontinuation of treatment should not therefore be regarded as failure. Discontinuation rates in our study were relatively low (Table 1), and were similar between the two groups.

CONCLUSION

Hypnotherapy and CBT can be applied with similar high success rates in the treatment of vaginismus. However, success may be achieved with fewer sessions with hypnotherapy.

The authors declare no conflict of interest..

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RESEARCH ARTICLE

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Shear Wave Ultrasound Elastography and Diffusion-Weighted Magnetic Resonance Imaging Findings of Pleural Based Masses with Histopathologic Correlation

ABSTRACT

Objective: The study aims to evaluate the usefulness of non-invasive diagnostic methods, shear wave elastography (SWE), and diffusion-weighted magnetic resonance imaging (DWI) to differentiate benign and malignant lesions in the thoracic pleural based masses by comparing them with histopathological findings.

Methods: Sixty-three patients having a pleural-based peripheral mass on computed tomography (CT), admitted to the interventional radiology department for transthoracic biopsy, were included in the study. All patients underwent DWI, and ADC values of the groups were measured. Transthoracic biopsy was performed with the guidance of US from the area where the highest shear wave velocity (SWV) value was calculated. ADC and SWV values of histopathologically proven benign and malignant lesions were statistically compared.

Results: Fifty-six patients were male, and seven were female. The mean age was 64.68±10.13 years (41-85 years). Fourty-four patients were malignant, and 19 were benign. The maximum SWV was found to be 4.13±0.59 m/s in malignant cases and 3.55±0.71 m/s in benign cases, and the difference was significant (p = 0.001). Mean ADC value was measured as 1.04±0.30 x 10-3 mm2/s in malignant cases and 1.32±0.33 x 10-3 mm2/s in benign cases on DWI and the difference was significant (p = 0.002). In malignant cases, the minimum ADC was 0.73±0.29 x 10-3 mm2/s, and 0.99±0.44 x 10-3 mm2/s in benign cases, the difference was significant (p = 0.024). ROC analysis revealed a cut-off value of ≥4.08 m/s for SWVmax, ≤1.01x10-3 mm2/s for mean ADC, and ≤0.8x10-3 mm2/s for minimum ADC showed a significant performance in distinguishing malignant and benign lesions.

Conclusions: Transthoracic US elastography and DWI are useful in differentiating malignant and benign lesions in appropriate cases. Both SWE and DWI are useful in routine use because they are non-invasive and do not contain radiation. In particular, SWE is suitable for biopsy guidance and may prevent the possibility of insufficient material.

Keywords: Shear Wave Elastography, Diffusion-Weighted MRI, Biopsy, Mass, Thorax.

Plevra Tabanlı Kitlelerde Shear Wave Elastografi Ve Difüzyon MRG Bulgularının Histopatolojik Bulgular İle Korelasyonu

ÖZET

Amaç: Non-invaziv tanısal yöntemler olan shear wave elastografi (SWE) ve difüzyon ağırlıklı magnetik rezonans görüntülemenin (DAG), toraksta plevra tabanlı kitlelerde benign ve malign lezyonların ayırımında kullanılabilirliklerinin histopatolojik bulgular ile karşılaştırılarak değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Mart 2015 ile Mart 2018 tarihleri arasında girişimsel radyoloji ünitesine transtorasik biyopsi amacıyla başvuran, bilgisayarlı tomografide (BT) plevra tabanlı kitle izlenen ve biyopsiye uygun bulunan 63 olgu çalışmaya dahil edilmiştir. Tüm olgulara DAG yapılmış ve kitlelerin ADC değerleri ölçülmüştür. Tüm olgulara SWE uygulanmış ve en yüksek SW hızı ölçülen alandan transtorasik biyopsi yapılmıştır. Histopatolojik olarak benign ve malign olduğu belirlenen lezyonların DAG ve SWE bulguları karşılaştırılmıştır.

Bulgular: Olguların 56'sı erkek, 7'si kadındı. Ortalama yaş 64.68±10.13 idi (41-85). Olguların 44'ü malign, 19'u ise benigndi. Malign olgularda maksimum SW hızı ortalama 4.13±0.59 m/sn, benign olgularda ise 3.55±0.71 m/sn ölçülmüş olup fark anlamlı idi (p=0.001). Malign olgularda mean ADC 1.04±0.30 x 10-3 mm2/sn, benign olgularda ise 1.32±0.33 x 10-3 mm2/sn ölçülmüş olup fark anlamlı idi (p=0.002). Malign olgularda minimum ADC 0.73±0.29 x 10-3 mm2/sn; benign olgularda ise 0.99±0.44 x 10-3 mm2/sn ölçülmüş olup fark yine anlamlı idi (p=0.024). ROC analizi sonucu maksimum SW hızı değeri ≥ 4.08 m/sn, mean ADC değeri ≤1.01x10-3 mm2/sn ve minimum ADC değeri ≤ 0.8x10-3 mm2/sn malign tanısı için cut-off değeri olarak alındığında, başarılı şekilde malign-benign ayrımı yapılabilmekteydi.

Sonuç: Transtorasik US elastografi ve difüzyon MR, uygun olgularda malign-benign lezyon ayrımında yararlıdır. Hem SWE, hem de difüzyon MR incelemesi, radyasyon içermemeleri ve non-invaziv olmaları nedeniyle rutin kullanımda kullanışlı yöntemlerdir. Özellikle SWE, biyopsi kılavuzluğu için uygun olup yetersiz materyal olasılığını engelleyebilir.

Anahtar Kelimeler: Shear Wave Elastografi, Difüzyon MRG, Biyopsi, Kitle, Toraks.

INTRODUCTION

Ultrasound elastography can detect soft tissue elasticity and hardness and has been used more frequently in diagnosing thyroid, breast, prostate, and liver cancers and evaluating liver fibrosis in the recent decade (1-6). Diffusion MR imaging, although primarily used in neuroradiology, is an imaging method that can be applied to many parts of the body and is increasingly used in differentiating benign and malignant lesions. Its use in the thorax is also becoming widespread (7-10). Both methods are easy-to-apply, fairly rapid, non-invasive, and safe imaging methods used in research to distinguish malignant vs. benign lesions. Computed tomography (CT) is mostly used for the diagnosis of thoracic lesions due to the bone structure of the chest wall and the air content of the lungs, and tomography-guided biopsy may be taken from suspicious lesions. CT-guided biopsy is a valuable method and an accurate, safe and effective procedure when performed in an adapted environment (11,12). However, radiation is used in CT, albeit at a low dose. Besides, if the lesion is necrotic and/or close to vessels or cannot be distinguished from accompanying atelectasis, it may be necessary to use contrast material during biopsy in some cases (12). CT cannot provide information about tissue stiffness, viable tumor tissue may not be determined clearly in some cases, the biopsy material may not have sufficient diagnostic value, and the biopsy may have to be repeated. This study aims to find the area where the tumor cells in the tissue to be biopsied by applying SWE and diffusion MRI before transthoracic biopsy for definitive diagnosis of pleural-based (pleural or subpleural) masses, to reduce the possibility of insufficient material and to prevent the need for repetition of the biopsy. Also, by correlating the histopathological diagnosis (benign/malignant feature) of the biopsy material with elastography and diffusion MRI findings, it will be investigated whether the imaging methods will determine the nature of the tumor without the need for invasive procedures.

MATERIAL AND METHODS

The study was conducted prospectively between March 2015 and March 2018. The cases were selected among the patients who had a chest CT-detected pleural-based solid mass, suitable for biopsy, MR, and US imaging. A total of 155 subjects referred to the interventional radiology unit with a transthoracic biopsy request were evaluated and 63 suitable cases were included in the study.

The criteria for inclusion in the study are:

- Having a pleural-based solid mass in chest CT and applying to our hospital's interventional radiology unit with the indication of biopsy.
- No contraindications for MR examination (contraindications include metallic foreign body in the body that are not compatible with MRI, metallic operation material such as a pacemaker, mechanical heart valve, severe claustrophobia, pregnancy (can be done by consulting a gynecologist and obstetrician))
- Being able to cooperate with all examinations

The exclusion criteria are:

- Central localization of the lesion (without pleural surface extention)
- Pure cystic lesions
- Previous diagnosis and treatment of the mass
- Contraindications for MRI and biopsy
- Not being able to cooperate with an examination

Informed consent form from all patients and ethics committee approval were obtained.

Diffusion MRI was performed to the patients first. Then they were taken to US and the images were compared.

Diffusion-weighted imaging (DWI) was performed with a 1.5 T MRI device (Hitachi Echelon, Tokyo, Japan) using a body coil, without breath-holding.

It was performed using two b values (b0 and b1000) in the axial plane, with a slice thickness of 5-10 mm and a slice interval of 1 mm, depending on the size of the lesion.

ADC (Apparent Diffusion Coefficient) measurements were made at the workstation from the area showing the most diffusion restriction in each lesion, and ADCmean (mean or average ADC) and ADCmin (minimum ADC) values were obtained.

Ultrasound and SWE examinations were performed using a Siemens ACUSON S2000 device and 4-MHZ 4C1 convex probe. ARFI (Acoustic Radiation Force Impulse) method (Virtual TouchTM Quantification/VTQ, Siemens, Germany) was used as the SWE technique. Scanning was performed with minimal scanning pressure applied by the operator and the patients were asked to stop breathing to minimize motion. A standard ROI (region of interest) box was used for sampling. This ROI has a predefined size provided by the system (1x0.5 cm). Sampling was not made

from necrotic and cystic components. Sampling was done 3-10 times from solid parts, depending on the size of the lesion. The highest shear wave velocity value (SWVmax) was recorded. The biopsy was attempted to be taken from the places with the highest shear wave velocity values.

Skin cleansing was provided with povidone-iodine in patients who were found suitable for biopsy in ultrasonography. After applying prilocaine (0.1 ml/kg) as a local anesthetic agent to the skin, subcutaneous and intercostal area, tru-cut biopsy (several samples) was taken from the mass with an 18-gauge biopsy needle after waiting one minute. The removed tissue was sent to the Pathology Department Laboratory in 10% formol solution. The patients without complications were discharged after the general condition of the patient was followed, and the pneumothorax control was performed on the PA chest radiographs taken 2 hours later.

The slides having 4 um-tissue sections were routinely stained by H&E and by immunohistochemistry whenever needed. The reporting was based on the 2015 WHO classification of Lung, Pleura, Thymus and Heart tumors.

Two cases for whom SWE measurement could not be performed were excluded from the study. During the biopsy procedure, minimal pneumothorax developed in only one case, which did not require tube thoracotomy. No complications were developed in other patients. There was no case in which insufficient material was reported histopathologically.

Imaging results were compared with histopathological findings in terms of benign versus malignant diagnosis.

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Statistical Analysis: Normal distribution prerequisite for continuous variables was examined with Shapiro-Wilk test and group comparisons were made with Independent Samples t-test. Relationships between categorical variables were examined with Pearson's chi-square or Fisher's exact test. ROC curve analysis was performed to determine cut-offs for parameters found to be significant. Statistical analyzes were made with the SPSS v.22 package program and the level of significance was taken into account as 0.05.

RESULTS

A total of 63 cases were included in the study. Fifty-six of the cases were male and seven were female. The mean age was 64.68 ± 10.13 (41-85). Forty-four of the cases were malignant, and 19 were benign. Of the malignant cases, 40 (90.9%) were male, 4 (9.1%) were female, and the mean age was 64.80 ± 10.41; of the benign cases, 16 (84.2%) were male, 3 (15.8%) were female, and the mean age was 64.42 ± 9.72. The demographic characteristics of the cases are shown in Table 1.

Table 1. The demographic characteristics of the cases

	Benign (n=19)	**Malignant (n=44)**	**p**	**Total(n=63)**
Age	64.42±9.72	64.80±10.41	0.894	64.68±10.13
Gender				
Male	16 (%84.2)	40 (%90.9)	0.422	56 (%88.9)
Female	3 (%15.8)	4 (%9.1)		7 (%11.1)
Smoking				
No	4 (%21.1)	4 (%9.1)	0.229	8 (%12.7)
Yes	15 (%78.9)	40 (%90.9)		55 (%87.3)

There were 44 malignant (32 non-small cell lung carcinoma (NSCLC), 4 small cell carcinoma (SCLC), 2 metastatic adenocarcinoma, 1 sarcomatoid carcinoma, 1 large cell neuroendocrine carcinoma, 1 malignant mesothelioma, 1 diffuse large B-cell lymphoma, 1 Hodgkin lymphoma, 1 malignant mesenchymal tumor) and 19 benign lesions (12 chronic inflammatory lesions, 4 acute inflammation/pneumonia, 1 tuberculosis, 1 solitary fibrous tumor, 1 thymoma).

Images of case samples are shown in Figure 1 and 2. The highest SWV (SWVmax) obtained from the measurements made from the lesions, ADCmin and ADCmean values calculated in DWI, the widest dimensions (measured on CT), and localization of the lesions (right-left lung) are shown in Table 2. Accordingly, a statistically significant difference was found between SWVmax, ADCmin, ADCmean, and size and malignant-benign characteristics of the lesion ($p < 0.05$).

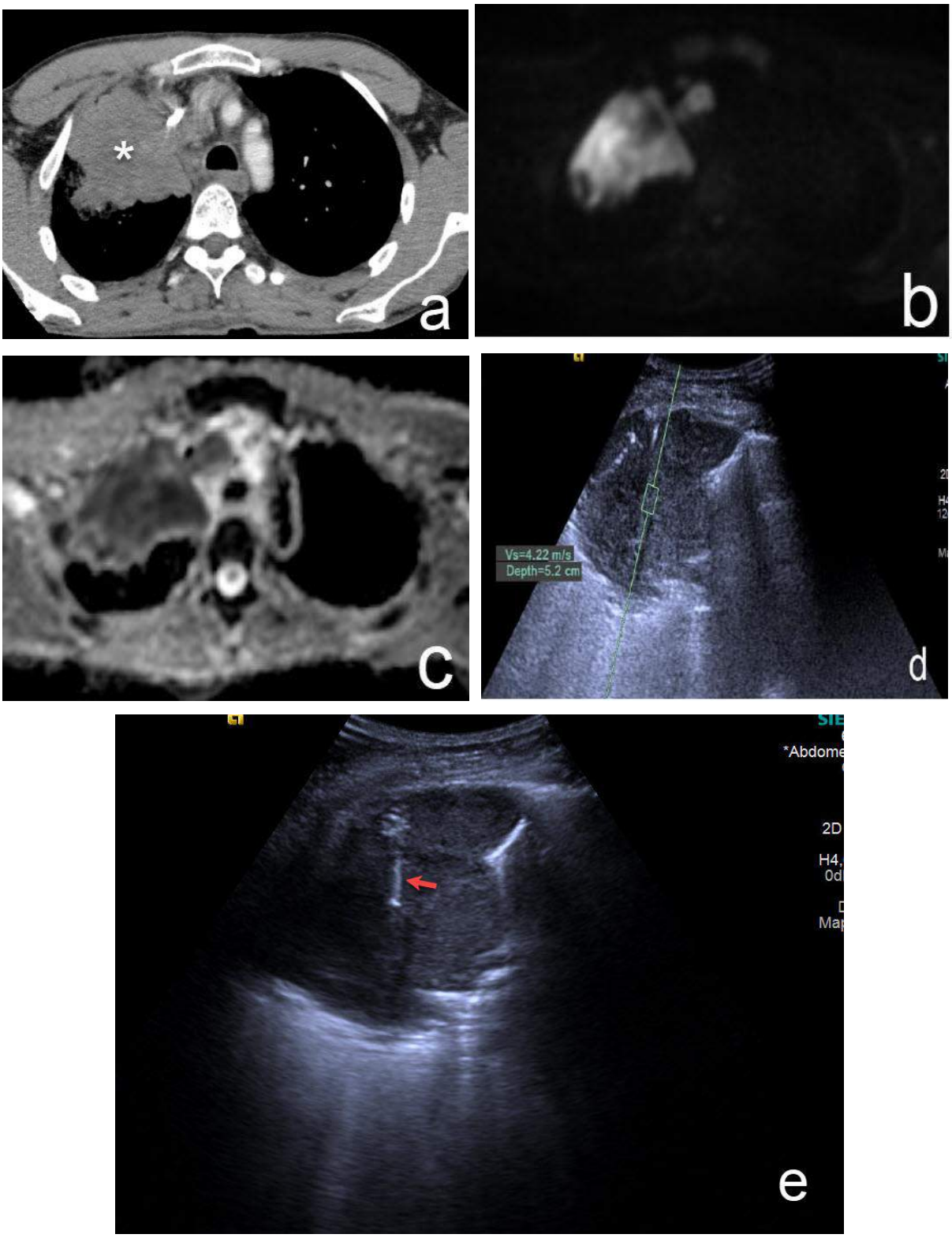

Figure 1. A 54-year-old smoker male with malignant right upper lobe mass (NSCLC). a. Axial CT image of the mass (asterisk). Axial DWI (b) and ADC map (c) show restricted diffusion. The mean ADC was 0.7x10-3 mm2/s and minimum ADC was 0.46x10-3 mm2/s. The maximum SWV value of the mass is 4.22 m/s (d) and the biopsy needle (e, arrow) is shown.

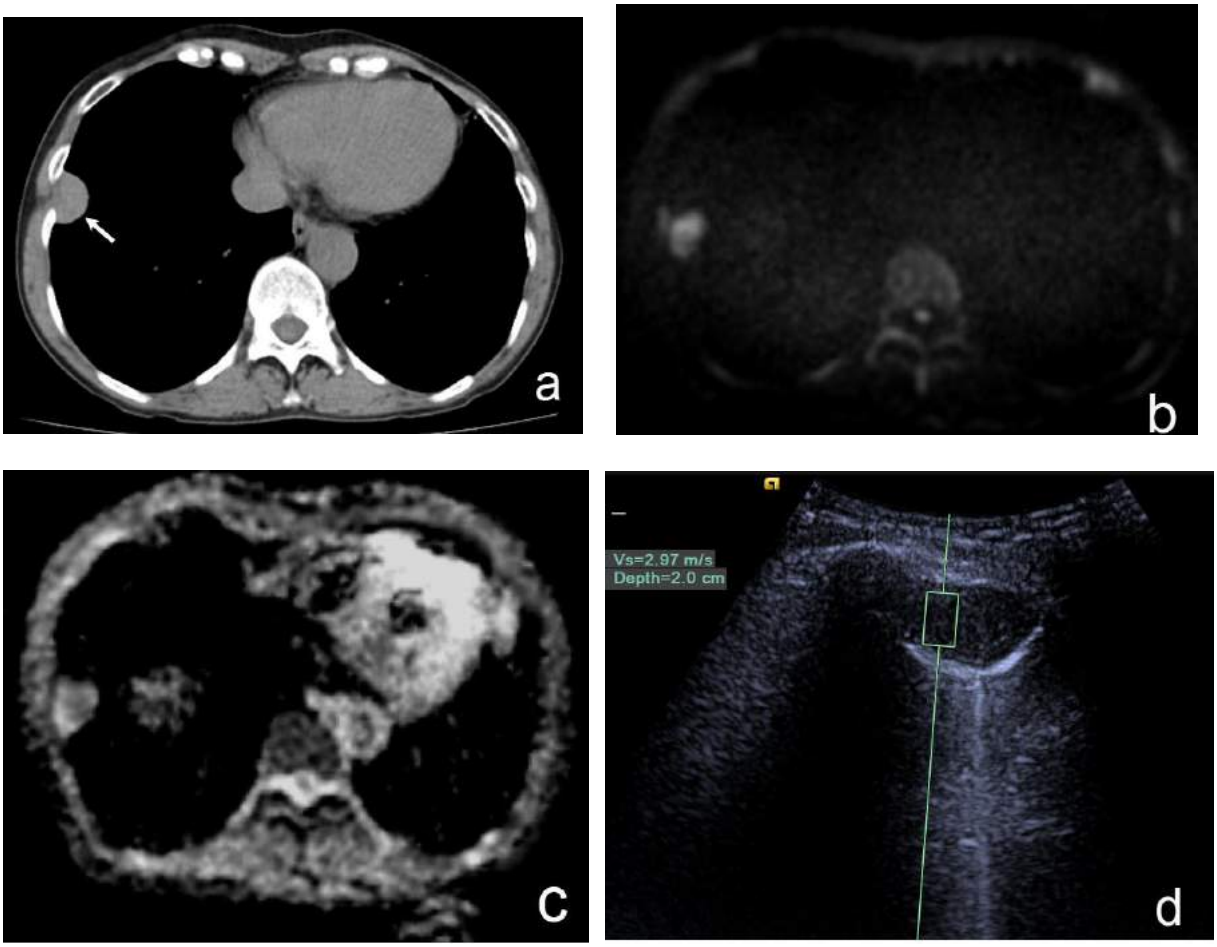

Figure 2. A 62-year-old smoker female with benign right pleural-based mass (solitary fibrous tumor). a. Axial CT image of the mass (arrow). Axial DWI (b) and ADC map (c). The mean ADC was $1.115x10^{-3}$ mm^2/s and minimum ADC was $0.3x10^{-3}$ mm^2/s. The maximum SWV value is 2.97 m/s (d).

Table.2. The SWV values, ADC values, size and sides of the lesions

	Benign (n=19)	**Malignant (n=44)**	**p**	**Total (n=63)**
SWVmax	3.55±0.71	4.13±0.59	***0.001***	3.95±0.68
ADCmin	0.99±0.44	0.73±0.29	***0.024***	0.81±0.35
ADCmean	1.32±0.33	1.04±0.30	***0.002***	1.13±0.33
Size	4.47±1.94	6.31±2.48	***0.006***	5.75±2.46
Side				
Right	13 (%68.4)	24 (%54.5)	0.305	37 (%58.7)
Left	6 (%31.6)	20 (%45.5)		26 (%40.0)

ROC analysis revealed that ADCmin cut-off value ≤$0.8x10^{-3}$ mm^2 / s (AUC = 68.1%; 95% CI = 51.6% to 84.7%; p = 0.023) to be a potential marker of malignancy with a sensitivity of 65.9% and specificity of 73.7%. The cut-off value of ≤$1.01x10^{-3}$ mm^2 / s for the ADCmean generated the combination of 61.4% sensitivity and 79% specificity in distinguishing malignant and benign cases (AUC=%73,6; 95% CI: 59,9% to 87,2%; p=0,003). And when the SWVmax value of ≥4.08 m / s is taken as the cut-off value for malignant diagnosis, it makes a successful distinction with 68.2% sensitivity and 84.2% specificity (AUC = 76.5%; 95% CI = 63.8% to 89.2; p = 0.001).

The ROC analysis results for benign vs. malignant lesion distinction are shown in Table 3.

Table.3. The ROC analysis results

	AUC	95% CI	p	Cut-off	Sensitivity	Specificity
SWV max	0.765	0.638 – 0.892	**0.001**	≥4.08	68.2	84.2
ADC min	0.681	0.516 – 0.847	**0.023**	≤0.80	65.9	73.7
ADC mean	0.736	0.599 – 0.872	**0.003**	≤1.01	61.4	79.0

DISCUSSION

Ultrasound elastography is a noninvasive imaging method that provides information about tissue stiffness and elasticity, has been increasingly used in recent years. When an external force is applied to a tissue, the tissue is deformed. The ability of the tissue to reach its original shape and size when the external force disappears is called elasticity. Tissue deformation is inversely proportional to the stiffness of the tissue. There are two basic elastography techniques: strain elastography and shear wave elastography. SE measures tissue stiffness by applying external tissue pressure by using probe pressure or through endogenous mechanical force (e.g. carotid pulsation). It is operator-dependent and may lead to inter-observer differences and can not give quantitative information. In shear-wave based elastography, a tissue shear-wave is induced by the imaging system. Measurement of shear wave velocity, tissue flexibility is evaluated qualitatively and quantitatively. In this mode, a short duration (0.3-0.4 ms), high power (frequency 2.67 MHz) acoustic radiation force impulse (ARFI) is applied to the tissue with US probes instead of external compression. Shear wave velocity is directly proportional to the hardness of the tissue (in m / s or kilopascals). In this technique, mild probe compression is sufficient, and user dependency is eliminated. However, if too much pressure is applied from the outside, there may be a false height in elasticity values (13,14). SWE was used in our study to eliminate user dependency and to obtain objective quantitative results.

Although ultrasonography in the chest is limited, it can be used for peripheral parenchymal, pleural, and chest wall diseases. Pleural thickening, pleural effusion, pneumothorax, pneumonia, or bronchopneumonia consolidations can be demonstrated by US (15,16). However, there is no specific US finding for the distinction between inflammation and malignancy in solid lesions. USE, on the other hand, has been a method that has been studied in the recent decade, as it provides information about tissue stiffness and malignant lesions are mostly harder than benign lesions (17-21). Sperandeo et al. (19) found that lung cancer is stiffer than pneumonia and concluded that USE could improve the accuracy and and yield of fine-needle aspiration biopsy as well as our study. Our results are similar to those of Sperandeo et al, but they used the compression elastography technique instead of SWE. Lim et al. (20) also found that the strain ratio of primary lung tumors was higher and stiffer than metastatic tumors. In the study of Ozgokce et al., it was emphasized that SWE is very useful in predicting malignancy in subpleural solid lesions, and it is a non-invasive method that can be used in the evaluation of subpleural lesions (21). The results of our study also support this study. In Ozgokce et al.'s study, not all cases were diagnosed histopathologically, and the findings were not evaluated together with diffusion MRI. In our study, all subjects were additionally visualized by DWI and confirmed histopathologically. Wei et al. assessed the diagnostic value of USE in differentiating between benign and malignant peripheral lung lesions by using conventional US, ARFI and point shear wave elastography (22). All cases were confirmed histopathologically. They concluded that USE helps to distinguish malignant lesions from benign lesions and ARFI elastography was more effective in diagnosing peripheral lung lesions. Our results are similar. Wei et al. reported the cut-off value of 1.951 m/s with a sensitivity of 70.9% and a specificity of 69.4% (22). Ozgokce et al. was found the cut-off value 2.47 m/s for the SWV value with sensitivity and specificity of 97.7% (21). When 4.08 m / s was selected as a cut-off value, a sensitivity of 68.2% and specificity of 84.2% were obtained in our study. We used the highest SWV value because we aimed to obtain a biopsy from the hardest part of the lesion. We used the highest SWV value because we aimed to obtain a biopsy from the hardest part of the lesion. Other studies have used the average-mean of multiple measurements from the lesions. The difference between the values is thought to be due to the difference in measurement techniques.

Although the use of MRI in the thorax is limited due to reasons such as respiratory and cardiac movements, vascular pulsations and sensitivity artifacts arising from the air-tissue interface, its use gradually increases. Due to the possibility of functional evaluation, DWI has begun to play an important role in the evaluation of tumoral diseases of the lung, mediastinum and lymph nodes (7,8). The density of the image in DAG increases or decreases with the diffusion ability of the molecules. Normal or increased diffusion, i.e. high ADC values, are seen in healthy tissues or benign pathologies. Diffusion restriction, i.e. low ADC values, indicates hypercellularity, cytotoxic edema, or dense content (hemorrhage or protein). Diffusion is restricted in malignant cells and low ADC values are observed. Because of this feature, DWI is also used in the differential diagnosis of malignant and benign diseases. Its clinical uses include evaluation of pulmonary nodules, characterization of lung tumors, differentiation of post obstructive pneumonia-tumor, evaluation of response after chemotherapy, evaluation of mediastinal lymph nodes and masses, and evaluation of pleural diseases (7,8, 23-25). A standard ROI (region of interest) measurement area or number has not been reported for ADC measurement from lesions. Besides, there is no full consensus on which ADCmin and ADCmean value should be used (9). In our study, both ADCmin and ADCmean were measured from each lesion. In the study of Luna et al. (23), DWI was reported to have

83% sensitivity and 74% specificity in distinguishing malignant lesions if the ADC value was accepted as $\leq 1.4x10^{-3}$ mm^2/s. In our study, when the ADCmin value $\leq 0.8x10^{-3}$ mm^2 / s is taken as the cut-off value for malignant diagnosis, it makes a successful distinction with 65.9% sensitivity and 73.7% specificity, and when the ADCmean value $\leq 1.01x10^{-3}$ mm^2 / s is taken as the cut-off value for malignant diagnosis, it makes a successful distinction with 61.4% sensitivity and 79% specificity.

Our study has some limitations. The masses could not be wholly visualized by ultrasonography (primarily due to the obstruction of the ribs) in all patients, diffusion images could not be fused with SWE and the biopsy needle could not be directed to the desired point in all cases.

CONCLUSION

Our study has shown that SWE and DWI are useful diagnostic methods for predicting malignancy in pleural-based masses. In particular, SWE is a suitable method for biopsy guidance. Since it is a non-invasive method that is easy to use, does not contain radiation and no need for contrast administration, it can be preferred to take the biopsy from the most suitable part of the lesion and can eliminate the possibility of insufficient/unsatisfactory material for histopathological evaluation as well.

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RESEARCH ARTICLE

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Does Excessive Meat Consumption During the Feast of Sacrifice Worsen Chronic Kidney Damage? The Effect of Intensive Meat Consumption on Chronic Kidney Damage

ABSTRACT

Objective: Chronic kidney disease (CKD) is precisely described as the availability of kidney damage or decreased kidney fonction that lasts for three months or more, regardless of its cause. Dietary factors may affect the progression and complications of the disease. Our aim is to investigate the effects of excessive meat consumption of Muslims on CKF during the Feast of Sacrifice.

Methods: The study was performed on 203 patients with stage III-V CKD. The biochemical values of the patients who applied to the nephrology outpatient clinic at least one month before and one month after the Eid al-Adha were recorded. Patients who regularly consumed sacrificial meat for 4 days during the feast of sacrifice were included in the study.

Results: The blood urea nitrogen (BUN), creatinine, albumin, potassium (K), calcium (Ca), vitamin D, and base excess (BE) levels of the patients were foundap to be significantly higher after the Feast of Sacrifice ($p=0.014$, $p<0.001$, $p=0.031$, $p<0.001$, $p=0.002$, $p<0.001$and $p=0.009$). The mean e-GFR of the patients before the Feast of Sacrifice was 32.221±14.756. It was found to be 31.474±15.229 after the feast of sacrifice, indicating a statistically significant decrease ($p=0.042$). A slight decrease was observed in the blood pH ($p=0.002$) and bicarbonate (HCO3) ($p=0.002$) levels of the patients. The change in the amount of creatinine with the feast showed a significant difference by CKD stages ($p<0.001$). There was no significant difference between stage IIIa (0.066±0.191), stage IIIb (0.067±0.318) and stage IV (0.137±0.547) patients ($p>0.05$). In stage V patients, creatinine level (0.580±1.124) showed a significant increase ($p<0.001$) due to the short-term intense meat consumption during the Feast of Sacrifice.

Conclusions: In this study, we observed a progressive deterioration in kidney function due to high protein diet caused by excessive meat consumption in a short time during the feast of sacrifice.

Keywords: Chronic Kidney Disease, Feast of Sacrifice, Meat Consumption, Progression of Kidney Disease.

Kurban Bayramında Yoğun Et Tüketimi Kronik Böbrek Hasarını Hızlandırır mı? Yoğun Et Tüketiminin Kronik Böbrek Hastalığına Etkisi

ÖZET

Amaç: Kronik böbrek hastalığı (KBH), nedene bakılmaksızın üç veya daha fazla ay boyunca böbrek hasarı veya azalmış böbrek fonksiyonunun varlığı olarak tanımlanır. Diyet faktörleri böbrek hastalığının ilerlemesi ve komplikasyonları üzerinde etkili olabilir. Çalışmamızda, kurban bayramında toplumda yoğun et tüketiminin KBH progresyonu üzerindeki etkilerini araştırmayı amaçladık.

Gereç ve Yöntem: Çalışma evre III-V KBH tanısı alan 203 hasta üzerinde gerçekleştirildi. Kurban Bayramı'ndan en az bir ay önce ve bir ay sonra nefroloji polikliniğine başvuran hastaların biyokimyasal değerleri kaydedildi. Çalışmaya 4 gün boyunca kurban bayramında düzenli olarak kurban eti tüketen hastalar dahil edildi.

Bulgular: Hastaların kan üre azotu (BUN) ($p=0.014$), kreatinin (Cre) ($p<0.001$), albumin ($p=0.031$) , potasyum (K) ($p<0.001$), kalsiyum (Ca) ($p=0.002$) vitamin-D ($p<0.001$), ve baz açığı (BE) ($p=0.009$) düzeyleri kurban bayramı sonrası anlamlı yüksek bulundu. Hastaların kurban bayramı öncesi e-GFR ortalaması 32.221±14.756 idi. Kurban bayramı sonrası ise istatistiksel olarak anlamlı bir düşüş göstererek 31.474±15.229 oldu ($p=0.042$). Hastaların kan pH ($p=0.002$) ve bikarbonat (HCO3) ($p=0.002$) düzeyinde de bir miktar azalma oldu. Kreatinin miktarında bayram ile meydana gelen değişim ise KBH evrelerine göre anlamlı farklılık gösterdi ($p<0.001$). Evre IIIa (0.066±0.191), evre IIIb (0.067±0.318) ve evre IV (0.137±0.547) hastaları arasında anlamlı fark yoktu ($p>0.05$). Evre V hastalarında ise bayram sürecindeki kısa süreli yoğun et tüketimine bağlı olarak kreatinin düzeyi (0.580±1.124) anlamlı bir artış gösterdi ($p<0.001$).

Sonuç: Bu çalışmada, kurban bayramı boyunca kısa sürede aşırı et tüketiminin neden olduğu yüksek proteinli diyete bağlı olarak böbrek fonksiyonlarında ilerletici bir bozulma olduğunu gözlemledik.

Anahtar Kelimeler: Kronik Böbrek Hastalığı, Kurban Bayramı, Et Tüketimi, Kronik Böbrek Hastalığında Progresyon.

INTRODUCTION

Chronic kidney Disease (CKD) is described as the availability of kidney damage or decreased renal function that lasts for three months or more, regardless of its cause. This disease, which is common worldwide (8% - 16%), is a global health problem that causes millions of deaths each year (1). There are two primary important risk factors for CKD; genetic, environmental. Diabetes mellitus (DM), hypertension (HT), Obesity, infections, inflammation, malnutrition are important causes of environmental factors (2). It is known that food intake is one of the changeable risk factors for kidney dysfunction. Dietary factors may affect the progression and complications of the disease. Among patients with CKD, excessive food consumption causes sodium and volume overload, hypercalcemia, hyperphosphatemia, and accumulation of toxic metabolites generated by protein degradation. On the other hand, poor nutrition increases the risk of malnutrition. However, the most appropriate nutritional approach in patients with CKD is still unknown, and conflicting results have been obtained from the clinical trials conducted so far. The individual optimal diet for patients with CKD varies depending on the estimated glomerular filtration rate (e-GFR), type of CKD (proteinuric or non-proteinuric), and the availability of other comorbidities such as HT either heart failure. Daily protein intake is recommended as 0.8 grams per kilogram of body weight in non-dialysis subjects with CKD (eGFR of <60 mL /min /1.73 m2)(3).

At one study, after 11 years of followup, a western-style diet characterized by processed red meat, saturated fats, and sweets has been shown to worsen kidney function. In the same study, it was claimed that another diet model with a elevated percentage of fruits, vegetables, leguminous plants, fish, poultry, crops preserved kidney function (4).

Appropriate dietary approaches may have a positive effect on clinical outcomes among patients with CKD. However, there is no consensus regarding the most appropriate nutritional approach in patients with CKD, and conflicting results have been reported in the clinical trials conducted so far.

Taking measures get under control the progression and development of complications is of great importance since CKD is an important public health problem. During the Eid al-Adha, there is intense meat consumption in the whole society for 4 days. Our aim is to investigate the effects of excessive meat consumption of Muslims on CKD during the Feast of Sacrifice.

MATERIAL AND METHODS

Before starting the study, approval numbered 2019/128 and dated 12/09/2019 was gained from the Clinical Research Ethics Committee of our university. The study included 203 patients with stage III-V CKD who were admitted to the Nephrology outpatient clinic one month before and one month after the 2020 Feast of Sacrifice (31/07/2020-03/08/2020). All cases consumed 150 grams of red meat (each piece of meat 10 g, a total of 15 pieces 150 grams) at each meal in 3 meals for 4 days during the Feast of Sacrifice . An e-GFR value of less than 60 ml/dk/1.73m^2 was considered as the diagnostic criteria for CKD.The Modification of Diet in Renal Disease (MDRD) study was used to measure e-GFR (5).In accordance with the CKD stages, the patients were classified as stage IIIa (e-GFR of 45-59 ml/dk/1.73m^2), stage IIIb (e-GFR 30-44 ml/dk/1.73m^2), stage IV (e-GFR of 15-29 ml/dk/1.73m^2) and stage V (e-GFR of <15 ml/dk/1.73m^2) (1).At least one month before and after the Feast of Sacrifice, 12-hour fasting blood samples were collected from the patients in the morning. COBAS c501 (Roche, Basel, Switzerland) device was used for routine biochemical analysis (creatinine, C-reactive protein (CRP), uric acid, potassium, sodium, calcium), while CELL-DYN RUBY (Abbott, IL, USA) was used for hemogram test.

Patients with active infections, those who were vegetarian, those who had malignancy, patients with cachexia, and those receiving renal replacement therapy (hemodialysis, peritoneal dialysis) were excepted from the study.

RESULTS

Two hundred three subjects were evaluated in our study. Of all patients, 107 (52.7%) were male and 96 (47.3%) were female. The mean age of the patients was 66.36± 12.91 years, from 19 to 89 years. The mean age of the male and female subjects was 67.81±12.55 and 64.74±13.18 years, respectively (p=0.092).The etiology was diabetes mellitus 81 (39.9%), hypertension 88 (43.3%), and others disease 34 (16.7%). The drugs used by the cases, respectively; 551 Insulin 39 (19.2%), oral antidiabetic 26 (12.8%), angiotensin converting enzyme inhibitors (ACE-I) –angiotensin receptor blockers (ARB) 48 (23.6%), calcium channel blocker 42 (20.7%) and multiple drug use was 48 (23.6%).

The change in the blood parameters before and after the Feast of Sacrifice is presented in Table 1. The blood urea nitrogen (BUN), creatinine, albumin, potassium (K), calcium (Ca), vitamin D, base excess (BE) levels of the subjects were found to be significantly higher after the feast. Following the feast, the BUN level increased from 34.045±15.920 to 35.981±17.633 (p=0.014), the creatinine level increased from 2.378±1.366 to 2.549±1.640 (p<0.001), and the mean albumin level increased from 4.231±0.403 to 4.267±0.406 (p=0.031). The mean e-GFR of the subjects before the feast was 32.221±14.756. It was found to be 31.474±15.229 after the feast, and

this decrease was statistically significant (p=0.042). No statistically significant change was observed following the feast in terms of other blood parameters (p>0.05).

Pearson's correlation coefficient was used to analyze the correlation of creatinine and e-GFR levels with uric acid and albumin levels (Table 2).

Table 1. Changes in blood parameters before and after the Feast of Sacrifice

	n	Before		After		t	p
		Mean	SD	Mean	SD		
Glucose(mg/dl)	203	128.419	57.166	127.665	48.195	0.231	0.818
BUN(mg/dl)	203	34.045	15.920	35.981	17.633	-2.473	0.014*
Creatinine(mg/dl)	203	2.378	1.366	2.549	1.640	-4.065	<0.001
eGFR(ml/dk/1.73m^2)	203	32.221	14.756	31.474	15.229	2.042	0.042*
Cholesterol(mg/dl)	203	191.296	44.636	188.015	45.832	1.462	0.145
HDL(mg/dl)	203	46.064	12.952	45.079	12.123	2.029	0.044*
Triglyceride(mg/dl)	203	181.581	116.310	160.852	90.293	3.323	0.001**
LDL(mg/dl)	197	109.663	36.987	109.351	37.455	0.156	0.876
Albumin(g/dl)	203	4.231	0.403	4.267	0.406	-2.168	0.031*
K(mmol/l)	203	4.853	0.622	5.004	0.629	-3.947	<0.001
Ca(mmol/l)	203	9.172	0.721	9.289	0.687	-3.119	0.002**
P(mmol/l)	203	3.864	0.957	3.891	0.895	-0.578	0.564
CRP(mg/dl)	203	0.918	1.754	0.851	1.330	0.489	0.625
Uric acid(mg/dl)	203	6.609	1.634	6.794	1.659	-1.974	0.051
HB1AC(%)	203	6.283	1.393	6.333	1.440	-1.083	0.280
ACR(mg/g)	202	1153.851	1776.789	1075.581	1731.522	1.097	0.274
BCR(mg/mg)	203	15.754	5.272	15.735	5.325	0.071	0.944
HGB(g/dl)	203	12.049	1.857	12.015	1.934	0.415	0.679
PLT	203	225906.404	77396.025	223157.635	70877.141	1.006#	0.315
Folate(ng/ml)	203	7.960	4.224	7.866	4.488	0.302	0.763
B12 (ng/ml)	203	382.001	260.847	374.630	176.271	0.466	0.642
Ferritin(ng/ml)	203	303.759	447.893	308.059	417.487	-0.295	0.768
PTH(pg/ml)	200	126.945	123.620	124.002	97.756	0.541	0.589
Vitamin D	202	16.034	8.461	17.708	8.520	-3.697	<0.001
PH	203	7.345	0.048	7.335	0.055	3.170	0.002**
HCO3(mEq/L)	203	25.138	3.515	24.667	3.839	2.302	0.022*
PCO2(mmHg)	203	45.855	5.577	46.149	6.331	-0.742	0.459
BE	203	-0.463	4.621	-1.188	4.390	2.642	0.009**

#*Wilcoxon Signed Rank Test Z-Value*, t=Paired t-test

*=<0.05, **=0.01

BUN:The blood urea nitrogen , e-GFR: estimated glomerular filtration rate, HDL: high density lipoprotein, LDL: Low density lipoprotein, K:potassium, Ca: calcium, P: phosphor, crp: C-reactive protein, HB1AC: glycosylated hemoglobin, ACR: Urinary albumin/creatinin ratio, BCR: blood urea nitrogen to serum creatinine ratio , HGB: hemoglobin, PLT: platelet, B12: vitamin B12, PTH: parathyroid hormone,

Table 2. Correlation between subjects' albumin levels and creatinine and eGFR levels

		Correlation Coefficient		Regression Coefficient			
		r	p	b	Std. Error	t	p
Creatinine	Before the Feast	-0.234	0.001**	-0.794	0.232	-3.416	0.001**
	After the Feast	-0.162	0.021*	-0.654	0.281	-2.329	0.021*
e-GFR	Before the Feast	0.323	<0.001	11.815	2.445	4.832	<0.001
	After the Feast	0.284	<0.001	10.632	2.535	4.194	<0.001

e-GFR: estimated glomerular filtration rate

r=Pearson correlation coefficient, b=Linear regression coefficient

*=<0.05, **=0.01

A significant weak negative correlation was detected between creatinine and albumin levels before (r=-0.234, p=0.001) and after the feast (r= -0.162, p=0.021). Likewise, albumin level was found to be correlated with e-GFR. There was a significant weak positive correlation between the albumin levels and e-GFR levels before (r=0.323, p<0.001) and after the feast (r=0.284, p<0.001). In other words, creatinine levels decreased and e-GFR levels increased as the albumin level increased. According to the calculated linear regression coefficients, the creatinine level was estimated to decrease by 0.794 mg/dL (p=0.001) before the Feast and by 0.654 mg/dL (p=0.021) after the Feast

as the albumin level increased by 1 mg. On the other hand, the eGFR level was estimated to decrease by 11.815 mL/min/1.73m^2 ($p<0.01$) before the Feast and 10.632 mL/min/1.73m^2 ($p<0.01$) after the Feast as the albumin level increased by 1 mg. The correlation coefficients calculated between uric acid and both creatinine and e-GFR showed that there was no significant correlation between the variables before and after the Feast ($p>0.05$). The distribution of the subjects before and after the feast by their CKD stages was compared using the McNemar-Bowker test and no significant difference was found ($p=0.091$, Table 3).

One-way ANOVA was carried out to determine at which CKD stage (Stage IIIa, Stage IIIb, Stage IV, Stage V) the amount of change (paired difference) in creatinine,

The blood urea nitrogen (BUN), blood urea nitrogen to serum creatinine ratio (BCR), and eGFR levels after the feast was greater (Table 4).

Table 3. Distribution of subjects before and after the Feast by CKD stages

			After the Feast				Total	p
			Stage IIIa	Stage IIIb	Stage IV	Stage V		
Before the Feast	Stage IIIa	n	38	12	0	0	50	0.091
		%	77.6	20.0	0.0	0.0	24.6	
	Stage IIIb	n	10	45	11	0	66	
		%	20.4	75.0	20.0	0.0	32.5	
	Stage IV	n	1	3	41	8	53	
		%	2.0	5.0	74.5	20.5	26.1	
	Stage V	n	0	0	3	31	34	
		%	0.0	0.0	5.5	79.5	16.7	
	Total	n	49	60	55	39	203	
		%	100.0	100.0	100.0	100.0	100.0	

Stage IIIa: 45-59 mL/min/1.73 m^2; Stage IIIb: 30-44 mL/min/1.73 m^2
Stage IV: 15-29 mL/min/1.73 m^2; Stage V=<15 mL/min/1.73 m^2

Table 4. Descriptive statistics values according to CKD stages

		n	**Mean**	**SD**	**F**	**p**
Creatinine	Stage IIIa	50	0.066[b]	0.191	7.099	<0.001
	Stage IIIb	66	0.067[b]	0.318		
	Stage IV	53	0.137[b]	0.547		
	Stage V	34	0.580[a]	1.124		
BUN	Stage IIIa	50	1.666	6.189	0.820	0.484
	Stage IIIb	66	0.421	7.422		
	Stage IV	53	3.077	16.013		
	Stage V	34	3.497	13.544		
BCR	Stage IIIa	50	.261	3.869	0.821	0.493
	Stage IIIb	66	-.534	3.476		
	Stage IV	53	.475	4.584		
	Stage V	34	-.200	2.760		
eGFR	Stage IIIa	50	-2.004	5.935	1.556	0.201
	Stage IIIb	66	-0.116	6.181		
	Stage IV	53	-0.168	4.360		
	Stage V	34	-1.024	2.206		

BUN:The blood urea nitrogen , BCR: blood urea nitrogen to serum creatinine ratio, e-GFR: estimated glomerular filtration rate, Stage IIIa: 45-59 mL/min/1.73 m^2; Stage IIIb: 30-44 mL/min/1.73 m^2
Stage IV: 15-29 mL/min/1.73 m^2 ; Stage V=<15 mL/min/1.73 m^2
F= One-way ANOVA
Means that do not share a common letter are significantly different ($p<0.001$).

There was no significant difference between the CKD stages in terms of the change in e-GFR, BUN, and BCR levels after the feast ($p>0.05$). The change in the amount of creatinine with the feast showed a significant difference by CKD stages ($p<0.001$). There was no significant difference between subjects with stage IIIa (0.066±0.191), stage IIIb (0.067±0.318), stage IV CKD (0.137±0.547) ($p>0.05$), while a significant increase was detected in creatinine levels (0.580±1.124) of subjects with stage V CKD due to the short-term excessive meat consumption during the feast ($p<0.001$).

DISCUSSION

The current study demonstrated that extraordinary excessive meat consumption for a short time during the Feast of Sacrifice worsened the kidney function in subjects with stage III-V CKD.

Chronic Kidney Disease is a majority disease affecting approximately 10–13% of adults (6). It is thought to cause a partial increase in traditional risk factors including HT, DM, and metabolic syndrome, and to significantly increase cardiovascular risk. The protein intake has been one of the most discussed dietary practices in CKD. Urea, creatinine, and uric acid, degradation products caused by protein metabolism are eliminated by the kidneys. Kidneys are involved in amino acid metabolism through the conversion of phenylalanine to tyrosine and of glycine to serine as well as in the extraction. Therefore, certain abnormalities occur in amino acid plasma concentrations in CKD. There is not enough common consensus about the restriction of certain foods or supplementation of certain nutrients affecting the morbidity or mortality of kidney failure. (7).

A healthy diet is related to lower mortality rates in subjects with CKD. Protein amount of 0.8 g/kg/day, which does not cause malnutrition or progression, is advised for non-dialysis CKD subjects with e-GFR of less than 60 mL/min/1.73m^2 (3). Increasing the consumption of fruits, vegetables, fish, and legumes and cutting down the amount of red meat, refined sugar, and sodium intake can be effective to lower mortality rates in people with renal failure. A balance between protein metabolism and protein intolerance or protein poisoning should be established in subjects with CKD. Limiting protein intake in diet has been a common practice used to control uremia and delay the progression of CKD (6). A meta-analysis suggested that low dietary protein intake decelerate the progression of CKD and residual renal function loss in subjects with advanced stage CKD (7). In a study by Fouque et al. (8) investigating a high-protein diet in subjects with CKD, the mortality rate in subjects with no protein restriction in their diet was found to be approximately 31% compared to those treated with a low protein diet. Kasiske et al. (9), asserted dietary low protein intake delayed the decline in kidney function, however was not sufficient alone.

Krebs et al. (10) reported that a low-carb and highly protein nourishment had no negative act upon creatinine and e-GFR levels. Larsen et al. (11) observed that a high observed that a high-protein diet caused no increase in creatinine levels in type 2 DM subjects with normal kidney functions.In a study by Tirosh et al. (12), an increase was reported in e-GFR levels of subjects who were following a high-protein diet, particularly in those with stage III CKD.In a study by Knight et al. (13), no high-protein diet-induced change was observed in e-GFR levels in cases with normal kidney function and high intake of non-dairy animal protein was related to increased e-GFR reduction in mild CKD.Cirillo et al. (14) described that high protein intake was cross-sectionally associated with higher GFR in middle-aged adults but was related to even greater GFR decline in the long term. Lew et al. (15) suggested that red meat consumption elevated the hazardous of end-stage renal disease.Similarly, unusual high red meat intake, albeit for a short time, has been observed to increase the loss of kidney function (increase in BUN and creatinine levels; decrease in e-GFR) in the present study. The progression in creatinine level has been observed to be more pronounced in non-dialysis subjects with stage V CKD.

Kidneys have a significant role in maintaining potassium homeostasis. The risk of hyperkalemia is higher in subjects with CKD, which is an important cause of comorbidities, such as cardiac arrhythmia and arrest, and mortality. The average potassium intake is 50-100 mEq/day in the Western pattern diet .The factors that determine the plasma potassium concentration are the amount of potassium intake in the diet, potassium distribution between cells and extracellular fluid, and the relation among plasma potassium and urinary potassium excretion.In the literature, the prevalence of hyperkalemia in CKD subjects has been reported to range from 1% to 50%, depending on the threshold level of serum potassium used for diagnosis (16). Diets rich in plant-based foods such as vegan or vegetarian diets have positive effects in subjects with CKD compared to diets high in alkalis and fiber (19).An elevated in serum potassium levels of subjects with CKD is a uncommon symptom in subjects following a vegetarian diet with low protein content (17). In line with the literature data, a high protein diet was observed to cause hyperkalemia in the present study. Although limiting potassium-rich foods is very important in subjects with CKD, attention is uncommonly paid to this during clinician visits. There is a need for studies investigating the effect of potassium diet management in subjects with severe CKD.

Chronic Kidney Disease is described as a e-GFR level less than 60 mL/min/1.73 m^2 or an urine albumin/creatinine ratio greater than 30 mg/g (5).Although there are studies observing no change in the urine microalbumin level despite high-protein diet (11,12), Friedman et al. (18) reported an increase in proteinuria.In the present study, no change was observed in the amount of urine ACR in subjects with CKD, who followed a high-protein diet. Our study is consistent with the literature in this regard.

Maintaining pH balance is one of the kidney functions. Decreased GFR in subjects with CKD is the foremost risk factor for metabolic acidosis. Furthermore, each 1 g/dl increase in albumin is the cause of a 35% increase in metabolic acidosis (19) .A fruit and vegetable-based diet that reduces kidney acid load by 50% can reduce kidney damage, including albuminuria (20). Metabolic acidosis is associated with increased risk of adverse kidney outcomes and mortality in patients with

non-dialysis dependent chronic kidney disease (21).In this study, a high protein diet was detected to worsen metabolic acidosis in subjects with CKD. Our study is consistent with the literature in this regard.

High FGF-23 levels inhibit 1α-hydroxylase activity as kidney functions decrease, and the resulting gastrointestinal absorption of decreased 1.25(OH) vitamin D_2 and calcium results in hypocalcemia (22). In the present study, the high protein diet was observed to have a positive effect on vitamin D and calcium. Considering the harmful effects of a high-protein diet, attention ought to be paid to this, the long-term results of which are unknown. In our study, although we found low triglyceride levels, no positive change was observed in LDL and total cholesterol levels. Studies with larger populations and longer follow-up are needed for the effects of high consumption of red meat on lipid metabolism during Feast of Sacrifice.

This study has several limitations. Firstly, the amount of red meat consumed by the subjects was not clear and the study was conducted in a regional area. Secondly, it was the limitation of our study that it was not taken into account what kind of meat consumption (cow, sheep) was. Another limitation of our study was that CKD etiologies were not questioned. Finally repeat measurements were not performed to determine the long-term effects of sacrificial meat consumption on kidney function.

CONCLUSION

In conclusion, subjects with CKD had a progressive deterioration in their kidney functions due to the high-protein diet caused by excessive meat consumption during the Feast of Sacrifice.A marked deterioration was observed in the blood gas besides the renal dysfunction. Considering the progression of CKD, the positive effect seen in vitamin D and calcium levels is negligible. The result that we found in our study, that acute intense meat consumption adversely affects renal functions, reminds us to be very careful about this issue. We believe that a protein-restricted diet not causing protein malnutrition in subjects with CKD may have positive effects on the course of the disease, and that clinicians need to follow their subjects more carefully. There is a need for studies with a larger patient population. We believe that our study will shed light on future studies to be conducted with larger populations.

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RESEARCH ARTICLE

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Evaluation of Quality Assurance Indicators and Contamination Rate in Blood Culture

ABSTRACT

Objective: Blood culture are of vital importance in patient follow-up, as they enable the identification and production of sepsis causative microorganisms, initiate antibiotic treatment in a timely manner and reduce mortality and morbidity. In this study, it is aimed to evaluate the microorganisms grown in the automated blood culture in the microbiology laboratory of the hospital in terms of quality indicators.

Methods: In this study, microorganisms grown from automated blood culture BACTEC-9120 (Becton Dickinson, USA) system from the blood culture samples sent to Duzce University Medical Microbiology Laboratory were evaluated retrospectively. For this purpose, the rejection and contamination rate of the samples for which blood culture was requested, the result of Gram staining-final identification compliance, the number of samples sent from a single bottle, and the growth times of microorganisms after incubation were determined.

Results: 5037 blood culture samples were sent to the laboratory from various clinics. 1.7% of these samples were rejected as inappropriate samples. Gram stain-final identification compatibility of blood cultures was investigated and it was determined as 97.8%. The single bottle number of the samples sent was found to be 511. For the 5037 samples included in the study, growth was detected in 20.7%, of which 10.2% were considered as contaminants. In our study, the average breeding time of the factors examined for breeding time was determined to be 30.29 hours.

Conclusions: As conclusion, there is no gold standard to distinguish true pathogens from contaminant agents in blood cultures.

Keywords: Blood Culture, Bacteremia, Quality Indicators.

Kan Kültüründe Kalite Güvence Göstergelerinin ve Kontaminasyon Oranının Değerlendirilmesi

ÖZET

Amaç: Kan kültürü, sepsise neden olan mikroorganizmaların üretilmesini ve tanımlanmasını sağladığı, antibiyotik tedavisini zamanında başlamayı ve mortalite ve morbiditeyi azalttığı için hasta takibinde hayati öneme sahiptir. Bu çalışmada hastanemiz mikrobiyoloji laboratuvarında otomatik kan kültür sisteminde üretilen mikroorganizmaların kalite göstergeleri açısından değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Bu çalışmada, Düzce Üniversitesi Tıbbi Mikrobiyoloji Laboratuvarına gönderilen kan kültürü örneklerinden otomatize kan kültürü BACTEC-9120 (Becton Dickinson, ABD) sisteminde üreyen mikroorganizmalar retrospektif değerlendirilmiştir. Bu amaçla kan kültürü istemi yapılan örneklerin reddedilme ve kontaminasyon oranı, Gram boyama sonucu-son identifikasyon uyum oranı, tek şişe gönderilen örnek sayısı ve inkübasyon sonrası mikroorganizmaların üreme süreleri belirlenmiştir.

Bulgular: Laboratuvara çeşitli kliniklerden gönderilen 5037 kan kültür örneği dahil edilmiştir. Bu örneklerden %1,7'si uygunsuz numune olarak reddedilmiştir. Gram boyama -son identifikasyon uyumu araştırılmış ve %97,8 olarak saptanmıştır. Gönderilen örneklerin tek şişe sayısı 511 olarak bulunmuştur. Çalışmaya alınan 5037 örneğin, %20,7'sinde üreme saptanmış, bunların %10,2'si kontaminant olarak kabul edilmiştir. Araştırmamızda üreme süresi incelenen etkenlerin ortalama üreme süresi 30,29 saat olarak saptanmıştır.

Sonuç: Sonuç olarak, kan kültürlerinde gerçek patojenleri kontaminant ajanlardan ayırt etmek için altın standart yoktur.

Anahtar Kelimeler: Kan Kültürü, Bakteriyemi, Kalite Göstergeleri.

INTRODUCTION

Despite some limitations in the diagnosis of bloodstream infections, blood culture is still the gold standard. Blood culture samples taken in accordance with the guidelines are of vital importance in patient follow-up, as they enable the identification and production of sepsis causative microorganisms, initiate antibiotic treatment in a timely manner and reduce mortality and morbidity. However, difficulties are encountered in the separation stage of true pathogen and contaminant microorganisms that are reproduced from inappropriate blood culture samples. While detection of a true pathogen may help the clinician to determine the cause of sepsis and provide antibiotic susceptibilities, reporting of contaminant microorganisms as an agent may be detrimental to patient care. Furthermore, it increases the length of hospital stay, hence increases costs for patient, and antimicrobial resistance (1–4).

In this study, it is aimed to evaluate the microorganisms grown in the automated blood culture BACTEC-9120 (Becton Dickinson, USA) system in the microbiology laboratory of the hospital in terms of quality indicators for two years.

MATERIAL AND METHODS

The blood culture results sent to the Medical Microbiology Laboratory of XXXX University Medical Faculty Hospital between April 1, 2017 and May 31, 2019 from departments and emergency services were examined retrospectively. Blood samples which were taken under aseptic conditions and sent in appropriate blood culture bottles were examined on a BACTEC automated blood culture device (Becton Dickinson, USA). All samples giving positive signal were examined by Gram staining, then they were cultured in 5% sheep blood agar, Eosin Methylene Blue agar and Chocolate agar and evaluated after for 24-48 hours of incubation at 37 °C. Microorganisms that grew in culture were identified with VITEK 2 (bioMérieux, France) fully automated identification system and traditional methods (5, 6). Strains of isolated coagulase negative staphylococci, diphteroids, Bacillus spp., Micrococcus spp, Propionibacterium acnes, and Corynebacterium spp were accepted as contaminant (7). It was accepted as a true pathogen when coagulase negative staphylococci growth was detected in two or more samples of one patient (2). The contamination rate was calculated according to the following formula (8). Blood culture samples included in the study were evaluated according to quality indicators.

Number of contaminated blood cultures / Total number of blood cultures = Contamination rate

The time between the loading of blood culture samples sent from the patients to the BACTEC automated blood culture device and the growth signal were measured. In this study, the number of single bottle blood culture samples sent from the services and clinics was determined. After the reproductive signal, cohesiveness of the images of the samples in Gram stain were compared to the final identification and recorded. Simultaneous catheter cultures were not included in the study (3, 9).

XXX University Faculty of Medicine Ethics Committee approval was obtained for the study (15.04.2019, Decision number: 2019/97)

Statistical Analysis: SPSS 17 software was used for statistical evaluation of the data. Categorical data are summarized as frequency and percentage. Pearson chi-square test and Fisher's exact test were used to evaluate the contamination and single bottle sample rates according to the clinics. In the comparison of reproductive time of microorganisms, the significance test of difference between two means were applied and Mann Whitney U Test were applied in cases where there was no agreement to normal distribution. $P < 0.05$ was considered significant.

RESULTS

A total of 5037 blood culture samples of 2767 male and 2270 female patients sent from various clinics to our laboratory were included in the study. According to this evaluation, 90 (1.7%) of the samples were rejected as they were found inappropriate. The Gram stain -Final identification" agreement of the Gram stained blood cultures of samples which showed reproductive signal was 97.8% (23/1045). The distribution of microorganisms that are incompatible with gram staining and final identification are shown in Table 1.

Table1. Gram staining and distribution of discordant microorganisms in final identification

Gram Staining Result (n)	Blood Cultur Result (n)		
	Microorganism1	Microoragnism2	Microorganism3
No microorganisms (n:2)	CNS* (2)	-	-
Gram positive cocci (n:3)	*A.baumannii* ** (1)	No growth (2)	-
Gram negative cocci (n:1)	*Salmonella* spp (1)	-	
Gram positive bacillus (n:2)	*Kocuria rosea* (1)	*R. planticola* , *** (1)	
Gram negative bacillus (n:4)	CNS	No growth	
Gram positive cocci and Gram negative bacillus (n:6)	CNS (4)	*Klebsiella* spp (1)	*Enterococcus* spp (1)
Gram positive cocci and yeast (n:2)	*A. baumannii* ** (1)	*Enterococcus* spp(1)	
Gram negative cocci (n:1)	*Proteus mirabilis* (1)		
Yeast (1)	CNS (1)	-	-

*CNS:Coagülase negative cocci ** *Acinetobacter baumanii* ****Raoultella planticola*

1045 (20.7%) of the 5037 samples included in the study were found growt. In the study, the number of contaminations was determined as 514 (10.2%). When the contamination rates were examined according to the clinics, it was found that the rate of contamination in the intensive care units was similar to that of the other services (p = 0.662), whereas it was lower in the surgical services compared to the intensive care units and other services (p = 0.030). It was determined that 511 of the samples were single bottles. The rate of sending blood culture in one bottle was found to be highest in neonatal intensive care units (p>0.001) in intensive care units and in neonatal service (p>0.001) in the other services. The most common isolate which is accepted as contaminant was identified as Coagulase negative staphylococci.

The distribution of the samples identified as contaminants and sent as single bottles according to the clinics is shown in Table 2.

Table 2. Distribution of isolates identified as contaminants sent as single bottles according to services

Intensive Care Units	**Total number (n)**	**Number of single Bottles**		**Contamination**	
		n	**%**	**n**	**%**
İnternal medicine	1178	31	2,6	119	10,1
Neonatology	319	**190**	**59,6**	29	9,1
Anesthesia	315	6	1,9	31	9,8
Pediatry	91	30	33	12	13,2
Coroner	90	5	5,6	13	14,4
Neurosurgery	64	5	7,8	7	10,9
Cardiovascular surgeon	27	1	3,7	3	11,1
Total	**2084**	**268**	**12,9**	**214**	**10,3**
Internal Units					
Internal medicine	767	39	5,1	75	9,8
Emergency medicine	518	22	4,2	71	13,7
Chest diseases	384	23	6	40	10,4
Infection disease	266	30	11,3	24	9
Nephrology	139	10	0,7	11	7,9
Pediatry	137	36	26,3	15	10,9
Hematology	129	10	7,8	13	10,1
Neurology	127	10	7,9	19	15
Oncology	72	4	5,6	3	4,2
Neonatology	37	**26**	**70,3**	6	16,2
Cardiology	30	6	20	0	0
Gastroenterology	27	1	3,7	3	11,1
PM&R *	6	2	33,3	1	16,7
Dermatology	5	1	20	-	0
Forensic medicine	1	1	100	1	100
Total	**2645**	**221**	**8,4**	**282**	**10,7**
Surgery Units					
Urology	104	9	8,7	6	5,8
General surgery	96	2	2,1	3	3,1
Orthopedics	37	5	13,5	4	10,8
Gynecology	34	4	11,8	0	0
Neurosurgery	15	-	0	-	0
Otorhinolaryngology	10	2	20	4	40
Thoracic surgery	8	0	0	-	0
Cardiovascular surgeon	2	0	0	1	50
Ophthalmology	2	0	0	-	0
Total	**308**	**22**	**7,1**	**18**	**5,8**
General Total	**5037**	**511**	**10,1**	**514**	**10,2**

PM&R: Physical medicine and rehabilitation

The growth span of 1045 samples with true pathogen and contaminant growth was examined and the average growth span was found to be 44.45 hours. *Streptococcus pneumoniae* was found to

reproduce more rapidly than other microorganisms. While it was found that the growth span of the contaminant bacteria is statistically similar to yeasts, it is significantly longer than Gram-positive cocci and Gram-negative bacilli (p = 0.897, p = 0.005, p = 0.025, respectively). The growth span of Gram-positive cocci and Gram-negative bacilli was found to be statistically similar (p = 0.147). The growth spans of bacteria and fungi from isolated microorganisms are shown separately and on average in Table 3.

Table 3. Isolated microorganisms and growth times

Microorganism		Growth time (h)	Avarage growth time (h)
Gram positive cocci	*Streptococcus pneumoniae*	11,5	
	Streptococcus agalactia	22,3	
	Staphylococcus aureus	22,6	
	Enterococcus spp	23,7	22,2±6,9
	CNS*	30,85	
Gram negative bacillus	*Acinetobacter* spp	16,7	
	E. coli	19,2	
	Enterobacter spp	19,5	
	Klebsiella spp	22,3	
	Pseudomonas spp	27,3	
	Salmonella spp	28,5	
	Other	28,6	30,7±11,5
	Burkholderia spp	29,3	
	Citrobacter spp	35,3	
	Proteus spp	42,7	
	Morganella morganii	45,5	
	Serratia spp	53,5	
Yeast	*Candida tropicalis*	22,3	
	Candida parapsilosis	34,4	
	Candida albicans	60	59,2±27,6
	Stephanoascus ciferrii	60,2	
	Candida glabrata	84,5	
	Blastoschizomyces capitatus	93,6	
Contaminant	Alfa hemolitic streptococcus	27,4	
	CNS*	32,7	
	Veillonella spp	33,4	
	Other	35,2	
	Corynebacterium spp	56,6	65,8±47,7
	Micrococcus spp	85,6	
	Kocuria spp	87,7	
	Propionebacterium spp	168	

CNS: Coagulase negative staphylococci

DISCUSSION

Contamination of blood cultures is the source of chain of mistakes in health care (10). In this study, blood culture contamination rate was calculated as 10.42%. This ratio was considered high when compared with the literature. Although the target rates for blood culture contamination are below 3%, the actual rates range from 0.6% to 6% among institutions. In a prospective study focusing on blood culture contamination caused by coagulase negative staphylococci, Souvenir et al. reported that almost half of the patients who received false positive results were treated with antibiotics, usually vancomycin (11, 12). Ramli et al. found a significant relationship between pre- and post-corrective action in their study to reduce blood culture contamination. They stated that a multidisciplinary approach that includes various strategies on raising awareness, lifelong training, technical improvement and monitoring of contamination rate may provide an important solution to decrease the contamination rate in the long term (13). Veranyurt et al. found the average contamination rate as 4.30% in their study comparing the years 2016-2018. They stated that as the contamination rate is above the quality standards, in-service trainings are needed, and each laboratory needs to establish a quality assurance program that includes quality control (14). The 10.42% contamination rate found in our study is within unacceptable limits. The reason is thought to be lack of in-service training, non-compliance

with disinfection rules, non-continuous monitoring of contamination rate and lack of personnel.

It was reported in different studies that the growth span of microorganisms isolated in blood cultures had a critical role in the separation of agent and contamination. Balıkçı et al. suggested that the growths detected in the first 12 hours would be interpreted as the causative agent, the ones in 24 hours as highly likely causative agent and the growths in the first 48 hours and more would be interpreted as contaminant agent. However, they reported that the growth span of methicillin-resistant staphylococci, causative agent or not, is longer than 24 hours (3). Durmaz et al. found average growth span of Gram-positive bacteria, Gram-negative bacteria and yeasts as 18.83, 15.67 and 23.87 hours, respectively, in their study (15). In their study, Dierig et al. stated that bacterial growth in blood cultures in children with sepsis is positive in 90% of the children within the first 36 hours of incubation, so it is not valid to treat all children for at least 48 hours. On the contrary, they suggested that the decision to continue empirical antibiotic treatment in the absence of blood culture would be reviewed after 24 and 36 hours and antibiotic treatment would be discontinued if the children are not diagnosed with sepsis (16). In this study, the average growth span was 22.2 hours for Gram-positive bacteria, 30.7 hours for Gram-negative bacteria, 65.8 hours for contaminants, and 59.2 hours for yeasts. This finding shows that bacteria identified as true agents grow in the first 36 hours. However, the fact that the growth span of yeast fungi is similar to contaminant agents should be taken into consideration especially in patients with fungemia.

Single blood cultures are often collected during suspected bacteremia events. Guidelines for obtaining blood culture guide clinicians to determine if patient needs blood culture or not and how many cultures they will get from the patient (17). Taking too many sets is not cost effective and not having enough number of sets and the lack of anaerobic or aerobic vials in one set may delay accurate diagnosis. Of the 5037 blood cultures included in the study, 511 were sent as single bottles (Table 2). Single-bottle samples are commonly sent from neonatal intensive care units and pediatric services. Although it is not recommended to send a single bottle sample, when evaluating post-reproductive factors in pediatric units where amount of blood is low and colleting blood is difficult, these difficulties should be taken into consideration. This reveals the importance of the communication between the clinic and the laboratory.

In our study, noncompliant samples such as leaky, insufficient or incompletely identified, with quality processes and guidelines were preanalitically rejected and this rate is 1.7%. Even if some of the preanalytical errors that constitute a significant part of laboratory errors are possible to prevent by rejecting these kinds of samples, it increases the cost of the patient and causes delays in diagnosis.

In their study, Sogaard et al. found the sensitivity of Gram staining as 91.3-99.7% and specificity as 98.9-100% in positive blood culture samples and they reported that the interpretation and evaluation of Gram staining performed by experienced personnel gives fast, cheap and high accuracy results (16). In our study, Gram staining and final identification agreement rate was found as 97.55% which is high. Assuming that delays in bacterial isolation and identification in blood cultures increase the mortality rate by 1.2% for each day of delay (17), it is suggested that Gram staining performed with well-trained experienced personnel would be more effective together with molecular methods which are being used more frequently nowadays.

As conclusion, there is no gold standard to distinguish true pathogens from contaminant agents in blood cultures. There is no one and only reason for blood culture contamination; but reasons may be various such as inadequate sampling, sampling with inappropriate technique, insufficient number of set or insufficient number of bottles in a set and patient's disease profile. Although coagulase negative staphylococci are the most frequently isolated contaminant, it should be kept in mind that these microorganisms are the most common causative agent of nosocomial infection. Hospitals and / or units should monitor blood cultures by evaluating contamination rates and quality indicators reported in the guidelines in order to reduce patient costs and prevent inappropriate antibiotic therapy and the associated antibiotic resistance. Furthermore, it is thought that regular training and continuous feedback on personnel compliance will ensure continuity in this regard; contamination rates will decrease, and quality indicators will improve.

Disclosure statement

No potential conflict of interest was reported by the authors.

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RESEARCH ARTICLE

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The Prevalence of Multimorbidity Among Adults Aged 40 Years and Above in Primary Care Setting: A Cross-Sectional Study

ABSTRACT

Objective: Coordination function of primary care (PC) enables continuous, efficient, and cost-effective health care provided to patients with chronic disease and multimorbidity (MM). The aim of this study was to identify the most common chronic diseases and to determine the prevalence of MM in PC registries.

Methods: Our study is a cross-sectional study. All the individuals aged 40 and over who were registered to the primary care units (PCUs) of the Uskudar district of Istanbul have formed the population of the study. A systematic cluster sampling was used. The patient list of each family physician in Uskudar district was accepted as a cluster and an equal number of patients from each cluster were enrolled. Only the information on the patients' MM data was requested from the primary care physicians.

Results: The 108 physicians of the Uskudar district (response rate: 73.4%) gave consent to participate in the study. The 1187 (40.3%) of registered patients of all PCUs were 40 years old and over. The multimorbid patients were found as 330 (27.8%).

Conclusions: Approximately, one of four patients have multimorbidity. So, the policy of primary care services should be redesigned for the management of MM patients including the 'goal-oriented care' approach.

Keywords: Multimorbidity, Physicians, Primary Care, Prevalence, Health Policy.

Birinci Basamakta 40 Yaş Ve Üzeri Yetişkinlerde Multimorbidite Prevalansı: Kesitsel Bir Çalışma

ÖZET

Amaç: Birinci basamağın (BB) koordinasyon işlevi, kronik hastalığı ve multimorbiditesi (MM) olan hastalara sağlanan sağlık hizmetlerinde sürekli, verimli ve uygun maliyetli sağlık bakımını sağlar. Bu çalışmanın amacı BB kayıtlarında en sık görülen kronik hastalıkları ve MM prevalansını belirlemektir.

Gereç ve Yöntem: Çalışmamız kesitsel bir çalışmadır. İstanbul'un Üsküdar ilçesine bağlı Aile Sağlığı Merkez'lerine (ASM) kayıtlı 40 yaş ve üzerindeki tüm bireyler çalışmanın evrenini oluşturmuştur. Örneklemin seçiminde sistematik küme örneklemesi metodu kullanılmıştır. Üsküdar ilçesindeki her aile hekiminin hasta listesi küme olarak kabul edilmiş ve her kümeden eşit sayıda hasta kaydedilmiştir. Birinci basamak hekimlerinden sadece hastaların MM verileri ile ilgili bilgiler istenmiştir.

Bulgular: Üsküdar ilçesinin 108 hekimi (yanıt oranı:% 73,4) çalışmaya katılmayı kabul etmiştir. Tüm PKB'lerde kayıtlı hastaların 1187'si (% 40,3) 40 yaş ve üzerindeydi. Multimorbid hastalar 330 (% 27,8) olarak bulunmuştur.

Sonuç: Yaklaşık olarak dört hastadan biri multimorbiditeye sahiptir. Bu nedenle, BB sağlık hizmetleri politikası, MM hastalarının yönetimi için "hedefe yönelik bakım" yaklaşımı dahil olmak üzere yeniden tasarlanmalıdır.

Anahtar Kelimeler: Multimorbidite, Birinci Basamak, Hekim, Sağlık Politikası, Prevalans.

INTRODUCTION

The World Health Organization (WHO) defined 'multimorbidity' (MM) as the presence of two or more chronic diseases simultaneously in the same individual (1). MM was also defined as any combination of chronic disease with at least one other disease (acute or chronic) or bio-psychosocial factors (associated or not) or somatic risk factors by The European General Practice Research Network (EGPRN) (2).

The biggest challenge in dealing with MM is the definition of chronic disease. There are also different definitions for chronic disease. WHO defines the chronic disease as a health problem requiring follow-up or treatment for many year (3). According to ICPC-2 (International First Step Classification-2), chronic disease has a pattern of recurrence or worsening for at least 6 months that is expected to continue, with a poor prognosis, which may lead to consequences or sequelae that may affect the quality of life of the person (4).

Family medicine, with its holistic, person centred and comprehensive approach, plays an important role in the management of chronic diseases. Especially, coordination function of primary care enables continuous, efficient and cost effective health care provision to patients with chronic conditions. Also, it is important to know the prevalence of MM to develop and improve health policy for primary care (5).

Barnett et al. found MM prevalence as 23.2% among registered patients and the prevalence of MM increased substantially with age and was present in most people aged 65 years and older (6). Prevalence of MM was reported as between 14.5% and 29.0% in primary care settings (7). In Dutch study, the MM data was collected from family medicine registries and the prevalence was reported as 34.7% among 40-59 years old, 63.1% among 60-79 years old, and 78.2% among 80+ years old (8). In Turkey, we have some data regarding individual prevalence of major chronic diseases like diabetes prevalence from The Turkish Diabetes Epidemiology Study (TURDEP), to our knowledge, there is no data regarding MM prevalence of the registered population to primary care units (PCUs) (9,10).

The aim of this study was to identify the most common chronic diseases and to determine the prevalence of MM in the older than 40 years population enrolled in the PCUs in Uskudar district of Istanbul in primary care registries.

MATERIAL AND METHODS

Our study is a cross-sectional study. In a systematic review of MM prevalence, Fortin et al. found that the prevalence of MM in individuals aged 40 years and older showed a sharp increase compared to under 40 years of age (11). Therefore, all the individuals aged 40 and over who were registered to the PCUs of the Uskudar district of Istanbul have formed the population of the study. Our study was conducted between 04/31/2015 - 08/31/2015. In the district of Uskudar, a population of 40 years and over was identified as 208964 persons who registered to PCUs. In order to represent the research population, with 95% confidence level and 3% standard deviation, the estimated sample size was 893.

A systematic cluster sampling was used. The patient list of each family physician in Uskudar district was accepted as a cluster and an equal number of patients from each cluster were enrolled. There were 147 primary care physicians (PCPs) in the Uskudar district. In order to reach 893 patients with a presumption of 60% of physicians' participation into the study, 11 patients from the patient registration list of each PCP were randomly selected using the national identification numbers of the patients. Online program called 'Research Randomizer' was used for randomization (12). PCPs accepted to participate in the study were in charge of the randomization process and sent the requested data from the patient records anonymously to the researchers.

Only the information of the patients' MM data was requested from the family physicians. In our study, we used the definition of Julie O'Halloran et al. and the definition of WHO for MM(1,4).

The database used in primary care in Turkey includes all state (including primary care) and private outpatient visits of the patients. The type of visit (primary or secondary care) and diagnosis were the main variables gathered from the data provided by PCPs. The researchers visited each PCU at least 2 times during the study period. Patients, who could not be reached due to reasons such as off day and sickness, absence during these two visits, were not included in the study. Patients of PCPs refused to participate in the study were also excluded.

Our study was approved by Marmara University Institute of Health Sciences Ethics Committee. (Date/Protocol number: 29.04.2015-20/60)

SPSS 16.0 program was used to analyze the data. Firstly, descriptive statistics (percentage, mean standard deviation, etc.) of the data were calculated. Then, in the comparative analysis, chi-square was used to test the difference between the two groups and the t-test was used for the significance of the difference between the two means. The p-value <0.05 was considered significant.

RESULTS

108 PCPs (response rate: 73.4%) gave consent to participate in the study and share their patients' characteristics and diagnosis (Fig 1). The 40 years and over ages registered patients of all PCUs were determined as 1187 (40.3%).

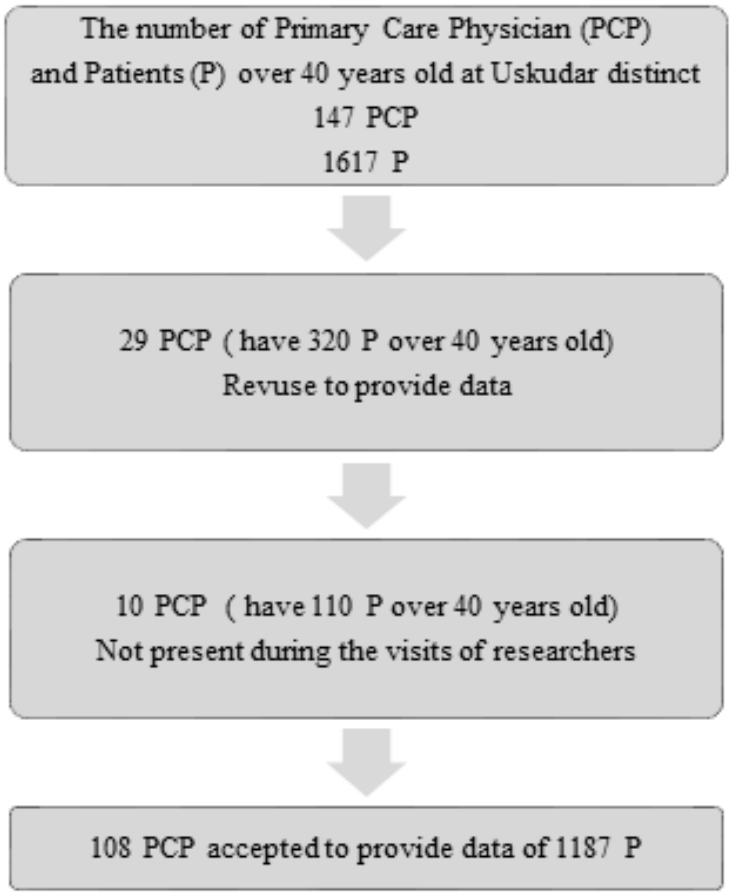

Figure. 1. Flow charts for participation status of primary care physicians

Among the 1187 patients, 596 (50.2%) were female and 591 (49.8%) were male. The mean age was 55.5 ± 12.2 years (56.6 ± 12.4 years for female, 54.4 ± 11.9 years for male). The 917 (77.4%) of the patients were under 65 years of age and 267 (22.6%) of them were 65 years and above.

Considering all the participants, the MM patients were found as 330 (27.8%). The prevalence of MM among women was significantly higher than the men. Additionally, the prevalence of MM in patients aged 65 years and older was significantly higher than below 65 years old (Table 1).

Table 1. Prevalence of multimorbidity distribution by gender and age of 65 years

$x^2=40,81$ $p<0,001$		Gender		Total
		Women N (%)	Men N (%)	
MM	No	381 (63.9)	476 (80.5)	857 (72.2)
	Yes	215 (36.1)	115 (19.5)	330 (27.8)
Total		596 (50.2)	591 (49.8)	1187 (100.0)
$x^2=137,73$ $p<0,001$		Age		Total
		65<y N (%)	**65>y** N (%)	
MM	No	738 (80.5)	119 (44.1)	857 (72.2)
	Yes	179 (19.5)	151 (55.9)	330 (27.8)
Total		917 (77.3)	270 (22.7)	1187 (100.0)

MM: Multimorbidity

Patients with MM had significantly more visits to PCUs and hospitals within a year compared to their peers without MM. *(PCU: t:26,13 p<0,001; Hospital t:11,30 p<0,001)*

There was a significant relationship between age and chronic disease number, shown on Table 2. There was no significant relationship for gender and number of chronic diseases ($p > 0.05$).

Table 2. Prevalence of multimorbidity distribution by gender and age of 65 years

		MM Only 2 CD	MM 3 and over CD	Total
Age *p: 0.031*	Below 65 years old, N (%)	83 (25.1)	117 (35.6)	200 (60.6)
	65 years and older, N (%)	38 (11.4)	92 (27.9)	130 (39.4)
Total, N (%)		121 (36.5)	209 (63.5)	330 (100.0)
		MM Only 3 CD	MM Over 3 CD	Total
Age *p: 0.046*	Below 65 years old N (%)	60 (28.5)	33 (16.0)	93 (44.5)
	65 years and older N (%)	57 (27.5)	59 (28.0)	116 (55.5)
Total		117 (56.0)	92 (44.0)	209 (100.0)

MM: Multimorbidity, CD: Chronic Disease

While 519 (43.7%) of the participants had at least 1 chronic disease, women were 340 (57.0%) and men were 179 (30.3%). No any chronic disease was detected in 602 (65.6%) of individuals under 65 years of age. This rate falls to 63 (23.6%) in 65 years and older.

The most common disease in our study was hypertension found in 318 (26.8%) patients. The second one was diabetes mellitus observed in 130 (11%) and the third one was depression as 90 (7.6%) (Fig 2).

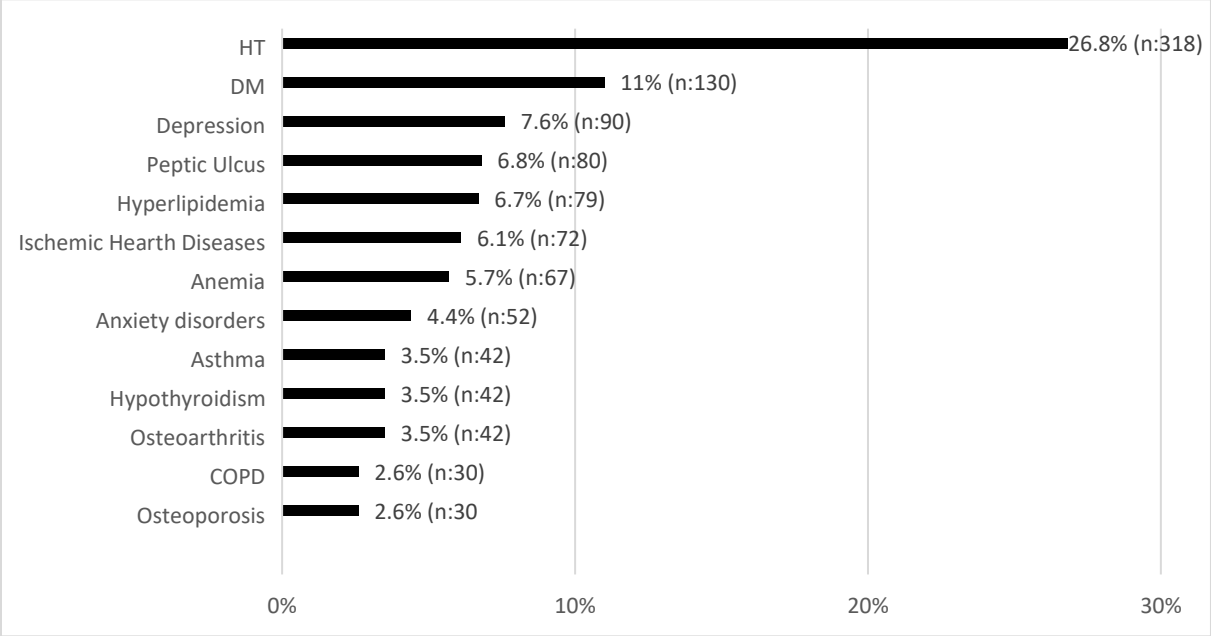

Figure 2. The most common chronic diseases seen on multimorbidity patients

In women, the most common diseases were: hypertension 202 (33.9%), diabetes mellitus 85 (14.3%) and depression 64 (10.7%). In men, that was the most important difference between women and the general population, depression was not included in the first 3 most common diseases, and ischemic heart disease was located in the 3rd place.

A dramatic increase in the prevalence of hypertension was observed in patients aged 65 and older. In patients aged 65 years and older, the prevalence of hypertension was 168 (62.9%), the prevalence of diabetes was 57 (21.3%), and the prevalence of ischemic heart disease was 46 (17.2%).

DISCUSSION

In our study, the prevalence of MM was found as 27.8% for the population aged 40 and above. The prevalence of MM among women was statistically significantly higher than the men, and the prevalence of MM in patients aged 65 years and older was 55.9% and significantly higher than below 65 years old. It was observed that individuals aged 65 years and over were more likely to visit the CPUs and hospitals in a year than the 40-65 age

group. The most common disease in our study was hypertension found in 318 (26.8%) patients. The number of chronic diseases in MM patients aged 65 years and over was higher than in the 40-64 age range, but no significant difference was found in increasing chronic disease numbers by sex.

Designing the prevalence studies of MM have some difficulties due to the existence of different definitions of MM and chronic diseases, different patient data sources. The number of patients included in the study, the age of patients, the number of diseases taken into account, the region where the study is done, the variety of data sources (date based on individual reports, questionnaires or medical record systems, etc.) lead to a variety of prevalence information (13). Different studies have been designed with different chronic disease codes in primary care. Hwang et al. consider 185 diseases and symptoms as chronic within 585 diagnostic codes, were identified in the ICD-9 (14). Taking these differences into consideration comparisons of the MM studies should be done with caution. As our study, some other studies in primary care settings accepted MM definition as 2 or more chronic diseases (15). We used ICPC-2 to characterize any disease as chronic disease (4).

The prevalence of MM was found 66.2% based on medical data of patients over 50 years of age enrolled in three PCUs in Ireland. The number of visits to the PCUs in a year increased in parallel with the number of chronic diseases (16). This finding is similar with our study. Brett et al. stated the prevalence of MM as 52%. According to the age ranges of patients, the prevalence of MM was found to be 75,5% for 45-64 years, 87,5% for 65-74 years and 97,1% for older than 75 years (17). In our study, prevalences in these ranges were as follows; 24.1%, 51% and 62.7%. Brett et al. evaluated only the applicants, but we also selected the non-applied population to PCUs based on an online registry system listed to represent the whole population. Therefore, our study represented low prevalences. Although MM prevalence was studied previously, especially in developed countries, there are a limited number of studies for Turkey. Our study is the last study to determine the prevalence of MM in primary care, so the results are important in terms of giving an idea about the Turkish population.

In Switzerland, the study investigating the chronic disease patterns of MM patients, used ICPC-2, the rate of chronic diseases in MM patients was 74% hypertension, 31% diabetes and 29.1% ischemic heart disease (18). Differently, the first three common chronic diseases in our study were hypertension, diabetes and depression.

In the study of Gulbayrak et al., data of 3038 patients over 60 years of age who applied to a primary care unit were screened from polyclinics, and as a result 51.2% of patients had chronic disease and 5.1% had comorbidities (19). But, in this study there was no randomisation and the study population based on patients visited PCUs. Since our study has a representative sample, our results reflect prevalence more precisely. In our study, the rate of MM was found 77.3% and the prevalence of 3 most common diseases were hypertension 168 (62.9%), diabetes 57 (21.3%) and ischemic heart disease 46 (17.2%) in patients 65 years old and over.

In 2011, 'The Prevalence and Risk Factors of Chronic Diseases Study in Turkey' determined the prevalence of hypertension as 24%, diabetes mellitus 11%, and hyperlipidemia 11.2% (9). According to the TURDEP-2 study, the prevalence of hypertension was 25.6% and the frequency of diabetes was 13.7% (10). It can be emphasized that our hypertension and diabetes prevalence are similar to 'The Prevalence and Risk Factors of Chronic Diseases Study in Turkey' and TURDEP-2 studies.

According to the data of the Ministry of Health, patients are admitted to a health care units on average 8.2 times in a year (2.9 times for PCUs, 5.3 for hospitals) and multimorbid patients had more visits in PCUs (mean: 7.01 vs 1.6) and hospitals (mean: 5.5 vs 2.1) within a year compared to non-multimorbid patients (20). Our results showed that the patients visited the health care units with a total of 6.05 times within a year (3.05 times to PCU and 3.00 to the hospital) which were less than the data of the Ministry of Health. These differences may be the cause of our methods of getting patients data.

According to our study, the frequency of MM is not to be neglected in our population. Parallel to the increasing frequency of MM, the responsibility of PCPs have increased in multimorbid patients' follow-up.

The current approach, based on the partial handling of multiple chronic diseases by different experts in hospital settings, is expensive and burdensome. Also, hospital based approaches with various medical specialities have uncertain benefits, and also have potential to cause harmful effects to multimorbid patients (21).

Effective primary care reduces the risk of hospitalization by preventing impairment of health, so it helps to control acute disease periods and to cope with chronic conditions (22). PCPs should better manage this situation in principles of family medicine (23).

It was stated that a care model focusing on eradication of disease and decrease of mortality have not fit very well to the management of chronic diseases. The researchers therefore proposed a 'goal-oriented care' approach, which encourages each individual to reach the highest levels of health care as defined by patients (24). Goal-oriented approach is very important for MM, because when the to-do list becomes too long and complex, it is necessary to make a ranking of importance with

multimorbid patients. This approach strengthens competencies rather than eliminating insufficiencies, which stimulates the patient's self-management and induces to get better by putting resistance instead of anxiety. This is the most rational and appropriate way to determine the patient's own goals. The task that is difficult to achieve in a goal-oriented approach is to find suitable ways for the patient to discover his treatment goals. One of the important challenges for PCPs is to explain the concept of goal-oriented care to colleagues, patients and their relatives. PCPs should also have to overcome the effects of a cultural and political climate where ordinary people are hard to hear in a health system which focuses on diseases more than the patients (25).

The chronic diseases management should start in the medical school training and continue by updating according to the requirements in practice after graduation. Besides the basic and clinical knowledge, effective communication skills and counseling, patient advocacy, and skills to be used to create behavioral change in society should be developed.

In management of the chronic disease, a team consisting of PCPs and allied health professions including the nurse, dietitian and psychologist should work together to improve care and ensure changes in the health behaviors of chronic patients. Therefore, the structure of primary care should be redesignated as multi-professional teams for the management of chronic diseases (9).

The limitations of our study can be listed as follows;

- Since the basis of our data is the diagnostic codes entered in the registration system, it was not possible to obtain confirmation from the patient or the physician.
- Diagnosis based on electronic records filled by PCPs. We were not able to check accuracy of the given diagnosis.
- Our results reflect only the Uskudar district of Istanbul and can be generalized to the whole Turkey but to many similar urban districts like Uskudar.

CONCLUSION

Approximately, one of four patients, and more than half of those with a chronic disorder, have MM. The main reasons why MM has gained importances are the ageing of population and financial pressures by increasing MM. The challenges associated with MM have become more visible, and now, the management of multimorbid patients are more important than yesterday. The current approach, based on the partial handling of multiple chronic diseases by different specialists in hospital settings, is expensive and burdensome. PCPs handle multimorbid patient's problems and overcomes responsibilities with a holistic and patient-centered approach, which are included in characteristics of family medicine. So, primary care should be strengthened and taken to ensure that each MM patient can access PCPs. Indeed, even in a health system where patients have direct access to medical specialists, PCPs should play a key role as coordinator for multimorbid patients. In conclusion, the structure of primary care should be redesigned for the management of multimorbid patients including ‘goal-oriented care’ approach and giving the responsibility of coordination of care to family physicians.

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RESEARCH ARTICLE

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The Prevalence and Associated Factors of Elderly Abuse: A Cross-Sectional Study

ABSTRACT

Objective: The prevalence of elderly abuse varies between 2.2% and 30.1% in European countries. There is a limited number of studies that have investigated elderly abuse in Turkey. The aim of this study is to detect the prevalence and risk factors of elder abuse, identify the factors that can affect elderly abuse, and assess the possible measures to prevent this problem.

Methods: We stratified the districts enrolled in family health centers to ensure that participants were from diverse social, cultural, and economic backgrounds of Edirne and formed a representative sample of 211 people. In addition to sociodemographic characteristics, our survey consisted of the Hwalek-Sengstock Elder Abuse Screening Test, the Geriatric Depression Scale-short form, the Standardised Mini-Mental State Examination, the Barthel Index for activities of daily living, and the Lawton-Brody instrumental activities of daily living scale.

Results: The prevalence of elderly abuse was determined as 9.9%, and high abuse risk was 15.2%. We found that abuse risk was higher among older people who had no social security, lived alone, were abused physically or emotionally before, reported having bad family relations, and had fewer rooms at home which leads to a lack of privacy. Furthermore, we found significant relationships between abuse risk and the depression score.

Conclusions: Elderly abuse is a risk for every person regardless of gender, education level, and economic status. As an invisible problem for societies, elderly abuse brings a great burden by leading to the loss of physical, mental, and psychological health. Preventive measures should be the primary goal. All results suggest that governments, non-governmental organizations, and health care providers should combat this problem by increasing patient literacy and ensuring lifestyle changes.

Keywords: Elderly Abuse, Risk Factors, Living Arrangements, Community Health.

Yaşlı İstismarı Prevalansı ve Etkileyen Faktörler: Kesitsel Bir Çalışma

ÖZET

Amaç: Yaşlı istismarı prevalansı Avrupa ülkelerinde %2,2 ile %30,1 arasında değişmektedir. Türkiye'de yaşlı istismarını inceleyen sınırlı sayıda çalışma mevcuttur. Bu çalışmanın amacı yaşlı istismarı prevalansı ve risk faktörlerini saptamak, yaşlı istismarını etkileyen faktörleri tespit etmek ve nu sorunu önlemek için alınabilecek tedbirleri değerlendirmektir.

Gereç ve Yöntem: Katılımcıların tüm sosyal, kültürel ve ekonomik kesimlerden olması için aile sağlığı merkezleri nüfusları üzerinden tabakalandırma yapılarak 211 kişilik örneklem oluşturulmuştur. Sosyodemografik özelliklere ek olarak Hwalek-Sengstock Yaşlı İstismarı Tarama Testi, Geriatrik Depresyon Ölçeği Kısa Formu, Standardize Mini Mental Durum Testi, Barthel Günlük Yaşam Aktiviteleri İndeksi ve Lawton-Brody Enstrümental Günlük Yaşam Aktiviteleri Ölçeği ankete dahil edilmiştir.

Bulgular: Yaşlı istismarı prevalansı %9,9 ve yüksek istismar riski %15,2 olarak tespit edilmiştir. Sosyal güvencesi olmayan, yalnız yaşayan, daha önce fiziksel veya duygusal istismara uğramış, aile ilişkilerinin kötü olduğunu bildiren ve mahremiyet eksikliğine yol açacak şekilde evinde az sayıda odası olan yaşlılarda istismar riskinin daha yüksek olduğu tespit edilmiştir. Yapılan regresyon analizinde istismar riski ile depresyon skoru arasında anlamlı ilişki bulunmuştur.

Sonuç: Yaşlı istismarı cinsiyet, eğitim düzeyi ve ekonomik durumu ne olursa olsun her insan için bir risktir. Toplumlar için görünmez bir sorun olan yaşlı istismarı, fiziksel, zihinsel ve psikolojik sağlık kaybına yol açarak büyük bir yük getirmektedir. Önleyici tedbirler öncelikli hedef olmalıdır. Tüm sonuçlar hükümetlerin, sivil toplum kuruluşlarının ve sağlık hizmeti sağlayıcılarının hasta okuryazarlığını artırarak ve yaşam tarzı değişiklikleri sağlayarak bu sorunla mücadele etmesi gerektiğini göstermektedir.

Anahtar Kelimeler: Yaşlı İstismarı, Risk faktörleri, Yaşam Düzenlemeleri, Toplum Sağlığı.

INTRODUCTION

The share of elderly people is increasing within the total population as populations age. The number of older people aged above 65 will increase from 9% to 16% globally between 2019 and 2050 (1). By 2030, the elderly population is expected to increase by 140% in low- and middle-income countries and by 51% in high income countries (2). An increase in the elderly population comes with new problems that differ markedly from problems presented by young populations. One of those problems is elderly abuse, which also has a legal aspect.

The U.S. National Academy of Sciences defines abuse as 'intentional actions that cause harm or serious risk of harm (whether or not harm is intended) to a vulnerable elderly persons by a caregiver or other person who stands in a trusting relationship to the elder or failure by a caregiver to satisfy the elderly person's basic needs or to protect the elderly person from harm' (3,4). While elderly abuse is considered as a type of violence, it has not been studied as much as other types of violence. Elderly abuse can be classified as physical, sexual, psychological, financial, and anti-constitutional.

According to data from around the world, 6% of older people experience abuse once a month at best (5). Furthermore, various studies on this topic have suggested the ratio of elder abuse varies between 7.4% and 11.4 % in the U.S.A. and between 2.2% and 30.1% in some European countries (6). A meta-analysis, which was supported by WHO and which included 52 studies from 28 geographically-diverse low and middle income countries, found that the prevalence of elderly abuse was 15.7% (7). It was notable that 64.2% of elderly abuse cases were reported by health staff (8).

Prevention is the most important factor in terms of abuse, as for every other health issue. Our evidence-based information is insufficient to prevent abuse, and most information is either anecdotal or based on poorly designed and executed studies (6). Once abuse happens, it leads to severe physical, psychological, and social problems that are very difficult to reverse (7). The risk factors associated with elder abuse should be eliminated through interventions for both elderly people that are open to abuse and potential abusers (9-11).

The most effective method of preventing abuse is to raise awareness among older people regarding this topic. A study showed that patient training on preventing elder abuse can decrease abuse by 21% by itself (11).

Elderly abuse and neglect have become more frequent with the growth of the elderly population. Studies have shown that abuse is a preventable problem (6). Family physicians are health professionals who can easily observe older people in their environment, so they can detect the presence or risk of abuse more easily. Older people may hide abuse as they fear legal processes which may break family ties. Therefore, it is important for health professionals to know the risk factors of abuse to eliminate them.

This study aimed to detect the prevalence and risk of elderly abuse and identify the factors that can affect elderly abuse. Our study was the only one that heads towards elderly abuse in Edirne, Turkey which is a European border city with European relations and interactions are intensive.

MATERIAL AND METHODS

This study was conducted in Edirne city centre. According to Edirne Provincial Health Directorate, there were 15678 people aged 65 and over whom formed our universe. To calculate the minimum sample volume, we used the study by Ergin et al. (12) conducted in Aydın, where the prevalence of elderly abuse was 14.2%. We used that study because Aydın and Edirne share similar socioeconomic and cultural structures.

Assuming the true prevalence of 14.2%, and using 5% type 1 error and 80% power, we made a stratification according to the districts enrolled to 20 family health centres (31 units inside the centres); thus the participants were from all social, cultural, and economic backgrounds of Edirne. The number of males and females calculated separately according to the ratio in the total elderly population until the total number exceeded the minimum sample size.

We received approvals from the Scientific Researches Ethics Council of Trakya University (numbered 2017/70) and from the Provincial Public Health Directorate of Edirne. We randomly chose 211 participants between March and June 2017 and met with 103 females and 108 males aged over 65, who lived in the city centre of Edirne. These randomly selected people were reached by phone or by going to their neighbourhood and a meeting time scheduled. One researcher met the participants face-to-face and alone in the family health centres or in the participants homes, depending on the participants' request, and implemented the questionnaires. The researcher was trained on the use of scales beforehand and applied all the questionnaires to ensure standardization. Participants' personal identity information was not recorded. They were informed verbally, and their consent was received before participation. If they didn't want to participate, didn't want to continue because of any reason, they were excluded from the study and replaced by another random chosen elderly from the same district. Each questionnaire took about 30 minutes to apply.

The survey first provided information regarding the topic; and has been checked by receiving feedback. Then, it listed 34 questions on the following; participants' sociodemographic characteristics; whether they had any chronic

diseases; relationship with family, relatives, neighbours and friends; whether they experienced abuse; the features of their residence; and whether they knew about the social support hotline '183' for abuse counselling.

In addition, the survey included the following; the Hwalek-Sengstock Elder Abuse Screening Test (HS-EAST), including 14 questions that evaluated abuse risk; the Geriatric Depression Scale-short form (GDS), including 15 questions that evaluated depression in older people; the Standardised Mini Mental State Examination (SMMSE), evaluating cognitive functions; the Barthel Index for Activities of Daily Living (BI-ADL), evaluating daily life activities; and the Lawton-Brody Instrumental Activities of Daily Living Scale (LBIADLS), evaluating the instrumental activities of daily life. Although the highness of the HS-EAST score indicates a potential increase in the risk of elder abuse, a score of 3 or more can be interpreted as the presence of abuse (13). They all have Turkish validity and reliability studies and suitable for using in Turkish elderly population (13-17).

We checked normality assumption using Shapiro-Wilk tests prior to the hypothesis tests. Mann-Whitney U test was used to compare two independent groups, while Kruskal-Wallis test was used to compare more than two independent groups. Spearman correlation coefficient was used to evaluate relationships between numerical variables. Multiple linear regression with stepwise selection was used to investigate relationships between HS-EAST and other scales. Median and interquartile range were used for numerical variables, while frequency and percentage used for categorical variables. A $p<0.05$ considered as statistically significant.

RESULTS

Of the 211 elderly people in the study, 48.8% (n=103) were women. The mean age was 72.0±6.5 (65-92) years. The prevalence of elderly abuse was 9.9% (n=21; seven females, 14 males). When we evaluated the abuse risk with using HS-EAST, there was no difference between genders ($p>0.05$), but abuse happened twice as much in females. Mean HS-EAST score was 1 (0-11). HS-EAST score was 3 or more in 15.2% (n=32) of participants which can be interpreted as the presence of abuse.

The abuse risk was higher among elderly people who had no or low social security ($p=0.016$), were abused physically ($p<0.001$) or emotionally ($p<0.001$) before, reported having bad family relations ($p<0.001$), and had fewer rooms at home ($p=0.002$). Only one abused person knew about the social support hotline '183' for abuse counselling, and this person never called the hotline.

We found negative correlation between the amount of total house income and abuse risk ($p=0.001$); but there was no relationship between abuse risk and the amount of self-income ($p>0.05$). Table 1 indicates the relationship between HS-EAST score and some sociodemographic characteristics of the participants.

Table 1. The relationship between HS-EAST score and sociodemographic characteristics of participants

	n (%)	HS-EAST Median Score (IQR*)	p
Gender			
Male	108 (51.2)	1 (2)	p = 0.876
Female	103 (48.8)	1 (2)	
Education			
Illiterate	17 (8.1)	1 (4)	
Literate	27 (12.8)	1 (1)	
Primary school	115 (54.5)	1 (2)	p = 0.835
Secondary school	14 (6.6)	1 (2)	
High school	25 (11.8)	1 (1)	
University	13 (6.2)	1 (1)	
Marital status			
Single	5 (2.4)	2 (7)	
Married	143 (67.8)	1 (2)	p = 0.069
Widow	63 (29.9)	1 (2)	
Working status			
Not working	197 (93.4)	1 (2)	p = 0.665
Working	14 (6.6)	1 (2)	
Have self income			
No	49 (23.2)	1 (2)	p = 0.081
Yes	162 (76.8)	1 (2)	
Living in own home			
No	75 (35.5)	1 (2)	p = 0.169
Yes	136 (64.5)	1 (2)	
Living alone			
No	171 (81.1%)	1 (2)	**p = 0.033**
Yes	40 (18.9%)	1 (3)	
Chronic disease			
No	38 (18)	1 (1)	p = 0.259
Yes	173 (82)	1 (2)	
Incompatibility in home			
No	191 (90.5)	1 (2)	**p = 0.005**
Yes	20 (9.5)	2 (3)	

* Interquartile Range

According to the cognitive status, we found that 21.3% (n=45) had moderate dementia, and only 1.4% (n=3) had severe dementia. There was no significant relationship between cognitive status and abuse risk ($p>0.05$). The median GDS score was 3 (0-15). We found a relationship between depression and abuse risk ($p<0.001$).

The median BI-ADL score was 100 (min:60 max: 100). Mean LBIADLS score was 7.1 ± 1.25 (median: 8). We found no significant relationship between abuse risk and daily life activities ($p > 0.05$) and between abuse risk and instrumental activities of daily living ($p>0.05$) (Table 2). Table 2 shows the relationship between HS-EAST score and SMMSE, GDS, BI-ADL and LBIADLS scores.

Table 2. Relationship between HS-EAST and SMMSE, GDS, BI-ADL, LBIADLS

	n (%)	HS-EAST Median score (IQR*)	p
SMMSE			
normal	163 (77.2)	1 (2)	
moderate dementia	45 (21.3)	1 (2)	p = 0.063
severe dementia	3 (1.5)	1	
GDS			
normal	138 (65.4)	1 (1)	
mild depression	48 (22.7)	1 (2)	**p < 0.001**
moderate depression	17 (8.1)	2 (3)	
severe depression	8 (3.8)	5 (3)	
BI-ADL			
fully independent	165 (78.2)	1 (2)	
mildly dependent	24 (11.4)	1 (2)	p = 0.242
moderately dependent	21 (10)	1 (2)	
highly dependent	1 (0,4)		
LBIADLS	211 (100)	8 (1)	p = 0.251

* Interquartile Range
SMMSE: Standardised Mini Mental State Examination; GDS: Geriatric Depression Scale-short form; BI-ADL: Barthel Index for Activities of Daily Living; LBIADLS: Lawton-Brody Instrumental Activities of Daily Living Scale

Multiple linear regression analysis is performed to investigate the effects of clinical variables on HS-EAST score. The results showed that only GDS has a significant, independent and negative effect on HS-EAST score (p<0.001) (Table 3).

Table 3. Multiple linear regression of SMMSE, GDS, BI-ADL and LBIADLS on HS-EAST score

	Coefficient	Standard Error	p
SMMSE	0.322	0.241	0.182
GDS	0.247	0.032	**<0.001**
BI-ADL	0.003	0.021	0.874
LBIADLS	-0.059	0.101	0.557

SMMSE: Standardised Mini Mental State Examination
GDS: Geriatric Depression Scale-short form
BI-ADL: Barthel Index for Activities of Daily Living
LBIADLS: Lawton-Brody Instrumental Activities of Daily Living Scale

DISCUSSION

In our study, the prevalence of elderly abuse was 9.9%. There was no statistically significant differences between genders (p>0.05).

A study in Manisa reported that elder abuse was 8% (18); and the study by Ergin et al. (12) found that the prevalence of elderly abuse was 14.2%. It is difficult to reach sufficient and correct data about elderly abuse which is a hidden and social issue. Although the definition of elderly abuse has not changed, the differences between cultures can affect the perception and detection of elderly abuse. Elderly people and aging people should know the definition of elderly abuse; and they should be aware of the results of elderly abuse and its effects on health (19).

We found that the abuse risk was lower among older people who had social security. Similarly, Ergin et al. (12) found that lack of social security was a risk factor for psychological abuse. In particular, lack of social security leads older people to loneliness and prevents them from getting health services due to financial difficulties. Therefore, the existence of social security is a protective factor against abuse (10). In Turkey, the state guarantee for infants and children can be implemented for older people, and it can serve as a powerful measure to prevent abuse.

In our study, there was no significant relationship between education level and abuse risk. Similarly, the systematic review by Johannesen et al. (9) reported that education level was not a risk factor for abuse. This makes us consider the possibility that abuse is a problem for older people from all sociocultural levels.

We found negative correlation between the amount of total house income and abuse risk; but the self-income of the elderly did not affect the risk of abuse. Economic status of the family has a significant effect on elderly abuse. This result makes us think that, if we want to prevent elderly abuse, we need to raise not only the economic level of the elderly, but families to a better level.

The abuse risk was higher for elderly people who lived alone (9). Whereas some studies have reported that those living with caretakers and children had a higher risk of abuse, other studies have reported results similar to our study (9,10,20). Living alone can cause social isolation, depression, and physical, emotional, economic, and medical neglect. In addition, those living alone are more vulnerable to abuse as they are more defenceless. Therefore, having more active social lives protects older people from abuse as well (10).

Our study found that the abuse risk was higher among elderly people who defined their domestic relations as problematic. Studies by Kissal

and Johannesen reported similar findings (9,19). As possible domestic problems affect the whole family, counselling should be provided for family members, and attention should be paid to keeping domestic relations healthy (19).

We found that repetition risk was higher among previously abused elderly people. In our study, 4.7% of participants experienced physical abuse, and 7.6% experienced emotional abuse. Any case of abuse detected around older people should be alarming and preventive measures should be taken without delay.

Elderly abuse is probably higher than reported cases. It may be difficult for older people to report abuse due to various reasons. Perception of abuse may also change due to cultural differences.

Home environment can pose a risk for elderly abuse. In our study, we found that fewer rooms in a house and probably certain types of heating could be risk factors. It is not possible to have privacy in houses with stoves because families usually gather in one room. This may lead to intolerance and abuse. Studies by Keskinoglu and Goodrich reported that an unfit home environment can lead to abuse and neglect for older people (21,22). Risks in living environments of older people can be detected by making house calls, and remedial measures can be applied (23). Also, health care providers can detect abuse by examining clues. Visible lacerations or bruises on the skin during examination are alarming (19). Conditions can be improved for poor families with the support of state entities and nongovernmental organisations (NGOs).

Due to the Covid-19 pandemic, social isolation has increased for older people who are at higher risk. Curfew has been declared in Turkey and many other countries. Time spent at home has increased globally. The expected result of home isolation and increased time spent with family in closed quarters is an increased risk of abuse and neglect for older people in some families (20). Particularly with the addition of psychological burden and intolerance, this may lead to worse problems. Health professionals will have a bigger role to play after the pandemic to prevent those problems.

We found a positive and significant relationship between depression score and elderly abuse risk. Depression or depressive symptoms have been associated specifically with emotional and physical abuse in the United Kingdom, China, and Canada (3). We found no studies in Turkey regarding depression. We thought that depression causes social exclusion in older people and makes them more dependent on other people, thus increasing the risk of abuse.

Although we did not find a significant relationship between cognitive functions and abuse risk, some studies like Dong et al. (24) reported that lowered cognitive functions were associated with increased risks of physical and emotional abuse in the USA. Living with and caring for a dependent older person with low cognitive functions may trigger burnout syndrome. This challenging situation can lead to elder abuse. Providing training to caregivers can build awareness of this and prevent abuse (19).

As the limitation of our study; although we could not find a significant relationship between elderly abuse and BI-ADL and LBIADLS scores, the number of participants remained low to achieve definitive results.

CONCLUSION

Elderly abuse is a risk for all elderly persons regardless of gender and education level. In addition, living alone, incompatibility at home, having bad family relations, scarcity of total house income, history of abuse, lack of social security and factors that can cause depression are risk factors for elderly abuse. Preventive measures should be the primary goal. We think that the supportive role of the society can reduce these problems with the help of the state and NGOs.

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RESEARCH ARTICLE

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Mediation Effect of Depression on the Association between Food Addiction and Body Image in Individuals with Obesity

ABSTRACT

Objective: This study aimed to examine the mediation effect of depression on the association between food addiction and body dissatisfaction in patients who seek for treatment for obesity.

Methods: The study population consisted of 105 patients admitted to an obesity center in a university hospital. Data from were collected with the patient information form, the Yale Food Addiction Scale, the Beck Depression Inventory, and the Body Image Scale. The direct relationship between food addiction and body dissatisfaction and the mediating effect of depression in the relationship between these two constructs were examined using multi-group structural equation modeling analysis by gender.

Results: The mean age of the patients was 50.22±10.05, 86.8% of them were females. The mean body mass index of the patients was calculated as 40.29±6.67. It was determined that 38.7% of the sample met the food addiction diagnosis criteria. It was found that 39.1% of females and 35.7% of males had food addiction. As a result of the modeling analysis, it was determined that there was no direct pathway between body dissatisfaction and food addiction, depression symptoms complete mediated the relationship between these two constructs. Results of multi-group analysis showed that the mediation model was consistent across gender.

Conclusions: In the treatment of obesity cases in which food addiction and body image disorders coexist, examining the existence of depression and treating it can increase the success rate.

Keywords: Food Addiction, Body Image, Depression, Obesity, Mediation.

Obezite Sorunu Olan Bireylerde Yeme Bağımlılığı ile Beden İmajı Arasındaki İlişkide Depresyonun Aracılık Etkisi

ÖZET

Amaç: Bu çalışmada, obezite sorunu olan ve tedavi programına başlamış hastalarda yeme bağımlılığı ile beden memnuniyetsizliği arasındaki ilişkide depresyonun aracılık etkisinin incelenmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmanın örneklemini bir üniversite hastanesinin obezite merkezine başvuran 105 hasta oluşturdu. Veriler hasta bilgi formu, Yale Yeme Bağımlılığı Ölçeği, Beck Depresyon Envanteri ve Beden İmajı Skalası ile toplandı. Yeme bağımlılığı ile beden memnuniyetsizliği arasındaki direkt ilişki ve bu iki yapı arasındaki ilişkide depresyonun aracılık etkisi cinsiyetlere göre çoklu grup yapısal eşitlik modellemesi analizi ile incelendi.

Bulgular: Çalışmaya katılan hastaların yaş ortalaması 50,22±10,05 ve %86,8'i kadındı. Hastaların beden kitle indeksi ortalaması 40,29±6,67 olarak hesaplandı. Örneklemin %38,7'sinin yeme bağımlılığı tanı kriterlerini karşıladığı belirlendi. Kadınların %39,1'inde, erkeklerin %35,7'sinde yeme bağımlılığı olduğu saptandı. Modelleme analizi sonucunda yeme bağımlılığı ile beden memnuniyetsizliği arasında doğrudan bir ilişkinin olmadığı, depresyonun bu iki yapı arasındaki ilişkiye tam aracılık ettiği tespit edildi. Çoklu grup analizinin sonuçları, aracılık etkisinin cinsiyetler arasında tutarlı olduğunu gösterdi.

Sonuç: Yeme bağımlılığı ve beden imajı bozukluklarının bir arada olduğu obezite vakalarının tedavisinde depresyon varlığının incelenmesi ve tedavi edilmesi başarı oranını artırabilir.

Anahtar Kelimeler: Yeme Bağımlılığı, Beden İmajı, Depresyon, Obezite, Aracılık.

INTRODUCTION

Obesity, which arises as a result of imbalance between energy intake and energy expenditure, has a complex etiology (1). Although there have been significant advances in studies on obesity in recent years, the increase in its prevalence is continuing, which has caused different factors to come to the fore in the etiology of this chronic disease. Within this framework, food addiction (FA) has entered into the literature as a new concept related to food intake (2,3).

Eating behavior is regulated by two different systems. It is stated that the balance can be maintained in eating controlled by the homeostatic system; however, in the hedonic system, the association of the reward system of brain with taste and pleasure is triggered by certain foods, which results in overconsumption of these foods (3). FA involves the notion that tasty foods, which are usually processed and contain high amounts of carbohydrate and calories, might have an addictive potential. Moreover, overeating in certain forms might represent addiction behavior (5). Some foods affect the reward system of brain and the regions associated with dopaminergic system, which results in the stimulation of reward pathways, the development of withdrawal symptoms, and the loss of control over the behavior of eating (2,3). FA particularly overlaps with Bulimia Nervosa (BN) and Binge Eating Disorder (BED) in terms of psychopathology (for example, decreased control over the behavior of eating, ongoing use despite negative consequences). However, FA is characterized by biopsychological symptoms such as withdrawal and tolerance. (5,6).

FA is most commonly assessed through the Yale Food Addiction Scale (YFAS), which was prepared based on the addiction criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (4). In prevalence studies carried out in the general population using the YFAS, FA varied between 4% and 26% (7-9). This rate increased from 7% to 38% in studies carried out with obese patient groups (10-13) and from 16% to 54% in patients who underwent bariatric surgery (14-16). Moreover, society-based studies report that FA is observed more in female sex (7,17,18), while studies carried out in obese patient groups report that sex difference did not affect FA prevalence (10,12,14). There are different results in the literature related to age variable, another predictor of FA. In the meta-analysis by Pursey et al. (201418), it was found that FA is observed more among individuals aged over 35 years. Moreover, in their study conducted with patients applying for obesity treatment, Eichen et al. (12) reported that FA severity is negatively correlated with age.

Studies carried out in obese patient groups demonstrate that FA is strongly correlated with psychopathological status (12,13,19). Addiction processes and depressive symptoms are affected in dopaminergic ways, which may affect food choice and eating behaviors in affective disorders (3). A positive relationship was reported between depression and FA among obese adults by Burmeister et al. (19) and among overweight and obese women in Özkan et al. (13). Furthermore, Bourdier et al. (20), in their study with young adults, reported that there is a positive association between FA and psychological distress (depression and anxiety) regardless of sex. The same study also reported that FA has a meditating role in the effect of psychological distress on body mass index (BMI).

Body image (BI) has been conceptualized as a complex and multidimensional construct with perceptual, affective, cognitive, and behavioral components. Body image is formed during the personal developmental process of individuals by their experiences, the value attached to their own BI, the ideas and attitudes of others about their physical appearance, and the reactions they show to them. When there is a discrepancy between the body appearance and the ideal BI of individuals at any period, their BI perception may also change (21). When compared with other psychopathological structures often associated with FA in recent years (for instance emotion dysregulation and depression), BI was a topic that was less emphasized (6). However, in studies carried out recently with different clinical or non-clinical age groups, it was shown that there is a negative relationship between FA symptoms and body satisfaction (17) and body uneasiness is independently related with FA symptoms (6). Studies conducted with obese patients report that those with a FA diagnosis have higher anxiety related to weight and body shape (22) and body shame increases as the severity of FA rises (19). In these studies, it is possible that the association between FA and body dissatisfaction may be mediated by other potential socio-demographic (e.g., sex and age) and clinical (e.g., depressive symptoms, emotion dysregulation, BMI) variables, though partially.

In the light of previous knowledge, this study aimed to assess the mediation effect of depression on the association between food addiction and body dissatisfaction in patients who seek for treatment for obesity and who will participate in programs in which behavioral change is applied according to sex by means of the Structural Equation Model (SEM). At the same time, the suitability of the mediation effect model was tested by including the variables of BMI and age, which can be shared variables, into the modelling.

MATERIAL AND METHODS

Study Sample: The study population consisted of patients applying to an obesity center in a university hospital. The obesity center was

taken into service in November 2018 and it implements behavioral change treatment for obesity. From the date the center was taken into service to the date when the study was planned (November 2019), a total of 144 patients applied to the center.

Patients aged over 18 years with a BMI of 30 and over, who were literate and were accepted to the weight loss program, were taken into the study scope. Those who had major central nervous system diseases (epilepsy, dementia, etc.) or diagnosed psychiatric disorders (bipolar disorder, depression, schizophrenia, etc.) and who used psychiatric medication were not included in the study.

The sample size was determined, on the basis of a 95% confidence interval and 5% sampling error, using the formula shown below. The frequency rate of a case was accepted as 0.5 to calculate the maximum sample size for the population. The formula used for the calculation of sample size:

N: Number of patients in the universe
n: Number of individuals to be sampled
p: Frequency rate of a case (probability of occurrence)
q: Frequency rate of the absence of a case (probability of non-occurrence)
t: Theoretical value found according to table t, at a specific significance level
d: Accepted sampling error according to incidence of the case

$$n = \frac{N \times t^2 \times p \times q}{d^2 (N-1) + t^2 \times p \times q} = 105$$

Data Collection: The data were collected through the Patient Information Form, the Yale Food Addiction Scale (YFAS), the Beck Depression Inventory (BDI), and the Body Image Scale (BIS).

Patient Information Form: The question form developed by the researchers involved questions related to socio-demographic characteristics such as age, sex, marital status, employment status, educational status. The existence of chronic diseases, the history of psychiatric disorders, and the use of cigarette-alcohol were questioned with regard to the patients' health characteristics.

Yale Food Addiction Scale: The YFAS was developed by Gearhardt et al. (23) in order to determine the symptoms of addiction to certain kinds of food. Turkish validity and reliability of the scale was performed by Bayraktar et al. (24) and the Cronbach's alpha value was found to be 0.93. It was calculated as 0.72 (Kuder-Richardson's alpha) in our study. The YFAS is a 27-item scale used to find out eating behaviors like addiction in the last 12 months. The questions in the scale are similar to the criteria related to drug addiction in DSM-IV and the development of the test was completed in line with these criteria. The following substance dependence symptoms were revised to apply to eating behaviors: (1) substance taken in greater quantity and for longer than intended; (2) persistent desire or unsuccessful repeated attempts to quit; (3) great time and effort to obtain, use, and recover from substance; (4) involvement in important life activities stopped or reduced; (5) continued use despite problems; (6) tolerance; and (7) withdrawal. The scale has two scoring systems. Experiencing a situation regarding clinical sensitivity and encountering 3 or more symptoms out of 7 are accepted as the reasons for reaching a diagnosis. Moreover, a continuous score is calculated by adding the number of symptoms encountered. In this study, the option of diagnostic scoring (descriptive statistics section) was used to assess the prevalence of persons who met FA criteria and the option of counting the number of symptoms was used for the rest of the analyses.

Beck Depression Inventory: The inventory was developed by Beck et al. (25) and its validity and reliability for Turkey was performed by Hisli (26). It is a self-assessment scale consisting of 21 items with 4 choices [a (0), b (1), c (2), d (3) points]. It questions how individuals have felt within the last week, including the day the test is implemented. In the assessment of the scale, the scores are added (it is possible to collect 63 points at most) and a high total score indicates the level or severity of depression is high. The Cronbach's alpha coefficient of the scale was calculated as 0.76 for this study.

Body Image Scale: This scale was developed by Secord and Jourard (27). Its validity and reliability was tested and the scale was adapted to the Turkish society by Hovardaoğlu (28). The scale, which is used to find out the ideas of individuals about their body features, consists of 40 items scored between 1 and 5 and the total score that can be obtained from the scale varies between 40 and 200. A high total score indicates a high BI satisfaction ["very satisfied (5)", "moderately satisfied (4)", "undecided (3)", "slightly unsatisfied (2)", and "very unsatisfied (1)"] (Hovardaoğlu, 1993). The Cronbach's alpha coefficient of the scale was calculated as 0.70 for this study.

The data were collected through face-to-face interview method. The height of the patients was measured without shoes by a stadiometer in the patient training room. The body weight, on the other hand, was measured with one layer of clothing on, without shoes and any extra clothing, using a Tanita BC418 Body Analysis Device.

Ethical Considerations: The present study protocol was conducted in accordance with the Declaration of Helsinki. Ethical permission to carry out the study was obtained from the Non-Invasive Clinical Research Ethics Committee of Düzce University (Dated: 04.11.2019, Consent No: 2019/235). The aim of the study was explained to

the patients and their written approvals were obtained.

Statistical Analysis: The analysis of the data was completed using the IBM SPSS 21.0 software and IBM SPSS AMOS 22.0 software. Continuous variables were displayed as mean ± standard deviation and categorical variables as number and percentage. The Cronbach's alpha and the Kuder-Richardson's alpha of reliability were used to measure internal consistency. The normality of data distribution was assessed with the Kolmogorov-Smirnov test. The correlation between variables that did not show a normal distribution and continuous variables were tested using the Spearman's Rho. Comparisons in terms of the sex variable were performed with the Mann-Whitney U and the Yates Chi-Square tests.

In the second step of the analysis, multiple-group analysis for structural equation modeling was carried out in terms of the variables observed to be correlated (age, FA, BI, depression) and sex. This step also investigated the mediation effect of depression on the relationship between food addiction and body image perception. In the model established according to the correlation between variables, age was included in the model as external and FA, BI, and depression as internal variables. The data that met the condition of multivariate normal distribution were tested using the maximum likelihood method. First, the suitability of the model was assessed. As the chi-square (χ^2) test, one of the fit indices, is sensitive to the sample size, the chi-square/df value, which is less affected by the sample size, was taken into consideration ($\Delta\chi^2$/df, good fit if <3, acceptable fit if 3< $\Delta\chi^2$/df <5). The other fit indices used were: Root Means Square Error Approximation (RMSEA, good fit if < 0.05, acceptable fit if < 0.08), Standardized Root-Mean-Square Residual (SRMR, good fit if < 0.05, acceptable fit if < 0.08), Goodness of Fit Index (GFI, good fit if > 0.95, acceptable fit if > 0.90), Tucker-Lewis Index (TLI, good fit if > 0.95, acceptable fit if > 0.90), Adjustment Goodness of Fit Index (AGFI, good fit if > 0.95, acceptable fit if > 0.90), Comparative Fit Index (CFI, good fit if > 0.95, acceptable fit if > 0.90) (29,30). Finally, bootstrapping analysis with 5000 bootstrapped samples was conducted to test the statistical significance of the mediation effects based on the bias-corrected percentile confidence intervals produced from the bootstrapping analysis. The mediation effect was determined based on whether the values within the 95% confidence interval obtained with mediation effect analysis performed using the Bootstrap method included zero or not (29). A significance level of .05 were used for all statistical analyses.

RESULTS

Sample Description: The mean age of the patients was 50.22±10.05, 86.8% of them were females, 43.4% were primary and secondary education graduates, and 78.3% were unemployed. Among the sample, 74.5% had one or more chronic diseases and 37.7% had a history of psychiatric disorder. With respect to drug abuse, 12.3% used cigarettes and 1.9% used alcohol. The mean BMI of the sample was 40.29±6.67 (Table 1).

Table 1. Distribution of socio-demographic characteristics of the obese patients (n=106)

Characteristics		**n**	**%**
Sex	Female	92	86.8
	Male	14	13.2
Age. years	50.22±10.05	(Min.-Max. = 24 - 68)	
Marital status	Married	92	86.8
	Single	14	13.2
Status of employment	Employed	23	21.7
	Unemployed	83	78.3
Educational status	Primary-Secondary School	46	43.4
	High School	35	33.0
	University	25	23.6
Chronic disease	Yes	79	74.5
	No	27	25.5
Psychiatric disease history	Yes	40	37.7
	No	66	62.3
Smoking	Yes	13	12.3
	No	93	87.7
Alcohol use	Yes	2	1.9
	No	104	98.1
BMI kg/m^2	40.29± 6.67	(Min.-Max. = 30.02 – 60.88)	

BMI: Body Mass Index, Mean ± Standard Deviation, Min.-Max.: Minimum-Maximum

Bivariate Associations: Correlation relationships was presented in Table 2. It was determined that there was a moderately positively association between YFAS and BDI and a weak negatively association between YFAS and BIS. However, there was a moderately negative association between BDI and BIS. While no association was detected between BMI and YFAS and between BDI and BIS, a moderately negative association was found between YFAS and age and between BDI and age (Table 2).

Table 2. Correlation matrix of the variables of interest

Variables	1	2	3	4	5
1. YFAS-Symptom Count	-				
2. BDI	0.342**	-			
3. BIS	-0.225*	-0.508**	-		
4. BMI	0.159	0.121	-0.172	-	
5. Age	-0.303**	-0.332**	0.150	0.037	-

*YFAS: Yale Food Addiction Scale, BDI: Beck Depression Inventory, BIS: Body Image Scale, BMI: Body Mass Index, *p<.05, **p<.01*

Group Comparisons According to Sex Differences: There was no statistically significant difference between female's and male's age, BMI, and the mean YFAS score. However, the mean BDI score of females was significantly higher than that of males. Similarly, the mean BIS score of females was significantly lower than that of males. The rate of those who met the FA diagnosis criteria was 38.7% in all the sample. Among the females, 39.1% met the FA diagnosis criteria, while 35.7% of the males met these criteria. There was no statistically significant difference between groups in terms of FA prevalence (Table 3).

Table 3. Characteristics of the sample and sex differences

	All (n=106)	Females (n=92)	Males (n=14)	Test Statistic	p
Age	50.22±10.05 (24-68)	49.67±9.82 (24-68)	53.79±11.91 (34-68)	-1.644	0.100
BMI	40.29± 6.67 (30.02-60.88)	40.18±6.78 (30.02-60.88)	40.97±6.04 (32.11-49.18)	-0.504	0.614
YFAS-Symptom Count	3.30±1.62 (0-7)	3.38±1.66 (0-7)	2.79±1.25 (1-5)	-1.304	0.192
BDI	16.79±6.99 (3-32)	17.53±6.91 (3-32)	11.93±5.58 (3-23)	-2.828	0.005
BIS	119.94±25.24 (70-182)	117.84±24.36 (70-182)	133.79±27.49 (91-175)	-1.965	0.049
FA	41 (38.7)	36 (39.1)	5 (35.7)	0.000	1.000
Non-FA	65 (61.3)	56 (60.9)	9 (64.3)		

Mean ± Standard Deviation (Minimum-Maximum), n(%), YFAS: Yale Food Addiction Scale, BDI: Beck Depression Inventory, BIS: Body Image Scale, BMI: Body Mass Index

Structural Equation Model: Multiple-group analysis for structural equation modeling was carried out in terms of the variables observed to be correlated (age, FA, depression, BI) and sex in the second step of the analysis. The modelling investigated the mediation effect of depression on the relationship between food addiction and body image perception. The structural model established in the study is given in Figure 1. Within the scope of the analysis, it was investigated whether there was multicollinearity between study variables in the model by the Durbin-Watson coefficient and variance inflation factor (VIF) methods. All these tests produced results confirming that no multicollinearity existed between independent variables (Durbin Watson=1,883, VIF< 5).

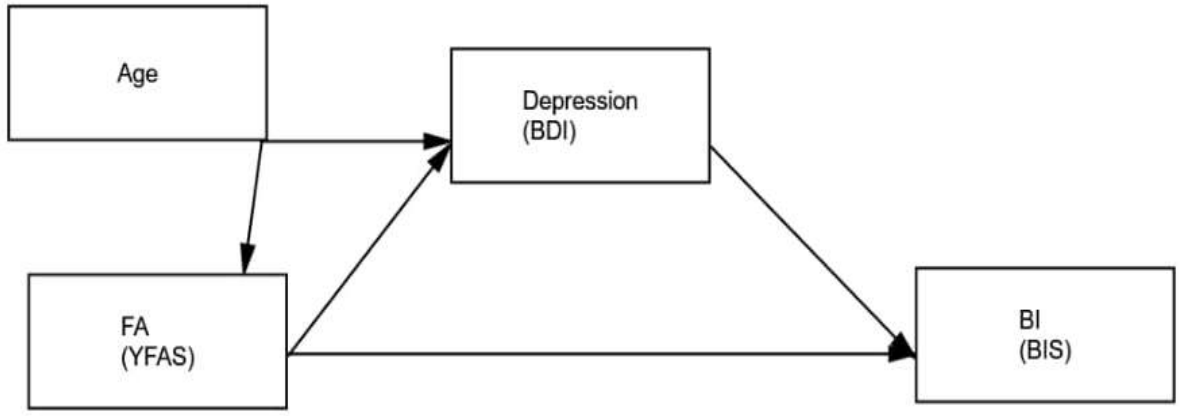

Figure 1. Structure Equation Model

When the fit indices of the model were examined, it was determined that it had good fit values ($\Delta\chi^2$/df=0.142, SRMR=0.0092, RMSEA=0.000, GFI=0.999, TLI=1.092, AGFI=0.993, CFI=1.000).

Table 4 presents the analysis results of the SEM. It was observed that in females, as age decreased, FA symptoms increased, whereas in males age did not have a significant effect on FA symptoms (females: β=-0.31, p=0.002; males: β=-0.14, p=0.613). Similarly, in females, depression was negatively affected as age decreased; however, in males, age did not have a significant effect on depression (females: β=-0.27, p=0.006; males: β=-0.01, p=0.979).

Table 4. Direct, indirect, and total effects of the Structural Equation Model

	Female			Male		
	β	**SE**	**p**	**β**	**SE**	**p**
Age -->FA	-0.31	0.02	0.002	-0.14	0.03	0.613
Age -->DEP	-0.27	0.07	0.006	-0.01	0.16	0.979
FA -->BI **(Total effects)**	-0.24	1.44	0.016	-0.15	1.44	0.016
R^2		0.06			0.02	
FA -->DEP	0.25	0.39	0.008	0.20	0.39	0.008
R^2		0.18			0.04	
FA --> BI **(Direct effects)**	-0.06	1.39	0.533	-0.04	1.39	0.979
DEP -->BI	-0.46	0.33	<0.001	-0.44	0.33	<0.001
R^2		0.24			0.21	
	Effect	**SE**	**95% Confidence Interval**	**Effect**	**SE**	**95% Confidence Interval**
Indirect effects	-0.12	0.05	-0.222 -0.010	-0.09	0.05	-0.187 -0.007

Bootstrap resampling: 5000, Standardized regression coefficients have been given. YFAS: Yale Food Addiction Scale, BDI: Beck Depression Inventory, BIS: Body Image Scale, SE: Standard error

In both sexes, it was found out that the total effect of FA on BI was significant and FA negatively affected BI (females: β=-0.24, p=0.016; males: β=-0.15, p=0.016). In both females and males, it was seen that FA negatively affected depression, which was the mediating variable, (females: β=0.25, p=0.008; males: β=0.20, p=0.008) and depression also affected BI negatively (females: β=0.46, p=<0.001; males: β=-0.44, p=<0.001). When FA and depression, the mediating variable, were included in the model at the same time, the significant effect of FA on BI disappeared (females: β=-0.06, p=0.533; males: β=-0.04, p=0.979). According to the results, the indirect effect of the mediating variable of depression was significant on both females and males (females: β=-0.12, 95% CI [-0.222, -0.010]; males: β=-0.09, 95% CI [0.187, -0.007]). In line with these results, it was determined that depression had a complete mediating role in the relationship between FA and BI.

DISCUSSION

The mechanisms affecting food intake are complicated in obesity, which is defined as a chronic disease. In recent years, it has been suggested that FA might be effective in the fact that obese persons cannot exhibit healthy eating behaviors even though they have a serious health issue (2,3). Studies show that FA has a strong association with psychopathological conditions such as depression, anxiety, poorer emotion regulation, lower self-esteem, internal stigmatization with regard to weight, body dissatisfaction, and boy shame. This study investigated the FA rates in individuals participating in behavioral change treatment for obesity and the mediation effect of depression on the relationship between food addiction and body dissatisfaction.

At the end of the study, the rate of those who met the FA criteria and received a FA diagnosis in the obese patient group was found to be 38.7%. The weighted mean prevalence of FA was reported to be 19.9% in a meta-analysis carried out by Pursey et al. (18), in which they reviewed 20 studies conducted with different populations. It is seen that the rate of FA is lower (4-26%) in society-based studies (7-9). However, in studies carried out with individuals seeking for obesity treatment, it was seen that this rate varied between 7% and 54% and it was higher compared to the general population (10-12,16). In the study by Özkan et al. (13), which was carried out with patients applying for obesity treatment, who were of the same ethnic origin as the present study, the rate of FA was detected as 38%, similar to the results of this study. The FA rates have a wide range in the literature, which suggests that the studies might have been affected by numerous factors such as sample size, ethnic origin, and sex distribution.

Different from this study, the results of society-based studies indicate that FA rate or FA symptoms is higher in females compared to males (7,17,18). This is explained with the fact that females and males have different hormonal profiles and dietary preferences. In studies carried out with patient groups applying for obesity treatment, it was seen that sex did not affect food addiction, which is similar to the results of this study (10,12,14).

Although people with a psychiatric diagnosis were excluded from the study, the results revealed that depressive symptoms were higher in the group with FA and there was a positive association between the FA symptoms and depression, similar to previous studies (10,12,13,31). It is assumed that addiction processes and depressive symptoms are affected by dopaminergic ways. Furthermore, affective disorders such as depression and anxiety can affect food choice and eating behaviors (3). Therefore, it is an expected result that depressive symptoms are high in the group with FA.

Body dissatisfaction is the negative subjective assessment of a person with respect to their body image and it has a consistent and significant relationship with eating disorders (5,32). Studies carried out with patients diagnosed with BED and BN particularly in Western cultures indicated that factors like depression, anxiety, self-esteem, and being exposed to teasing about body image in childhood mediated the association between eating disorders and body dissatisfaction (11,33-37). Previous studies carried out in clinical and non-clinical populations in the Turkish society and in different cultures indicate that those with food addiction have lower body satisfaction level and higher body uneasiness and anxiety levels with respect to their weight and body shapes, and that they are ashamed of their body shapes (6,17,19,22). In the present study, different from the previous studies, it was established that food addiction had a total effect on body dissatisfaction but no direct effect. It was indicated that the negative effect of food addiction on body image appeared by mediation of depression. It was seen that this total mediation effect was valid for both sexes. FA has significant psychopathological overlap (e.g., reduced control over eating, continued use despite problems) with BN and BED. However, FA is not characterized by symptoms related to body image (5,6). The results of the present study support this, indicating that food addiction does not have a direct effect on body image.

Similar to the previous studies carried out with obese patient groups, no significant relationship was detected between BMI and the number of FA symptoms in this study (11,14,19). However, in society-based studies, a correlation was reported between BMI and the number of FA symptoms (8, 9,17). Meule (38) reported that there was a cubic relationship rather than a linear one between BMI and FA based on empirical data. In a cubic relationship, positive correlations are observed in the number of FA for overweight and moderately obese individuals, but this relationship may not be observed in symptoms of severely obese individuals. The mean BMI of the sample included in the study is 40.29±6.66, but the minimum and maximum range is wide. There are persons with a severe obesity problem in the sample group. There is no correlation between the FA symptoms and BMI, which can be explained with cubic relationship.

CONCLUSION

In conclusion, it was determined that food addiction rates were high in both female and male obese patients who sought for treatment and the negative effect of food addiction on body image was mediated by depression. FA is one of the important factors that might lead to obesity and it may negatively affect the efforts to lose body weight, and even if positive results are achieved, it may make maintaining the weight difficult. In the treatment of cases in which food addiction and body image disorders coexist, examining the existence of depression and treating it can increase the success rate. Furthermore, we are of the opinion that there is a need for studies on obesity in which surgical and non-surgical treatment methods are used and which are carried out with larger samples with different socio-demographic and psychological characteristics.

Limitations

Though the results of the present study have a unique value, there are limitations with respect to generalizability. To begin with, the study was carried out in a center with a sample group comprising a high female population who sought for treatment. Secondly, although the data collection tools used in the study are valid and reliable, a risk of biased reporting exists as they are self-reporting tools. When assessing food addiction, the previous YFAS version based on the criteria about drug addiction in DSM-IV was implemented. Finally, only depression was assessed among psychopathological conditions for the relationship between food addiction and body image.

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RESEARCH ARTICLE

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Evaluation of Cyber Victimization and Self-Esteem Level in High School Students

ABSTRACT

Objective: The aim of this study is to determine the prevalence of cyber victimization among high school students, to examine some possibly related variables and to evaluate the relation with level of self-esteem in Sivrihisar district of Eskişehir.

Methods: This is a cross-sectional study conducted between May-June 2018. The study group consisted of 712 students. The questionnaire used in the study includes The Revised Cyber Bullying Inventory-II and Rosenberg Self-Esteem Scale. Chi-square test, Mann Whitney U test and Logistic Regression Analysis were performed to analyze the data. It was considered significant if $p \leq 0.05$.

Results: The 60.1% of the students were female, and the mean value of ages was 16.3±1.2 in years (ranged 13-20). The prevalence of cyber victimization was 51.3% (n=365). When compared to other groups in same subtitle, the risk of being cyber victim was 1.66 times higher in the 9th and 10th grades (CI: 1.20-2.30), 4.56 times higher in individuals with poor family income (CI: 1.18-17.64), 1.53 times in the middle ones (CI: 1.10-2.16), 3.15 times in individuals with social media accounts (CI: 1.00-9.85), and 2.80 times higher in individuals having problems with anyone on the internet (CI: 1.96-4.02). Rosenberg Self-Esteem Scale scores were higher in cyber victims (p=0.027).

Conclusions: It was concluded that cyber victimization is an important problem among high school students in Sivrihisar, and cyber victimization is observed higher in the group with low self-esteem.

Keywords: Cyber Victimization, Self-Esteem, High School Student.

Lise Öğrencilerinde Siber Mağduriyet ve Benlik Saygısı Düzeyinin Değerlendirilmesi

ÖZET

Amaç: Bu çalışmada Eskişehir ili Sivrihisar ilçesinde öğrenim görmekte olan lise öğrencilerinde siber mağduriyet sıklığının belirlenmesi, ilişkili olduğu düşünülen bazı faktörlerin incelenmesi ve benlik saygısı düzeyi ile ilişkisinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışma Mayıs-Haziran 2018 tarihleri arasında yapılan kesitsel tipte bir araştırmadır. Çalışma grubu toplam 712 öğrenciden oluştu. Çalışmada kullanılan anket form Yenilenmiş Siber Zorbalık Envanteri-II ve Rosenberg Benlik Saygısı Ölçeği'ni içermektedir. Analizler için Ki-kare testi, Mann Whitney U testi ve lojistik regresyon analizi kullanıldı. İstatistiksel anlamlılık değeri olarak $p \leq 0.05$ kabul edildi.

Bulgular: Öğrencilerin %60.1'i kadındır. Yaşları 13-20 arasında değişmekte olup ortalama 16.3±1.2'dir. Siber mağduriyet görülme sıklığı %51.3 (n=365) olarak bulundu. Siber mağdur olma riski 11 ve 12. sınıflara göre 9 ve 10. sınıflarda 1.66 kat (GA: 1.20-2.30), aile gelir durumu iyi olanlara göre kötü olanlarda 4.56 kat (GA: 1.18-17.64), orta olanlarda 1.53 kat (GA: 1.10-2.16), sosyal medya hesabı olmayanlara göre olanlarda 3.15 kat (GA: 1.00-9.85), internette herhangi biriyle sorun yaşamayanlara göre yaşayanlarda 2.80 kat (GA: 1.96-4.02) daha fazla saptandı. Siber mağdur olanlarda Rosenberg Benlik Saygısı Ölçeği puanı daha yüksek bulundu (p=0.027).

Sonuç: Sivrihisar'da öğrenim görmekte olan lise öğrencileri arasında siber mağduriyetin önemli bir sorun olduğu, benlik saygısı düşük olanlarda siber mağduriyetin daha fazla olduğu görüldü.

Anahtar Kelimeler: Siber Mağduriyet, Benlik Saygısı, Lise Öğrencisi.

INTRODUCTION

With technological improvements, functional developments in technological devices have led to the emergence of new environments and cultures in communication, and smaller size of the devices has increased availability and continuity, making the time spent in these environments prolonged and become an indispensable part of people's life. These emerging virtual platforms have become an important factor shaping people's social life, especially friendships (1-3). There are many negativities brought about by all of these. People face many problems such as cyber fraud in virtual environments, personal information stolen or given to the others, psychological and sexual abuse (4-6).

Damaging behaviors that an individual or group carries out in a repetitive manner towards an individual or group that cannot defend itself are called bullying. Bullying is applied to a person or group with less durable in physical and physological way and aims to intentionally damage in a continuous period (7-9). Cyberbullying is defined as the malicious and repetitive use of information and communication technologies by an individual or group to harm other individuals (10).

Cyber victimization is the situation in which an individual or group, a private or legal person, is exposed to harmful behaviour in technical or relational manner and is materially or morally harmed by such behavior (8, 11). Individuals may experience technical grievances such as the capture of their personal information and passwords as a result of virtual attacks on e-mail or websites, they may also experience psychological-based grievances such as constant harassment, mockery, spreading a gossip about them in the virtual environment, being exposed to insults, spreading private photos without their consent or threatening with it (5, 8, 12, 13).

It has been reported that the prevalence of cyber victimization among high school students varies between 10-83.8% in various countries (14-20). In Turkey, it is seen that it varies between %7.0-63.3 (6, 10, 13, 21, 22). It was reported that %8.9-72.2 of students in Turkey both make cyberbullying and experience cyber victimization (6, 10, 13).

People who are exposed to cyberbullying may experience some negative outcomes that may lead to closure, withdrawal from society and asocialization, cooling and escaping from school, a decrease in school success, humiliation and revenge, aggressive behavior, a decrease in self-esteem and even suicide (1, 5, 10, 12, 23). Among these concepts, self-esteem is a subjective phenomenon that can be defined as the positive and negative attitudes of the individual towards him/her. Self-esteem has an important place in personality development and it is a whole of perceptions, emotions and thoughts that are important for the individual. The relation of self-esteem level with cyber victimization is one of the issues that arise curiosity. There are studies in the literature that low self-esteem level increases cyber victimization, along with studies that state that cyber victimization decreases self-esteem level, that is, there is a bi-directional interaction (2, 18, 21).

In this study, it was aimed to determine the prevalence of cyber victimization among high school students studying in Sivrihisar district of Eskişehir, to examine some factors that are thought to be related, and to evaluate relationship with self-esteem level.

MATERIAL AND METHODS

The study is a cross-sectional study of high school students studying in Sivrihisar district of Eskişehir between May-June 2018.

Ethics committee permission required for the study was obtained from Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee with the report dated 24.04.2018 and numbered 25403353-050.99-E.43225. In order to collect data in schools, necessary written permissions were obtained from the provincial and district national education directorates.

Eskişehir is a city located in Western Turkey with high development index. The population of Eskişehir is 860,620, of which 429,078 (49.9%) are male and 431.542 (50.1%) are female. The population of Sivrihisar district, which is 100 km away from the city center, is 20,449 (10,358 (50.6%) male and 10.091 (49.4%) female) (24). There are 7 high schools that provide education in Sivrihisar district, 1089 students study in these high schools in total. It is aimed to reach all the students in this study.

A questionnaire was prepared using the literature in order to collect data (2, 11, 17, 18, 20, 22). The first part of the questionnaire forms some socio-demographic characteristics of students (school, grade, age, gender, family income status, family type, personality type) and some features related to internet use (daily average internet usage time, preferred device in internet access, presence of social media account, internet usage purpose). The second part of the questionnaire consists of the questions of the Revised Cyber Bullying Inventory-II, and the third part consists of the questions of Rosenberg Self Esteem Scale.

In order to collect data, the days and times of the survey were determined by informing the school administrators in advance. It was ensured that the students gathered in their classrooms by going to the schools on the specified days and hours. The students were informed about the subject and pupose of the study. The questionnaire form, which was administered by obtaining verbal consent from those who agreed to participate in the study, was filled in approximately 10-15 minutes by the students under observation. Those who did not agree to participate in the study (n=5), those who did not attend the school on the day and time of study (n=359) and those who did not respond adequately to the questionnaire (n=13) were not included in the study. A total of 712 (65.4%) students constituted the study group.

The Revised Cyber Bullying Inventory-II, which is used to determine cyber victimization, was first developed by Erdur-Baker and Kavşut in 2007

(25). It was revised by Topçu and Erdur-Baker (7). In the scale consisting of 10 items answered in the 4-point Likert type and two parallel answer forms, the cyber bullying situation is evaluated in the "I did it" section, and the cyber victimization situation in the "Made to me" section. Answers are scored as none=1 point, once=2 points, two-three times=3 points, more than three=4 points. The total score that can be obtained from the scale varies between 10-40. It is accepted that the level of cyber victimization increases as the total score obtained from the "Made to me" section increases. In addition, those who has scored a total of 10 points from the scale are considered non-cybervictims, and those who has scored 11 points or more are considered as cyber victims (7).

The Rosenberg Self-Esteem Scale (RSES) was developed by Morris Rosenberg in 1965 (26). Turkish validity and reliability study of the scale was done by Çuhadaroğlu in 1986 (27). In the scale, which consists of 10 proposals of four Likert type, items 1,2,4,6 and 7 are positive; Items 3,5,8,9 and 10 are negative. Answers given for negative items are very correct 4 points, correct 3 points, wrong 2 points, very wrong 1 point; The answers given for positive items are scored the opposite. The total score that can be obtained from the scale varies between 10-40, and the self-esteem decreases as the score gets Higher (28).

In this study, family income status was evaluated as "good", "medium" and "bad" according to one's own perception. Those who are hasty, disciplined, agile and impatient were considered as "A type personality", and those who were patient, comfortable, calm and emotional were accepted as "type B personality".

The evaluation of the data was done with SPSS (v15) Statistical Package Program in computer. For analysis, Chi-square test, Mann Whitney U test and logistic regression analysis were used. $p \leq 0.05$ was accepted as the statistical significance value.

RESULTS

428 (60.1%) of the study group are female and 284 (39.9%) are male. Their ages vary between 13-20 and on mean 16.3±1.2 years. The prevalence of cyber victimization in the study was 51.3% (n=365). The distribution of those with and without cyber victimization according to some socio-demographic characteristics is given in Table 1.

Table 1. Distribution of those with and without cyber victimization in the study group according to some socio-demographic characteristics

Socio-demographic Characteristics	Cyber Victimization			Statistical Test Value
	No n (%)*	Yes n (%)*	Total n (%)†	χ^2; p
School				
Vocational High School	127 (53.4)	111 (46.6)	238 (33.4)	3.948; 0.267
Science High School	105 (44.3)	132 (55.7)	237 (33.3)	
Imam Hatip High School	20 (50.0)	20 (50.0)	40 (5.6)	
Anatolian High School	95 (48.2)	102 (51.8)	197 (27.7)	
Grade				
9-10	189 (44.9)	232 (55.1)	421 (59.1)	**6.089; 0.014**
11-12	158 (54.3)	133 (45.7)	291 (40.9)	
Age range				
≤15	91 (45.0)	111 (55.0)	202 (28.4)	2.387; 0.303
16-17	178 (48.9)	186 (51.1)	364 (51.1)	
≥18	78 (53.4)	68 (46.6)	146 (20.5)	
Gender				
Female	215 (50.2)	213 (49.8)	428 (60.1)	0.963; 0.326
Male	132 (46.5)	152 (53.5)	284 (39.9)	
Father's educational status				
Primary school and below	105 (47.3)	117 (52.7)	222 (31.2)	0.614; 0.736
Middle school	99 (51.0)	95 (49.0)	194 (27.2)	
High school and above	143 (48.3)	153 (51.7)	296 (41.6)	
Mother's educational status				
Primary school and below	171 (46.2)	199 (53.8)	370 (52.0)	3.325; 0.190
Middle school	95 (48.7)	100 (51.3)	195 (27.4)	
High school and above	81 (55.1)	66 (44.9)	147 (20.6)	
Family income status				
Good	122 (54.5)	102 (45.5)	224 (31.5)	**9.248; 0.001**
Medium	222 (47.0)	250 (53.0)	472 (66.3)	
Bad‡	3 (18.8)	13 (81.2)	16 (2.2)	
Family type				
Nuclear family	279 (50.5)	274 (49.5)	553 (77.7)	3.202; 0.202
Extended family	49 (41.5)	69 (58.5)	118 (16.6)	
Broken family	19 (46.3)	22 (53.7)	41 (5.8)	
Personality type				
A	171 (51.5)	161 (48.5)	332 (46.6)	1.911; 0.167
B	176 (46.3)	204 (53.7)	380 (53.4)	
Last year grade point average				
≤69	100 (43.1)	132 (56.9)	232 (32.6)	5.085; 0.079
70-84	167 (52.8)	149 (47.2)	316 (44.4)	
≥85	80 (48.8)	84 (51.2)	164 (23.0)	
Any history of psychiatric illness diagnosed by a physician				
Yes	33 (51.6)	31 (48.4)	64 (9.0)	0.225; 0.635
No	314 (48.5)	334 (51.5)	648 (91.0)	
Total	347 (48.7)	365 (51.3)	712 (100.0)	

*The value reflects the percentage of row; †The value reflects the percentage of column; ‡The group that makes difference.

583 (81.9%) of the study group stated that they use the internet every day, 422 (59.3%) use the internet 3 hours a day or more. 669 (94.0%) of the students had a device with their own internet access.

The number of students with a social media account was 689 (96.8%). The distribution of those with and without cyber victimization according to some features related to internet usage is given in Table 2.

Table 2. Distribution of students with or without cyber victimization according to some features of internet usage

Some Features About Internet Usage	Cyber Victimization			Statistical Test Value
	No n (%)*	Yes n (%)*	Total n (%)†	χ^2; p
Internet usage frequency				
At least once every day‡	269 (46.1)	314 (53.9)	583 (81.9)	
2-3 times a week‡	56 (58.3)	40 (41.7)	96 (13.5)	**9.358; 0.009**
2-3 times a month‡	22 (66.7)	11 (33.3)	33 (4.6)	
Daily average internet usage time (hours)				
≤1	79 (54.5)	66 (45.5)	145 (20.4)	
2-3	141 (53.2)	124 (46.8)	265 (37.2)	**9.436; 0.009**
≥4‡	127 (42.1)	175 (57.9)	302 (42.4)	
The presence of her/his own room in her house				
Yes	252 (48.0)	273 (52.0)	525 (73.7)	0.433; 0.510
No	95 (50.8)	92 (49.2)	187 (26.3)	
Having a device with internet access				
No	24 (55.8)	19 (44.2)	43 (6.0)	0.918; 0.338
Yes	323 (48.3)	346 (51.7)	669 (94.0)	
Family's restriction on internet use				
Limited	133 (48.9)	139 (51.1)	272 (38.2)	0.005; 0.946
No limitation	214 (48.6)	226 (51.4)	440 (61.8)	
Having social media account				
No	19 (82.6)	4 (17.4)	23 (3.2)	**10.915; 0.001**
Yes	328 (47.6)	361 (52.4)	689 (96.8)	
Acceptance of friendship of people they do not know				
Accepting	90 (39.6)	137 (60.4)	227 (31.9)	**11.017; 0.001**
Not accepting	257 (53.0)	228 (47.0)	485 (68.1)	
Number of friends in social networks compared to real life				
More‡	112 (42.3)	153 (57.7)	265 (37.2)	
The same	151 (53.7)	130 (46.3)	281 (39.5)	**7.487; 0.024**
Less	84 (50.6)	82 (49.4)	166 (23.3)	
Feeling stronger in social networks than in real life				
Positive	86 (42.0)	119 (58.0)	205 (28.8)	**5.304; 0.021**
Negative	261 (51.5)	246 (48.5)	507 (71.2)	
A history of having problems with anyone on the internet				
Experienced	69 (29.6)	164 (70.4)	233 (32.7)	**50.689; 0.001**
Not experienced	278 (58.0)	201 (42.0)	479 (67.3)	
Speaking of things on the internet that can't be said in real life				
Speaking	112 (40.7)	163 (59.3)	275 (38.6)	**11.502; 0.001**
Not speaking	235 (53.8)	202 (46.2)	437 (61.4)	
Sharing a problem that occured on internet with someone in real life				
No	121 (54.3)	102 (45.7)	223 (31.3)	
Yes	226 (46.2)	263 (53.8)	489 (68.7)	**3.966; 0.046**
Total	347 (48.7)	365 (51.3)	712 (100.0)	

*The value reflects the percentage of row; †The value reflects the percentage of column; ‡The group that makes difference.

As the electronic devices used in internet access, the students responded by mobile phone with 74.8% (n=641), computer with 14.2% (n=122) and tablet with 11.0% (n=94). 68.7% of the students constituting the study group reported that they shared the problem they experienced with anyone on the internet with others. The people with whom students shared a problem they experienced on the internet were 51.8% (n=341) friends, 37.7% (n=248) parents, 4.2% (n=28) teachers, 3.8% (n=25) school administrators and 2.4% (n=16) others. (Since more than one answer was given, the numbers were evaluated based on the answers given, not the individuals).

The scores that students got from RSES ranged from 10 to 37 and the mean was 20.3±5.2 (median 20.0). The RSES scores of cyber victims ranged from 10 to 37, with a median of 21. The RSES scores of non-cybervictims ranged from 10 to 35, with a median of 20. Those with cyber victims had higher RSES scores so their self-esteem was found to be lower (z=2.213; p=0.027).

It was determined that the aim of the students to use the internet is to enter and chat on social media with 37.3%, and to follow the news with at least %8.0. Students' reasons for using the internet are given in Table 3.

Table 3. Reasons for students to use the internet

Reasons for Using the Internet	n (%)*
Entering and chatting on social media	868 (37.3)
Fun and games	613 (26.4)
Doing homework	352 (15.1)
Doing research on any subject	298 (12.8)
Following the news	187 (8.0)
Other	6 (0.2)
Total	2324 (100.0)

*Since more than one answer was given, the numbers were evaluated based on the answers given, not the individuals.

Logistic regression analysis was performed with the variables found to be significant in univariate analyses. When compared to other groups in same subtitle, the risk of being cyber victim was 1.66 times higher in the 9th and 10th grades (CI: 1.20-2.30), 4.56 times higher in individuals with poor family income (CI: 1.18-17.64), 1.53 times in the middle ones (CI: 1.10-2.16), 3.15 times in individuals with social media accounts (CI: 1.00-9.85), and 2.80 times higher in individuals having problems with anyone on the internet (CI: 1.96-4.02). The results of logistic regression analysis created with variables which are found to be related to cyber victimization are given in Table 4.

Table 4. Logistic regression analysis results based on the variables determined to be associated with cyber victimization

Variables	p	OR	%95 CI
Grade (Reference: 11-12)			
9-10	**0.002**	1.66	1.20-2.30
Family income status (Reference: Good)			
Medium	**0.016**	1.53	1.1-2.16
Bad	**0.028**	4.56	1.18-17.64
Internet usage frequency (Reference: 2-3 times a month)			
2-3 times a week	0.231	0.73	0.44-1.22
At least once a day	0.162	0.54	0.22-1.28
Average internet usage time per day (Reference: ≤1 hour)			
2-3 hours	0.579	0.87	0.54-1.41
≥4 hours	0.825	1.06	0.64-1.74
Social media account presence (Reference: No)			
Yes	**0.049**	3.15	1.00-9.85
Acceptance of friendship of people they do not know (Reference: Not accepting)			
Accepting	0.393	1.18	0.81-1.72
Number of friends in social networks compared to real life (Reference: Less)			
The same	0.562	0.88	0.59-1.34
More	0.675	0.91	0.58-1.42
Feeling stronger in social networks than real life (Reference: Not feeling so)			
Feeling so	0.232	1.24	0.87-1.78
An experience of having problems with anyone on the internet (Reference: No experience)			
Experienced	**0.001**	2.80	1.96-4.02
Speaking on the internet what one can't say in real life (Reference: Not speaking)			
Speaking	0.266	1.21	0.86-1.69
Sharing a problem that occured on internet with someone in real life (Reference: No)			
Yes	0.171	1.27	0.90-1.80
Constant: B=-2.173, p=0.001			

DISCUSSION

In this study, the prevalence of cyber victimization was found to be 51.3%. In some studies conducted in Turkey, it is reported that cyber victimization prevalence among students varies between 7.0-63.3% (6, 10, 13, 21, 22), the prevalence of students who are both cyberbully and cyber victims varies between 8.9-72.2% (6, 10, 13). In some studies conducted in various countries, it is reported that the prevalence of cyber victimization varies between 10-83.8% (14-20), the prevalence of both cyber victims and cyberbullies varies between 6.4-11.2% (18, 19). Cyber bullies easily find themselves victims, as they can hide their personal identity on the internet and quickly reach large audiences in a short time (29). The frequent use of the internet today also makes cyber victimization widespread. This may be one of the important reasons that approximately half of the students are exposed to cyberbullying in our study. Among the reasons for the different results reported in various studies may be presented as: the studies were conducted in different schools, different age groups, with different measurement tools, and the criteria for accepting a person as a cyber victim and the time interval questioned were varied.

In our study, no difference was found between age and prevalence of cyber victimization. There are also researchers reporting similar results (5, 10, 11, 17, 22). In some studies, it is reported that age increase is a risk factor for cyber victimization (21, 30). In a study by Pabian and Vandebosch young adolescents were reported to be more risky in terms of cyber victimization than older adolescents (15). It is the late childhood and adolescence period when the individual is most susceptible to risks within the developmental periods. Negative issues such as spending a lot of time on the internet, exhibiting asocial behavior, and cyber victimization are common in this period (29). Since our study was conducted only in high school students and covers a certain age range, there may be no difference between age and presence of cyber victimization.

In the study group, no difference was found between male and female in terms of the prevalence of cyber victimization. Similar results have been reported in some studies conducted in various countries and Turkey (9-11, 14, 30). Although there are studies reported that the prevalence of cyber victimization is higher in male (6, 8, 22), there are also studies reported to be higher among female (15, 17, 19). The fact that both males and females have access to the internet and have the ability to use them, makes cyberbullies reach everyone without gender discrimination and this may have caused no difference between cyber victimization and gender.

The prevalence of cyber victimization among students studying in 9-10 grades of schools, found higher than those studying in 11-12 grades. Similar results were reported in the study conducted by Kessel Schneider et al. (20). In the study conducted by Dalmaç Polat and Bayraktar, cyber victimization was reported to be the highest 10th grade, however in the study conducted by Göldağ, it was reported to be the highest in the 11th grade (9, 11). There are also studies reported that there is no difference between grades in terms of prevalence of cyber victimization (6, 8). The situations may be the reason of higher prevalence of cyber bullying in 9th and 10th grades compared to advenced grades; such as increased usage of internet in new generation, the change in circle of friends and social relationships, the switch in concentration of the advenced classes due to exams related to their career.

In our study, it was found that the prevalence of cyber victimization was higher in those with poor family income. While some studies reported that socioeconomic level does not predict cyber victimization and cyber victimization does not differ according to family income status (9-11), in some studies, it was reported that cyber victimization is higher in those with high family income (8, 22). In our study, cyber victimization may have been found more frequent in low family income group because of the economic related factors like sociocultural facilities and educational background.

People can share about themselves through the accounts they create on social media, they can add other people as friends and communicate. People who have never met the person and who is not on the list of friends can also see the posts (29). Those who interact with other people from their social media accounts, share their photos, videos and thoughts are more likely to be cyber victims than those without a social media account. In our study, the presence of social media accounts was found to be one of the risk factors for cyber victimization. Safaria et al. reported that students mostly experienced cyber victimization on social networking sites such as Facebook and Twitter (16). Olenik-Shemesh and Heiman also reported that about a quarter of adolescents experience cyber victimization through social networks (14).

The concept of cyberbullying involves using the internet and technological tools to harm another person, threats, insults, aggression and bullying (5). Those who have problems with anyone on the internet may act like cyberbullier with emotions such as anger as a result of their problem and become a cyber victim. As expected in our study, it was found that having problems with anyone on the internet is an important risk factor for cyber victimization.

Risky internet behaviors such as chatting with foreign people and sharing personal information and photos increase cyber victimization (18). Easy access to the internet, spending a lot of

time on the internet and not knowing the safe internet use also increases the chance of engaging in risky behaviors and being a cyber victim (5, 21, 29, 30). In many studies, the increase in internet usage time has been associated with cyber victimization (4, 6, 9, 17, 22). In the univariate analysis conducted in our study, it was found that the prevalence of cyber victimization was higher in those who had higher internet usage and daily average internet usage time, who accepted the friendship of people they did not know, and those who had more friends in social networks than in real life. As a result of the logistic regression analysis, it was seen that these situations, which were found significant in univariate analyzes, lost their significance. In addition, situations such as having a student's own room at home, having a device with internet access, and not limiting the family's use of the internet are factors that may lead to risky internet behavior (8, 29, 30). However, in our study, no relation was found between these factors and the presence of cyber victimization. Similar results have been reported in some studies (10, 11, 29).

The person who is a cyber victim suffers psychologically, various fears develop, mental illnesses such as depression and anxiety and problematic behaviors appear. These problems are reflected on students' school achievement, leading to a low grade point average (23, 29). It has been reported that those with low school success are more cyber victims (11, 17, 23). In our study, no difference was found between those with and without a psychiatric disease in terms of the prevalence of cyber victimization. Similarly, it was observed that there was no relationship between the grade point average of the previous year and the prevalence of cyber victimization. In a study conducted by Özdemir, it was reported that there was no relationship between academic success and cyber victimization, in the study conducted by Peker et al, there was no predictive effect of academic success on cyber victimization (4, 5).

Despite the damage they have exposed, most cyber victims do not share their grievances with feeling of embarrassment and fear of restriction of their internet use (5). Safaria et al, reported that only a quarter of cyber victims, Kessel Schneider et al. one-third shared this situation with others (16, 20). Support from the close environment reduces cyber victimization (5). Cyber victimization will increase in those who do not share their problems with their immediate environment and do not receive support. In the regression analysis conducted in our study, the student's failure to share a problem on the internet with his / her relatives was not found as a risk factor for cyber victimization. The development of cyber victimization skills of the students on their own without the support of another person can be shown as a reason to explain this situation.

The family is the place where the child receives first education, is socialized first, and the foundations are laid in personality development. The characteristics of family may affect the risk of cyber victimization. Children who are raised in unhealthy families with poor family functionality and emotional bonds experience more cyber victimization (29). It is reported that cyber victimization decreases as the relations with the mother and father increase and, increase in the presence of oppressive, authoritarian or irrelevant parental attitude (5, 6, 8). Parental education level and personality type can affect cyber victimization by affecting family relationships. But in our study, no relation was found between the cyber victimization and the parental education level and personality type. In various studies, it has been reported that cyber victimization did not differ according to the education level of parents (10, 11, 17, 22). Dalmaç Polat and Bayraktar reported that cyber victimization scores did not differ according to the behavior of individuals (calm, aggressive, shy, sociable) (11).

One of the serious problems occurring in cyber victims is reported to be a decrease in self-esteem (29). Self-esteem, which results from the positive and negative attitudes himself/herself of the individual, is affected by some environmental factors. The self-esteem of the children, who are valued by their surroundings and feel that they are important, is high, those who are exposed to negative events such as cyberbullying also have low self-esteem. Those with low self-esteem are less self-confident, non-extroverted, shy, and these individuals are reported to be victims of cyberbullies and experience more cyber victimization (21). In our study, it was found that cyber victims had lower self-esteem. In the studies conducted both in Turkey and in the World, the decrease in self-esteem has been associated with an increase in cyber victimization, and cyber victims have been reported to have lower self-esteem similar to our study (2, 18, 21, 23, 30).

The limitations of the study are the inability of generalization of results due to monocenter localization, some absent students (participation was 65.4%), absence of causality due to characteristics of a cross-sectional study. The strengths of the study are that the research topic is a current and new one and reaching all high schools in the research region.

CONCLUSION

As a result, in this study, it was observed that cyber victimization is a significant problem among high school students studying in Sivrihisar, and cyber victimization is higher in those with low self-esteem. In addition, being 9-10 grade students, poor family income, having a social media account and having problems with anyone on the internet were found to be risk factors for cyber victimization. In order to reduce the cyber

victimization of the students, it will be beneficial to provide information studies and trainings about cyber victimization and safe internet use. In addition, it is important to raise awareness of families and teachers, who are supporters and guides of students, about cyber victimization.

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RESEARCH ARTICLE

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The Use of Neutrophil Lymphocyte Ratio in Patients Presenting to the Emergency Department with Chest Pain

ABSTRACT

Objective: Objective: In this study, we aimed to determine the roles of neutrophil, MPV, and NLR, in the diagnosis of ACS and the differentiation of ACS subtypes (ST-elevation myocardial infarction and non-ST elevation myocardial infarction), in patients presented to the emergency department with chest pain and were diagnosed with ACS (acute coronary syndrome).

Methods: This study was designed as a single-center, cross-sectional, and retrospective. 402 patients who were applied to University Hospital Emergency Department between January 2020 and November 2020; and registered to hospital automation system with chest pain; and underwent further examinations and treatments were included in the study. Ethical approval was obtained from the Local Clinical Research Ethics Committee before the study. Patients who were hospitalized after further examination, who received medical treatment, and did not undergo PCI (Percutaneous coronary intervention) were accepted as NSTMI (n = 202). Patients who were hospitalized after further examination and underwent PCI were accepted as STMI (n = 200).

Results: 36.3% of the patients were female (n = 146) and 63.7% (n = 256) were male. The mean age of the cases was detected to be 61.46 ± 14.06. The number of hospitalized ACS patients for NSTMI suspicion and received medical treatment was 202. The number of patients who underwent PCI and accepted as STMI was 200.Mean neutrophils, MPV, NLR, and Troponin values were also significantly higher than those who are not hospitalized ($p < 0.001$). The mean WBC, Neutrophil, NLR, and Troponin values of the patients underwent PCI were also significantly higher than those without PCI ($p < 0.001$).

Conclusions: We believe that NLR is a diagnostic valuable that can be used as a biomarker in diagnosing ACS and determining the PCI.

Keywords: Emergency Department, Chest Pain, Acute Coronary Syndrome, Percutaneous Coronary Intervention, Neutrophil Lymphocyte Ratio.

Acil Servise Göğüs Ağrısı ile Başvuran Hastalarda Nötrofil Lenfosit Oranının Kullanımı

ÖZET

Amaç: Biz çalışmamızda acil servise göğüs ağrısı şikayeti ile başvuran ve AKS(Akut koroner sendrom) öntanısı alan olgularda; Nötrofil, MPV, NLR, nin AKS tanısı koymada ve AKS subtip ayrımını (ST elevasyonlu myokard enfarktüsüve non St elevasyonlu myokard enfarktüsü) yapabilme durumunu saptamayı amaçlanmıştır.

Gereç ve Yöntem: Bu çalışma tek merkezli, kesitsel ve retrospektif olarak yapıldı. Çalışmaya Üniversite hastanesi acil servisinin 2020-Ocak, 2020-Kasım tarihleri arasında hastane otomasyon sistemine göğüs ağrısı tanısı girilip ileri tetkik ve tedavi yapılan 402 hasta dahil edilmiştir. Çalışma için öncesinde Lokal Klinik Araştırmalar Etik Kurulu'ndan etik onay alındı. İleri tetkik sonrasında hastaneye yatışı yapılan, medikal tedavi alan ve PCI (Perkütan koroner girişim) yapılmayan olgular NSTMI olarak (n=202) kabul edilmiştir. İleri tetkik sonrasında hastaneye yatan ve PCI yapılan olgular STMI (n=200) olarak kabul edilmiştir.

Bulgular: Hastaların %36.3'ü kadın (n=146), %63.7'si (n=256) erkek olarak saptandı. Olguların yaş ortalaması 61.46±14.06 olarak tespit edildi. Hastaneye yatan AKS düşünülen olgulardan NSTMI düşünülen ve medikal tedavi ile alan hasta sayısı 202 iken, PCI tedavisi uygulanan ve STMI kabul edilen olgu sayısı 200 olarak saptanmıştır. Nötrofil, MPV, NLR ve Troponin ortalamaları da yatış yapmayanlardan anlamlı derecede yüksekti ($p<0.001$). PCI yapılan hastaların WBC, Nötrofil, NLR ve Troponin ortalamaları da PCI yapılmayanlardan anlamlı derecede yüksekti ($p<0.001$).

Sonuç: AKS tanısı konmasında ve PCI tedavi yönteminin belirlenmesinde NLR' nin tanı değeri olan bir biyobelirteç olarak kullanılabileceği kanaatindeyiz.

Anahtar Kelimeler: Acil Servis, Göğüs Ağrısı, Akut Koroner Sendrom, Perkütan Koroner Girişim, Nötrofil Lenfozit Oranı.

INTRODUCTION

Acute coronary syndrome (ACS) is a clinical picture that occurs due to acute myocardial ischemia. In patients with ACS are divided into 2 subgroups. The pathology at the myocardial level in patients with non-ST elevation myocardial infarction (NSTMI) is cardiomyocyte necrosis that can be measured by troponin release, or less commonly, myocardial ischemia without cell damage. Generally, the risk of death is significantly lower in this group and they benefit less from aggressive pharmacological and interventional approaches (1). The other subgroup is ST-elevation myocardial infarction (STMI). STEMI is a clinical picture that often manifests itself with chest pain and damage to the heart muscles due to ischemia. ACS in this group is the clinical picture recommended to be hospitalized and treated by applying percutaneous coronary intervention (PCI) as soon as possible (2). In cases with STMI, PCI is a fast and effective method. By improving myocardial blood flow by PCI, the infarct area can be reduced, and mortality can be prevented. Incorrect or late diagnosis of ACS, even late or non-performing PCI in cases with ACS diagnosis, increases the rate of mortality and morbidity (3).

Nowadays, despite many diagnostic and treatment options, acute coronary syndrome continues to be the most important cause of morbidity and mortality in the world. Quick and accurate diagnosis of patients with the acute coronary syndrome in emergency services is very important. However, it may not always be possible to diagnose acute coronary syndrome (ACS) in patients presenting with chest pain and to make the percutaneous coronary intervention (PCI) indication for every diagnosed patient (4). In addition to routine diagnostic options (anamnesis, physical examination, ECG, cardiac markers), the ratio of neutrophil count to lymphocyte count (N/L ratio) has shown itself as a predictor used to show the diagnosis and prognosis of many cardiovascular diseases such as ACS (5). Clinical studies have shown the correlations between NLR and arterial stiffness, the progression of atherosclerosis, high coronary calcium scores, and increase in first diagnosed AF. In addition, complete blood count (CBC) is important, inexpensive, easily accessible, and can be performed easily in many laboratories (6).

In our study, in cases presented to the emergency department with chest pain and diagnosed as a pre- ACS; We aimed to determine the importance of neutrophil, MPV, and NLR in the diagnosis of ACS and the ability to distinguish the ACS subtype (STMI and NSTMI).

MATERIAL AND METHODS

Study Design and Groups: This is a retrospective study conducted in an emergency department of a University Hospital. The Emergency Service of the University Hospital, with approximately 150,000 applications per year to the emergency department. The patients who were registered to the automation system with chest pain between 01/01/2020 and 31/12/2020 were retrospectively scanned and a study group was formed. All cases over the age of 18 and who were stated that they had chest pain to the health personnel in triage and registered to the automation system were examined (n = 879).

The patients (n = 477) who were pre-diagnosed with chest pain and discharged without blood examination were considered as non-cardiac chest pain and were excluded from the study. All patients who were registered to the hospital automation system with chest pain and underwent further examination and treatment were accepted as cardiac chest pain (n = 402).

Patients who were hospitalized after further examination, who received medical treatment, and PCI did not apply were accepted as NSTMI (n = 202). Patients who were hospitalized after further examination and underwent PCI were accepted as STMI (n = 200). The preliminary diagnosis in the hospital system was accepted as anamnesis.In addition, laboratory values could be examined ECG of the patients could not be recorded in the hospital information system, so they could not be evaluated. This was considered among the limitations of the study.

Laboratory Methods: CBC, biochemistry and Troponin parameters were obtained from the results of venous blood samples taken during admission to the emergency department and analyzed retrospectively. CBC analysis was performed via LH 780 Analyzer (Beckman Coulter, Miami, USA). Blood for biochemical analysis such as urea, creatinine, AST (aspartate aminotransferase), ALT (alanine aminotransferase), LDH (lactate dehydrogenase), and troponin was taken during admission to the emergency department and was performed via ADVIA 2400 (Siemens, NY, USA). Among CBC parameters, red blood cell (Rbc), hemoglobin (Hb), hematocrit (Hct), mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), RDW, platelet (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), white blood cell (WBC), neutrophil count, lymphocyte count, and neutrophil/lymphocyte ratio (NLR) were examined. The relationships of these parameters with the hospitalization decision of patients with chest pain and the decision of PCI in hospitalized patients was examined.

Ethics Consideration*:* Ethics approval was obtained from the Ordu University Clinical Research Ethics Committee before the study (24/12/2020 No: 2020/268). Since the study was designed retrospectively, the informed consent forms of the patients were waived. The study was carried out following the Helsinki Declaration.

Data Analysis: The parametric test assumptions were analyzed with the Levene test

and the Kolmogorov Smirnov test. When appropriate, independent samples t-test was used. When the assumptions were not provided, Welch's t-test was used. ROC analysis was used to evaluate the diagnostic performances of the study variables. Youden's index was used as a criterion for choosing an optimal cut-off value. All statistical tests were performed using SPSS v26 (IBM SPSS, IBM Corp) at the significance level of p < 0 .05.

RESULTS

In this study, data of 879 cases registered to hospital automation system with chest pain between January 2020 and November 2020 in a university hospital emergency department were analyzed. From these cases, 402 patients who were thought to have cardiac chest pain and needed further examination were included in the study. 36.3% of the included cases were female (n = 146) and 63.7% (n = 256) were male. The mean age of the cases was 61.46 ± 14.06. The demographic characteristics of the included patients are shown in Table 1.

The number of hospitalized patients after further examinations was 402. Among the inpatients with ACS pre-diagnosis, the number of cases which thought to be NSTMI and ACS treatment was administered with medical treatment was 202. The number of patients underwent PCI after hospitalization and accepted as STMI was determined as 200.

Table 1. Demographic characteristics of the included cases.

		n	%
Gender	Female	146	36.3
	Male	256	63.7
DM	Yes	97	24.1
	No	305	75.9
HT	Yes	119	29.6
	No	283	70.4
PCI	Yes	69	17.2
	No	333	82.8
COPD	Yes	30	7.5
	No	372	92.5
ASTHMA	Yes	10	2.5
	No	392	97.5
	Yes	161	40.0

DM; Diabetes mellitus, HT; Hypertension, PCI; Percutaneous Coronary Intervention, COPD; chronic obstructive pulmonary disease

The comparison of study variables according to hospitalization is given in Table 2. According to the t-test, there was no significant difference between hospitalization status in terms of Lymphocyte, Hemoglobin, and PLT (p> 0.05). The mean age of hospitalized patients (64.07 ± 12.87) was significantly higher than the non-hospitalized patients (58.87 ± 14.74) (p <0.001). Similarly, the mean WBC, Neutrophil, MPV, NLR, LDH, AST, ALT, and Troponin values of the hospitalized patients were significantly higher than the non-hospitalized patients (p <0.001). Mean Creatine value was also significantly higher in hospitalized patients than non-hospitalized patients (p <0.05).

Table 2. Comparison of study variables according to hospitalization.

Variables	Hospitalization	n	Mean	SD	p
Age	No	202	58.87	14.74	**<0.001*** **
	Yes	200	64.07	12.87	
WBC	No	202	8.05	2.68	**<0.001*** **
	Yes	200	9.68	3.52	
Neutrophil	No	202	4.86	2.19	**<0.001*** **
	Yes	200	6.53	3.27	
Lymphocyte	No	202	2.34	1.12	0,976
	Yes	200	2.34	1.78	
Hb	No	202	13.48	1.93	0,457
	Yes	200	13.96	8.95	
PLT	No	202	236.41	60.47	0,422
	Yes	200	231.56	60.33	
MPV	No	202	10.01	0.82	**<0.001*** **
	Yes	199	10.33	0.88	
NLR	No	202	2.58	2.21	**<0.001*** **
	Yes	166	3.91	2.94	
LDH	No	202	205.06	44.47	**<0.001*** **
	Yes	196	345.43	280.88	
AST	No	202	19.70	7.40	**<0.001*** **
	Yes	200	67.95	93.11	
ALT	No	202	19.51	11.47	**<0.001*** **
	Yes	200	29.58	30.53	
Troponin	No	202	0.10	0.00	**<0.001*** **
	Yes	193	12705.01	29447.19	
Creatinine	No	202	0.92	0.34	**0,037***
	Yes	200	1.04	0.71	

WBC; White Blood Cell, Hb; Hemoglobin, PLT; Platelet, MPV; Mean platelet volume, NLR; Neutrophil lymphocyte ratio, LDH; lactate dehydrogenase, AST; Aspartate aminotransferase, ALT; Alanine aminotransferase;
Ki-kare testi *<0.05 ** <0.01 ***<0.001

The comparison of study variables according to hospitalization status is given in Table 2. According to the t-test, Lymphocyte, Hemoglobin, and PLT did not differ significantly according to hospitalization status (p> 0.05). The mean age of the hospitalized patients (64.07 ± 12.87) was significantly higher than the non-hospitalized patients (58.87 ± 14.74) (p <0.001). Similarly, the mean WBC, Neutrophil, MPV, NLR, LDH, AST, ALT, and Troponin values of the inpatients were significantly higher than the outpatients (p <0.001). The mean creatine value was also significantly higher in inpatients than non-hospitalized patients (p <0.05).

The comparison of study variables according to the PCI status is given in Table 3. The mean age of the inpatients (62.78 ± 12.55) was higher than the outpatients (60.57 ± 14.95), but it was not statistically significant according to the t-test (p> 0.05). Similar situation was valid for Lymphocyte, Hb, and creatine (p> 0.05). In addition, also the mean PLT values did not change according to hospitalization (p> 0.05). In inpatients, the mean WBC, Neutrophil, NLR, LDH, AST, ALT, and Troponin values were also significantly higher than the outpatients (p <0.001). MPV values of inpatients (10.32 ± 0.83) was lower than non-hospitalized patients (10.07 ± 0.88) and this was statistically significant (p <0.01).

Table 3. Comparison of study variables according to PCI status.

Variables	PCI	n	Mean	SD	p
Age	No	241	60.57	14.95	0.110
	Yes	161	62.78	12.55	
WBC	No	241	8.10	2.73	**<0.001*** **
	Yes	161	10.01	3.57	
Neutrophil	No	241	4.97	2.28	**<0.001*** **
	Yes	161	6.76	3.37	
Lymphocyte	No	241	2.28	1.11	0.338
	Yes	161	2.44	1.92	
Hb	No	241	13.40	1.92	0.214
	Yes	161	14.21	9.93	
PLT	No	241	234.59	59.97	0.811
	Yes	161	233.11	61.16	
MPV	No	241	10.07	0.88	**<0.01** **
	Yes	160	10.32	0.83	
NLR	No	241	2.78	2.43	**<0.001*** **
	Yes	127	3.95	2.87	
LDH	No	241	206.87	46.50	**<0.001*** **
	Yes	157	377.52	304.40	
AST	No	241	20.18	8.21	**<0.001*** **
	Yes	161	78.92	100.65	
ALT	No	241	19.34	11.28	**<0.001*** **
	Yes	161	32.28	33.11	
Troponin	No	241	0.1004	0.0036	**<0.001*** **
	Yes	154	12705.0072	29447.1869	
Creatinine	No	241	0.95	0.41	0.182
	Yes	161	1.03	0.73	

PCI; Percutaneous Coronary Intervention, WBC; White Blood Cell, Hb; Hemoglobin, PLT; Platelet, MPV; Mean platelet volume, NLR; Neutrophil lymphocyte ratio, LDH; lactate dehydrogenase, AST; Aspartate aminotransferase, ALT; Alanine aminotransferase
Ki-kare testi *<0.05 ** <0.01 ***<0.001

The comparison of study variables according to the PCI is given in Table 4. The mean age of the patients underwent PCI (62.78 ± 12.55) was higher than the non-hospitalized patients (60.57 ± 14.95), but it was not statistically significant according to the t-test (p> 0.05). Similar situation was valid for Lymphocyte, Hb, and Creatine (p> 0.05). Also, the mean PLT did not change according to the PCI (p> 0.05). The mean WBC, Neutrophil, NLR, LDH, AST, ALT, and Troponin values of the patients underwent PCI were also significantly higher than those did not (p <0.001). The MPV values (10.32 ± 0.83) of the patients underwent PCI were lower than those did not (10.07 ± 0.88), and this was statistically significant (p <0.01).

Table 4. Area Under the ROC Curve (AUC), sensitivity and specificity by optimized cut-off points for study variables in PCI.

Variables	AUC (95% CI)	Cut-off according to the Youden index	Sensitivity (%)	Specificity (%)	p
WBC	0.666 (0.608-0.724)	8.42	61.2	60.6	**<0.001**
NEU	0.687 (0.630-0.745)	5.20	65.3	65.6	**<0.001**
MPV	0.593 (0.533-0.654)	10.15	54.5	56.8	**<0.01**
NLR	0.691 (0.634-0.747)	2.53	65.3	66.4	**<0.001**
LDH	0.741 (0.680-0.802)	224.50	66.9	69.7	**<0.001**
AST	0.770 (0.709-0.830)	21.50	72.7	68.9	**<0.001**
ALT	0.695 (0.637-0.753)	19.50	64.5	61.4	**<0.001**
Troponin	0.968 (0.943-0.993)	2.43	90.9	99.6	**<0.001**

PCI; Percutaneous Coronary Intervention, WBC; White Blood Cell, NEU; Neutrophil, MPV; Mean platelet volume, NLR; Neutrophil lymphocyte ratio, LDH; lactate dehydrogenase, AST; Aspartate aminotransferase, ALT; Alanine aminotransferase

ROC Curve Analysis: The diagnostic value of NLR, which was determined to show a significant change according to the PCI, was examined by ROC analysis. As a result of ROC curve analysis, there is no 0.5 value in the 95% confidence interval (CI) calculated for Area Under the ROC Curve (AUC) in both female and male patients (Table 4). NLR predicted the presence of PCI with 58.3% Sensitivity and 57.0% Specificity (with a positive likelihood ratio of 1.36) in women if it was> 2.215. NLR predicted the presence of PCI with 73.6% Sensitivity and 62.4% Specificity (with a positive likelihood ratio of 1.96) in men if it was> 2.345. Therefore, NLR may be a diagnostic biomarker for both men and women. However, it is more effective in males than females in terms of PCI decisions. For these reasons, while NRL can be used for PCI decisions in male patients, it needs additional biomarkers in female patients.

DISCUSSION

In this study, systemic inflammation biomarkers from CBC, routine emergency biochemistry, and troponin panel examinations of patients presenting with chest pain were examined. Neutrophil, MPV, and NLR values of the inpatients (ACS) were found to be significantly higher than the outpatients (for ACS diagnosis). In addition, the Neutrophil, MPV, and NLR values were significantly higher in STMI inpatients (underwent PCI), than NSTMI inpatients who did not undergo PCI. In the pathogenesis of ACS, it is known that there is a dysfunction in the inflammatory system. Dysfunction in this system makes the plaques more unstable and causes ACS (7). Neutrophil-lymphocyte ratio (NLR) shows the balance between regulatory factors and inflammation that occurs from various reasons. Therefore, it is considered as a new biomarker of thrombosis. Various studies about inflammatory response reported associations between NLR and many clinical conditions such as diabetes, malignant tumors, ACS, atherosclerosis, obesity, heart failure, and dyslipidemia (8,9). In a study conducted by Karagun, in inflammatory and infective events, an increase in neutrophil and thrombocyte count was observed, and a decrease in lymphocyte counts was reported. He also reported that NLR increases in many disease groups such as sepsis, cardiovascular diseases, neurovascular diseases, and malignancies, and it can be used in the prognostic follow-ups (10). Although mean platelet volume (MPV), which is another parameter in the CBC, is generally used to evaluate platelet functions in routine practice, it has been reported to show inflammatory load and disease activity. Also, MPV has been reported to be associated with disease activity in unstable angina, ulcerative colitis, myocardial infarction, pre-eclampsia, and Crohn's disease (11). In our study, we detected that neutrophil, MPV, and NLR values were significantly higher in patients diagnosed with the acute coronary syndrome in the emergency department (inpatients) than patients who were not diagnosed with ACS (outpatients).

NSTMI is the ACS subgroup that has less myocardial damage. Generally, the mortality rate in this group is lower than STMI, medical treatment sare recommended rather than invasive treatments. Therefore, patients in this group are hospitalized and generally, the medical treatment protocol is preferred (1). High sensitivity troponin (hs-Tn) measurement is recommended in the diagnoses of ACS. The second cTn test time interval can be shortened with the use of hs-cTn kits, due to their higher sensitivity and diagnostic accuracy in MI detection at the time of admission. It is recommended to use 0 hour/1-hour (best option) or 0 hour/2-hour (second-best option) algorithms (1).

Another subgroup of ACS is ST-elevation myocardial infarction (STMI). STMI is a clinical picture that usually manifests itself with chest pain and heart muscle damage due to ischemia. Among the ACS subgroups, this clinical picture has the highest mortality. This group is recommended to be hospitalized and treated with PCI as soon as possible. If ischemia is not resolved in the first 4 hours following coronary occlusion, myocardial damage increases, and heart contraction deteriorates. If reperfusion can be achieved during this period, it will prevent infarction. Therefore, (early) opening of the occluded vessel without expanding the area of ischemic necrosis; decreases mortality, decreases the risk of complications, and

contributes positively to the life expectancy of the patient (2). Therefore, opening of the occluded vessel before ischemic necrosis expands (early) decreases mortality and the risk of complications thus prolongs the life expectancy (2). In a study, it was emphasized that even minutes are very important in emergency reperfusion treatment, and PCI should be performed as quickly as possible because it reduces mortality and complications in ACS (12). For this reason, ACS patients should be diagnosed and underwent PCI quickly. Rapid diagnosis protocol with anamnesis, physical examination, and high-precision cardiac troponin test is recommended for ACS (13). Besides, there are publications reporting that Neutrophil, MPV, and NLR values can be used in the diagnosis of ACS subtypes (8). In addition, the relative lymphopenia observed in STMI patients compared to NSTMI patients causes a higher rate of NLR. In this direction, NLR can be used in the differentiation of STMI patients and NSTMI patients (14). In another study, it was reported that neutrophil, MPV, and NLR values can be used in the diagnosis of ACS and in determining the poor prognosis (15). Similarly, to the study of Tamhane et al., Azab et al. also found troponin levels of ACS patients with higher NLR levels significantly higher (16,17). In their study, Aydın et al. reported that neutrophil, MPV, and NLR values can be used in the diagnosis of STMI (8). Similar to the literature, in our study, MPV, Neutrophil, and Troponin values of patients with ACS (STMI) who underwent PCI were found to be higher than ACS without PCI patients (NSTMI). It is thought that the unavailability of troponin tests, especially in peripheral hospitals, and long intervals needed for control tests such as 2 hours at the earliest may cause delays in the decision of PCI. CBC parameters such as WBC, Neutrophil, MPV, and NLR are inexpensive, common, and reproducible. Therefore, we believe that they can be used in the diagnosis of ACS and in making PCI decisions.

CONCLUSION

In conclusion, in our study, the diagnostic specificity and sensitivity of Troponin were found to be significantly high in diagnosing ACS and determining the PCI. In addition, diagnostic specificity and sensitivity of NLR were also found to be high. Although troponin is important for the diagnosis of ACS in emergency departments, we believe that NLR too can be used as a diagnostic biomarker, especially in male patients with suspected ACS.

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RESEARCH ARTICLE

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Foreign Body Aspiration in Children; Duzce University Five-Years Results

ABSTRACT

Objective: Foreign body aspiration is a preventable cause of mortality and morbidity especially in younger than three years old children. The aim of this study is to determine the risk factors, causes and prognosis in patients with foreign body aspiration.

Methods: In this study, laboratory and examination findings of 35 patients who underwent bronchoscopy, because of suspected foreign body aspiration, were retrospectively analyzed.

Results: Of the 35 patients included in the study, 19 were boys and 16 were girls. The mean age was 3,2. The most causes of application were cough, and wheezing. Foreign body was detected in the right main bronchus in 62,8%, in the left main bronchus in 25,7%, in the trachea in 5,7% and in both bronchi in 5,7% of the patients.

Conclusions: Early diagnosis and intervention significantly reduce the mortality and morbidity in foreign body aspirations. Prevention of foreign body aspirations is possible with the education of babysitters and family members.

Keywords: Foreign Body Aspiration, Childhood, Bronchoscopy.

Çocuklarda Yabancı Cisim Aspirasyonları; Düzce Üniversitesi, 5 Yıllık Sonuçlar

ÖZET

Amaç: Yabancı cisim aspirasyonu, özellikle 3 yaşından küçük çocuklarda önlenebilir bir mortalite ve morbidite nedenidir. Bu çalışmanın amacı yabancı cisim aspirasyonu nedeniyle başvuran hastalarda risk faktörleri, nedenleri ve prognozu belirlemektir.

Gereç ve Yöntem: Yabancı cisim aspirasyonu şüphesiyle bronkoskopi yapılan 35 hastanın şikayetleri, laboratuvar ve muayene bulguları retrospektif olarak incelendi.

Bulgular: Çalışmaya alınan toplam 35 hastanın 19'u erkek ve 16'sı kızdı. Hastalar ortalama 3,2 yaşındaydı. Hastaların hastaneye başvuru nedeni en sık öksürük ve hırıltılı solunum idi. Yabancı cisim hastaların %62,8'inde sağ ana bronşta, %25,7'sinde sol ana bronşta, %5,7'sinde trakeada ve %5,7'sinde de her iki bronşta saptandı.

Sonuç: Yabancı cisim aspirasyonlarında hızlı tanı ve erken müdahale ile mortalite ve morbidite oranları belirgin şekilde azalmaktadır. Yabancı cisim aspirasyonlarının önlenmesi ancak bebek bakıcılarının ve aile bireylerinin eğitimi ile mümkündür.

Anahtar Kelimeler: Yabancı Cisim Aspirasyonu, Çocukluk Çağı, Bronkoskopi.

INTRODUCTION

Foreign body aspiration is defined as the aspiration of a foreign body into the tracheobronchial tree (1). As the result of inhalation of materials such as foods, toys, bones, seeds occur acute-onset upper respiratory airway obstruction. The main reasons are tendency to talk, cry and move while eating or put objects in the mouth unconsciously. On the other hand, the absence of molar teeth is another risk factor for aspiration. Even though aspiration occurs with non-food products, such as small plastic toys, metal objects etc., most of the cases occur with food (2). Foreign body aspiration is a preventable cause of mortality and morbidity especially in younger than three years old children (3).

Cough, cyanosis and wheezing are the most symptoms and findings (4). In many cases, cardiovascular arrest and sudden death are observed (5). Rarely any symptoms are seen (6). Complications may occur such as emphysema, bronchial collapse and pneumonia as the result of aspiration (7). X-ray is not always supported foreign body aspiration findings (8). Bronchoscopy is the best-known technique for diagnosis and treatment (9).

In this study, foreign body aspiration causes, risk factors and morbidity rates were evaluated retrospectively in the five years period in patients who admitted to our emergency department.

MATERIAL AND METHODS

Between August 2014 and November 2019, patients who applied to Duzce University Faculty of Medicine Hospital Paediatric Emergency Department because of foreign body aspiration were retrospectively analysed. The diagnosis was confirmed with bronchoscopy. Bronchoscopy was performed in the operating room under general anaesthesia. The gender, age, symptoms, physical examination and radiological findings, location and the type of the foreign body, time until bronchoscopy and the discharge time after bronchoscopy, the complications after the procedure and the seasonal relationship of the foreign body aspiration were evaluated.

Statistical Analysis: Data obtained in this study evaluated with descriptive statistics such as mean, standard deviation, numbers and percentages. Also Fisher's exact test was used to analyse categorical variables between groups. IBM SPSS version 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) statistical package program. P values of 0.05 was considered statistically significant..

RESULTS

Of the 35 patients included in the study, 19 (54%) were boys and 16 (46%) were girls. The mean age was 2,41± 2,12 (10 months-7 years) of the boys and was 4,16± 4,69 (8 months-16 years) of the girls. 25 cases (71%) were under three years old. 10 (28%) patients applied in the spring (March, April, May) and similarly, 10 patients (28%) applied in the autumn (September, October, November). On the other hand, the most common application time was in May (n=5) and the least application was in February (n = 1). The most causes of application were cough, and wheezing. 51% (n = 18) of aspirations took place under the babysitter supervision. 97% (n = 34) of the patients applied to a hospital on the same day and 74% of the patients were referred from another hospital. None of the patients had low oxygen saturation. In the physical examination, wheezing and rales were detected in 24 patients (68%). Diminished breath sound was found in 17 patients (48%). 5% of patients (n = 2) had no pathological breath sound. Posteroanterior chest radiography was performed in all cases. Computed tomography (CT) was performed in 2 patients (5%) due to clinical and radiological suspicion and the diagnosis was confirmed. The most common localization of the foreign body in the right main bronchus (62%). The other localizations were in the left main bronchus, trachea and both bronchi. Bronchoscopy was performed in 82% of the patients (n = 29) in the day of admission. 82% (n = 29) of the foreign bodies were food. On the other hand, needle aspiration was significantly high in patients over three years old ($p<0.05$). In a case with a recurrent pneumonia, CT was performed. In this case, part of the toy was removed by bronchoscopy after the diagnosis with CT. No complication was detected in 92% of the patients (n = 32) after bronchoscopy. However, pneumonia developed in 8% of patients (n = 3). Mean hospitalization period after

bronchoscopy was 1,2 days. 88% (n = 31) of the patients were discharged one day after bronchoscopy, the longest hospitalization time was 7 days. No patient was needed intensive care unit and none of the patient died. Demographic characteristics and findings were shown at Table 1, 2.

Table 1. Symptoms and findings of the patients according to age three

		<3 years (n=25)	>3 years (n=10)	p
Symptom; n (%)				
	Swallowing needles	1 (4.0)	1 (10.0)	NS
	Frequent lower respiratory tract infections	0	1 (10.0)	NS
	Coughing	19 (76.9)	8 (80.0)	NS
	Wheezing	5 (20.0)	0	NS
Foreign body type; n (%)				
	Needle	0	**3 (30.0)***	**0.03**
	Food	22 (88.0)	7 (70.0)	NS
	Toy	3 (12.0)	0	NS
Breath sound; n (%)				
	Normal	0	2 (20.0)	NS
	Bilateral rales, wheezing	7 (28.0)	4 (40.0)	NS
	Diminished breath sounds in the right side	10 (40.0)	1 (10.0)	NS
	Coarse breathe sound in the right side	3 (12.0)	0	NS
	Diminished breath sounds in the left side	4 (16.0)	2 (20.0)	NS
	Retraction, wheezing	0	1 (10.0)	NS
	Coarse breathe sound in the left side	1 (4.0)	0	NS
Radiographic findings; n (%)				
	Normal	11 (44.0)	8 (80.0)	NS
	Atelectasis in the right lower lobe	1 (4.0)	1 (10.0)	NS
	Hyperaeration in the right lung	7 (28.0)	0	NS
	Hyperaeration in the left lung	3 (12.0)	0	NS
	Total atelectasis on the left lung	1 (4.0)	0	NS
	Fissuritis on the right	0	1 (10.0)	NS
	Atelectasis in the left lower lobe	1 (4.0)	0	NS
	Total atelectasis on the right lung	1 (4.0)	0	NS
Localization; n (%)				
	Right main bronchi	17 (68.0)	5 (50.0)	NS
	Left main bronchi	6 (24.0)	3 (30.0)	NS
	Trachea	1 (4.0)	1 (10.0)	NS
	Bilateral	1 (4.0)	1 (10.0)	NS

NS: non-significant

DISCUSSION

Foreign body aspiration is a major cause of mortality and morbidity, especially in under 3 years old children. Acute respiratory distress, chronic and irreversible lung injury and death are important complications (3). In the literature, death caused by foreign body aspiration is between 0 and 1.5% in all age groups (10). The main causes of death are asphyxia, pneumonia and sepsis, delay in diagnosis, sudden death, cardio-pulmonary arrest, anaesthesia and bronchoscopy complications (11). In our study, no mortality was detected due to foreign body aspiration. Early application, experienced medical team and early intervention could be the main reasons of no mortality.

Foreign body aspiration is frequently encountered under three years old children. They desire to bring foreign bodies to their mouths, when playing, running or crying, and their swallowing functions, mouth, chin, larynx and epiglottis anatomy are not sufficiently developed (3). On the other hand because of they are more active than girls, aspiration is more commonly seen in boys (10). Similarly literature, in our series, most of our patients were under 3 years old and were boy, but there was no statistically significant difference between the sexes (p>0.05).

Table 2. Symptoms and findings of the patients according to gender and age

	Girls (n=16)			Boys (n=19)		
Age; mean± SD (years)	2,41± 2,12 (10 months-7 years)			4,16± 4,69 (8 months-16 years)		
	<3 years (n=11)	>3 years (n=5)	p	<3 years (n=14)	>3 years (n=5)	p
Symptom; n (%)						
Swallowing needle	0	1 (20.0)		0	0	
Frequent lower respiratory tract infections	0	1 (20.0)		0	0	
Coughing	10 (90.9)	3 (60.0)	NS	10 (71.4)	5 (100)	NS
Wheezing	1 (9.1)	0		4 (28.6)	0	
Foreign body; n (%)						
Needle	0	2 (40.0)		0	1 (20.0)	
Food	10 (90.9)	3 (60.0)	NS	12 (85.7)	4 (80.0)	NS
Toy	1 (9.1)	0		2 (14.3)	0	
Breath sound; n (%)						
Normal	0	1 (20.0)		0	1 (20.0)	
Bilateral rales, wheezing	2 (18.2)	3 (60.0)		5 (35.7)	1 (20.0)	
Diminished breath sounds in the right side	5 (45.5)	0		5 (35.7)	1 (20.0)	
Coarse breath sound in the right side	2 (18.2)	0	NS	1 (7.1)	0	NS
Diminished breath sounds in the left side	2 (18.2)	0		2 (14.3)	2 (40.0)	
Retraction, wheezing	0	1 (20.0)		0	0	
Coarse breath sound in the left side	0	0		1 (7.1)	0	
Radyographic findings; n (%)						
Normal	3 (27.3)	3 (60.0)		8 (57.1)	5 (100)	
Atelectasis in the right lower lobe	0	1 (20.0)		1 (7.1)	0	
Hyperaeration in the right lung	4 (36.4)	0		3 (21.4)	0	
Hyperaeration in the left lung	2 (18.2)	0		1 (7.1)	0	
Total atelectasis on the left lung	1 (9.1)	0	NS	0	0	NS
Fissuritis on the right	0	1 (20.0)		0	0	
Atelectasis in the left lower lobe	0	0		1 (7.1)	0	
Total atelectasis on the right lung	1 (9.1)	0		0	0	
Localization; n (%)						
Right main bronchi	7 (63.6)	4 (80.0)		9 (64.3)	1 (20.0)	
Left main bronchi	3 (27.3)	0	NS	3 (21.4)	3 (60.0)	NS
Trachea	1 (9.1)	1 (20.0)		0	0	
Bilateral	0	0		2 (14.3)	1 (20.0)	

NS: non-significant

Seasonal foreign body aspiration cases have been reported in the literature. In a study, Albirmawy et al were found that the highest frequency of foreign body aspirations in Spring and Summer months. They stated that a high percentage of watermelon and peanut are consumed in summer (12). Tan et al. concluded that some geographic and seasonal variations, were the important factors of foreign body aspirations. They found that peanut and the other nuts were the most common foreign bodies. As these foods are consumed more in the summer, it could be thought that the possibility of aspiration of these foods increases (13). Most of the food that was aspirated were nuts and seeds in our study. Thus, we found that the aspirations took place during the spring and summer seasons generally, similar to the previous literature.

The first step in the diagnosis of foreign body aspiration is carefully taking the history and making the physical examination. The most common symptoms and findings are; cough, wheezing and rapidly developing respiratory distress (4). Symptoms and signs may vary depending on the duration, location, size of the foreign body and characteristics of aspiration material in course of time. Sometimes patients may be completely asymptomatic. In this case, aspiration is diagnosed with the patient's history. In our study, there was no asymptomatic patient. The most common symptoms were sudden cyanosis, cough and wheezing. On the physical examination, wheezing, stridor or rales were the most common findings on the aspirated side of the lung.

The first diagnostic approach is chest radiography in patients with suspected foreign body aspiration. If there is a radiopaque foreign body, the diagnosis can be made easily. However, most of the foreign bodies are food, 90% of them are non-opaque and they are generally not seen on radiography (8). In case of the absence of radiographic findings, foreign body aspiration does not exclude. If the history and the patient's

symptoms are compatible for foreign body aspiration, bronchoscopy must be performed (14). Although bronchoscopy is a simple and reliable procedure, it may lead to complications such as pneumonia, pneumothorax, pneumo-mediastinum, airway oedema, respiratory stress and cardiac arrest (15). For this reason, bronchoscopy should be done by experienced hands. While most of our patients did not have any complications after bronchoscopy, only 3 patients developed pneumonia. Pneumonia may occur due to interventional procedures or may be associated with delay in diagnosis. A broad spectrum antibiotic is recommended for the treatment of the pneumonia secondary to foreign body aspiration (16).

The most common radiographic finding of cases with foreign body is the hyperaeration in the aspirated side (14). The right main bronchus is shorter, thicker and more vertical than the left main bronchus in children. Therefore, more air enters into the right system in inspiration. For this reason, foreign bodies especially must seek in the right main bronchus (10). Similar to the literature, most of the foreign bodies were in the right main bronchus in our patients and the hyperaeration was in the right lung in X-ray.

CONCLUSION

Foreign body aspiration is a common reason for applying to the emergency room, especially in children younger than 3 years old. Rapidly diagnosis and early intervention significantly reduce the mortality and morbidity. CT helps in the differential diagnosis in patients who have been complaining for a long time. Bronchoscopy is the gold standard in diagnosis and treatment. It should be performed in the operating room and by experienced hands to minimize complications. Prevention of foreign body aspirations is possible with the education of babysitters and family members.

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RESEARCH ARTICLE

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Evaluation of the Protective Effect of the Cup Therapy on the Epileptic Seizure in Rats

ABSTRACT

Objective: Cup therapy has an important place in traditional and complementary medicine applications. The purpose of our study, this is the first time to investigate the protective effect of cup therapy in rats on experimentally generated epileptic seizures in new rat modeling created by different anatomic regions.

Methods: A total of 42 Wistar albino rats were randomly divided into 6 groups (n:7). The "new dry cup" was applied to the G1 group, and the "new wet cup" model was applied to the G2. In the G3 group, an "epilepsy model" (PTZ, 35 mg / kg) was created and "diazepam" (2.5 mg / kg) was given to G4. "Dry cup" and "wet cup" models were applied to the G5 and G6 groups, respectively. 24 hours after the cupping therapies, the rats were injected with PTZ and the epilepsy behavior scores of the rats in all groups were recorded for 20-30 minutes.

Results: In the 'Open Area' and 'Elevated Plus Maze' tests, there was no behavioral difference between the cup therapy group and the control group ($p > 0.05$). Given all the parameters, the G4 group significantly reduces the seizure compared to other groups ($p < 0.05$). There is a significant difference in G2, G5 and G6 groups compared to G3 in the phases parameter ($p < 0.05$).

Conclusions: In this study, the new wet cup therapy (G2), which was applied for the first time, had a protective effect on seizures. G2, G5 and G6 groups are observed to suppress seizures compared to G3. Our findings are expected to contribute greatly to animal model analysis in the future.

Keywords: Epilepsy, Seizure, Cup Therapy, Hijama, Rat, Animal Model.

Kupa Terapisinin Ratlarda İndüklenen Epileptik Nöbet Üzerine Koruyucu Etkisinin Değerlendirilmesi

ÖZET

Amaç: Geleneksel ve tamamlayıcı tıp uygulamaları içerisinde kupa terapisi önemli bir yer almaktadır. Çalışmamızın amacı, ilk kez sıçanlarda kupa terapisinin farklı anatomik bölge tayini ile oluşturulan yeni rat modellemesinde, deneysel olarak oluşturulmuş epileptik nöbetler üzerine koruyucu etkisinin araştırılmasıdır.

Gereç ve Yöntem: Çalışmamızda, 42 adet Wistar albino cinsi 3-4 aylık (200-250 gr) sıçanlar kullanılmıştır. G3 ve G4 dışındaki diğer dört gruba (n=7), kupa terapisi uygulamasından 24 saat sonra, PTZ (35 mg/kg, sc., 0,2 cc) enjekte edildi ve ardından davranışsal epilepsi skorlaması yapılmıştır.

Bulgular: Toplamda 42 adet Wistar albino sıçan rastgele 6 gruba (n:7) ayrılmıştır. G1 grubuna "yeni kuru kupa", G2'ye ise "yeni yaş kupa" modeli uygulanmıştır. G3 grubunda, "epilepsi modeli" (PTZ, 35 mg/kg) oluşturulmuş ve G4'e diazepam (2,5 mg/kg) verilmiştir. G5 ve G6 gruplarına ise "kuru kupa" ve " yaş kupa " modelleri sırasıyla uygulanmıştır. Kupa terapilerinden 24 saat sonra, sıçanlara PTZ enjekte edilmiş ve daha sonra tüm gruplardaki sıçanların epilepsi davranış skorları 20-30 dakika boyunca kaydedilmiştir.

Sonuç: Bu çalışmada, ilk defa uygulanmış olan yeni yaş kupa terapisinin (G2) nöbetler üzerine koruyucu etkisi bulunmuştur. G2, G5 ve G6 gruplarının G3'e kıyasla nöbeti baskıladığı gözlemlenmektedir. Bulgularımızın ileride bu konuda yapılacak hayvan modeli analizlerine büyük ölçüde katkı sağlaması beklenmektedir.

Anahtar Kelimeler: Epilepsi, Nöbet, Kupa Terapisi, Hacamat, Rat, Hayvan Modeli.

INTRODUCTION

Epilepsy is a progressive neurodegenerative disease characterized by recurrent seizures as a result of abnormal and synchronous neuron hyperactivity due to multifactorial causes. It was observed that the incidence of epilepsy was higher in childhood and old age, and it was at a lower level in early adulthood (1, 2). According to the International Association for Combating Epilepsy (ILAE) criteria, the diagnosis of idiopathic epilepsy is seen in the rate of 36-44 / 1000 (3). According to clinical information and electroencephalography (EEG) changes, no underlying pathological process was detected in idiopathic epilepsies (4).

Pentylenetetrazole (PTZ) induced animal model is widely used in the investigation of epilepsy pathophysiology. It is known to be effective by binding to γ aminobutyric acid type A (GABA-A) receptors associated with the postsynaptic Cl- channels, which are the binding site of picrotoxin in general. In the message regulated with N-Methyl-D aspartate (NMDA) receptors, it plays an important role in the formation of PTZ-induced generalized tonic-clonic seizures (6).

Traditional and complementary medicine (TCM) includes 14 different types of application areas within the scope of the Ministry of Health. It is used in the treatment of many diseases such as asthma, cellulite, fibromyalgia, hypertension, ischemia and allergic rhinitis, as well as in pathological conditions affecting the nervous system (7, 8). Cup therapy is an important part of TCM applications.

Cup therapy has been widely used in many regions of the world for centuries in the diagnosis and treatment of different diseases (9, 10). Although there are many variations of cup therapy, there are two most used forms. The first of these is a dry cup treatment known as “cupping” and there is no incision in this method and no blood is drawn after cupping (11). In the second cugging method known as Hijama, after the incision is applied to certain points in the body, the blood is released by creating negative pressure with the cup. In the literature, there are studies evaluating the use of wet cup therapy in diseases affecting the nervous system, such as migraine (12), neuralgia, manic depression and mental diseases (13), as well as in patients with epilepsy (14). Although there are many publications in the literature evaluating the application of cup therapy on humans, studies in experimental rat models are limited. In addition, no study investigating the effects of cup therapy has been found in experimentally created epilepsy animal models.

In a study by Subadi et al., cup therapy was applied only in the paralumbar region (15). However, the regions selected for cup therapy applications in neurodegenerative diseases such as migraine in humans; cervical 7, thoracic 3 interscapular region, acupuncture areas such as thoracic 7. Our study, lack of an effective cup therapy model in the literature in experimental studies on neurodegenerative diseases and it is important in terms of understanding stress-related processes in the application.

Therefore, the aim of our study is to investigate the protective effect of experimentally generated epileptic seizures in the new rat modeling created by different anatomic region determination of cup therapy in rats.

MATERIAL AND METHODS

Experimental Animals: In the study, 3-4 months old (200-250 g) rats of Wistar albino type were used. The experimental animals used in the study were obtained from the Bolu Abant Izzet Baysal University Experimental Animals Application Research Center. The animals were fed ad libitum in type IV cages for 12 hours in a light / dark environment with a relative humidity of 55-60%. Each group was determined to have 7 rats. Accordingly, a total of 42 rats were divided into 6 groups (Figure 1).

Experimental Design: Before applying dry and wet cup therapy, 90/10 mg/kg intamuscular ketamine/xylazine anesthesia was applied to each rat (Figure 2).

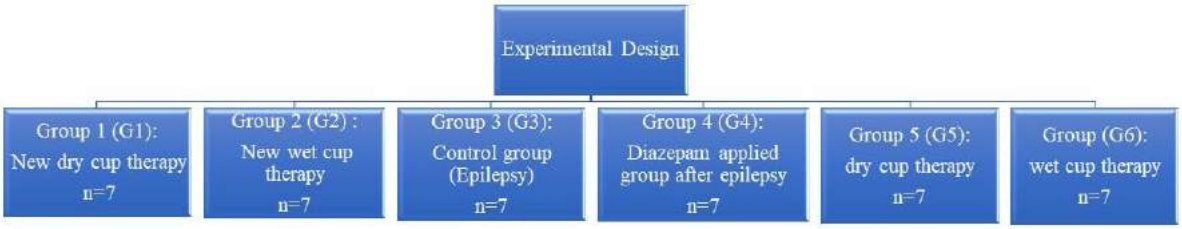

Figure 1. Experimental Groups

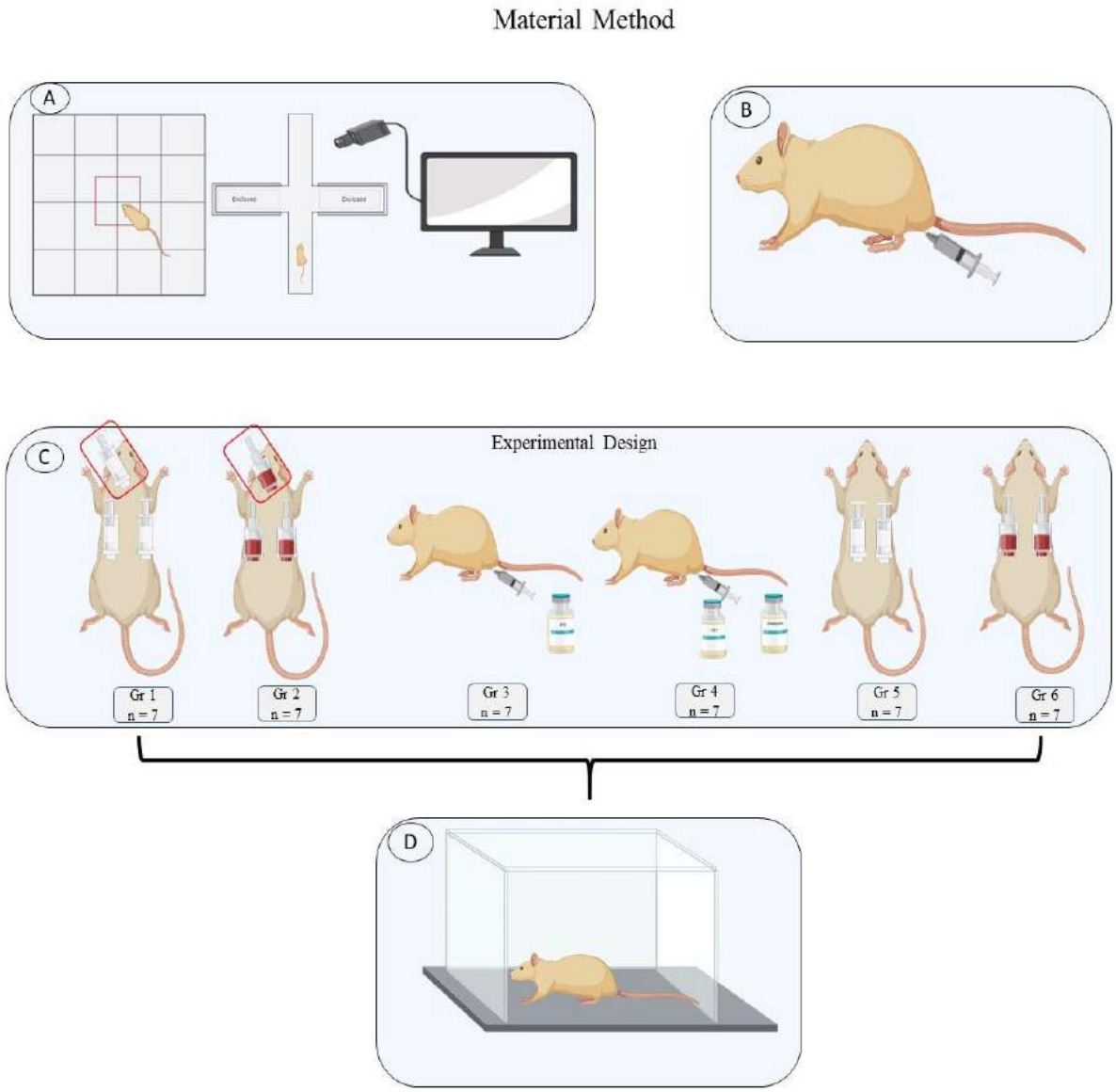

Figure 2. Material Methods

A: 'Open Field' and 'Elevated Plus Maze' Tests. **B:** Animals were anesthetized intramuscular (im) with 90 mg/kg ketamine and 10 mg/kg xylazine.**C:** Experimental Design (New dry cup therapy, New wet cup therapy, Control, Diazepam applied group after epilepsy, dry cup therapy, wet cup therapy, respectively). **D:** After epilepsy modeling, the behavior of the subjects was recorded with a camera for 20 minutes. Three measurement methods were used to evaluate the seizures: (1) Racine's Convulsion Scale (RCS), latency times of 'first myoclonic jerk' (FMJ), latency times of 'first generalized seizure' (FGS)

Cup Therapy Models:

Wet Cup Therapy: According to the method made by Subadi et al. (15), the skin of the left and right paralumbar regions of the G6 rats were punctured with a lancet, and then sterile cups (1 cm in diameter) were placed and negative pressure (-200 mm Hg) was applied for 5 minutes (Figure 3-A).

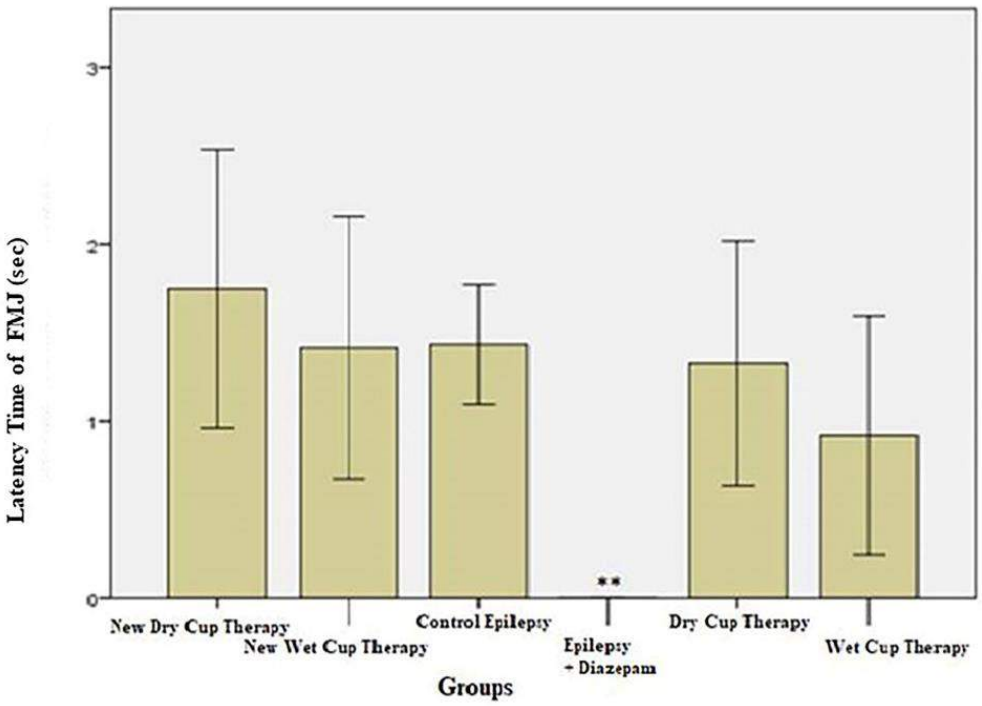

Figure 3. Latency Time of 'First Myoclonic Jerk' (FMJ) (sec)

Dry Cup Therapy: According to the method made by Subadi et al. (15), sterile cups (1 cm in diameter) were placed in to the skin of the left and right paralumbar regions of the G5 rats and negative pressure (-200 mm Hg) was applied for 5 minutes.

New Cup Therapy Models:

New Wet Cup Therapy: In addition to the left and right paralumbar areas made by Subadi et al. (15), the skin of the cervical 7 (C7) region of the G2 rats were also punctured with lancet, sterile cups (1 cm in diameter) were placed and then, negative pressure (-200 mm Hg) was applied for 5 minutes (Figure 3-B).

New Dry Cup Therapy: In addition to the left and right paralumbar areas made by Subadi et al. (15), sterile cups (1 cm in diameter) were also placed in to the skin of the cervical 7 (C7) regions of the G1 rats and negative pressure (-200 mm Hg) was applied for 5 minutes.

Animal Model of Epilepsy and Behavior Scoring: PTZ used in epilepsy modeling was provided by P6500-Sigma-Aldrich. PTZ (35 mg/kg or 3.5mg/mL) was prepared by dissolving in a volume of 10 ml/kg in 0.9 % physiological salt solution (16). Epilepsy modeling was performed by subcutaneous injection of 0.2 cc for each subject from this prepared solution (17). 24 hours after cup therapy applications to G1, G2, G5 and G6 groups, PTZ injections were made. After epilepsy modeling, the behavior of the subjects was recorded with a camera for 20 minutes.

Three measurement methods were used to evaluate the seizures:

(1) Racine's Convulsion Scale (RCS) (18) (Table 1),

(2) latency times of 'first myoclonic jerk' (FMJ) (19)

(3) latency times of 'first generalized seizure' (FGS) (20).

In this experiment, the time to get at least 3 points represents the rat's FMJ (19) and the time to get at least 4 points represents FGS (20).

Table 1. Racine's Convulsion Scale (RCS) (18)

0	No Seizure
1	Twitching of vibrassae and pinnae
2	Motor arrest with more pronounced twitch
3	Motor arrest with generalized myoclonic jerks
4	Tonic clonic seizure while remaining on animal feed
5	Tonic -clonic seizure with loss of correction reflex
6	Fatal seizure witching of vibrasse and pinnae

Statistical Analysis: Statistical analysis of all groups were carried out using the SPSS (version.20) program. The statistical significance was assessed by one-way ANOVA and $p < 0.05$ values were considered statistically significant.

RESULTS

'Open Field' and 'Elevated Plus Maze' Tests: Before studying the effect of cup therapy on epileptic seizures, different groups have been formed and whether the cup therapy applications cause stress or not has been evaluated in the 'Open Field' and 'Elevated Plus Maze' tests. No behavioral difference was found between the cup therapy (incision+cupping) and control (non cup therapy) ($p > 0.05$).

Anti-epileptic Effects of Cup Therapy: Compared to other groups, we showed that the diazepam group significantly reduced PTZ-induced epileptic seizures in rats, with a greater decrease in mean RCS, and greater prolongation in FMJ and FGS, ($p < 0.05$) (Fig. 3,4). On the other hand, there is a decrease in means of RCS in G2, G5 and G6 groups compared to G3 ($p < 0.05$) (Fig. 5). There was no statistically significant difference between the other groups in terms of antiepileptic effects ($p > 0.05$).

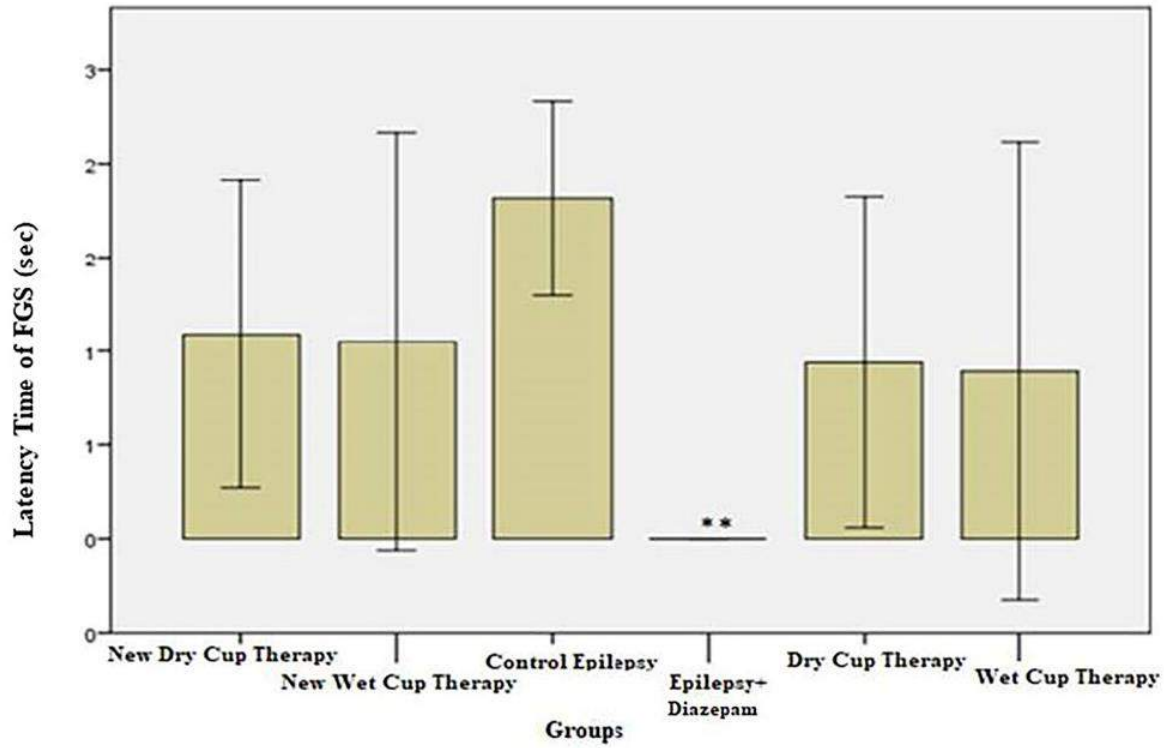

Figure 4. Latency Times of 'First Generalized Seizure' (FGS) (sec)

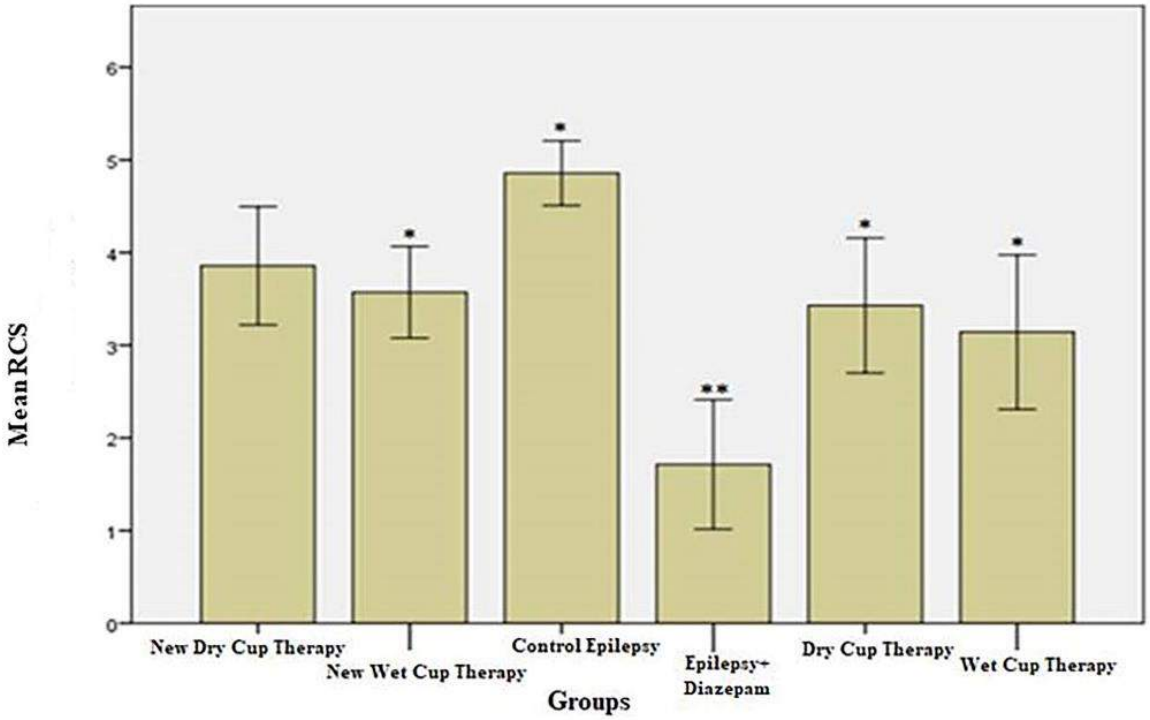

Figure 5. Mean Racine's Convulsion Scale (RCS)

DISCUSSION

Cup therapy is a very old method used as a complementary treatment in many diseases in the world (21). The history of the cup theory in China goes back over 2000 years, and its various versions have been used in parts of India, Arabia, Europe and Africa (22). It is used for many conditions such as infections, pain, mental disorders, heart diseases, various common diseases and skin diseases (21). It is known to be used in high blood pressure, especially tension type headaches, migraine, musculoskeletal pain, asthma, stroke, acne and some rheumatic diseases. In addition, cup therapy is recommended for pain and paralysis, stroke rehabilitation and complications, and neurological diseases such as Parkinson's disease (23). Eghbalian et al. from Iran, reported that wet cup therapy can be used in the treatment of epilepsy by applying it to the back of both legs (24). In the treatment of epilepsy, wet cup is used in the cervical, shoulder, leg and occipital regions, and dry cup is used in the head and legs (21).

Although different theories have been proposed, in epilepsy treatment, the mechanism of action of cup therapy has not yet been elucidated by experimental evidence. In the national health survey covering 23,393 people in the USA, they compared individuals with neurological diseases (tension headache, migraine, back and leg pain, stroke, dementia, epilepsy, memory loss) to healthy individuals. It has been observed that the use of TCM is high in patients with neurological diseases (44.1% vs. 32.6%) (25). In another study, it was emphasized that cup therapy removes oxidants and reduces oxidative stress (26). In the literature, although there are many studies investigating the effectiveness of cup therapy in neurological diseases, including epilepsy in humans, the number of animal model studies in which cup therapy is applied is very low.

Many theories have been proposed to explain the various effects and mechanisms of action of cup therapy (27). Various researchers have proposed biological and mechanical processes associated with cup therapy. For example, pain reduction is caused by the biomechanical properties of the skin, which is explained by the "Pain-Gate theory" (28), "Common Pest Inhibitory Controls" (29) and "Reflex Zone Theory" (30). Reflex Zone Theory and Pain-Gate Theory draws attention especially for the effect mechanism of cup therapy related to the nervous system (27, 31). According to the Reflex Zone Theory, the connections with the internal organs in the relevant regions of the segments formed by the spinal nerves are known as the Cutivesceral/viscerocutaneous reflex. In any pathological situation, skin changes or pain may occur in this area with the signal to the relevant skin area. According to this mechanism, it has been suggested that it is possible to contribute to the treatment of the organ with cup therapy to be made on the part related to the diseased organ. According to the Pain-Gate Theory, the thick unmyelinated A delta fibers are stimulated through the post-vacuum incision created with wet cup therapy, and the entrance doors of the pain signals reaching the medulla spinalis with the C group thin myelinated nerve fibers in the substantia gelatinosa are closed. In addition, with the stimulation of mechanoreceptors, other pain stimulation is prevented over nociceptive afferent fibers and its transport is prevented (31,32).

In order to contribute to the mechanism of action, we designed an experimental study on rats related to epilepsy and cup therapy for the first time in the literature. According to the findings in our study, no significant result was obtained for the antiepileptic effects related to FMJ and FGS in groups other than the G4 group ($p > 0.05$). Compared to other groups, we showed that the diazepam group significantly reduced PTZ-induced epileptic seizures in rats, with a greater decrease in mean RCS, and greater prolongation in FMJ and FGS, ($p < 0.05$). Diazepam group has higher protection compared to all cup therapy models ($p < 0.05$). Strikingly, in RCS, G6, G5, and G2 appear to suppress seizures compared to G3. To put it more clearly, in dry cup, wet cup and new wet cup therapy model groups, cup therapy has a protective effect compared to the group that has epilepsy ($p < 0.05$), while the new dry cup therapy model does not have a protective effect on seizures ($p > 0.05$). In addition, there is no significant difference in other groups RCS parameter ($p > 0.05$) (Figure 2-4). With the exception of the new dry cup therapy modeling, the suppressive effect of cup therapy on all seizures is surprising. This can cause many different underlying causes. Between these two different modeling, there are existing differences in terms of anatomical zoning and dry cup therapy has a significant effect on seizures as much as wet cup therapy. It is noteworthy that dry cup therapy, which is applied only to paralumbar areas, has a protective effect on seizures as well as wet cup therapy and new wet cup therapy. Further studies are needed to clarify the existing differences in terms of anatomical regions in two different models. In addition, epigenetic and anatomical differences in animals may cause errors in statistical results. In this context, in order to clarify the causes of differences, peripheral blood analyzes and histopathological brain tissue studies should be examined in detail. It is thought that detailed investigations and meta analysis studies will shed light on further studies to be carried out in the future.

CONCLUSION

While there is a significant difference in the new wet cup therapy group compared to the epilepsy group, the new dry cup therapy group (G1) created with C7 in addition to the paralumbar

region does not have a protective effect compared to G3. As a result; In RCS, G2, G5 and G6 groups seem to suppress seizures compared to G3. However, there is no significant difference in RCS when other groups are compared among themselves. Compared to other groups, the diazepam (G4) group further extended FMJ and FGS, thereby demonstrating its protective efficacy on their seizures. However, there is no significant difference between FMJ and FGS parameters among other groups.

This study is the first to investigate the protective effect of newly created cup therapy modeling on experimental epilepsy rat modeling. Our findings are expected to contribute greatly to future studies.

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RESEARCH ARTICLE

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Evaluation of Doctors' Knowledge of Rational Laboratory Use, a Descriptive Study from Turkey

ABSTRACT

Objective: The effects of health expenditures on the economy of countries have become more evident in recent years. Especially unnecessary and inappropriate laboratory tests increase both the cost and the workload. In this study, it was aimed to evaluate the level of knowledge of physicians about rational laboratory use and procedure for frequently ordered tests in clinical practice.

Methods: This study was planned to be a descriptive study. A questionnaire based on the current circular about 'Rational Laboratory Use' and including sociodemographic data was applied to physicians working at Turgut Ozal Medical Center.

Results: The questionnaire was applied to a total of 400 physicians working in internal medicine and surgical branches. The average age of the physicians was 33.01 ± 5.97 (min = 22, max = 59) years. The question about order period of blood lipids was answered correctly by 3.3% of physicians, HbA1c by 80.8%, Urea / creatinine by 64.5%, and vitamin D and vitamin B12 was answered by 40% of physicians. On the other hand 85.3% of the physicians were not aware of the rational laboratory test ordering procedure and 94% had not received any training on rational laboratory use.

Conclusions: It was found that physicians had insufficient knowledge about rational laboratory use and they did not receive any training about the test procedures. In order to reduce health expenditures, more training on this subject should be organized for physicians and awareness should be raised.

Keywords: Rational Laboratory Use, Unnecessary Test Order, Test Order Period.

Doktorların Akılcı Laboratuvar Kullanımı Bilgilerinin Değerlendirilmesi, Türkiye'den Tanımlayıcı Bir Çalışma

ÖZET

Amaç: Sağlık harcamalarının ülkelerin ekonomisi üzerine etkileri son yıllarda daha aşikar duruma gelmiştir. Özellikle gereksiz ve uygunsuz istenen laboratuvar tetkikleri hem maliyeti hem de iş yükünü artırmaktadır. Laboratuvarların akılcı kullanılması ve gereksiz test istemlerinin azaltılması için çeşitli düzenlemeler geliştirilmiş olmasına karşın hala bu konuda yetersizlikler bulunmaktadır. Bu çalışmada hekimlerin akılcı laboratuvar kullanımı hakkındaki farkındalıklarını ve klinik pratikte sık istenen testlere ait test istem prosedürü hakkındaki bilgi düzeylerini ölçmek amaçlandı.

Gereç ve Yöntem: Tanımlayıcı olarak planlanan çalışmada Turgut Özal Tıp Merkezi'nde çalışmakta olan hekimlere 'Akılcı Laboratuvar Kullanımı' hakkında mevcut olan genelge baz alınarak hazırlanan sorulardan ve sosyodemografik verilerden oluşturulan anket formu uygulandı.

Bulgular: Dahili ve cerrahi branşlarda toplam 400 hekime anket uygulandı. Hekimlerin yaş ortalaması 33.01±5.97 (min=22, maks=59) yıl idi. Hekimlerin %3.3'ü, kan lipitleri, %80.8'i HbA1c, %64.5'i Üre/kreatinin, %40'ı D vitamini ve B12 vitamini istem periyodu hakkındaki soruyu doğru yanıtladı. Hekimlerin %85.3'ü akılcı laboratuvar test istem prosedüründen haberdar değildi ve %94'ü akılcı laboratuvar kullanımı ile ilgili herhangi bir eğitim almamıştı.

Sonuç: Hekimlerin akılcı laboratuvar kullanımı hakkındaki bilgi düzeyleri yetersiz olduğu ve testlerin istem prosedürü hakkında eğitimlerinin olmadığı bulundu. Sağlık harcamalarını azaltabilmek için bu konuda hekimlere eğitimler düzenlenmeli ve farkındalık oluşturulmalıdır.

Anahtar Kelimeler: Akılcı Laboratuvar Kullanımı, Gereksiz Test İstemi, Test İstem Periyodu.

INTRODUCTION

Although physical examination and taking anamnesis are the basis in the diagnosis of diseases, many laboratory tests have gained an important place in the diagnosis, thanks to the developing technology. In a study, it was reported that the results of laboratory tests have a two-thirds effective role in the clinical decision making process (1). Currently, the importance of laboratory tests in clinical decision making is indisputable. However, a certain amount of time is needed to conduct all these laboratory tests and to get results. This need comes with an additional cost and increased workload. Besides the contribution of new analyzes with faster turnaround times, brought by technological advances; due to reasons such as an increase in the number of elderly and patients with chronic diseases, and physicians' concerns about malpractice, the number of tests studied in clinical laboratories have been increasing (2,3).

Sometimes, physicians may request more than necessary laboratory tests, which have an important place in clinical decision making. The reasons for this situation, include physicians' anxiety due to legal responsibilities at the stage of clinical decision making, the large number of the patients, the lack of time dedicated for patients, and difficulty in making decisions (4). It has been reported that between 7.5% and 30% of the tests studied in the laboratory constitute repeated and unnecessary tests (5). Ordering inappropriate and extra tests by clinicians leads to a significant increase in costs and workload on health expenses. Increasing workload may cause delays in finalization of laboratory tests and increase in laboratory errors. In health institutions, physicians' unawareness of avoiding unnecessary laboratory tests prevents laboratories from providing services effectively and makes laboratory applications challenging (6).

Given these reasons, many strategies have been developed to use the laboratory studies rationally and effectively, to reduce the inappropriate or unnecessary tests, to manage the increasing demands, and to optimize the clinical use of the tests. The limitation of the number and frequency of laboratory orders is one of these strategies (7). In our country, in recent years, important provisions have been made by the Ministry of Health to ensure rational laboratory use. The "Rational Test Ordering Procedure" has been prepared and communicated to all healthcare providers with a circular, in order to regulate the use of laboratory tests and to reduce the number of unnecessary test orderings. As part of this procedure, a "Test Ordering Period List" was created, which defines the recommended time to re-order the same test after the first order for a patient (8).

In this study, it was aimed to evaluate the awareness of physicians about rational laboratory use and the level of knowledge about the test ordering period for frequently requested tests in clinical practice.

MATERIAL AND METHODS

This study was conducted at Inonu University Medical Faculty Turgut Ozal Medical Center, between April 20 2019 and October 20 2019, with the permission of the Scientific Research and Publication Ethics Committee of Inonu University, dated 07/05/2019 and numbered 2019 / 9-10. All applications within the scope of this descriptive study were carried out in accordance with the latest version of the Helsinki Declaration and the "Good Clinical Practices Directive".

This study included 400 volunteer physicians, 200 from the internal branches, 200 from the surgical branches, in the Inonu University Faculty of Medicine Turgut Ozal Medical Center. Within the scope of the study, a 19-question questionnaire was applied to the physicians who volunteered to participate in the study to evaluate the physicians' level of knowledge about "Rational Laboratory Use". Questionnaire questions were prepared by referring to the "Rational Test Ordering Procedure" issued by T.C. Ministry of Health, General Directorate of Health Services / Research and Diagnosis Services Department with the number of "Procedure No 95966346" (8).

The questionnaire included multiple choice questions regarding the shortest interval required for re-ordering routinely used biochemical parameters and questions investigating whether they were aware of "Rational Laboratory Use", whether they have received training regarding this subject and whether they needed training, and their opinions about restrictions on rational use of laboratories in health policies, as well as demographic data including age, gender, branch, year of working in the profession.

The SPSS version 22.0 statistical packaged software (SPSS 22.0 version, SPSS Inc., Chicago, Illinois, USA) was used for data analysis. Descriptive values were indicated by numbers, percentages, means, and standard deviations. The categorical variables were compared using Chi-square analysis (Pearson Chi-square) between groups. The statistical significance level was accepted as $p<0.05$ in the analyzes.

RESULTS

The average age of the physicians included in the study was 33.01 ± 5.97 (min = 22, max = 59) years. 200 (50.0%) of the participants are women, 200 (50.0%) of the participants are working in the internal branches, and 135 (33.8%) physicians have been working in the profession for 1-5 years. Sociodemographic characteristics of physicians are given in Table 1.

Table 1. Sociodemographic characteristics of physicians

		Mean ± SD	Min-Max
Age		33.01±5.97	22-59
		n	**%**
Gender	Female	200	50.0
	Male	200	50.0
Branch	Internal	200	50.0
	Surgery	200	50.0
Years in profession	0-1 year	43	10.8
	1-5 years	135	33.8
	5-10 years	117	29.3
	>10 years	105	26.3

The number of physicians who were aware of the rational laboratory test ordering procedure was 59 (14.8%), while 24 (6.0%) of them had received rational laboratory training. While 285 (71.3%) physicians stated that they needed training about rational laboratory use, 251 (62.7%) physicians thought that restrictions should be implemented on rational laboratory use, in health policies (Table 2).

Table 2. Physicians' awareness of rational laboratory use

	Yes (n/%)	No (n/%)	No idea (n/%)
Have you received rational laboratory use training?	24 (6.0)	376 (94.0)	-
Are you aware of rational laboratory test ordering procedure?	59 (14.8)	341 (85.3)	-
Do you need rational laboratory use training?	285 (71.3)	46 (11.5)	69 (17.3)
Do you think restrictions should be implemented on unnecessary laboratory use?	251 (62.7)	89 (22.3)	60 (15.0)

The highest number of correct answer was given by the physicians to the question asking the minimum interval for reordering HbA1c with a rate of 80.8% , followed by BUN/Creatinin with 64.5%, CRP with 60.5%, Hepatitis marker test with 59.0%, Vitamin B12 with 41.3%, Vitamin D with 40.8%, AST, ALT with 36.0%, complete urine analysis with 28.0%, with thyroid hormones 17.3%, and Ferritin with 13.5%, whereas only 3.3% the physicians answered the question regarding the minimum interval for blood lipids. The distribution of the answers given by the physicians to the questions evaluating their knowledge about the minimum interval required for re-ordering routinely used biochemical parameters is given in Table 3.

Table 3. Distribution of physicians' answers to questions about the minimum interval required for re-ordering routinely used biochemical parameters

	Correct (n/%)	Incorrect (n/%)	No idea (n/%)
What should be the shortest interval before reordering ferritin?	54 (13.5)	315 (78.8)	31 (7.8)
What should be the shortest interval before reordering complete urine test?	112 (28.0)	243 (60.8)	45 (11.3)
What should be the shortest interval before reordering BUN and creatinin?	258 (64.5)	116 (29.0)	26 (6.5)
What should be the shortest interval before reordering ALT/AST??	144 (36.0)	229 (57.3)	27 (6.8)
What should be the shortest interval before reordering CRP?	242 (60.5)	138 (34.5)	20 (5.0)
What should be the shortest interval before reordering blood lipids?	13 (3.3)	360 (90.0)	27 (6.8)
What should be the shortest interval before reordering Hepatitis marker tests?	236 (59.0)	139 (34.8)	25 (6.3)
What should be the shortest interval before reordering thyroid hormones?	69 (17.3)	307 (76.8)	24 (6.0)
What should be the shortest interval before reordering HbA1c?	323 (80.8)	67 (16.8)	10 (2.5)
What should be the shortest interval before reordering Vitamin B12?	165 (41.3)	202 (50.5)	33 (8.3)
What should be the shortest interval before reordering Vitamin D?	163 (40.8)	192 (48.0)	45 (11.3)

Those whose professional years were between 5-10 years answered the question of ferritin demand interval at the highest rate (p=0.04). The knowing rate of women was found to be significantly higher than men (p=0.038). The rate of knowing this question was found to be significantly higher for those with a 0-1 year professional year (p=0.001). The rate of knowing the CRP examination request interval question in internal sciences was found to be significantly higher than those in surgical sciences (p=0.033). The rate of knowing the question of blood lipids in those who were trained in rational laboratory use was found to be significantly higher than those who did not (p=0.033). The rate of knowing the HbA1c examination request interval question was found to be significantly higher than the others (p=0.014). The rate of knowing the question of Vitamin B12 examination request interval was found to be significantly higher among those in the internal branches than those in the surgery branches(p=0.031) (Table 4).

Table 4. Comparison of physicians' answers to questions about rational laboratory use according to sociodemographic parameters

	Gender		**Branch**		**Years in profession**			
	Female	Male	Internal	Surgery	0-1 year	1-5 years	5-10 years	≥10 years
Ferritin	21 (10,5)	33 (16,5)	20 (10,0)	34 (17,0)	0 (0,0)	14 (10,4)	22 (18,8)	18 (17,1)
p*	0,160		0,089			**0,04**		
Complete urine test	61 (30,5)	51 (25,5)	65 (32,5)	47 (23,5)	12 (27,9)	45 (33,3)	27 (23,1)	28 (26,7)
p*	0,409		0,126			0,149		
BUN and creatinin	137 (68,5)	121 (60,5)	132 (66,0)	126 (63,0)	32 (74,4)	75 (55,6)	81 (69,2)	70 (66,7)
p*	**0,038**		0,806			**0,001**		
ALT/AST	76 (38,0)	68 (34,0)	81 (40,5)	63 (31,5)	11 (25,6)	49 (36,3)	46 (39,3)	38 (36,2)
p*	0,659		0,168			0,453		
CRP	120 (60,0)	122 (61,0)	130 (65,0)	112 (56,0)	24 (55,8)	82 (60,7)	75 (64,1)	61 (58,1)
p*	0,897		**0,033**			0,908		
Blood lipids	5 (2,5)	8 (4,0)	7 (3,5)	6 (3,0)	1 (2,3)	7 (5,2)	3 (2,6)	2 (1,9)
p*	0,691		0,592			0,798		
Hepatitis marker tests	117 (58,5)	119 (59,5)	119 (59,5)	117 (58,5)	25 (58,1)	73 (54,1)	67 (57,3)	71 (67,6)
p*	0,825		0,968			0,518		
Thyroid hormones	34 (17,0)	35 (17,5)	35 (17,5)	34 (17,0)	10 (23,3)	19 (14,1)	20 (17,1)	20 (19,0)
p*	0,912		0,991			0,873		
HbA1c	158 (79,0)	165 (82,5)	158 (79,0)	165 (82,5)	33 (76,7)	122 (90,4)	89 (76,1)	79 (75,2)
p*	0,630		0,643			**0,014**		
Vitamin B12	75 (37,5)	90 (45,0)	91 (45,5)	74 (37,0)	13 (30,2)	56 (41,5)	53 (45,3)	43 (41,0)
p*	0,307		**0,031**			0,499		
Vitamin D	80 (40,0)	83 (41,5)	86 (43,0)	77 (38,5)	10 (23,3)	61 (45,2)	54 (46,2)	38 (36,2)
p*	0,923		0,201			0,068		

Only the percentage of those who answered the Question correctly was taken. *Chi square test.

DISCUSSION

In our study, the rate of physicians who were not aware of the rational laboratory test ordering procedure was 85.3% and only 6% of the physicians reported that they received training about rational laboratory use.

In a survey study 100 physicians were asked whether they have received any training regarding clinical use of the diagnostic tests used in the laboratories and 56 of them answered "Yes" and 44 replied "No". In the same study, 91 out of 100 physicians to the question whether you need training on diagnostic tests and clinical use, used in laboratories (9). In the study of Berkem and Ozbek, 24% of physicians stated that they received training on rational laboratory use, during their specialization education and 12% of physicians stated that they found this training sufficient. In the same study, 91% of physicians stated that they needed training on rational laboratory use (9). In the study conducted by Allan et al., which they evaluated knowledge level of physicians about rational laboratory use and awareness about the test costs, which constitute an important part of the rational laboratory use, it was found that a minority of the physicians (6.7%) received training on this subject (10). In a cross-sectional study conducted by LuísaSá et al, it was reported that only 7% of family physicians had knowledge about test costs. According to this study, Portuguese family physicians were found to have limited awareness of diagnostic use and costs of laboratory tests. In this study, the need for improved training in this area was emphasized (11). In our study, we found that 14.8% of the physicians were aware of the rational laboratory test ordering procedure, only 6.0% of them received rational laboratory usage training, and 71.3% needed training related to rational laboratory use. Although a wide scope training regarding diagnosis and treatment has been provided in the medical education, it is seen that the training for rational laboratory use is insufficient. The results of ours and other studies in the literature show that physicians are not aware of rational laboratory use, do not have sufficient information, do not receive sufficient training on the subject, and there is need for training on this subject.

Physicians generally tend to make laboratory orders based on their past knowledge and habits and the routine practices of the clinics they have been working. Rational laboratory use practices have been obstructed due to the reasons including the effectiveness of education and guidebooks to be less than expected, physicians not wanting to change their habits, understanding of defensive medicine, and insistence of some patients on undergoing more tests. Although it has been shown that, physicians needed to receive training on rational laboratory use, either in our study or in similar studies, the nature and the usefulness of the training that should be provided is still controversial. According to the study conducted by Yeh et al., it was observed that the trainings given to the health professionals working in the clinics were not at the desired rate, and physicians whose impact on health expenditures was reported to be 80%, returned to their old habits of ordering tests, after a certain period (12). It has been shown that training activities for changing physician practices reduce unnecessary laboratory test requests up to 25%, however these reductions are temporary and limited to a certain period of time after training (13). In some studies it has been suggested that replacement of items on the laboratory order forms was more useful than the trainings and its effect lasted longer. Kobkitjaroen et al. reported that they had a 44.2% reduction in unnecessary test orders by replacing the items on the test order form (14).

Unnecessary laboratory test orders have been observed to be more common in training hospitals, since less experienced trainee or resident physicians are responsible for the majority of the test orders in these centers. In another study, it was observed that resident physicians made further and unnecessary orders than specialists, in a training and research hospital, and it was reported that a 50% decrease was achieved when instructors effectively questioned and discussed which tests should be ordered (15). Therefore, by appropriate and accurate trainings and strict follow-up of the applications after these trainings, may reduce unnecessary test orders.

One of the methods developed for rational laboratory use is to limit the test orders. It has been tried to prevent unnecessary tests by restricting the number and frequency of the tests and warning the physicians by the operating system. In our study, 62.7% of the physicians wanted the test orders to be restricted within the scope of rational laboratory practices. Although limiting the test orders has been shown to decrease the number of unnecessary test orders, it should be taken into consideration that such limitations may also limit physicians' effectiveness in terms of diagnosis and treatment. Rather than compulsory restrictions, it should be essential for the physicians to decide depending on their own knowledge and experience and not to order the tests that they cannot interpret (16).

In our study, the highest number of correct answer was given by the physicians to the question asking the minimum interval for reordering HbA1c with a rate of 80.8%, followed by BUN/Creatinin with a rate 64.5%, and CRP with a rate of 60.5%, Hepatitis marker test with 59.0%, respectively. This situation was attributed to the fact that, since these tests have been highly ordered in both internal and surgical branches and the disciplines under them, the physicians have more information about these tests. Again, in our study, the less correctly answered question was about blood lipids, with a rate of 3.3%. This situation was attributed to the

fact that, since evaluating lipid panel is not necessary for most diseases, physicians are less knowledgeable about these tests. In a cohort study conducted by Morgen and Naugler, identified and evaluated inappropriately reordering of six commonly used laboratory tests by using highly specific criteria based exclusively on test repeat time and test value in a population patient sample. The most commonly used tests were identified to include cholesterol, HbA1c, TSH, vitamin B12, vitamin D and ferritin tests. At the end of the study, they found that the rate of tests repeated at 3rd, 6th and 12th months were found to be 11%, 23% and 41%, respectively and it was found that that 16% of these six tests were unnecessarily repeated and represent an extra cost of 0.6 to 2.2 million dollars, per year (13).

According to the Ministry of Health Test Request Period List, Ferritin request should be made at the earliest every 28 days (8). In our study, the rate of those who answered the ferritin demand interval correctly was quite low (13.5%). The knowledge rate of the group with an occupational year of 5-10 years and 10 years or more was found to be significantly higher than the other residents. When this situation was evaluated especially in terms of ferritin, it was attributed to the fact that experienced physicians were more knowledgeable on this subject. In the study of Savaş and Köken, in which they investigated the unnecessary test request in the diagnosis of iron deficiency anemia, it was found that parameters for iron deficiency were requested unnecessarily in approximately 55% of the patients (17).

The HbA1c test is an important blood test for diagnosing diabetes and keeping the disease under control. According to the Ministry of Health Test Request Period List, the HbA1c demand interval should be done at the earliest every 2 months (8). In our study, the HbA1c demand period was known accurately at a rate of 80.8%. This rate was the highest rate obtained in our study. This was attributed to the fact that HbA1c is a specific test and it is frequently requested in the follow-up of diabetes, especially in internal branches. Özdin et al. found that there was a 7.5% decrease in the number of unnecessary HbA1c tests, thanks to the laboratory efficiency committee formed in their study (18).

According to the Test Request Period List of the Ministry of Health, the demand interval of blood lipids should be done every 13 days at the earliest (8). In our study, only 3.3% of the physicians answered the demand period of blood lipids correctly. In their study investigating unnecessary requests for serum lipid tests, Kocatürk et al. found that more than 50% of total cholesterol and HDL tests and nearly 50% of LDL tests were repeated within the first 15 days (19).

The demand period of vitamin D level, which is among the frequently requested examinations, was correctly known by 40.8% of the physicians who participated in our study. 40.13% of the participants got the Vitamin B12 demand period correctly. Vitamin levels are among the most frequently requested examinations in outpatient clinics and are among the tests frequently requested by patients. During routine examinations, requests outside of indications are frequently encountered. In his study, Esendemir found that approximately 10% of vitamin D requests were unnecessary requests, and this rate increased to 34.55% in repeated tests (20).

In our study, only 17.3% of the participants answered the request period of thyroid hormones correctly. In the study conducted by Demirci et al., only TSH test was requested in 4,308 (40.96%) of 8,583 patients for whom thyroid function test was requested, whereas in 4,275 (40.65%) of them, in addition to the TSH test, fT3, fT4 or both fT3 and both fT3 tests were required. They saw that fT4 tests were requested, and according to the results of the first test, they found that the rate of unnecessary tests decreased from 40.65% to 1.19% with the "Reflex test" application, which means a new test request if the criteria are met (21).

Urea, creatinine, AST, ALT, CRP and Complete urine test are not tests specific to a certain disease, but are required in many clinical situations. They are generally considered among routine blood tests and are often requested in panels. For this reason, they are among the tests with a high rate of unnecessary requests. In our study, the rate of accurate knowledge of the request period of these examinations by physicians varies between 36.0% and 64.5%. The fact that there are tests requested by physicians in all branches and that they are highly requested cause the awareness of physicians to be high.

There are some limitations in our study. Since, there are a few studies conducted on the subject of rational laboratory use and these studies were rather cost-effectiveness analyzes than evaluating the level of knowledge of the physicians, the comparability of our findings was limited. However, it was an advantage to be the first study on this regard. Our second limitation is that this study is a descriptive study and cannot be generalized to the universe.

CONCLUSION

In conclusion, in our country, the "Rational Test Ordering Procedure" has been prepared and communicated to all healthcare providers with a circular, by the Ministry of Health, in order to regulate the use of laboratory tests and to reduce the number of unnecessary test orders. Depending on the findings of our study, it was concluded that physicians are not aware of the rational laboratory use principles and they need a comprehensive training about this subject. In addition, it has been seen that the majority of physicians misunderstand the reordering periods of the tests frequently used in

clinical practice. This lack of correct knowledge information leads to an increase in the frequency of unnecessary test orders in clinical practice. In order to reduce health expenditures, trainings should be organized and awareness should be raised on this subject.

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RESEARCH ARTICLE

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A Different Look at Premarital Hemoglobinopathy Screening in Primary Care

ABSTRACT

Objective: Despite the high prevalence of hemoglobinopathies (HBP), the most common single-gene disorders in Turkey, data in some regions are lacking. We aimed to evaluate the effectiveness of the hemoglobinopathy premarital screening program (PMS) and to investigate the contribution of efficient use of complete blood count (CBC) parameters on cost-effectivity.

Methods: HMP diagnosed 49171 subjects in 4 years and CBC of subjects with HMP in a year were evaluated retrospectively.

Results: The total incidence rate of HBP was 3.41%, β-thalassemia trait (β-TT) was 1.98%, HMP incidence in the PMS group was 2.43%, β-TT was 1.08%. Moreover, HbF, HbD, HbC, HbS, HbE and HbJ were detected with the incidences of 0.49%, 0.14%, 0.05%, 0.04%, 0.007% and 0.009%, respectively. RDW/MCH ratio compared to other indices was the most successful for both sexes in diagnostic efficiency of HBP (AUC: male:0.922 - female:0.961) and β-TT (AUC: male;0.928 - female:0.961).

Conclusions: PMS was found to be an effective application program in HMP screening. RDW/MCH ratio was the most useful and easy parameter in detecting HBP and β-TT in PMS and in terms of reducing unnecessary test requests and cost-effectiveness in public health screenings.

Keywords: Hemoglobinopathy, Premarital Screening, β-Thalassemia Trait, RDW, MCH.

Birinci Basamakta Evlilik Öncesi Hemoglobinopati Taramasına Farklı Bir Bakış

ÖZET

Amaç: Türkiye'de en sık görülen tek gen hastalıkları olan hemoglobinopatilerin (HBP) yüksek prevalansına rağmen, bazı bölgelerde veri bulunmamaktadır. Hemoglobinopati evlilik öncesi tarama programının (PMS) etkinliğini değerlendirmeyi ve tam kan sayımı (CBC) parametrelerinin etkin kullanımının maliyet-etkililiğe katkısını araştırmayı amaçladık.

Gereç ve Yöntem: 4 yılda 49,171 HMP tanısı konan olgu ve bir yılda HMP'si olan olguların tam kan sayımları geriye dönük olarak değerlendirildi.

Bulgular: HBP'nin toplam insidans oranı %3.41, β-talasemi taşıyıcılığı (β-TT) %1.98 bulundu. PMS grubunda HMP insidansı %2.43, β-TT %1.08 idi. Ayrıca HbF, HbD, HbC, HbS, HbE ve HbJ sırasıyla %0.49, %0.14, %0.05, %0.04, %0.007 ve %0.009 oranında tespit edildi. ROC analizinde diğer indekslere kıyasla RDW/MCH oranı, HBP (erkek:0.922- kadın:0.961) ve β-TT (erkek;0.928- kadın:0.961) tanısal etkinliğinde her iki cinsiyet için de en başarılıydı.

Sonuç: PMS, HBP taramasında etkili bir uygulama programı olarak bulundu. RDW/MCH oranı; HBP ve β-TT'nin saptanmasında ve halk sağlığı taramalarında gereksiz test isteklerinin azaltılması ve maliyet etkinliği açısından en kullanışlı parametreydi.

Anahtar Kelimeler: Hemoglobinopati, Evlilik Öncesi Tarama, β-Talasemi Taşıyıcılığı, RDW, MCH.

INTRODUCTION

Hemoglobinopathy is a genetic disorder leading to an abnormal globin chain structure in the hemoglobin(Hb) molecule(1). Thalassemia types are more prevalent in the regions of the Mediterranean coastal line (Greece and Italy), the Arabian Peninsula, Iran, Ecuador, Africa, Asia, and Turkey. The genetic prevalence of thalassemia in these regions varies from 2.5% to 15.0%(2).

The diversity and heterogeneous distribution of Hb disorders make it necessary to develop strategies depending on the country. Due to the high rate of marriages between first-degree relatives in our country, a Hemoglobinopathy Control Program with pre-marital screening (PMS) has been initiated to prevent childbirth with HBP(3). As in the examples across the world (Tunisia, Bahrain, Saudi Arabia, Lebanon, United Arab Emirates, Iran, Qatar, and the Gaza Strip), national PMS in Turkey is mandatory and free of charge(4).

PMS and counseling services, in primary health care, aimed to minimize maternal and fetal risks, to prevent birth defects and genetic diseases, to reduce the economic burden on public health and for couples to obtain information about the situations due to potential risks (5). With these programs, carriers can be easily detected by routine haematological methods and pre-warned of reproductive risks (6). In this regard, while the number of couples who had their PMS tests in Turkey in 2003 was 30%, this rate reached 86% in 2013(7).

In this study, we aimed to investigate the prevalence of HMP among individuals who applied to Family Health Centers (FHC) in our province for PMS. Moreover, we planned to retrospectively assess the usefulness of the parameters and formulas based on CBC in detecting abnormal Hb variants among individuals with HBP.

MATERIAL AND METHODS

This study was approved with Ethics Committee Protocol number: 20:09.84.06.05, May 30th, 2019. In this retrospective study, individuals who applied to FHCs for PMS and other reasons were investigated between January 2016 and December 2019, from the public health laboratory electronic archive. CBCs have been measured in Beckman Coulter hematological autoanalyzer and hemoglobin variant analyses have been measured using high-pressure liquid chromatography (HPLC) technique of Arkray Adams A1c HA-8180T analyzer (Arkray, Inc., Kyoto, Japan). All demographic data and test results were taken from patient files retrospectively. Individuals with a recent medical history of systemic and other hematological disorders were excluded. CBC parameters of subjects with HMP (n=393) in 2019 and the healthy control group (n=100) were included in this study for evaluation of indices.

Subjects were considered to have β-TT if they had MCV <80 fl and MCH <27 pg and a hemoglobin A2 level >3.5%. HbF, HbD, HbC, HbS, HbE, HbJ, and other variants were also detected. HbA2 level between 3.1% and 3.5% was considered borderline. The discrimination erythrocyte (RBC) indices and formulas were calculated using the RBC indices as defined following: England&Fraser(8):MCV-RBC-5Hb-3.4 (Cut-off: <0), Mentzer index(9): MCV/RBC count (<13), Shine and Lal (SL-I)(10): MCV2xMCH/100 (Cut-off <1530), Green&King Index (G&K)(11): MCV2xRDW/100xHB (Cut-off <72), RDWI(12):MCV x RDW/RBC (Cut-off <220).

Statistical Analysis: The normal distribution of the variables was determined using the Kolmogorov-Smirnov test. Parametric variables were compared using the Student's t-test. Non-parametric data were analyzed with the Mann–Whitney U test. The AUC was found using a receiver operating characteristics (ROC) analysis to investigate the effectiveness of the methods used in showing marked β-TT and HBP. An AUC of ≤0.05 was evaluated as "the test has no diagnostic value". A p-value of less than 0.05 was considered statistically significant. All statistical analyses were carried out with SPSS IBM 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

In the present study, between January 2016 and December 2019, 44,790 participants of the total 49,171 participants applied for the HMP screening were investigated for PMS, and abnormal hemoglobin variants were detected in 1090 (2.43%) of them. Abnormal Hb variants were detected in 588 of 4381 participants who applied for other reasons (8.91%). The numbers of admissions and abnormal Hb variants' detection rates by years were presented in Table 1.

Table 1. Year-based Thalassemia Screening and Abnormal Hemoglobin Variant Analysis

Year	Total Test Number	Application based on marriage (Number/%)	Abnormal variant analysis as a result of application for marriage (Number/%)	Application for other reasons (Number/%)	Abnormal variant analysis as a result of application for other reasons (Number/%)	Abnormal hemoglobin variant rates in all groups
2016	13.069	12.499 (%95.64)	295 (%2.36)	570 (%4.36)	134 (%23.51)	429 (%3.28)
2017	12.506	11.874 (%94.95)	323 (%2.72)	632 (%5.05)	135 (%21.36)	455 (%3.63)
2018	12.248	11.629 (%94.95)	264 (%2.27)	619 (%5.05)	134 (%21.65)	398 (%3.24)
2019	11.348	8788 (%77.44)	208 (%2.37)	2560 (%22.56)	185 (%7.23)	393 (%3.46)
Total	49.171	44.790 (%91.09)	1090 (%2.43)	4381 (%8.91)	588 (%13.42)	1678 (%3.41)

The incidence of high HbA2, microcytosis, hypochromia, and β-TT was 1.08% in 393 subjects with abnormal hemoglobin variants, detected in PMS of 2019 yearly data. Moreover, HbF, HbD, HbC, HbS, HbE and HbJ were detected with the incidences of 0.49%, 0.14%, 0.05%, 0.04%, 0.007% and 0.009%, respectively. The prevalence rates among subjects applied for other reasons were as follows: 5.98% for β-TT, 0.86% for HbF, 0.16% for HbS, 0.12% for HbD, and 0.12% for HbE. The prevalence of β-TT among all applications was 1.98% (Table 2).

Table 2. Numbers of Abnormal Hemoglobin Variants for 2019

	Abnormal variant analysis as a result of application for marriage	Abnormal variant analysis as a result of application for other reasons	Total
HbA2	122 (% 1.08)	153 (% 5.98)	275 (% 1.98)
HbF Height	56 (% 0.49)	22 (% 0.86)	78 (% 0.56)
HbS Variant	5 (% 0.04)	4 (% 0.16)	9 (% 0.064)
HbC Variant	6 (% 0.05)	-	6 (% 0.043)
HbD Variant	16 (% 0.14)	3 (% 0.12)	19 (% 0.14)
HbJ Variant	1 (% 0.009)	-	1 (% 0.007)
HbE Variant	2 (% 0.017)	3 (% 0.12)	5 (% 0.035)
Total Hb Variant Number	208 (% 1.83)	185 (7.23)	393 (2.83)
Total Screening Person	**11.348**	**2560**	**13.908**

Hb: Hemoglobin

Two different genders were compared concerning CBC and indices in the group with HMPs (n=393) and the healthy control group (n=100). In females, RBC, HB, MCV, MCH, EF index, G&K-I, and SL-I values were significantly lower in the group with HMP than the control group (for all, $p<0.001$), whereas RDW and RDWI values were significantly higher (for both, $p<0.001$). In males, RBC, HB, HCT, MCV, MCH, MCHC, G&K-I, and SL-I values were significantly lower in the group with HMP than the control group (for all, $p<0.001$). On the other hand, RDW, RDWI, and Mentzer index values were significantly higher ($p<0.001$, $p<0.001$, and $p<0.01$, respectively) (Table 3).

Table 3. Hematological features of subjects at 2019

	FEMALE			MALE		
	Healthy Groups (n:52)	HBP Groups (n:210)	*P*	Healthy Groups (n:48)	HBP Groups (n:183)	*P*
Age (years)	33.57 (23 - 69)	30.46 (27 - 77)	0.240	33.15 (23-62)	30.33 (28-73)	0.114
RBC (/mm^3)	6.55 ± 0.42	5.46 ± 0.86	0.000	6.80 ± 0.53	5.25 ± 0.93	0.000
HB (g/dL)	13.11 ± 1.14	11.96 ± 1.77	0.000	15.39 ± 1.05	12.58 ± 1.85	0.000
HCT (%)	38.89 ± 3.01	39.95 ± 3.13	0.705	45.46 ± 3.24	38.82 ± 5.22	0.000
MCV	90.61 ± 6.56	69.08 ± 10.13	0.000	92.26 ± 3.73	75.58 ± 13.11	0.000
MCH	30.95 ± 1.56	22.41 ± 3.96	0.000	32.78 ± 2.26	24.58 ± 4.81	0.000
MCHC	33.08 ± 1.54	34.14 ± 2.4.	0.618	34.96 ± 2.23	32.38 ± 1.25	0.000
RDW	12.78 ± 1.06	17.26 ± 2.63	0.000	12.94 ± 0.94	15.88 ± 2.70	0.000
RDWI	176.84 (138.87 – 418.3)	226.21 (139.1 – 415.3)	0.000	175.46 (131 – 219.1)	230.71 (128.6 – 499.68)	0.000
Mentzer-I	13.87 ± 1.21	13.20 ± 3.98	0.108	13.55 ± 1.33	15.24 ± 5.37	0.007
E- F	15.08 (-1.27- 30.87)	0.42 (-23.1- 32.13)	0.000	5.03 (-5.52 – 14.29)	4.02 (-17.41 – 46.3)	0.586
G&K	13791.89±2210.82	9865.83 ± 3207.71	0.000	17041.85 ± 2569.5	11332.1 ± 3946.5	0.000
SL-I	2555.18±381.84	1148.46 ± 600.19	0.000	2798.29 ± 326.68	1542.22 ± 831.19	0.000
RDW/MCH	0.4±0.04	0.79±0.21	0.000	0.39±0.03	0.69±0.22	0.000

HBP Groups: Haemoglobinopathy Groups. RBC: red blood cells. HB: Hemoglobin. HCT: Hematocrit. MCV: Mean corpuscular volume. MCH: Mean corpuscular hemoglobin. MCHC: Mean corpuscular hemoglobin concentration. RDW: Red cell distribution width. RDWI: Red cell distribution width index. Mentzer-I: Mentzer-Index. E-F: England & Fraser index. G&K: Green and King index. SL-I: Shine Lal Index.

To distinguish HMP and β-TT subjects:

ROC analysis was performed to determine the precision of CBC parameters and indices in the HMP group. AUC values for RDW, MCH and RDW/MCH ratio were acceptable (>70%), concerning diagnostic efficiency for males (0.860, 0.918, 0.922 respectively) and females (0.958, 0.929, 0.961 respectively).

The optimal cut-off value for RDW/MCH ratio in men was 0.44 and the sensitivity was 83%, the specificity was 85% and the PPV was 94%. Besides, at the cut-off value of 0.48 for RDW/MCH ratio, a sensitivity of 91%, a specificity of 93%, and a PPV of 98% were determined in females (Figure 1, Table 4).

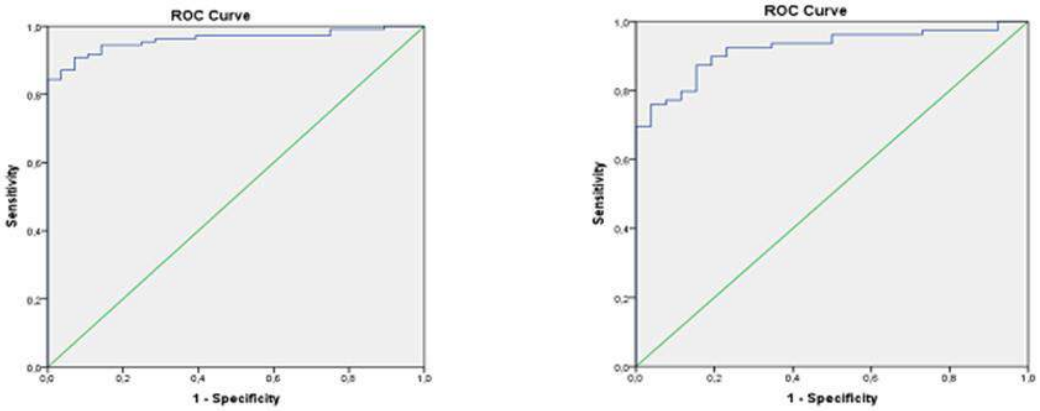

Figure 1. ROC curve analyses of RDW/MCH ratio in both genders with Hemoglobinopathy

Table 4. Comparison of diagnostic accuracy with optimal cut-off values (95% Confidence Interval)

	Sex	Indices	AUC	Cut Off	Sens	Spes	LR^+	LR^-	PPV	NPV	DA
HBP	Men	RDW	0.860	13.85	0.76	0.77	3.29	0.31	0.91	0.51	0.76
		MCH	0.918	30.13	0.78	0.77	3.38	0.29	0.93	0.49	0.78
		RDW/MCH	0.922	0.44	0.83	0.85	5.42	0.20	0.94	0.63	0.84
	Women	RDW	0.958	14.05	0.91	0.89	8.48	0.1	0.97	0.71	0.91
		MCH	0.929	29.17	0.88	0.86	6.15	0.14	0.97	0.6	0.87
		RDW/MCH	0.961	0.48	0.91	0.93	12.7	0.10	0.98	0.72	0.91
β-thalassemia trait	Man	RDW	0.855	13.75	0.78	0.77	3.37	0.29	0.88	0.63	0.78
		MCH	0.921	30.08	0.87	0.86	6.08	0.15	0.97	0.59	0.87
		RDW/MCH	0.928	0.45	0.78	0.85	5.06	0.26	0.91	0.65	0.80
	Women	RDW	0.946	13.94	0.91	0.89	8.48	0.10	0.97	0.71	0.91
		MCH	0.924	29.11	0.87	0.86	6.09	0.15	0.97	0.59	0.87
		RDW/MCH	0.961	0.48	0.91	0.93	12.7	0.10	0.98	0.72	0.91

Sens: sensitivity. Spes: specificity. LR: Likelihood ratio. PPV: Positive predictive value. NPV: Negative predictive value. DA: Diagnostic accuracy. RDW: Red cell distribution width. MCH: Mean corpuscular hemoglobin

When their roles in the detection of β-TT were examined, the AUC values of RDW, MCH, and RDW/MCH ratio parameters were considered significant in diagnostic efficiency with the values of 0.855, 0.921, and 0.928 for males, and 0.946, 0.924, and 0.961 for females, respectively. Regarding RDW/MCH ratio, at the cut-off value of 0.45, a sensitivity of 78%, specificity of 85%, and a PPV of 91% were determined in males. Besides, at the cut-off value of 0.48, a sensitivity of 91%, a specificity of 93%, and a PPV of 98% were determined in females (Table 4).

DISCUSSION

In our study, the prevalence of HMP in whole groups was 3.41% and HMP was detected in 2.43% of PMS in those years (Table 1). To our knowledge, our results are the first concerning revealing the data on HMP prevalence in our city with a population of approximately one million. The overall prevalence of HMP was 2.1%, and this rate reached up to 4.3% in the coastal areas of our country(7). Hence, the results in our province were similar to the HMP average of Turkey. It was noteworthy that the number of HMPs detected in PMS was higher than applications for other causes. This was a good example of how effectively the screening program could be used.

Yearly PMS results of 2019 in our province were analyzed, the prevalence of β-TT was 1.08% and it was 5.98% in people who applied for other reasons. When all applications were considered, the prevalence of β-TT was 1.98% (Table 2). The prevalence of β-thalassemia was reported to be 1.4% (125/8904) and the prevalence of sickle cell anemia was 0.06% (5/8904) in the PMS in our neighboring city, Canakkale(13). Moreover, in a study performed in Kocaeli province, also in the Marmara region, the prevalence of β-TT was 0.89% and sickle cell trait was 0.05%(14). Compared to

some screening programs performed in Turkey, there were significant regional differences. In our country, the highest prevalence of β-TT and HbS were in the Mediterranean region (respectively, 13.1% 10.0%)(15). When we examined the examples across the world, the prevalence of β-TT in Southern Italy, Iran, South Russia, India, and Southeast Asia ranged from 10% to 15%. The rate of β-TT in Greece was 5-15.0%, while it was 4-10.0% in Iran and 3.22% in Saudi Arabia(16). β-TT in our province had a lower prevalence compared to many countries close to average in Turkey.

In our study, analyzed the data of 2019 in PMS, the second-highest HMP was HbF with a rate of 0.49%, and this rate was 0.86% at admission for other reasons. Furthermore, other variants were detected also as seen in Table 2. In the PMS group, HbD was 0.46%, and HbS was 0.09%, HbE was 0.04% and HbD carrier was 0.04% in the Mediterranean region(17). When compared together, HMP rates have lower percentages in our province. Besides that, the HMP rates of our city are below the rates across the world(18). According to our findings, more detection of hemoglobin variants (such as HbC, HbD, and HbJ), less common in PMS compared to those presenting for other reasons, also support the success of the program.

Differentiation of abnormal HMPs from the healthy population has crucial clinical implications. Electrophoresis or chromatographic techniques should be employed for identification. Since the use of these methods in the field is limited, screening the whole society with these methods is challenging and expensive. Hence, it was suggested to use a series of algorithms that combine routine RBC parameters and indices to determine the people to be screened or avoid unnecessary tests on healthy people(19). The clue for thalassemia was low MCV or low MCH. The same results suggest iron deficiency anemia, which was likely to indicate thalassemia in ethnic populated regions of countries at risk(20). In the literature, specifically, MCH, MCV, and RDW parameters were used in the differentiation of HMPs(21–24). In our study, MCV, MCH, and RDW were significantly different in the groups with HMP in both genders than the control group. These results were consistent with the findings obtained in the previous studies(20,25–27). Particularly, RDWI, G&K, and SL-I derived indices from RBC parameters, were significantly different in both genders in the group with HMP, while the E-F index was significantly different in males and the Mentzer index in females than the control group (Table 3). Thus, these parameters could be used in determining subjects with HMP.

In our study, RDW/MCH ratio was diagnostically efficient for both genders in ROC analysis to determine the precision in detecting HMP (Figure 1). Upon literature review, similar studies have shown that the RDWI is an efficient parameter in differentiating beta-thalassemia patients from patients with iron deficiency anemia(11,28). Velasco-Rodrígue et al. (2017) revealed that RDW could differentiate Hb E- β -thal from β -thal (22) and suggested that it would be the most likely diagnosis at RDW ≥ 20% and/or MCH <19 pg in the differentiation of α-thalassemia and HbH disease. When evaluated together with our results, RDW/MCH ratio could play a role in HMP screening.

Likewise, the diagnostic efficiency of RDW/MCH ratio was significant in both genders in determining β-TT (Table 4). Contrary to our findings, Sudman AA et al. (2012)(25) examined the efficiency of the MCH and MCV parameters in the ROC analysis in differentiating those with β-TT from those with non-HMP and found the sensitivities to be 100% and the specificities between 64.0% and 71.0%. Compared to our study, more efficient and effective process management could be achieved than MCV and MCH if individuals above the cut-off values of RDW/MCH ratio in both genders were screened. Based on this, it was a remarkable finding that the number of subjects requiring further examinations for HMP diagnosis in the community would decrease considerably. Indeed, supporting our findings, Chatterjee et al. (2015)(29) revealed that MCH is superior to MCV for thalassemia screening (as it varies greatly in different HMP conditions). Charoenkwan P. et al.(30) found MCV below 95 fl with 100% sensitivity and 92.4% specificity in the demonstration of HMP presence in α-thalassemia screening.

One may solely perform CBC tests at the first step of a thalassemia screening program and effectively use the proposed indices. As already known, HPLC is 10-15 times more expensive than CBC. Variant analysis could be performed with HPLC test at the 2nd step, not only in PMS, but in all patients for the first step, by distinguishing the patients with the RDW/MCH ratio with an accuracy of 91% in women and 84% in men. With this algorithm, a cheaper and easier diagnosis could be made.

Conclusions: In the PMS data of Tekirdağ province, HMP prevalence was 2.43% and the prevalence of β-TT was 1.08%. The number of HMP s and rare variants (such as HbC, HbD) detected in people presenting with PMS were higher than those applicating with other causes. The use of MCH in men and RDW in women may confuse the diagnosis. Instead, RDW/MCH ratio would be more useful and simpler in decision making. RDW/MCH ratio was diagnostically efficient for both genders to determine the precision of detecting HMP and β-TT. It could be applied by calculating with automation like NLR as those days of COVİD19 pandemics. Using a single ratio and cut-off provides a more efficient application.

As a result, RDW/MCH ratio would both reduce unnecessary test requests and facilitate the selection of individuals who require further examination for a definitive diagnosis in community screenings with limited healthcare equipment and resources. It could be the basis for earlier, inexpensive and effective thalassemia screening in all patients, not just PMS.

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RESEARCH ARTICLE

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Systolic Blood Pressure Variability and Its Relationship with Surrogate Markers of Cardiovascular Risk in Hypertensive Patients

ABSTRACT

Objective: Systolic blood pressure variability (SBPV) is a measure of oscillations in SBP for 24 hours. There are conflicting data about the relationship between SBPV and cardiovascular (CV) diseases. In this study we aim to document relationship between SBPV and surrogate markers of CV damage in a hypertensive patient cohort.

Methods: Previously documented hypertension patients were enrolled. Patients with previous documented CV disease, diabetes mellitus and secondary hypertension were excluded. 24-hour ambulatory blood pressure monitoring (ABPM), echocardiography, electrocardiography and cardio-ankle vascular index (CAVI) measurements were performed. SBPV is defined as standard deviation of mean systolic blood pressure readings from ABMP records. The relationship between SBPV and QTc distance, QT dispersion, presence of fragmented QRS, CAVI results were examined.

Results: 64 patients were enrolled [mean age 50±8, 24(37%) were male]. Mean SBPV was 15.12±4.6 mmHg and there was not a significant correlation between SBPV CAVI, QTc measurements of the study patients but there was a significant positive correlation with QT dispersion values (28.6±15.2 msec, p=0.004, p=0.354). When patients were divided into two categories as high SBPV and low SBPV, QT dispersion was consistently longer in high SBPV group (p=0.006).

Conclusions: In hypertensive patients without documented CV disease and signs of hypertensive CV changes on clinical evaluation, SBPV is positively correlated with QT dispersion but high SBPV is not related with aortic stiffness according to CAVI results. These findings might be a sign of occult left ventricular fibrosis and high risk of arrhythmia in hypertensive patients with high SBPV.

Keywords: Systolic Blood Pressure Variability, Hypertension, Cardiovascular Risk.

Hipertansiyon Hastalarında Sistolik Kan Basıncı Değişkenliği ve Kardiyovasküler Riskin Vekil Belirteçleri Arasındaki İlişki

ÖZET

Amaç: Sistolik kan basıncı değişkenliği (SKBD) 24 saatlik kan basıncı takiplerinde sistolik kan basıncının gösterdiği yükselme ve düşme hareketinin bir ölçüsüdür. SKBD ile kardiyovasküler (KV) hastalıklar arasındaki ilişkiyi gösteren çelişkili bilgiler mevcuttur. Bu çalışmada, hipertansif bir kohortta SKBD ile KV hasarı gösteren vekil belirteçler arasındaki ilişkiyi araştırdık.

Gereç ve Yöntem: Esansiyel hipertansiyon hastalarının dahil edildiği çalışmada; belgelenmiş KV hastalık, diabetes mellitus ve sekonder hipertansiyon öyküsü olan bireyler dışlandı. 24 saat ambulatuar kan basıncı ölçümü (AKBÖ), ekokardiyografi, elektrokardiyografi ve kalp-ayak bileği vaskuler indeks (KAVİ) ölçümleri yapıldı. SKBD, AKBÖ kayıtlarında ortalama sistolik kan basıncı değerinin standart sapması olarak tanımlandı. SKBD ile EKG'de QTc mesafesi, QT dispersiyonu, fragmante QRS varlığı ve KAVİ sonuçları karşılaştırıldı.

Bulgular: 64 hasta çalışmaya dahil edildi [ortalama yaş 50±8 yıl 24(%37) erkek]. SKBD (ortalama 15.12±4.6 mmHg) ile KAVİ ölçümü, QTc mesafesi, fragmante QRS varlığı arasında bir korelasyon bulunamadı ancak QT dispersiyonu ile pozitif bir korelasyon izlendi. Hastalar ortanca SKBD değerine göre ikiye bölünüp yüksek ve düşük SKBD olarak ikiye bölündüğünde QT dispersiyonu yüksek SKBD grubunda tutarlı ve anlamlı olarak daha yüksekti (p=0.006).

Sonuç: Belgelenmiş KV hastalıkları ve hipertansif KV değişim belirteçleri görülmeyen hipertansiyon hastalarında SKBD değerleri, QT dispersiyonu ile pozitif korelasyon gösterirken, bir aort sertlik indeksi olan KAVİ ile ilişki görülmedi. Bu bulgular SKBD'si yüksek olan hipertansif hasta grubunda gizli sol ventrikül fibrozis varlığını ve buna bağlı artmış aritmi riskini gösteriyor olabilir.

Anahtar Kelimeler: Sistolik Kan Basıncı Değişkenliği, Hipertansiyon, Kardiyovasküler Risk

INTRODUCTION

Inadequate blood pressure control in hypertensive subjects is documented to be associated with adverse cardiovascular (CV) and cerebrovascular outcomes in numerous studies (1,2). This interaction designated hypertension as the primary target of risk factor modification in CV disease management and prevention. The measurable treatment goal of antihypertensive therapy is generally based on office blood pressure readings, presumed as a hypertensive patient's mean blood pressure for a specific time interval. On the other hand, blood pressure (BP) is not a constant value; instead, it exhibits oscillations through a 24-hour period. This variation in systolic and diastolic BP measurements is studied as an independent risk factor for CV system. Systolic blood pressure variability (SBPV), which is defined as the amount of variation in systolic blood pressure measurements in a certain time period, is documented to be an independent risk factor for end-organ damage and CV outcomes in hypertensive patients in a few studies (3,4). Temporal effects of high systolic blood pressure on the physiologic and histological structure of two main components of CV system, heart and major arterial tree, has been documented with several surrogate markers such as left ventricular mass index (LVMI), pulse wave velocity (PWV) or carotid intima-media thickness (CIMT) (5-7). On the other hand, the relationship between these markers of adverse CV outcomes and SBPV is of interest to answer the question of whether considering SBPV as a goal of treatment in the care of hypertensive patients or not.

In this study, we analyzed the relationship between SBPV and surrogate markers of end-organ damage in the CV system such as cardio ankle vascular index (CAVI), corrected QT distance (QTc), QT dispersion (QTd), and presence of fragmented QRS (fQRS) on ECG in hypertensive patients without CV risk factors and history of CV disease. CAVI is a relatively new marker of arterial stiffness, which differs from PWV as independent from instant blood pressure and heart rate values at the time of measurement (8). Measurements of fQRS, QTc, and QT dispersion are documented as markers of myocardial fibrosis and subsequent abnormalities in depolarization and repolarization in the left ventricle. (9-11)

MATERIAL AND METHODS

Patient Selection: This is a single-center study that had approval from Sakarya University School of Medicine Ethics Committee according to the principles of the Declaration of Helsinki. All the subjects (or their parents or guardians) have given their written informed consent. Sixty-four patients with a history of essential hypertension are selected from our hospital's outpatient cardiology clinic. Patients who have a primary disease leading to hypertension or cardiovascular damage or patients with a history of documented CV disease (coronary artery disease documented with conventional or computed tomography coronary angiography, ischemic or hemorrhagic cerebrovascular disease history), diabetes mellitus, peripheral artery disease, endocrine disorders including thyroid, adrenal and pituitary diseases , neoplastic disease, rheumatologic disease, and vasoactive drug abuse (cocaine etc.) were also excluded. Patients on beta blocker or nondihydropyridine calcium channel blocker therapy were excluded due to possible interaction with QTc measurements. Obesity and smoking status were not exclusion criteria unless they are related with aforementioned diseases because both conditions are common risk factors for essential hypertension. All patients underwent 2D and M-Mode transthoracic echocardiography with appropriate equipment (iE33, Phillips Medical Systems, Andover, Massachusetts). Patients with an ejection fraction lower than 50%, wall motion abnormality, more than mild mitral valve disease and any aortic valve disease, measurements of the aortic root and ascending aorta more than the upper normal limit, left ventricular wall thickness more than 13 mm were excluded.

Ambulatory Blood Pressure Monitoring and Assessment of Blood Pressure Variability: All subjects underwent a 24-hour ambulatory blood pressure monitoring with a validated device. During measurements, subjects were allowed to practice their daily routine except for heavy exercises. BP measurements were obtained every 15 minutes daytime (7 AM-11 PM) and every 30 minutes night time (11 PM-7 AM). SBPV was calculated as the standard deviation (SD) of mean SBP of 24 hours (12). SBPV for daytime and night time were calculated and analyzed separately.

Electrocardiographic Indices and CAVI Measurement: All patients underwent electrocardiographic (ECG) testing after medical history checking. The paper speed of ECG is set to 50 mm/sec, and the voltage amplitude grid is set to 2 mm as 1mV for more sensitive measurements of intervals and wave morphologies. QTc is measured according to Bazett's formula, and dispersion of QTc is defined as the difference between the longest and shortest QTc interval on a 12 lead ECG record. Patients with QRS duration longer than 120 milliseconds were excluded. fQRS is defined as the presence of additional R' waves or a notch in the nadir of the R or S wave (fragmentation) in two contiguous leads corresponding to a coronary territory in a routine 12-lead ECG. All measurements on ECG recordings are made by a single observer to eliminate interobserver variability. We did not have access to computer-based detailed ECG measurement and digital processing systems. CAVI measurements was done with VaSera VS-1000 device (Fukuda-Denshi Company, LTD, Tokyo, Japan).

Statistical Analysis: Data are expressed as mean ± standard deviation (SD) for normally distributed continuous variables, as median and interquartile ranges for skew-distributed continuous variables, and as frequencies for categorical variables. The means for normally distributed continuous variables were compared by independent-samples t-test. Skew-distributed continuous variables were compared using a Mann–Whitney U-test. Patients were divided further into two groups according to the median of the dependent variable SBPV as over-median (High SBPV) and below-median (Low SBPV) groups and were compared with each other for the independent variables again. A two-sided p-value <0.05 was considered statistically significant. Statistical analyses were performed with the SPSS software (version 15.0 for Windows; SPSS Inc., Chicago, IL, USA)

RESULTS

We studied 64 patients (mean age 50 ± 8 years); 24 were male (37%). Mean eGFR was 100.2 ± 8.7 mg/dL, and mean BMI was 29.9±4.6 kg/cm^2 (Table 1).

Table 1. Baseline demographics of study patients and mean values derived from tests in the study protocol.

Age (years)	50 ± 8
Male (%)	24 (37)
eGFR (mg/dL)	100.2±8..7
BMI	29.9 ± 4.6
Smokers (%)	34 (53)
CAVI	7.9±1.2
ABI	1.1±0.1
SBPV	15.2±4.5
QTc (msec)	420.5±29.5
QTd (msec)	28.6±15.2

(SBPV=systolic blood pressure variability, BMI=basal metabolic index, eGFR=estimated glomerular filtration rate, QTc=corrected QT distance according to Bazzett's formula, QTd=QT dispersion, CAVI=cardio-ankle vascular index, ABI=ankle-brachial index)

Mean SBPV was 15.12±4.6 mmHg (14.9±5.1mmHg for daytime and 11.9±5.1mmHg for night time), and there was not a significant correlation between SBPV and glomerular filtration rate (GFR), CAVI, ABI, QTc measurements of the study patients (100.2 ± 8.7, 7.9 ±1.2, 1.1 ± 0.1 and 420.5±29.5 msec, respectively), but there was a significant positive correlation with QT dispersion values (28.6±15.2, p=0.004, ρ=0.354) (Figure 1).

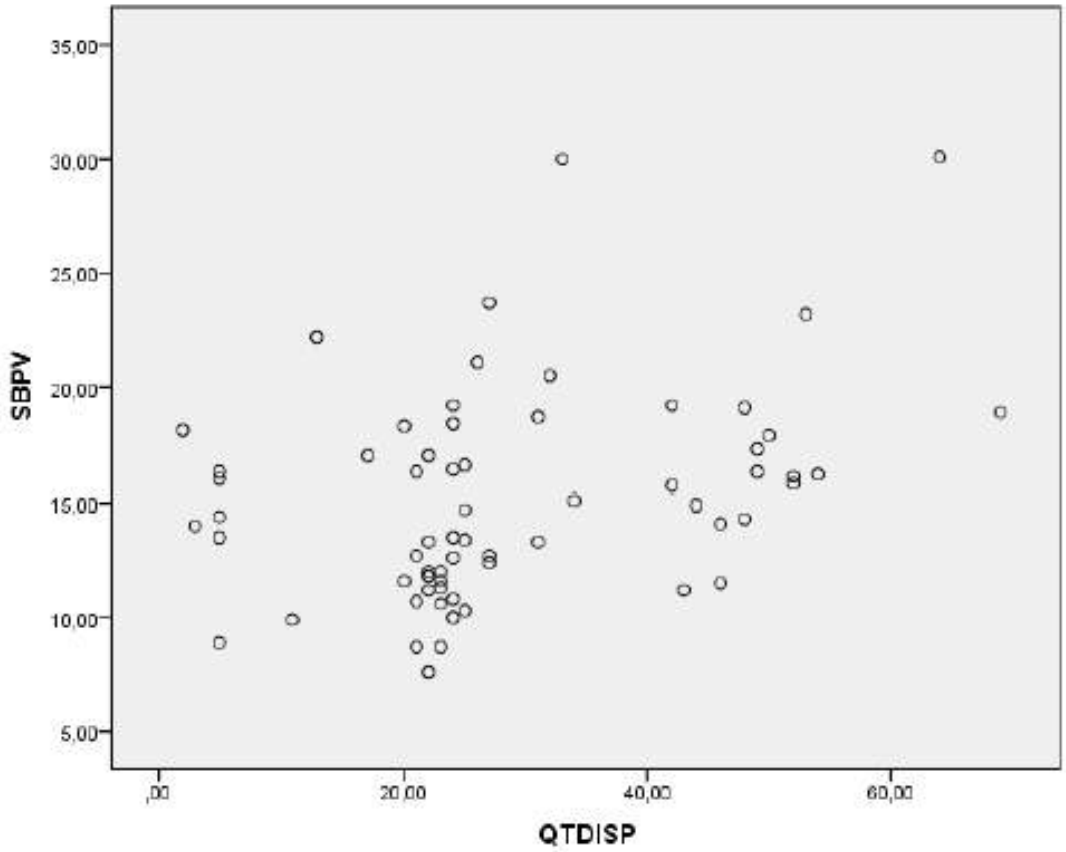

Figure1. SBPV and QTdisp correlation (SBPV=systolic blood pressure variability, QTDISP=QT dispersion)

The mean blood pressure of the study cohort was 131.9±14.9/ 86.1±10.9 mmHg for systolic/diastolic readings. When patients were divided into two categories as high SBPV and low SBPV, there was no statistically significant difference between the two groups in terms of GFR, CAVI, ABI, fQRS, and QTc values (Table 2), but high SBPV group patients had higher QT

dispersion comparing to low SBPV patients (21/23/25, 22/31/49, p=0.006, low and high SBPV values, respectively) (Table 2).

Table 2. Comparison of low and high SBPV patient groups according to laboratory and other test results representative of end organ damage. (Median SBPV=14,55 , Low SBPV is for values < 14,55 , High SBPV is for values > 14,55)

	Low SBPV (n=32)	High SBPV (n=32)	p value
SBPV (mmHg)	11,7±1,8	18,6±3,8	<0.001
Age (years) (mean ± SD)	49±9	51±8	0.261
Smoking status (n, %)	21 (65)	21 (65)	1.000
BMI	29,7±4,1	30,1±5,1	0.908
GFR (ml/min/1.73m$^{2)}$	100±9,3	100,3±8	0.373
QTc (msec)	419,6±25,7	421,3±33,3	0.158
QT d* (25th/50th/75th percentiles)	21/23/25	22/31/49	**0.006**
CAVI	8±1,4	7,8±1,1	0.247
ABI	1,1±0,1	1,1±0,1	0.495
fQRS (n, %)	16 (50)	20 (62)	0.313

*Skew distributed continuous variables are expressed in median and 25th-75th percentiles
(SBPV=systolic blood pressure variability, BMI=basal metabolic index, GFR=glomerular filtration rate, QTc=corrected QT distance according to Bazzett's formula, QTd=QT dispersion, CAVI=cardio-ankle vascular index, ABI=ankle-brachial index, fQRS=fragmented QRS)

DISCUSSION

Our main findings from the study are that SBPV was not associated with GFR, CAVI, ABI, fQRS, and QTc measurements of the study patients, but there was a positive correlation between SBPV and QT dispersion. This correlation was still significant when patients were divided into two groups according to the mean SBPV value of the whole study group as low and high SBPV subgroups. Patients in the high SBPV subgroup had significantly higher QT dispersion comparing to patients in the low SBPV subgroup.

QT dispersion is regarded as a measure of heterogeneity in left ventricular (LV) repolarization and refractoriness. Many factors, including sympathetic activity, history of previous CV diseases, circadian changes in hormonal and humoral elements, may also alter QT interval length and QT dispersion. Cardoso et al. (13) showed that QT dispersion is a predictor of CV events in diabetic patients. In a systematic review from Yitzchok et al. (14) it is suggested that QT dispersion might have a prognostic role in predicting mortality in stroke. These studies have documented that in patients with known cardiovascular risk factors such as diabetes and cerebrovascular event history, QTd might predict future CV events and prognosis. Therefore, the positive correlation of QTd and SBPV from our study results might be indicating a subclinical fibrosis and/or repolarization anomaly in LV and, therefore, an increased risk of CV events, including sudden cardiac death in the high SBPV group. Conversely, this difference might be related to any other factor that causes high SBPV and high QTd values simultaneously (decreased autonomic balance, dysfunctional baroreflex mechanism, etc.) since this is a cross-sectional study, and we cannot document a causal relationship (15). The absence of a relationship between other ECG marker of left ventricular fibrosis (fQRS) and SBPV in our cohort might be indicating that repolarization anomalies in LV appear, before alterations in LV afterload and high SPBV leads to LV hypertrophy (LVH) and fibrosis, as patients with documented LVH on echocardiography were excluded from this study (Table 1 and 2).

CAVI is a novel marker for arterial stiffness and increased CV risk (16,17). In this study, we could not document a relationship between CAVI measurements and SBPV. SBPV is documented to be associated with increased aortic stiffness but not carotid artery stiffness, according to previously published data from Zhou et al. (18). The patient cohort in this study was based on the Maastricht Study, which consists of type 2 diabetes mellitus patients, and PWV was measured to document aortic stiffness. Shin et al. also reported an association between daytime SBPV and arterial stiffness, which was also documented with PWV (19). PWV measurement has several limitations, such as estimation of the length of the arterial system, estimation of a unidirectional pathway for pulse pressure to travel and close relation with instant BP and heart rate at the time of measurement (20). We used CAVI instead of PWV to measure arterial stiffness, which is not affected by the instant BP or heart rate and, we have excluded all patients with documented CV risk factors, including diabetes, from the study. These two factors might have resulted in this conflicting result with the previous data. On the other hand, although statistically not significant, the mean CAVI measurement in the high SBPV subgroup was lower than the low SBPV subgroup. Nevertheless, our patient cohort is extremely small to draw a definite conclusion in this manner.

The significance of fQRS on routine ECG was first studied as a sign of myocardial scar in patients undergoing nuclear stress test (21). In this study, fQRS was documented as a marker of prior myocardial infarction (MI) and left ventricular scar with a higher sensitivity and negative predictive value comparing to the presence of q waves. Later, the prognostic value of fQRS in patients with different aspects of coronary artery disease, including ST-elevation MI and non-ST elevation MI, were studied separately (22,23). In both of these studies, fQRS on ECG was reported as associated with poor prognosis. A small study from Kadı et al. (24) has documented that in hypertensive patients with normal coronary arteries,

left ventricular mass (LVM) and LVMI of patients who had fQRS on their ECG was significantly higher than patients who did not have. This study proved that hypertension-related myocardial fibrosis is associated with fQRS independent of coronary artery disease. Furthermore, Eyuboglu et al. reported an association between fQRS presence and increased blood pressure in the absence of LVH (25). In our study, despite the higher frequency of fQRS among patients in the high SBPV group comparing to the low SPBV group, this difference did not reach statistical significance. This was an unexpected finding considering the aforementioned studies and reports. In the absence of LVH and CAD, with more patients enrolled in the study, we might have documented similar results with previous studies, or it might be postulated that in this selected group of patients, SBPV is not as a powerful predictor of myocardial fibrosis as mean SBP is.

We had planned a larger patient group initially, but due to the SARS-CoV-2 virus pandemic, we had to stop our patient recruitment process earlier than planned, so the low number of patients included in the study is the primary weakness of our study. CAD is excluded based on patients' medical history in this study, and it is impossible to be entirely sure about the absence of CAD in the study patients without a coronary angiography. This weakness might have an effect on study results. Moreover, this is a cross-sectional study, and we cannot derive a causal relationship between SBPV and other markers of CV system disorders.

CONCLUSION

In hypertensive patients without documented CV disease and in the absence of LVH, SBPV is positively correlated with QT dispersion, which might signify an increased risk of ventricular arrhythmia. High SBPV was neither related to increased arterial stiffness nor the presence of fQRS. Further studies are needed to understand the consequences of blood pressure variability on the cardiovascular system and help physicians refine their treatment protocols in patients with hypertension.

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RESEARCH ARTICLE

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ECG Evaluation in Patients with Pneumothorax Admitted to the Emergency Department: A Three years Analysis

ABSTRACT

Objective: Pneumothorax is one of the life-threatening differential diagnoses of patients presenting to emergency department (ED) with shortness of breath and chest pain. The place of dynamic electrocardiography (ECG) changes in diagnosis of pneumothorax was not well defined. The aim of our study was to reveal the clinical importance of ECG in pneumothorax.

Methods: Between 01.04.2014 and 01.04.2017, 147 patients who applied to our ED and take a diagnosis of pneumothorax were retrospectively examined. The patients were divided as Group 1 (with pneumothorax volume <20%), and group 2 (with pneumothorax volume≥ 20%). Patient demographics, mechanism of pneumothorax formation (traumatic or spontaneous), X ray and tomographic findings, ECG findings, hospitalization-follow-up periods, treatment methods; were derived from the hospital's data recording system and compared between groups.

Results: 109 (74.1 %) of 147 patients had a traumatic pneumothorax, and 38 (25.8%) had a spontaneous pneumothorax (p <0.001). 21 (55.2%) of the spontaneous pneumothorax cases are primary spontaneous pneumothorax. 64.6% (n=95) of the patients had chest pain. The two groups were similar in terms of age, hemoglobin level, GCS, number of days followed, gender and smoking status, (p> 0.05). When the ECG data was analyzed, a difference was found between the two groups. While 52.8% of the patients in group 1 had ECG changes, all of the patients in group-2 (100%) had unusual ECG findings (p = 0.004).

Conclusions: Pneumothorax is a condition that should not be overlooked at ED. Pneumothorax especially with large volume size (size≥20%) should be remembered in cases with abnormal findings in their ECG.

Keywords: Electrocardiography; Spontaneous Pneumothorax; Traumatic Pneumothorax.

Acil Servise Başvuran Pnömotoraks Hastalarında EKG Değerlendirilmesi: Üç Yıllık Bir Analiz

ÖZET

Amaç: Pnömotoraks, nefes darlığı ve göğüs ağrısı ile acil servise başvuran hastaların hayatı tehdit eden ayırıcı tanılarından biridir. Dinamik elektrokardiyografi (EKG) değişikliklerinin pnömotoraks tanısındaki yeri iyi tanımlanmamıştır. Çalışmamızın amacı, pnömotoraksta EKG'nin klinik önemini ortaya çıkarmaktır.

Gereç ve Yöntem: 01.04.2014 – 01.04.2017 tarihleri arasında acil servisimize başvuran ve pnömotoraks tanısı alan 147 hasta geriye dönük olarak incelendi. Hastalar Grup 1 (pnömotoraks hacmi <% 20) ve grup 2 (pnömotoraks hacmi≥% 20) olarak ayrıldı. Hasta demografik özellikleri, pnömotoraks oluşum mekanizması (travmatik veya spontan), Röntgen ve tomografi bulguları, EKG bulguları, hastanede yatış-takip süreleri, tedavi yöntemleri; hastanenin veri kayıt sisteminden elde edildi ve gruplar arasında karşılaştırıldı.

Bulgular: 147 hastanın 109'unda (% 74.1) travmatik pnömotoraks, 38'inde (% 25.8) spontan pnömotoraks vardı (p <0,001). Spontan pnömotoraks vakalarından 21'i (% 55.2) birincil spontan pnömotoraks (PSP) idi. Hastaların% 64.6'sında (n = 95) göğüs ağrısı vardı. İki hasta grubu yaş, hemoglobin düzeyi, GKS, takip edilen gün sayısı, cinsiyet ve sigara içme durumu açısından birbirinden farklı değildi (p> 0.05). EKG verileri incelendiğinde iki grup arasında fark bulundu; Grup 1'deki hastaların% 52,8'inde EKG değişiklikleri varken, grup-2'deki tüm hastaların (% 100) olağandışı EKG bulguları vardı (p = 0,004).

Sonuç: Pnömotoraks acil serviste gözden kaçırılmaması gereken bir durumdur. EKG'sinde anormal bulgular olan durumlarda pnömotoraks (Klinik olarak anlamlı pnömotoraks, boyut≥% 20) hatırlanmalıdır.

Anahtar Kelimeler: Elektrokardiyografi; Spontan Pnömotoraks; Travmatik Pnömotoraks.

INTRODUCTION

Pneumothorax is defined as the presence of free air in the space between the parietal and visceral membranes of the lung and associated lung collapse. Although the air in the pleural space can have many sources, the most common causes are rupture of the visceral pleura and air leakage from the lung parenchyma to the pleural space (1). Pneumothorax can be classified as non-traumatic (spontaneous) or traumatic (blunt or penetrating). Trauma is the most common cause of death in the first 4 decades of life (1, 2, 3). Thoracic trauma constitutes 25% of deaths due to trauma in prehospital settings (1, 4). Pneumothorax is observed in approximately 20% of patients with severe chest trauma (2). Spontaneous pneumothorax (SP) more frequently affects patients between the ages of 20 and 30 years, and 60-70 years (1). The male / female ratio was found to be 2.7 in the distribution by gender (1, 5). Most common complaints of pneumothorax are chest pain, shortness of breath, cough, tachycardia, and tachypnea (1, 2). Elimination of the patient's symptoms as much as possible complete re-expansion of the lung, prevention of complications and recurrences are targets of the treatment (1, 2, 6). Radiological imaging methods (x-ray, tomography) are the most critical parameters in diagnosis. However, the place of dynamic electrocardiography (ECG) changes in diagnosis of pneumothorax was not well defined. Most of the studies were conducted in small groups of patients and most frequently, the reports include isolated cases (7-13). The similar symptomatology of spontaneous pneumothorax and cardiac conditions (chest pain, dyspnea) together with ECG abnormalities may lead to misdiagnosis and delay in the treatment of pneumothorax (7-10). The aim of our study was to reveal the clinical importance of ECG in the diagnosis of pneumothorax in daily emergency department practice.

MATERIAL AND METHODS

After approval by the Institutional clinical research ethics committee (Decision no: 2017/10; date: 06.02.2017), this retrospective and descriptive study was performed in accordance with the ethical guidelines of the Declaration of Helsinki. In the study, 205142 patients who applied to our emergency department between 01.04.2014 and 01.04.2017 were retrospectively examined, and 147 patients aged 18 years and over with a diagnosis of pneumothorax were identified. Patient symptoms, age, gender, Glasgow coma scale (GCS), chronic diseases (diabetes mellitus, hypertension, coronary artery disease, hypothyroidism.), smoking history, mechanism of pneumothorax formation (traumatic or spontaneous), posterior-anterior chest radiography (PACR) thoracic computed tomography (CT), hemoglobin level, ECG findings, hospitalization-follow-up periods, treatment methods; were derived from the hospital's data recording system.

Patients were divided in two groups as Group 1 (patients with pneumothorax volume less than 20% of a hemithorax volume) and Group 2 (patients with pneumothorax volume equal to or greater than 20% of a hemithorax volume) according to the pneumothorax volumes measured using the Kircher method. We used <20% and≥ 20% as limits for patient grouping because pneumothorax up to 20% on PACR is considered as minimal pneumothorax and is followed conservatively in clinically stable patient, however pneumothorax above 20% is classified as massive pneumothorax and requires drainage by tube thoracostomy (1, 2).

12-lead ECG data were evaluated by an emergency medicine specialist and a cardiologist, and the findings were recorded. Distinct P waves, regular rhythm, heart rate of 60-100 / minute, the QRS complex following each P wave, the constant PR interval between 0.12-0.20 seconds, QRS width maximum 0.10-0.12 seconds, and fixed ST-segment on the isoelectric line were accepted as "normal ECG." ECGs other than these definitions were accepted as "ECG with abnormal findings" (14). After confirmation of pneumothorax size via PACR the treatment and follow-up for patients with pneumothorax was made by the same thoracic surgeon.

Kircher method was used to calculate the pneumothorax size (15). This method is based on measuring and calculating the hemithorax and collapsed lung area on chest radiography (%) = [(A x B) - (a x b)] / (A x B) (**Figure 1**). The formula requires measurements of lateral wall at the mid-point of the upper and lower halves of the hemithorax(B), diameter of collapsed lung(a), lateral wall at the mid-point of the upper and lower halves of the collapsed lung(b) and hemithorax diameter (A). A chest tube is required if pneumothorax is > 20% in clinically stable patient.

Statistical Analysis: Statistical evaluation of the data was made with the SPSS 19.0 package program. The compatibility of numerical variables to normal distribution was examined using the Shapiro-Wilk test. Descriptive statistics were expressed as arithmetic mean ± standard deviation and median (minimum-maximum) for numerical variables and as numbers and percentages for categorical data. In comparing the two groups in terms of numerical variables, the Mann-Whitney U test was used because parametric test assumptions were not provided. The differences between groups in terms of categorical variables and the relationships between variables were examined using Chi-square and Fisher's exact chi-square tests. A p-value of <0.05 was considered significant in the analysis. It is commented that a "statistically significant difference exists" for values equal or less than this value.

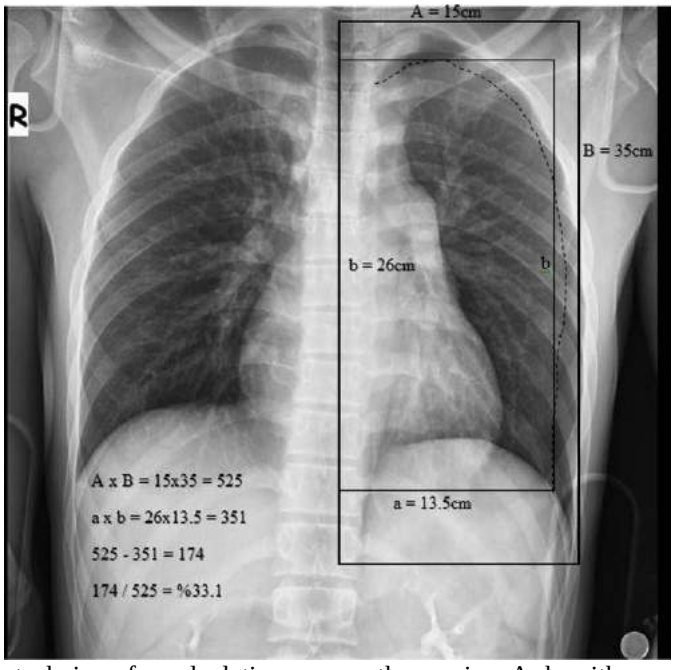

Figure 1. Kircher's technique for calculating pneumothorax size. A: hemithorax diameter- A line started at the mid-tracheal line and finished at lateral wall of hemithorax; B: the lateral wall at the mid-point of the upper and lower halves of the hemithorax; a: diameter of collapsed lung. b: the lateral wall at the mid-point of the upper and lower halves of the collapsed lung. It was taken from the archive of our School of Medicine hospital

RESULTS

Traumatic pneumothorax is seen in 109 (74.1 %) of 147 patients, and 38 of the patients had a spontaneous pneumothorax. While 55.2% of spontaneous pneumothorax cases were primary spontaneous pneumothorax (PSP), 44.7% were secondary spontaneous pneumothorax. The patients had chest pain (64.6% (n = 95)), shortness of breath (17.6% (n = 26)), change in level of consciousness (7.4% (n = 11)) and 6.8% (n = 10) of patients presented with back pain and 3.4% (n = 5) with another complaint during application to our emergency department.

The groups were not different from each other in terms of age, hemoglobin level, GCS, number of days followed, gender, smoking status, and chronic disease history (p> 0.05).

When the mechanism of pneumothorax is examined it was seen that traumatic pneumothorax was more common in group 1 patients and spontaneous pneumothorax was more common in group 2 patients (p = 0.004) (**Table 1**).

Table 1. Descriptive and comparative data of the patients groups

Patient group(n)		**Group1 (n=116)**	**Group2 (n=31)**	**p value**
Age (years)		45.5 (18 – 89)	47 (18 – 83)	0.831
Hemoglobin (g/dL)		14.1 (7.6 - 17.6)	14.3 (10.0-17.4)	0.183
GCS		15 (3 – 15)	15 (5 – 15)	0.192
Length of hospital stay (day)		4 (1 – 33)	3.5 (1 – 11)	0.938
Gender(n)	Male	103 (88.8%)	27 (87.1 %)	0.758
	Female	13 (11.2%)	4 (12.9%)	
Etiology of pneumothorax (n)	Spontaneous	21 (18.1%)	17 (54.8%)	0.001
	Traumatic	95 (81.9%)	14 (45.2%)	
Smoking* n=138	*Non-smoker*	*48 (44.4%)*	*15 (50.0%)*	*0.589*
	Smoker	*60 (56.6%)*	*15 (50.0%)*	
Comorbidity(n)	yes	56 (48.3%)	20 (64.5%)	0.160
	no	60 (51.7%)	11 (35.5%)	

Values are presented as medians (range), or n (%). * n = 138: 9 people with unknown smoking status were excluded from the analysis. Group 1 (patients with pneumothorax volume < 20% of a hemithorax volume); Group 2 (patients with pneumothorax volume ≥20% of a hemithorax volume), GCS: Glasgow coma scale. Significant at p <0.05 level

ECG changes were observed in the 30 (63.8%) (p = 0.004) of 47 patients whose ECG's could be evaluated. Unusual ECG findings were observed in all of the patients with pneumothorax volume ≥ 20% (**Table 2**).Incomplete right bundle branch block was the most common ECG finding **(Table 3)** in both patient groups.

Table 2. Distribution and comparison of ECG changes according to pneumothorax size

Parameter		Total Population (n=47; 100%)	Group 1 (n=36; 76.6%)	Group 2 (n=11; 23.4%)	p value
ECG	Usual findings	17 (36.2%)	17 (47.2%)	0 (0.0%)	0.004
	Unusual findings	30 (63.8%)	19 (52.8%)	11 (100%)	

*Significant at p<0.05 level

Table 3. ECG changes detected in our patients

ECG changes- Unusual findings	n
V1-V4 T negativity	2
V4-V5-V6 ST depression	1
V5-V6 ST elevation + D1 and AVL T negativity	1
V4-V5-V6 T negativity +Right branch block + atrial fibrillation	1
V1-V4 T negativity +Right axis deviation	3
V1-V4 ST depression +Right axis deviation + atrial fibrillation	1
Isolated R wave loss in D1 derivation	1
Reduction of P, QRS and T wave amplitudes in D1 leads	2
Right axis deviation + incomplete right bundle branch block	2
Right bundle branch block + D3 and T negativity in AVF	1
Incomplete right bundle branch block	**7**
Incomplete left bundle branch block	1
Atrial fibrillation	1
P pulmonale	1
D2-D3-AVF showed ST elevation and pathologic Q + V4 V5 V6 with T negativity	1
V2-V4 T negativity +ST segment depression, +Right axis deviation + right bundle branch block	1

DISCUSSION

Pneumothorax is an important life-threatening disease that all physicians must keep in mind and not overlook. Pneumothorax is characterized by collection of air and pressure increase in the pleural space between the lung and the chest wall (1, 2). Although cardiac causes are the first to come to mind, pneumothorax and other thoracic pathologies are the other options in the differential diagnosis in patients presenting with chest pain and shortness of breath in an emergency department. Patients with pneumothorax may be asymptomatic or can present with chest pain, shortness of breath, tachycardia, and tachypnea (1). Chest pain (64.6%) and shortness of breath (17.6%) was most common symptoms in our patients.

Acute chest pain conditions have a quite common symptoms and ECG is one of the most important diagnostic tool used in the differential diagnosis of these disorders (2). Many reasons, such as coronary artery diseases, pericardial diseases, ischemic stroke, electrolyte disturbances, and intoxications, can present with specific or non-specific findings on ECG (16-20). Clinical conditions that decrease venous return to the thoracic cavity, disrupt perfusion, and increase systemic vascular resistance cause ECG changes. Intrapleural pressure that increase in pneumothorax may gradually compress ipsilateral lung directly and opposite lung by mediastinal shift. Increased intrapleural pressure and mediastinal shift act on the venous flow and stroke volume (1, 5, 6). Decreased cardiac output, increased intrathoracic pressure, cardiac rotation around its long axis, right ventricular dilatation due to increased pulmonary artery pressure, and cardiac displacement are estimated with ECG changes in pneumothorax (7-10). In patients with pneumothorax various non-specific ECG findings such as right axis deviation, decreased QRS amplitude in the precordial leads, and T-wave inversion can be observed (7-13, 21, 22). ECG changes may be expected in both left-sided and right-sided pneumothorax alike. Changes reported for left-sided pneumothorax more frequently include right axis deviation, QRS amplitude changes, diminution in precordial R-wave voltage, T- wave inversions, and PR-segment elevation. Reported right-sided pneumothorax changes most commonly involve the QRS complex (particularly right bundle branch block) and T- wave inversion. ST elevation may be seen in both left-sided and right-sided pneumothorax (10-13). The possibility of such changes is most often mentioned in patients with spontaneous pneumothorax and tension pneumothorax (7-13). Yeom et al. found that ST-segment elevation can be observed in a case with minimal pneumothorax and that ECG returns to the normal by reducing the size of the pneumothorax (7). Tomiyama et al. found hypotension, decreased oxygen saturation, and decrease in R wave amplitude of ECG in cases which developed tension pneumothorax intraoperatively. They suggested that this could be an indicator of pneumothorax (8). However, there is evidence that ECG changes are related to the size of the pneumothorax (7, 9, 10). It has been shown that

detected change of ECG in patients with left PSP is helping in estimation of the size of pneumothorax, although it is not the only indicator for pneumothorax (9). Also in male patients with left PSP the size of the pneumothorax can be over 20% if the S wave in the V2 derivation of ECG is <12 mm, and the S wave in the V3 lead is <9 mm (10). In our study 17 (36.2%) of 47 patients whose ECG was examined had normal ECG findings and their pneumothorax volume is <20% of the hemithorax. ECG within normal limits was not observed in any of the patients with pneumothorax volume ≥ 20%. Incomplete right bundle branch block was the most common unusual ECG finding in our study.

We think that, pneumothorax has an important place in the differential diagnosis of the cases considered as cardiac emergencies. Our findings showed that pneumothorax especially with large volume size should be considered in patients with shortness of breath, chest pain, and unusual ECG findings.

Motor vehicle accidents are one of the most important causes of trauma-related mortality and morbidity (1, 5). Thoracic trauma accounts for about a quarter of emergency room admissions for trauma (2, 3, 5). Traffic accidents are a fundamental cause of traumatic pneumothorax due to blunt trauma (3, 23, 24). The most common etiologic cause of pneumothorax in our emergency department was trauma (74.1%). If our pneumothorax patients were compared within themselves rather than the whole population, the rate of traumatic pneumothorax / spontaneous pneumothorax was found to be more than twice of the rate in the study of Melton et al (25). This situation may be related to the differences of the districts where studies were conducted.

PSP etiology includes smoking, male gender, mitral valve prolapsus, Marfan syndrome, atmospheric pressure change, lung bulla/blebs, genetic factors (1, 2). In our study, 73% of PSP cases were smokers also 88.4% of 147 cases were male. Our study finding also showed that spontaneous pneumothorax more frequently presented with pneumothorax volume more than 20%.

The treatment of pneumothorax in emergency department varies according to the pneumothorax size and the severity of the clinic. Besides operative (tube thoracostomy, videothoracoscopy, thoracotomy) and non-operative (needle aspiration, percutaneous aspiration catheter) treatment options and conservative monitoring can also be performed (1, 4, 5, 26). The size of the pneumothorax may affect the treatment and length of stay in the hospital (26, 27). Thelle et al. found that the duration of hospital stay of PSP patients who underwent tube thoracostomy was approximately two times longer than those who underwent needle aspiration (28). In our study, no significant difference was found between the size of the pneumothorax and the length of hospital stay.

The limitations of our study included its retrospective nature, heterogeneity of patients, the small group of patients with ECG data and the absence of previous ECGs of patients. The missing ECG data was conducted with retrospectively design of our study. Lack of comparative ECG data may have affected the accuracy of the results.

CONCLUSION

ECG and Chest X ray are the most important diagnostic tools used in the differential diagnosis of patients with chest pain and dyspnea. Chest X ray should not be forgotten in patients with abnormal findings in their ECG. Pneumothorax (volume size ≥ 20%) should be included in the differential diagnosis in cases admitted to the emergency department with abnormal findings in their ECG. Further prospective studies are required to define the ECG changes in patients with pneumothorax and the underlying mechanisms of ECG changes.

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REVIEW

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Use of Youtube in Medical Education

ABSTRACT
The use of technologies is gradually increasing in undergraduate, postgraduate and continuing medical education. The internet has become not only an easily accessible resource for health services but also the biggest and latest source of medical knowledge. In this framework, Web 2.0 sites such as YouTube have become useful sources of information, and they are widely used by medical students as a learning resource. Educators should promote the use of YouTube particularly as a self-guiding method to enhance students' learning. YouTube provides an affordable and useful communication tool that students can access at any time. We believe that YouTube will continue to provide the skills and information needed in the learning processes in undergraduate and postgraduate medical education in the future as well.

Keywords: YouTube, Medical, Education, Medical Education

Tıp Eğitiminde Youtube Kullanımı

ÖZET
Lisans, lisansüstü ve sürekli tıp eğitiminde teknolojilerin kullanımı giderek artmaktadır. İnternet sadece sağlık hizmetleri için kolay erişilebilir bir kaynak değil, aynı zamanda en büyük bilgi kaynağı haline gelmiştir. Bu çerçevede, YouTube gibi Web 2.0 siteleri yararlı bilgi kaynakları haline gelmiştir ve tıp öğrencileri tarafından bir öğrenme kaynağı olarak yaygın şekilde kullanılmaktadır. Eğitimciler, öğrencilerin öğrenmesini geliştirmek için, özellikle kendi kendine rehberlik yöntemi olarak YouTube'un kullanımını teşvik etmelidir. YouTube, öğrencilere her zaman erişebilecekleri uygun ve kullanışlı bir iletişim aracı sağlar. YouTube'un gelecekte de mezuniyet öncesi ve mezuniyet sonrası tıp eğitiminde öğrenim süreçlerinde ihtiyaç duyulan bilgi ve becerileri sağlamaya devam edeceğine inanıyoruz.

Anahtar Kelimeler: YouTube, Tıp, Eğitim, Tıp Eğitimi.

INTRODUCTION

Medical education is changing rapidly, as it is affected by many factors such as the developments and changes in health service delivery, globalization, the internet, population diversity, the changing role of physicians, changing social expectations, rapidly changing medical science and the diversity of pedagogical techniques. The use of technologies is gradually increasing in undergraduate, postgraduate and continuing medical education, and the use of technology has been developing for years. This inclination towards the use of technology has developed as a response to the challenges experienced particularly in medical education. The aims of using technology in medical education include facilitating basic learning, improving decision making, improving skill coordination, making clinical decisions in rare or critical cases, learning teamwork and improving psychomotor skills. It is possible to achieve these aims through different technologies. Podcasts and videos, mobile devices with apps, video games, simulations (part-time trainers, integrated simulators, visual reality) are a few examples of current technological advancements. The use of computer technologies has the advantage of evaluating competencies and providing the necessary tools to continue lifelong medical learning. In addition, the use of technology in medical education should support learning (1). The internet has become not only an easily accessible resource for health services but also the biggest and latest source of medical knowledge. In this framework, Web 2.0 sites such as YouTube have become useful sources of information, and they are widely used by medical students as a learning resource. Easily accessible visual-auditory files both enhance patient knowledge and affect medical education. However, very little is known about their characteristics. Easily accessible video-posting sites such as YouTube are the internet applications that are commonly used by medical students and residency students. YouTube gives an opportunity for educational purposes. Since 2005, YouTube has been acknowledged as an important platform for sharing information. However, the quality and accuracy of online medical information is very heterogeneous. Inaccurate or misleading health information can appear on YouTube. YouTube is an important resource for different diseases and procedures (2). Considering that YouTube access can accelerate the learning of clinical procedures, it is important to enhance its scope and access to support student needs in addition to basic education (3). YouTube reaches billions of users and is a unique source of information dissemination and communication. It is a "participatory culture" site, where contributors upload a great variety of content from entities, enterprises and individuals (4). It is a resource of popular video blogs and short original videos uploaded by individuals. Most of the videos on YouTube are based on personal experience, but there are also many videos posted by professionals such as physicians. Diversity of authorship and lack of preliminary examination on YouTube may lead to misleading health information (5,6). Despite this, social media is widely used by patients and interns as an educational tool (7, 8, 9, 10). Doubtlessly, new technologies change the way students learn as well as the strategies used for designing and implementing medical and health curricula. Considering those changes, there are a series of technological tools that can promote learning for medical students. For example, network sites (Facebook and Twitter), media sharing sites (for example, YouTube and Flicker), blogs, wikis, podcasts and iTunes U can help users in discovering and downloading visual and auditory content. These online applications are built on contents posted by users and known as Web 2.0 (11). YouTube is the biggest online video site, where videos are viewed by more than 100 million viewers every day (12).

This study aims to examine the importance of using YouTube in medical education, the studies on the use of YouTube in medical education, and the advantages and disadvantages of using YouTube.

STUDIES REGARDING USE OF YOUTUBE IN PRECLINIC EDUCATION

Use Of Youtube In Teaching Anatomy: In the last decades, the way in which anatomy is taught and its resources have evolved significantly. One of these resources has been videos, and their role in anatomy education has developed with technological advancements. Successfully integrated anatomy videos are important for the curricula. Students watch and use these videos as a highly important resource for revision and preparation for examinations (13). The use of YouTube in medical education has remodeled and enhanced the teaching and learning of anatomy. A study conducted on 91 second-year medical students assessed the effectiveness of YouTube videos. According to its results, 98% of students used YouTube videos that emphasized applied aspects of anatomy as an online information resource, albeit in different frequencies. Based on these findings, YouTube can be considered as an effective tool to enhance anatomy education if the videos are scrutinized, diversified, and aimed toward course objectives (14). A survey made with first-year medical students at a medical school in Venezuela showed that 85% of them used YouTube as an online information resource to study human anatomy. 82.5% of them considered that human anatomy videos were a positive tool to learn human anatomy (15). Barry et al. surveyed second-year undergraduate medical and radiation therapy students (n=73) regarding their use of online social media in relation to anatomy learning and reported

that the majority of students used YouTube as their primary source of anatomy-related video clips (16). YouTube is an evolving platform for learning human anatomy as it is an easy-access and free service. Raikos and Waidyasekara made a quantitative and qualitative analysis of the human heart anatomy videos available on YouTube. In the study, the authors analyzed 294 videos. They used a scoring system to assess the anatomical quality and details, general quality, and the general data for each video. The results indicated that the human heart anatomy videos available on YouTube conveyed anatomical criteria poorly and that the general quality score was borderline (17).

Another study screened YouTube videos covering surface anatomy. For each video, information was collected on its title, authors, duration, number of viewers, posted comments, and total number of days on YouTube. Videos were grouped into educationally useful and non-useful videos. A total of 235 YouTube videos were screened, and 57 were found to have relevant information to surface anatomy. According to the results, 27% of the videos provided useful information on surface anatomy, while 73% of the videos were not useful educationally. The total average viewership per day was 750 for useful videos and 652 for non-useful videos. There were no video clips covering surface anatomy of the head and neck, blood vessels and nerves of upper and lower limbs, chest and abdominal organs/structures (18).

USE OF YOUTUBE IN TEACHING CLINICAL SKILL-RELATED TOPICS

Use Of Youtube In Teaching Heart Sounds And Murmurs: Camm et als'study aiming to assess the quality of videos relating to heart sounds and murmurs contained on YouTube hypothesized that the quality of video files purporting to provide education on heart auscultation would be highly variable and screened related videos. Their YouTube search found and scored 22 suitable videos. According to the results, the average score was 4.07 out of 7; 6 videos scored 5.5 or greater; and 5 videos scored 2.5 or less. In addition, there was no correlation between video score and YouTube indices of preference, and the quality of videos was highly variable (19).

Using Videos On YouTube For Surgical Preparation: The study by Rapp et al. questioned participants regarding the frequency and helpfulness of videos, video sources used, and preferred methods between videos, reading, and peer consultation to evaluate the surgical preparation methods of medical students, residents, and faculty with special attention to video usage. Survey participants included fourth-year medical students pursuing general surgery, general surgery residents, and faculty surgeons in the Department of Surgery. A total of 86 surveys were distributed, and 78 surveys were completed. It was found that 90% of respondents reported using videos for surgical preparation; the most used source was YouTube (% 86); and learners and faculty used different video sources (20).

Use Of Youtube In Teaching Physical Examination Of The Cardiovascular And Respiratory Systems: In a study analyzing YouTube videos about physical examination of the cardiovascular and respiratory systems, three assessors searched YouTube for videos covering the clinical examination of the cardiovascular and respiratory systems. For each video, information was collected on the title, authors, duration, number of viewers, and total number of days on YouTube. The three assessors rated the videos independently and grouped them into educationally useful and non-useful videos. According to the results, there were 56 videos covering the examination of adults; of these, 20 were relevant to cardiovascular examinations and 36 to respiratory examinations. Further analysis revealed that 9 provided useful information on cardiovascular examinations and 7 on respiratory examinations. The other videos (11 on cardiovascular and 29 on respiratory examinations) were not useful educationally. The study concluded that a small number of videos about physical examination of the cardiovascular and respiratory systems were educationally useful; these videos can be used by medical students for independent learning and by clinical teachers as learning resources (21).

Use Of Youtube In Teaching Cardiopulmonary Resuscitation And Basic Life Support: Another study aimed to analyze the videos on the YouTube video sharing site, noting which points addressed in the videos related to CPR and BLS, based on the 2010 Guidelines for the American Heart Association (AHA). The relevant videos on You Tube (n=61) were analyzed. They were mostly posted by individuals, and most of them were under the older 2005 guidelines, despite being added to the site after the publication of the 2010 AHA Guidelines, (22). Yaylacı et al. investigated the reliability and accuracy of the information on YouTube videos related to CPR and BLS according to the 2010 CPR guidelines. The authors examined the sources that uploaded the videos, the recording time, and the number of viewers in the study period. They rated the videos based on their display of the correct order of resuscitative efforts according to the 2010 CPR guidelines. Then, they analyzed the 209 videos meeting the inclusion criteria after the search in YouTube with four search terms, namely 'CPR', 'cardiopulmonary resuscitation', 'BLS' and 'basic life support'. They found that only 11.5% of videos were compatible with the 2010 CPR guidelines with regard to the sequence of interventions. Videos uploaded by 'Guideline bodies' had significantly higher rates of download when compared with the videos uploaded by other sources (23).

Duncan et al. evaluated 100 YouTube sites, approximately 1500 minutes or 25 hours' worth of content across 10 common clinical skill-related topics to assess the quality of clinical skills videos available on YouTube. The authors viewed 10 videos on YouTube for each topic. They found that the topic with the biggest number of both postings and views was cardiopulmonary resuscitation (CPR). Only one video out of the 100 analyzed could be categorized as 'good'. 60% of the CPR content was categorized as 'satisfactory' (24).

Use Of Youtube In Teaching ECG Diagnosis: Akgun et al. assessed the videos relating to ECG diagnosis on YouTube. Videos were assessed for usefulness, source and characteristics. The authors assessed the usefulness of videos using a checklist they developed. They included 119 videos in the analysis. They found that 56 videos were very useful and that 16 videos were misleading. Videos grouped as very useful videos comprised 90% of those uploaded by universities/hospitals and 45% of those uploaded by individuals. They found that the ratio of the misleading information in ventricular tachycardia videos was 42.9%. The results of this study indicated that ECG information on YouTube was not satisfactory (2).

Videos About Thermal Burn First Aid On Youtube: Butler et al. evaluated the clinical accuracy and delivery of information on thermal burn first aid on YouTube. Two independent reviewers scored the videos using a standardized scoring system and the scores were totaled to give each video an overall score out of 20. 47 videos were analyzed. This study concluded that videos covering thermal burn first aid available on YouTube were unsatisfactory. Its recommendation was that the organizations involved in managing burns and providing first aid care should be encouraged to produce clear, structured videos (25).

USE OF YOUTUBE IN TEACHING SYSTEMS

Use Of Youtube In Teaching Nervous System: Azer et al. assessed the videos covering the nervous system examination on YouTube. The authors collected the title, author/s, duration, number of viewers, number of posted comments, and total number of days on YouTube for each video. Videos were rated independently by three assessors and grouped into educationally useful and non-educationally useful videos. According to the findings, 129 videos had relevant information to the nervous system examination; 47% of videos provided useful information on the nervous system examination; while 53% videos were not useful educationally. This study reported that YouTube provided an adequate resource for learning the nervous system examination for medical students, but that there were deficiencies in videos covering examination of the cerebellum and balance system (26).

Use Of Youtube In Teaching Cardiovascular Mechanisms: Azer assessed the contents of YouTube videos on cardiovascular mechanisms and examined 29 YouTube videos. That study found that 16 of those videos were educationally useful while 13 videos were not educationally useful, and concluded that You-Tube videos were deficient in cardiovascular mechanisms (27).

Pant et al. assessed the credibility of YouTube video information on acute myocardial infarction by exploring the relationship between accuracy of information on the topic, source of expertise, and perceived credibility of the message. They categorized videos according to the source of the video. They analyzed content for discussing different aspects of the disease, ranging from pathophysiology to treatment. They found that only 6% of the videos touched upon all aspects of acute myocardial infarction. They reported that only 17% of the videos discussed the preventive aspects of the disease and stressed weight-loss and exercise programs, while very few videos stressed other risk factors (28).

Use Of Youtube In Teaching Anorexia-Related Misinformation Disseminated: Syed-Abdul at al. investigated anorexia-related misinformation disseminated through YouTube videos. Three doctors reviewed 140 videos with approximately 11 hours of video content, classifying them as informative, pro-anorexia, or others, and the 40 most-viewed videos (20 informative and 20 pro-anorexia videos) were assessed to gauge viewer behavior. According to the results, pro-anorexia videos were favored 3 times more than informative videos (29).

Use Of Youtube In Teaching Hip Arthritis: Koller et al. analyzed 133 YouTube videos on hip arthritis in terms of accurate information. They developed two quality assessment checklists with a scale of 0 to 12 points to evaluate available video content for diagnosing and treating hip arthritis. They grouped videos into poor quality (grade 0-3), moderate quality (grade 4-7) and excellent quality (grade 8-12), respectively. Three independent observers assessed all videos using the grading system and independently scored all videos. According to the results, 84% of videos had a poor diagnostic information quality, 14% a moderate quality and only 2% an excellent quality; 86% of videos had a poor treatment information quality, 11% a moderate quality and only 3% an excellent quality (30).

USE OF YOUTUBE IN TEACHING CLINICAL INTERVENTION

YouTube Videos On Knee Arthrocentesis: The study by Fischer et al. assessed the educational value of YouTube videos on knee arthrocentesis posted by health professionals and institutions. Two independent clinical reviewers assessed videos for procedural technique and educational value using a

5-point score, ranging from 1 = poor quality to 5 = excellent educational quality. According to the findings, 13 videos met the inclusion criteria. The most popular video had 1,388 hits per month, 8 videos were considered useful for teaching purposes, and 6 videos demonstrated full sterile conditions. At least two thirds of videos were considered useful for teaching purposes, but while some videos had a high educational quality, an improvement of most of the YouTube videos on knee arthrocentesis was recommended (31).

Lumbar Puncture (LP) And Spinal Anesthesia (SA) Videos On YouTube: In a retrospective study assessing the quality of lumbar puncture (LP) and spinal anesthesia (SA) videos available on YouTube, Rössler et al. evaluated the videos using essential key points (5 in SA, 4 in LP) and 3 safety indicators. They evaluated the violation of sterile working techniques and rated whether the video should be regarded as dangerously misleading. They evaluated 38 eligible videos. They found that 56% of SA videos contained 2–4 key points, while 19% did not contain any essential information. They reported that even though high quality videos were available, the quality of video clips was generally low. Although the fraction of videos with aseptic working techniques was low, these posed a substantial risk to patients, and that consequently, more high-quality, institutional medical learning videos should be made available (32).

Male Urethral Catheterization (UC) Videos On Youtube: Nason et al. aimed to assess the quality of YouTube as an educational tool regarding male urethral catheterization (UC) and to assess the experience of newly qualified doctors regarding UC. The authors identified 49 eligible videos. They found that, regarding the Safe Catheter Insertion Score, the mean score was 5.18 ± 1.64. Nine videos (18.4%) were deemed useful, 24 (49%) somewhat useful and 16 (32.7%) not useful. There was no difference in the number of views, duration of video or number of days online between those videos. Out of 26 interns, 21 completed the survey and reported that the video was a useful educational adjunct (33).

USE OF YOUTUBE IN PATIENT EDUCATION

- Stellefson et al. conducted a content analysis of chronic obstructive pulmonary disease (COPD) patient education videos on YouTube. Two independent coders evaluated each video to determine the topics they covered, media source(s) of posted videos, information quality as measured by HONcode guidelines for posting trustworthy health information on the internet, and viewer exposure/engagement metrics. The study found that more than half of the videos included information on medication management, while there were very few videos on smoking cessation. The study findings suggested that COPD education via YouTube had the potential to reach and inform patients but that existing video content and quality varied significantly (34).

- In Sood et als' study examining the effective use of YouTube as an information source on kidney stone disease, two physicians watched relevant videos and classified them as useful, misleading, or personal experiences. Total viewership, duration, rating, days since upload, source, and information content were noted. According to the results, 199 videos had relevant information about nephrolithiasis, 58.3% of the videos had useful information, and 18.1% were misleading. Useful videos had 47.2% of total viewership share, whereas misleading videos had 2.8%, so there was a statistically significant difference in viewership/day and rating among useful videos vs misleading videos (6).

USE OF YOUTUBE IN COUNSELING

Use Of Youtube In Teaching Cigarette-And Hookah-Related: Carroll et al. compared the characteristics of and messages conveyed by cigarette- and hookah-related videos on YouTube. The authors detected 66 cigarette-related and 61 hookah-related videos. They found that median view counts were 606,884 for cigarette-related videos and 102,307 for hookah-related videos, and that the number of comments per 1000 views was significantly lower for cigarette-related videos than for hookah-related videos (35).

YouTube Videos on Infantile Spasms: Fat et al. assessed YouTube videos for their efficacy as a patient resource for infantile spasms. Two neurologist raters assessed the technical quality, diagnosis of infantile spasms, and suitability as a teaching resource using the Medical Video Rating Scale. Mean rating for technical quality was 4.0 out of 5 for rater 1 and 3.9 out of 5 for rater 2. Raters found 60% and 64% of videos to accurately portray infantile spasms, respectively. Ten videos were considered excellent (36).

USE OF YOUTUBE IN PREVENTION

Use Of Youtube In Teaching The Human Papillomavirus (HPV) Vaccine: In a study making a content analysis of YouTube videos related to the human papillomavirus (HPV) vaccine, the authors examined 172 YouTube videos with respect to video sources, tones, and viewer responses. They found that most of these videos were news clips or consumer-generated content. They reported that the majority of the videos were negative in tone and disapproved of the HPV vaccine, and that negative videos were liked more by the viewers than positive or ambiguous ones (37).

USE OF YOUTUBE IN MASTER LEVEL

Another study explored how master's students (of occupational therapy) perceived the use of YouTube videos in the kinesiology course. The videos, taken on a smartphone, were uploaded to a

private YouTube URL created by the instructor and then linked to a pre-established Moodle learning platform. According to the post-course survey results, students perceived that the videos improved the quality of the course and increased their level of engagement and learning (38).

STUDIES ABOUT VIDEO LENGTH AND INFORMATION QUALITY

Buzetto-More investigated student perceptions and preferences regarding the implications of YouTube videos. According to the findings, the use of YouTube in the teaching and learning process enhances instruction. In addition, the study found that video length had an impact on student decisions regarding whether or not to watch a video, and that course delivery format impacted length and audio preferences (39).

THE ADVANTAGES AND LIMITATIONS OF USING YOUTUBE IN MEDICAL EDUCATION

YouTube has become an increasingly important resource for people to meet their needs for additional information regarding their medical conditions. YouTube can increase out-of-class learning opportunities and particularly promote self-regulatory learning (40). In addition, YouTube enables students to access the videos that they can use in their learning process all the time and everywhere (41). Today, medical students and assistants use technological opportunities frequently. If technology is used properly, it has the potential to make a big impact on medical education, but it can also cause harm if there are no recommendations on which resources will be used or how they will be used (42). Use of YouTube to exchange personal and professional information among university students is rapidly growing. In terms of medical education, YouTube is very important for enhancing the teaching-learning experiences of medical educators, physicians, librarians and students in a rich environment of networking and collaboration. YouTube videos focus students' attention and allow them to interact and thus include them in their own training. YouTube allows students to compare and analyze the perspectives of several videos and promotes critical thinking (43). Another questionable advantage of YouTube is that it makes distance training possible (41). Educators should promote the use of new technologies, choose the educational videos enhancing critical thinking for students, and use them in group studies. When YouTube is used for clinical education, it has a promising potential as a lifelong learning tool (44). Azer compared the contents of medical textbooks, eMedicine (Medscape) topics, and YouTube videos on cardiovascular mechanisms and found that they were also ideal for the molecular and clinical integration of contents and information. The author found that YouTube provided up-to-date and understandable education resources for medical students and increased interaction among users through user comments and feedback (27). However, despite all its benefits, there are problems to be addressed. One of them is that students can often be confused as to where to look for knowledge because there has been a recent overcrowding of YouTube (45). In today's world, the internet and social media are a part of everyday life. One of the most frequently used social media sites is YouTube, which was created in 2005 and now has over one billion users. Social media has great potential to provide easy access to medical information. Social media can help close the health literacy gap and present information in new ways that allow even illiterate populations to learn. However, with this increased opportunity, the chances also increase for the dissemination of inaccurate and even harmful information (46). With the rise of Web 2.0, the sharing of information on medical conditions by patients spreads through home videos, forums and blogs on the internet. Uploading home videos online has gained popularity since the creation of YouTube in 2005, and now numerous videos can be found online. Thus, it is easy to access information, and particularly YouTube can be the first source of information for patients. There are an increasing number of studies that detail the effect of YouTube on health services. Their topics include health promotion, disease perception and dissemination of proper health information (36). YouTube content is an attractive combination of active and didactic methods as a platform for learning skills or discussion. Medical students prefer web-based learning to conventional lecture-based classes because of its ease of use, accessibility, high medical image quality and repeated application advantage (31). Using YouTube can promote students to think about the materials in a medical curriculum. Students can have online discussions and make comments on videos in a familiar environment. In terms of feedback, the "insights" analytical tool of YouTube provides useful statistical data on the use of videos. These statistics relate to the viewing frequency in a certain time period, regional popularity, user demographics and how people mention videos. Such statistics are effective in making plans for future videos and providing a retrospective perspective for evaluating videos (14). YouTube is accepted as an important platform for sharing information and patient education because it is popular, easy to access and free (18). As in many health-related sources of information on the internet, online videos are not generally peer reviewed and the quality of information is variable (25). Another disadvantage is the high probability that YouTube videos will give wrong messages indirectly to people.

CONCLUSION

We recommend educators to explore the idea that YouTube will continue to provide the

skills and information needed in the learning processes in undergraduate and postgraduate medical education in the future as well. Therefore, we recommend educators to explore YouTube particularly as a self-guiding method to improve students' learning, as YouTube provides a communication environment that is affordable, useful, accessible at all times, and familiar to students.

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CASE REPORT

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The Diagnostic Role of Ascitic Fluid Adenosine Deaminase Activity in A Peritoneal Tuberculosis Case Presenting with Abdominal Pain and Diarrhea

ABSTRACT
A young case diagnosed with peritoneal tuberculosis with ascites will be presented here. Conditions that may pose a significant risk for the development of tuberculous peritonitis; poor hygiene, overpopulation, consumption of unpasteurized milk, cirrhosis, peritoneal dialysis, HIV infection, drug abuse and inadequate access to healthcare. In general, the tuberculosis agent reaches the gastrointestinal system via hematogenous route, ingestion of infected sputum, or direct spread. Peritoneal TB should be considered in the differential diagnosis in patients with abdominal pain, diarrhea, weight loss, anorexia, night sweats, presence of ascitic fluid, bilateral pleural effusion, pleural nodule appearance, and findings suggestive of peritonitis carcinomatosis, as in our case. Peritoneal tuberculosis is rarely diagnosed, without a high index of suspicion for this disease.

Keywords: Tuberculose, Ascites, Adenosine Deaminase

Karın Ağrısı Ve Diyare İle Başvuran Peritoneal Tüberküloz Olgusunda Asit Sıvısı Adenozin Deaminaz Aktivitesinin Tanısal Rolü

ÖZET
Assiti bulunan periton tüberkülozu tanısı alan genç bir vaka burada sunulacaktır. Tüberküloz peritonit gelişimi için önemli risk oluşturabilecek durumlar arasında; kötü hijyen, aşırı nüfus, pastörize edilmemiş süt tüketimi, siroz, periton diyalizi, HIV enfeksiyonu, uyuşturucu kullanımı ve sağlık hizmetlerine yetersiz erişim bulunmaktadır. Genelde tüberküloz ajanı, gastrointestinal sisteme hematojen yolla, enfekte balgam yutulmasıyla veya doğrudan yayılma yoluyla ulaşır. Karın ağrısı, ishal, kilo kaybı, iştahsızlık, gece terlemeleri, asit sıvısı varlığı, bilateral plevral efüzyon, plevral nodül görünümü ve olgumuzda olduğu gibi peritonit karsinomatozunu düşündüren bulguları olan hastalarda ayırıcı tanıda peritoneal TB akla gelmelidir. Periton tüberkülozu, yüksek bir şüphe indeksi olmaksızın nadiren teşhis edilir.

Anahtar Kelimeler: Tüberküloz, Assit, Adenozin Deaminaz.

INTRODUCTION

Tuberculosis is still an important public health problem in our country and other low-income countries. In the 2017 global tuberculosis report of the World Health Organization, the incidence of tuberculosis in our country is seen as 1.4 % (1).

Tuberculous peritonitis is a rare form with an incidence between 0.1% and 0.7% among all types of tuberculosis. The disease occurs equally in both genders, with most cases between the ages of 21 and 45 (2). Patients usually present with nonspecific symptoms such as abdominal discomfort and swelling, weight loss, fever, increased sweating, diarrhea. Delay in the diagnosis of patients causes an increase in mortality and morbidity. In this report, a case diagnosed with wet type (with ascites) peritoneal tuberculosis will be presented.

CASE

A 28-year-old male patient, who had no known history of chronic disease or drug use, first applied to the emergency service of our hospital with complaints of abdominal pain and diarrhea 20 days ago, was evaluated as acute infectious gastroenteritis and was discharged after treatment. The patient's complaints of abdominal pain gradually increased within 20 days after discharge, and diarrhea continued, and he was admitted to the emergency department again after 4 kilograms of weight loss in 20 days. The patient was admitted to the General Internal Medicine service due to the presence of free fluid in the abdomen and the findings suggesting possible peritonitis carcinomatosis in the abdominal computed tomography examination performed in the emergency department. Vital signs of the case were as follows; body temperature: 36.5 C, heart rate 80 / min, blood pressure 100/70 mm Hg, respiratory rate 16 / min. In the abdominal physical examination, although there was tenderness with palpation, defense and rebound were negative. There was no significant feature in other system examinations. When the systems were reviewed, it was learned that there was anorexia, night sweats, and watery diarrhea 8-10 times daily. In the case, whose lung examination was normal, an area compatible with minimal effusion was seen on posteroanterior chest radiography and thorax CT imaging was planned. The patient's cardiac examination was normal and his ECG had sinus rhythm, and his ECG was interpreted as normal. Whole blood count was as follows; white blood cells: 5700, Hgb: 12.6 g / dl, neutrophil: 3900, platelet: 240000. Biochemistry parameters showed no abnormal values except for albumin: 3.1 g / dl, globulin: 3.8 g / dl, CRP: 11.8. In viral serological tests of the patient; HBsAg, anti-HBs, anti HCV, anti-HIV, anti-HAV IgM was negative and anti HAV was IgG positive. Paracentesis was performed from the ascitic fluid of the patient with USG, and biochemistry parameters in the blood and ascitic fluid were examined and the ascitic fluid culture examination was requested. Ascites fluid biochemical tests were as follows; glucose: 70 mg / dl, potassium: 3.64 mmol / L, albumin: 2.6 g / dl, lactic dehydrogenase: 424, protein: 5.4 g / dl, sodium: 135 mmol / L. Albumin, protein and LDH levels were evaluated as high. In the ascitic fluid cell count, more than 1000 erythrocytes and 240 leukocytes per mm3 were seen. Ascitic fluid was evaluated to be compatible with exudate. The biopsy specimen taken from the left lower quadrant peritoneal implant with USG guidance was sent to the pathology laboratory. Bilateral pleural effusion and pleural nodule were observed in the chest CT of the patient. Pleural fluid examinations of the patient were planned considering peritoneal tuberculosis, peritonitis carcinomatosis, hematologic malignancy, and metastatic malignancy among the differential diagnoses. Under USG guidance, the fluid between the left visceral and parietal pleura was sampled by thoracentesis, and the biochemistry sample of the fluid, pleural fluid culture and pathological examination of the pleural biopsy material were requested. Biochemical analysis of pleural fluid was as follows; glucose: 88mg / dl, potassium: 3.8 mmol / l, albumin: 2.4 g / dl, LDH: 300, protein: 4.8 g / dl and interpreted as exudate according to Light's criteria. There was no bacterial growth in peritoneal and pleural fluid cultures. The result of the peritoneal biopsy sample was a lymphoplasmocytic inflammatory infiltrate accompanied by giant cells. Cytology sample was reported as "Blood, lymphocytes and histiocytes have been monitored, and it is recommended to investigate in terms of granulomatous diseases, especially tuberculosis." The pleural fluid of the case was also seen in favor of tuberculosis, resulting in Adenosine Deaminase level: 67 U / I. The patient was referred to Chest Diseases Hospital for 6 months of anti-tuberculosis therapy (isoniazid 300 mg / day, rifampicin 600 mg / day, pyrazinamide 1500 mg / day, ethambutol 1500 mg / day). At the control one month later, his general condition was good and improvement in his laboratory parameters was detected.

DISCUSSION

In addition to the initiation of antituberculosis treatment, the improvement in socioeconomic status has been associated with a decrease in all forms of tuberculosis (TB), including tuberculous peritonitis (3, 4). Although abdominal tuberculosis continues to be a major health problem in the developing world, the recent increase in the number of patients diagnosed with peritoneal tuberculosis in regions where TB is rare, is partly due to travel, migrations and HIV infection which increases susceptibility to opportunistic infection. In the literature, a frequent relationship between tuberculous peritonitis (TBP)

and cirrhosis particularly of alcoholic aetiology has been described in developed countries (3, 4, 5). Peritoneal dialysis and HIV patients include patients at high risk of developing TBP (3, 6, 7). While poor hygiene and overcrowding have been shown to have a causal relationship with TB, ingestion of unpasteurized milk may also be another factor in the rural area. HIV infection is the strongest among all these risk factors for TB development, as the Th1-type immune response, which is a defense weapon against Mycobacterium tuberculosis, is impaired in those with HIV infection (3). Diagnosis of peritoneal TB can easily be missed or inappropriately delayed unless there is a high degree of suspicion. In patients with suspected peritoneal TB, screening of Mycobacterium with the staining and culture of the ascitic liquid is of paramount importance. Mechanistically, ulcers and fistulas may develop as a result of the lesions in the intestines caused by bacilli reaching the intestines when the patient with active pulmonary tuberculosis swallows the infected sputum. On the other hand, there may be peritoneal tuberculosis and tuberculous ascites with spread from small bowel tuberculosis to mesenteric lymph nodes. A higher incidence of peritoneal tuberculosis has been reported in homeless, in prison, in immigrants, in persons with underlying conditions such as acquired immunodeficiency syndrome, malignancies, diabetes mellitus and peritoneal dialysis (3, 8). It has been suggested that peritoneal tuberculosis is caused by the reactivation of latent tuberculosis clusters in the peritoneum, which are usually caused by the spread of the primary lung focus through the hematogenous route (8). Insidious-onset ascites, which can accompany non-specific symptoms such as abdominal pain, weight loss, abdominal swelling, fever, and night sweats, can be counted among the clinical findings of tuberculous peritonitis. In other words, the most important symptom of tuberculous peritonitis is ascites and is observed in the vast majority of cases (9, 10, 11). Ascitic fluid white blood cell count ranges between 150-4000 / mm3 and lymphocyte dominance (3). Acidic fluid total protein levels> 25 g / L are known as a finding that can be seen in almost all cases with tuberculosis peritonitis. Because of a low serum-ascites albumin gradient (SAAG) (<11 g / L) is seen in 100% of patients with tuberculous peritonitis, SAAG (<11 g / L) should suggest tuberculosis peritonitis. A cutoff point of 39 IU / L (with 100% sensitivity and 97.2% specificity) was reported for the diagnosis of TBP, calculated by the ROC curve for the ADA value (8, 10). An increased ADA activity is thought to be related to the intensity of stimulation and the maturation state of the lymphocyte due to the immune cellular response to Mycobacterium tuberculosis (8). Ascitic fluid adenosine deaminase (ADA) activity, in addition to being recommended as a useful diagnostic test for abdominal TB, may be a useful screening test to study "ADA activity in ascitic fluid" in countries with a high incidence of TB and in high-risk patients (8, 10). In addition, in the diagnosis of peritoneal TB, it has been reported that the use of fast method like ascitic fluid ADA activity may be associated with a reduction in diagnosis time (8, 10, 12). In tuberculous peritonitis, the peritoneum is infiltrated with numerous yellow-white tubercles, lost its bright appearance, and becomes thick and hyperemic (13). Peritoneal tuberculosis can usually present in 3 different types: Wet type with ascitis; localized type; and fibrotic type with abdominal masses consisting of mesenteric and omental thickening. In tuberculous peritonitis, although the peritoneum is generally thickened and nodular, thickening on CT with minimal and significant enhancement and the presence of a "smooth" peritoneum suggest tuberculosis peritonitis; "nodular implants" and "irregular" peritoneal thickening suggest peritoneal carcinomatosis. While culture growth of Mycobacterium remains the " hallmark" for diagnosis, ADA screening in ascitic and/ or pleural fluid is a relatively new approach as in our case (13). "Caseation"; as a pathognomonic histologic lesion can only be seen in lymph nodes (13, 14) and therefore obtaining results from biopsy samples may be difficult. In this context, it is considered that the best diagnostic procedure for tuberculous peritonitis is peritoneal biopsy with laparoscopy (13, 14). Ascitic fluid adenosine deaminase (ADA) activity is thought to be a useful diagnostic test for tuberculosis peritonitis (13. 15). Abdominal tuberculosis has many different faces and a wide variety of clinical symptoms, and it may be necessary to review a wide range of diseases in patients with differential diagnosis because it is a difficult condition to diagnose (15, 16, 17). Peritoneal TB needs to be considered in the differential diagnosis when patients with abdominal pain, diarrhea, weight loss, anorexia, night sweats, the presence of ascitic fluid, bilateral pleural effusion, pleural nodule appearance and the findings suggesting peritonitis carcinomatosis are encountered as in our case. The internist should search for tuberculosis and exclude this curable disease in any patient presenting with a suitable clinical picture.

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CASE REPORT

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Rare Complications of COVID-19 Pneumonia: Pneumomediastinum and Atrial Fibrillation

ABSTRACT

Objective: Coronavirus disease 2019 (COVID-19) is considered as systemic disease involving many vital organs in addition to the lungs, including the heart, liver, and kidneys. Pneumomediastinum associated with COVID-19 pneumonia is a rare condition usually seen in patients with underlying lung pathology, infections, or mechanical intubation. We presented a case of late diagnosis of pneumomediastinum and atrial fibrillation in COVID-19 patient undergoing Noninvasive mechanical ventilation (NIMV).

Case: A 66-years-old male patient with a history of COVID-19 pneumonia and 19 days hospital follow up and a NIMV treatment was admitted to our emergency department with palpitations and dyspnea. Thoracic CT and electrocardiography revealed, scattered ground glass areas, pneumomediastinum and high-velocity atrial fibrillation, respectively.

Conclusion: We recommend regular checks with imaging methods and ECG during follow-up in patients with COVID-19. Clinicians should remember that ventilator-related lung damage may be seen in COVID-19 patients undergoing NIMV.

Keywords: COVID-19, Pneumomediastinum, Positive Pressure Ventilation, Atrial Fibrillation

COVID-19 Pnömonisinin Nadir Komplikasyonları: Pnömomediastinum ve Atriyal Fibrilasyon

ÖZET

Giriş: Koronavirüs hastalığı 2019 (COVID–19), akciğerlere ek olarak kalp, karaciğer ve böbrekler dahil olmak üzere birçok hayati organı içeren sistemik bir hastalık olarak kabul edilir. COVID–19 pnömonisi ile ilişkili pnömomediastinum, genellikle altta yatan akciğer patolojisi, enfeksiyonları veya mekanik entübasyonu olan hastalarda görülen nadir bir durumdur. Burada, noninvazif mekanik ventilasyon (NIMV) uygulanan COVID–19 hastasında geç tanı konulan bir pnömomediastinum ve atriyal fibrilasyon olgusunu sunduk.

Olgu: COVID–19 pnömonisi için 19 gün hastane takibi ve NIMV tedavisi öyküsü olan 66 yaşında erkek hasta, acil servisimize çarpıntı ve nefes darlığı şikayeti ile başvurdu. Torasik BT ve elektrokardiyografide sırasıyla dağınık buzlu cam alanları, pnömomediastinum ve yüksek hızlı atriyal fibrilasyon saptandı.

Sonuç: COVID–19 hastalarında takip sırasında görüntüleme yöntemleri ve elektrokardiyografi ile düzenli kontroller yapılmasını öneriyoruz. Klinisyenler, NIMV uygulanan COVID–19 hastalarında vantilatöre bağlı akciğer hasarının görülebileceğini akılda tutmalıdır.

Anahtar Kelimeler: COVID–19, Pnömomediastinum, Pozitif Basınçlı Ventilasyon, Atriyal Fibrilasyon.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), which was reported for the first time at the end of 2019, is considered as systemic disease involving many vital organs in addition to the lungs, including the heart, liver, and kidneys (1,2). Complications such as hypoxemic respiratory failure is the most common conditions leading to intensive care unit (ICU) admission among hospitalized COVID-19 patients with pneumonia. A comprehensive literature review of studies involving patients with COVID-19 pneumonia revealed 15 cases of spontaneous pneumomediastinum, a rare condition usually seen in patients with underlying lung pathology, infections, or mechanical intubation (3, 4, 5). Here we presented a case of late diagnosis of pneumomediastinum and atrial fibrillation in COVID-19 patient undergoing noninvasive mechanical ventilation (NIMV).

CASE

The 66-year-old male patient had a known diagnosis of benign prostatic hyperplasia. He was a 20 pack years former smoker who had not smoked for 30 years. He had had no regular medication or substance use. Forty days prior to admission to the emergency department of our hospital, the patient tested positive for SARS-CoV-2 by real-time reverse transcription polymerase chain reaction and he had been hospitalized in the ICU for 6 days due to severe lung involvement observed via thoracic computed tomography (CT) (Figure 1) and the need for a noninvasive mechanical ventilation (NIMV). He had been discharged home with methylprednisolone treatment after 19 days of follow-up. Fifteen days after first discharge, he was readmitted to our emergency department (ED) with palpitations and dyspnea.

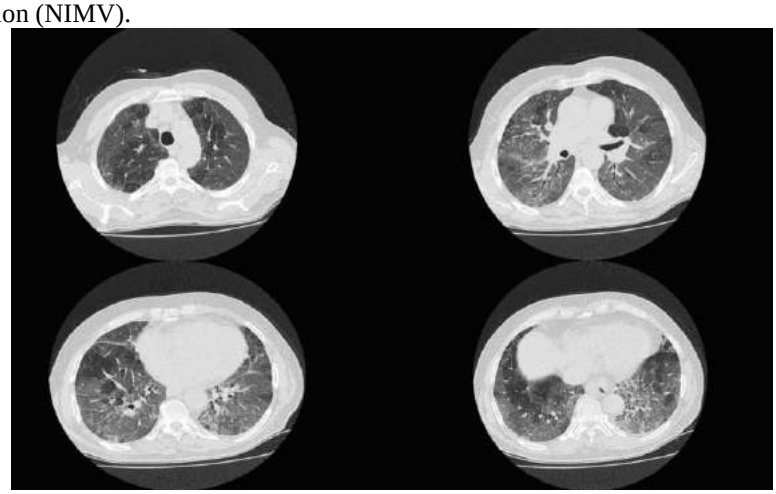

Figure 1. Thoracic CT images taken during the first hospitalization due to COVID-19 pneumonia, showed bilateral disseminated ground glass areas and normal mediastinal pathology.

Vital signs at the time of emergency admission were as follows: fever, 36.5°C; blood pressure, 138/68 mmHg; and oxygen saturation (sO2) 92% without external oxygen supplementation. Laboratory results were as follows: C-reactive protein , 6.5 mg/dL; white blood cell count, 10.5×103/μL; lymphocyte count, 1.43×103/μL; neutrophil count, 8.77×103/μL; d dimer, 0.43 g/mL; procalcitonin, 0.15 ng/mL; ferritin, >2000 ng/mL; troponin I, 0.41 ng/mL; aspartate aminotransferase, >891 IU/L; alanine aminotransferase, >1533 IU/L; and lactate dehydrogenase (LDH), 655 U/mL. Electrocardiography (ECG) revealed high-velocity atrial fibrillation (AF). Chest X ray (Figure 2) and Thoracic CT (Figure 3) were performed: The air collection was seen in the mediastinum and was diagnosed as pneumomediastinum. The scattered ground glass areas were observed in both lungs and were interpreted as compatible with pulmonary edema with COVID-19 sequelae. Echocardiography revealed moderate aortic regurgitation and minimal mitral insufficiency.

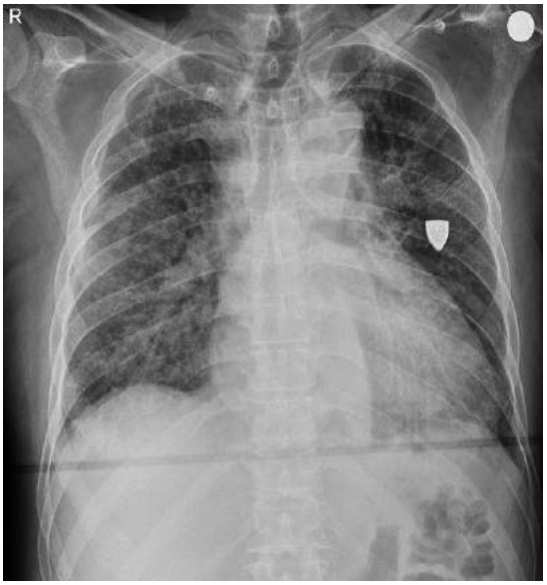

Figure 2. Chest X ray revealed a slight left deviation in the cervical trachea, increased mediastinal width and heart size, air around trachea and heart and bilateral disseminated ground glass areas.

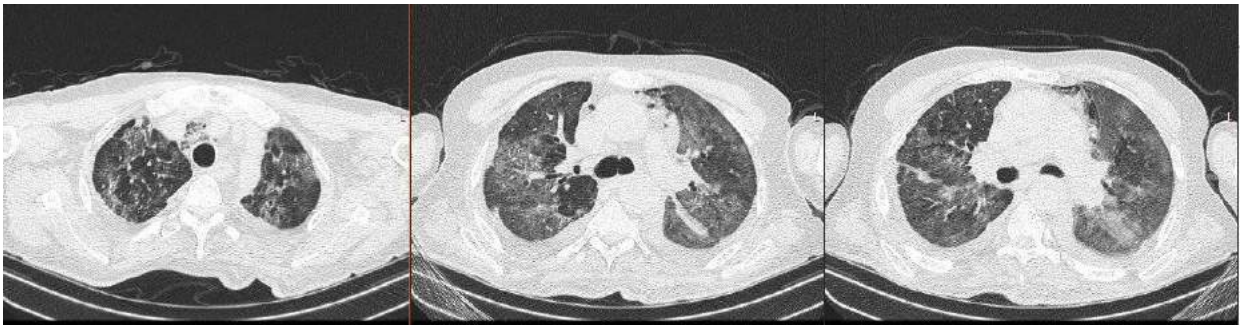

Figure 3. Thoracic CT revealed scattered ground glass opacity over all lobes in both lungs, bilateral minimal pleural effusion, adjacent compression atelectasis and air collection around the jugular veins in the neck and in the soft tissue around the trachea, which progressed around the aorta in the anterior mediastinum and continued in the soft tissue around the pericardium from the anterior. No pneumothorax and no air were seen around the bronchus or the bronchioles.

Retrospective examination of X-ray findings indicated that no other radiological evaluations had been made during ICU follow-ups or at discharge, except for thoracic CT, which was performed 40 days before for a diagnosis of COVID-19.

Liver function disorder was considered to have occurred secondary to hypoxemia. Bilateral minimal pleural fluid observed on CT was interpreted as compatible with AF and volume overload.

The patient was prescribed bed rest, oxygen therapy, and rhythm-regulating amiodarone infusion followed by amiodarone maintenance therapy, and diuretic and anticoagulant therapy. Conservative follow-up, avoidance of NIMV applications, and X-ray follow-up were performed for pneumomediastinum. He was discharged after 9 days of follow up with sO2 of 96% in room with no cough or shortness of breath. The patient outpatient clinic control at 10th day after discharge was uneventful and Chest X ray (Figure 4) was in normal limits.

Figure 4. Chest X ray taken at 10 th day after discharge, showed that all previous findings were regressed.

DISCUSSION

Pneumomediastinum, defined as the presence of free air in the mediastinum, is a rare condition most commonly observed in young, male patients (6,7). Pneumomediastinum can be spontaneous, iatrogenic, or traumatic. Mediastinal structures, such as the trachea and esophagus, in the mediastinum are covered with the mediastinal pleurae, which separate them from the pleural space. Although the pathophysiology of pneumomediastinum is unclear, air within the esophagus and trachea and air within the lung alveoli are potential sources of air for pneumomediastinum (7). In an experimental study in cats regarding the pathogenesis of pneumomediastinum performed in 1944, it was suggested that with the increase in alveolar interstitial pressure gradient, the air in the alveoli passes into the mediastinum through the perivascular and peribronchial sheaths and causes pneumomediastinum (8). In cases with only pneumomediastinum without passage of air into the pleural area, the lack of air collection in the bronchial walls or peribronchial area does not support the suggestion regarding air leakage secondary to alveolar rupture caused by alveolar pressure changes. It is thought that pneumomediastinum may occur when air is transported to a lower pressure environment between the soft tissues surrounding the mediastinal organs after an abnormal increase in pressure in the mediastinal region (7, 9). The development of pneumomediastinum has also been reported in excessive respiratory effort, such as coughing, vomiting, sneezing, defecation, and use of the voice at high volumes (7). During high NIMV or recurrent intense coughing attacks with high intratracheal pressure, air may pass through the separations in the pars membranacea fibers of the trachea and move toward the lower pressure mediastinal area, causing pneumomediastinum. Air in the mediastinum may develop as diffuse massive pneumomediastinum with air formation on all mediastinal surfaces or minimal air accumulation of 1 to 2 cm air. The development of massive pneumomediastinum is mostly seen in cases with long-term high NIMV treatment (7). Clinically, the

most common symptoms in pneumomediastinum are dyspnea and chest pain. Other symptoms include cough, hoarseness, swelling in the neck, nausea, swallowing difficulties, odynophagia, and rhinorrhagia (6,7). Chest X ray after clinical suspicion is helpful in the diagnosis of pneumomediastinum, while a definite diagnosis is made with thoracic CT (6,7). Our patient was male and 66 years old, and had no additional symptoms other than shortness of breath.

Alveolar damage caused by the inflammatory response in COVID-19 has emerged as the reason for symptoms of respiratory distress, or the need for a NIMV treatment, or pneumomediastinum as a potential complication of the disease (10). The 22% of hospitalized patients diagnosed with COVID-19 may require invasive mechanical ventilation (IMV) and in 15% of these patients who required IMV, may develop barotrauma related pneumothorax, pneumomediastinum, and pneumopericardium in multiple time periods (11).

High peak serum levels of LDH are thought to be associated with alveolar damage (10). It has been hypothesized that severe disseminated alveolar damage causes interstitial emphysema and alveolar rupture resulting in the leakage of air through the bronchoalveolar sheath (5). In our patient, the LDH level was 655 U/L at the time of ED, but thoracic CT indicated no air collection in the bronchoalveolar sheath or peribronchial area. In our case, mediastinal emphysema invading around the cervical trachea, and its extension to the lower pericardial area suggested the development of massive pneumomediastinum caused by damage at the tracheal level.

Our case had no history of blunt or penetrating thoracic trauma to the chest, or underlying chronic respiratory disease. Among causes of pneumomediastinum, there is a history of barotrauma or volutrauma. In addition, it was understood that radiological imaging was not performed during the history of noninvasive mechanical ventilation NIMV use or until admission to the ED of our hospital, and it was thought that pneumomediastinum had been left undiagnosed for a long time.

Arrhythmia in patients with COVID-19 infection is complex and multifactorial, and has been suggested to be caused by metabolic disorders, hypoxia, acidosis, intravascular volume imbalances, and neurohormonal and catecholaminergic stress (12). AF has been reported as the most common type of arrhythmia in COVID-19 patients (13). Indeed, 27.5% of COVID-19 patients admitted to ICU in the USA develop atrial tachyarrhythmia, and 63% of these have AF (14).

In some cases of pneumomediastinum, low voltage values in ECG, nonspecific acute coronary syndrome changes, and ST-T changes in lateral precordial leads have been observed (14). AF was thought to have developed secondary to COVID-19 infection in our patient, who was hospitalized in the ICU without known heart disease, and the pneumomediastinum secondary to NIMV may have been a facilitating factor for AF.

CONCLUSION

Respiratory disturbances in patients with COVID-19 may not always be due to pulmonary embolism or worsening infection. We recommend regular checks with X-ray and intermittent ECG during follow-up in patients with COVID-19. Clinicians should take in mind that ventilator-related lung damage usually may be seen in COVID-19 patients undergoing NIMV.

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