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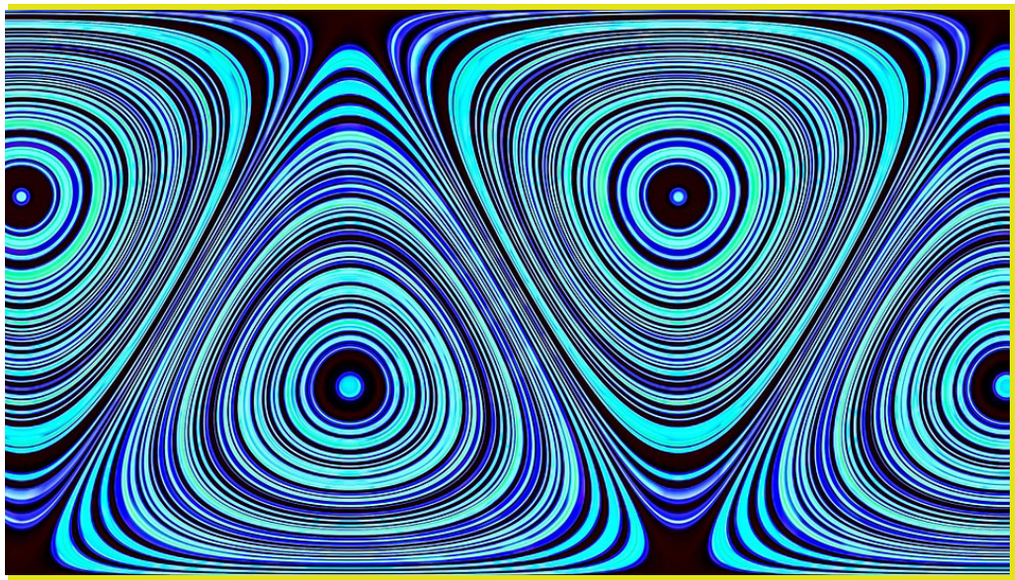

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DOKUZ EYLÜL UNIVERSITY INSTITUTE OF HEALTH SCIENCES

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J Basic Clin Health Sci 2023; 7: 553
RETRACTION- RESEARCH ARTICLE

RETRACTION: IS THE OCCURRENCE OF GESTATIONAL DIABETES MELLITUS IN PREGNANCIES HIGHER FOLLOWING IN VITRO FERTILIZATION TREATMENT? WHY? A RETROSPECTIVE COHORT STUDY

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NOTICE OF RETRACTION:

Related Article: Aypar-Akbağ NN, Aluş-Tokat M, Özöztürk S, Ünsal-Avdal E, Okyay RE, Doğan OE. Is the occurrence of Gestational Diabetes Mellitus in pregnancies higher following In Vitro Fertilization treatment? Why? A retrospective cohort study. J Basic Clin Health Sci 2023; 7: 94-102.

The article given details above and published in the 1st issue of 2023 on pp. 94-102 in the Journal of Basic and Clinical Health Sciences, has been retracted due to the investigation of ethical claims.

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RESEARCH ARTICLE

ASSESSING THE EFFECTS OF ORAL HEALTH KNOWLEDGE AND BEHAVIOURS OF MOTHERS ON ORAL HEALTH OF PRESCHOOL 4-6 YEARS OLD CHILDREN

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ABSTRACT

Purpose: Pre-school child health has always been one of the most important milestones for lifelong health research. Also, the knowledge and behaviour of the parents, especially mothers, affects children's health. The variable household-related factors and mothers, in particular, are considered to be the main role models that can improve pre-school children behaviour. To determine the knowledge and behaviours of the mothers and their impact on pre-school 4-6 years old children oral health status.
Material and Methods: A 27 subjects' questionnaire was prepared using previous questionnaires assessing mothers' knowledge and behaviours towards oral health. Children's oral and dental health was examined by the researcher and scores were calculated using dmft (decayed, missing, filled, tooth) index. Accordingly, the effect of knowledge and behaviour of the mothers on their children dmft score was analysed. Chi-Square and logistic regression tests were used in the statistical analysis.
Results: The study population consisted of 261 pre-school children and their mothers. Which included 126 males (48.3%) males and 135 females (51.7%). The mean mothers' oral health knowledge score was found to be 4.24 ± 1.94. The children oral health examination through dmft scoring showed that 71.3% of children had experienced dental caries. the mean value for dmft score was 2.32 ± 2.39.
Our study showed that the mother's cumulative oral health knowledge score has a statistically significant relationship to the children oral health status. The higher the mother's oral health knowledge scores the lower their children dmft scores ($p=0.001$).
Conclusion: Mothers oral health knowledge and dental health indices in our study are lagging behind the developed countries and the WHO goal for the 21st century showing an urgent need to improve the effectiveness of preventive care in oral health programmes.

Keywords: preschool children health, oral health knowledge, dental caries.

INTRODUCTION

The WHO defined oral health as "a state of being free from chronic mouth and facial pain, oral and throat cancer, oral sores, birth defects such as cleft lip and palate, periodontal (gum) disease, tooth decay and tooth loss, and other diseases and disorders that affect the oral cavity (1). Accordingly, the health word defines more than just the impact of healthy teeth on physical and psychological aspects of people life, it extends involving also the teeth influence on growth, function speech, aesthetics, socializing and social wellbeing (2). Health wellbeing research considers

preschool phase as a lifelong health construction phase guided by the parents. Mothers, in particular, are the main models improving pre-school children behaviour (3). The significance of parental background in children's health is evident in the resultant outcome due to large sociodemographic difference (4). It is extensively essential to initiate good basic oral health habits to create appropriate dental norms and standards that can be preserved in adult life. Add to that, the mothers can have a vital role in promoting their children's dental hygiene and nutritional habits acting as an advisor to improve children oral health (5). Considering health in general and oral health in particular, the role of parents is of massive importance since they are considered as the main caregivers during the first years of life (6).

It was found that the parents have a direct and indirect role in prevention and promotion of their children's oral health. Dental caries, a well-known morbid disease that can be evaded readily through a simple well organised health promotion programmes that can be directed towards the oral health of children through their mother's oral health literacy. Dentists and oral health professionals, in general, are accepting that the role of the caregivers and parents can be a vital one, resulting in a reduction of caries risk among their children (7). Therefore, mothers' oral health status and health literacy are correspondingly related to children's oral health and early childhood behaviours of the children (8).

Dental caries is recognised as one of the major problems in the world. the WHO reports that 60-90% of school children worldwide have experienced dental caries. However, the highest prevalence is in Asian and Latin American countries (9).

Few oral-health-related epidemiological surveys covering children have been done. Most of these were conducted in cities, in dental schools at universities, and included small numbers of participants (10–12). In Turkey, the general information regarding the oral health status of children originates from the two national surveys of 1988 and 2004 (13-15).

Some researchers examined the inter-relationship between the characteristics of caregivers and their children's oral health. While some studies showed that financial status or geographical isolation might affect the preschool children oral health through limiting the necessary social support (e.g., education, information, intervention) required by parents (16). These factors include oral health behaviours and demographic factors of the caregivers (7,8,17–19). Adding to the parents' role, some other factors, for instance, maternal education, occupation and their current knowledge also have an essential role in determining the oral health of their children (20). Mother's oral health knowledge and attitudes affect the oral health of children in particular at early ages (21,22). In Turkey, only a few studies have been done to determine the knowledge and attitudes of pre-school children's mothers and their interrelationship to children oral health.

Table 1. Child and mother's sociodemographic characteristics

Variable	frequency	
	N	%
Sex		
Males	126	48.3
Female	135	51.7
Child Age		
4	89	31.4
5	80	30.7
6	92	35.2
Child order in the Family		
1	183	70.1
2	60	23.0
3	18	6.9
Mother's Age group		
26 years and below	49	18.8
27-37 years	168	64.4
38 and above (recheck)	44	16.9
Marital status		
Married	252	96.6
Others	9	3.4
Family type		
Small Family (Mother, Father and children)	222	85.1
Others (Big family and separated family)	39	14.9
Children number		
1	111	42.5
2	113	43.3
3 and above	37	14.2
Education group		
Primary school	36	13.8
Middle school	66	25.3
High school	97	37.2
Diploma	21	8.0
Graduate and post-graduate	41	15.7
Work status		
Working	86	33.0
Non-working	175	67.0
Total	261	100

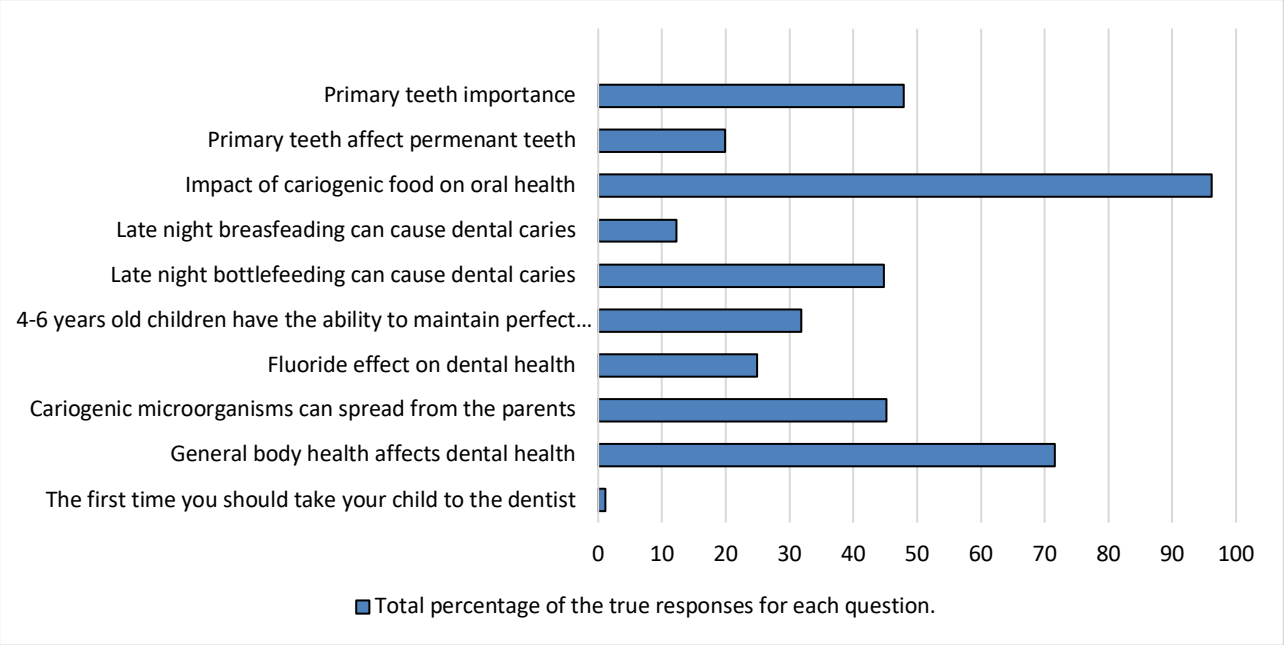

Figure 1. The total percentage of the mothers responded the true answer for each question.

The aim of this study is to determine the mothers' oral health knowledge and the effect of the mothers' oral health knowledge and behaviour on their preschool (4-6 years) old children's dmft score.

MATERIAL AND METHODS

The study is a descriptive cross-sectional study conducted at Dokuz Eylul University, Paediatrics Hospital policlinic and Dental clinic by examining the children aged 4-6 years old visiting the Paediatrics and dental polyclinics and correspondingly applying the questionnaires to the mothers.

The study was done during the period from February to May 2018.

The study population and sampling

By assuming that the dental caries prevalence was 70% in children aged 5 years old in Turkey which was found in 2004 national survey (14,15), 95% confidence level and 0.05 margin of error, the required sample to perform the study was 245 children and their mothers. The number of people we reached by taking as a reserve of 10% for reasons such as the limitations that may be experienced in reaching or refusal to participate in the survey is 270 children and their mothers. the mothers who accepted to participate in the study was 261, with 135 female and 126 male children.

Data collection and variables

The data was collected through face-to-face interviews with mothers.

Firstly, a questionnaire was used to study the children's sociodemographic variables, behaviour and their dental visit experiences, variables related to the mother's knowledge and behaviour towards oral health with a total of 27 questions. For the questionnaire, Chahbra et al (23) and the Oral health survey developed by the Texas health service department were used and some additional questions were added. Ten questions were prepared to examine the mother's knowledge. Questions were scored according to the true answer choice and counted every true answer as 1 point and the overall score was 10.

Secondly, the patients who accepted to be part of the study were examined according to dmft scoring standards and using examination sheet to record the patient's oral health as the number of decayed, missing and filled teeth number was calculated to obtain the overall dmft score. Children's oral and dental examinations were performed by the investigator and their scores were calculated using the dmft (decayed, missing, filled, tooth-tooth number) form. DMF indexes are used for permanent teeth in practice, primary teeth are explained in small letters as dmf index.

dmft scores were categorized into 3 categories, no obvious dental caries, low caries, and high caries according to the number of decayed missing and filled teeth.

Data analysis

In the descriptive analysis, continuous variables are given as mean and standard deviation (SD), categorical variables as number and percentage. T-test, chi-square, ANOVA and logistic regression analysis were performed to analyse the associations between dependent variables and independent variables.

Age, gender, sociodemographic characteristics were presented as frequency and percentage. From the questionnaire consisting of 27 subjects, a total of 10 oral health knowledge related subjects were scored and the general knowledge level was calculated (each true answer counted as 1 point) and mean, standard deviation, median and quartile values were reported.

The dmft score was determined by clinical dental examination and the mean, standard deviation, median and quartile values were calculated.

The difference between mean scores according to independent variables were analysed by t-test. Behavioural properties with independent variables were evaluated using the Chi-square test.

Statistical analysis was done using SPSS 20.0.

Logistic regression was performed for the association of independent variables of mother's and child characteristics to oral health, assessed by dmft score. dmft was categorized into two as no obvious dental caries and high caries group.

Ethics committee approval was obtained from Dokuz Eylul University Non-Interventional Research Ethics Committee (Date: 08.02.2018, Decision no: 2018/04-37) and a permission to conduct the research was approved by Dokuz Eylul University, Faculty of Medicine, Department of Child Health and Pediatrics.

RESULTS

Sociodemographic features

The study population consisted of 261 pre-school children and their mothers. Which included 126 males (48.7%) males and 135 females (51.7%). The percentages of 4, 5- and 6-years old children in the time of data collection who were included in the study were 31.4%, 30.7% and 35.2%, respectively.

The mothers' oral health knowledge had been analysed as cumulative score of total true answers.

Table 2. Mean and median values for oral health determinants

Variable	Mean ± SD	Median	Quartiles	
Mothers' Oral Health knowledge Score	4.24 ± 1.94	4.00	25	3.00
			50	4.00
			75	6.00
Child's Decayed Teeth	2.08 ± 2.28	2.00	25	0.00
			50	2.00
			75	3.00
Child missing Teeth	0.04 ± 0.29	0.00	25	0.00
			50	0.00
			75	0.00
Child's filled teeth	0.19 ± 0.76	0.00	25	0.00
			50	0.00
			75	0.00
Child's dmft score	2.32 ± 2.39	2.00	25	0.00
			50	2.00
			75	3.00

Half of the mothers (47.9%) knew that the primary teeth have an important role in the dental health and wellbeing. However, whether the primary teeth diseases have an impact the permanent teeth received less true answers as only one in five mothers (19.9%) considered that as true statement.

The mean mothers' oral health knowledge score was found to be 4.24 ± 1.94. When the mothers' knowledge was categorised into 3 groups poor, fair and good knowledge it was found 37.5%, 33.0% and 29.5%, respectively.

The children dental health examination using dmft scoring system showed that 71.3% of children had experienced dental caries. 47.2% had low caries, 24.1% had high caries and only 28.7 were considered not having obvious caries. the mean value for dmft score was 2.32 ± 2.39. The number of decayed teeth per child was 2.08 ± 2.28, 0.04 ± 0.29 for missing teeth and 0.19 ± 0.76 for filled teeth.

Children oral health status

Our main findings showed that the mother's cumulative oral health knowledge score has a statistically significant relationship to the children's dental health status. It was found that mother with higher oral health knowledge score had children having lower dmft scores while the children of the mothers with low oral health knowledge scores had higher dmft scores (p=0.001).

Children dmft score is statistically significant to the mother's education and work status. The higher

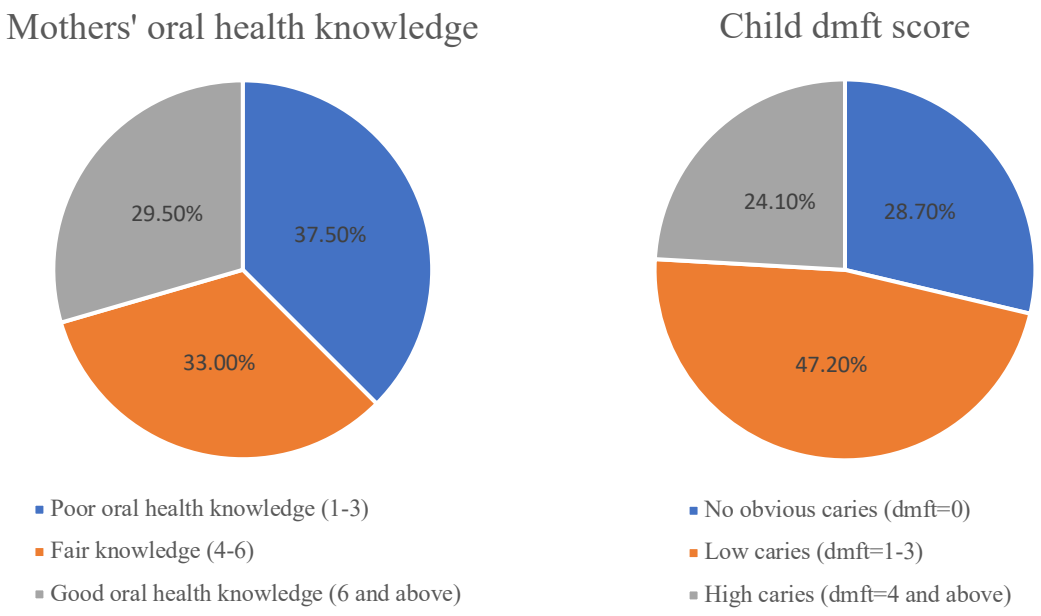

Figure 2. Mothers oral health knowledge and children dmft scores classified into groups.

education status of the mothers the better their children dental health status (p= 0.001). Also, working mother's children have a better dental health in comparison to non-workers. Another determinant factor for the children dental health is the child's oral hygiene behaviour. Lower dmft score is significantly related to the regular brushing behaviour of the child when compared to non-brushers and irregular brushers (p=0.001). add to that, the mother's role when their children are brushing their teeth is of significant relationship to the child's dental health. Mothers who observe and correct their children teeth brushing behaviour have children with lower dmft score when compared to the mothers who only give advice (p=0.001).

The mothers and their children dental visits frequency exhibited a significant impact on the children oral health status. For instance, children who were regular dental services visitor had a better dental health status in comparison to children who visits only for dental problems. However, children who had never been to the dentist also had a better oral health when compared to children who visit only for dental problems (p=0.019). On the other hand, the mothers who were regular visitors have children with better oral health, unlike the mothers who visit only for dental problems (p=0.002).

Logistic regression testing clearly revealed that the mothers' education level, work status, dental visits frequencies and pediatrics medical practitioner advice are the most significant factors affecting the mother's oral health knowledge. It had also showed that the determinant factors affecting the children oral health status (dmft score) were the child age, mothers' education level, brushing frequency and cariogenic food consumption frequency. However, when mothers' education level was excluded from the logistic regression model the mother's oral health knowledge score was the significantly affecting the child dmft score.

DISCUSSION

Our study was conducted in preschool children aged between 4 and 6 years in a university hospital pediatrics and dental clinics. It was significantly found that there's a relationship between the mothers' oral health knowledge and the dmft score of the children. This inverse relationship addresses that the higher the mothers' oral health knowledge scores the lesser their children dmft scores which means the better their dental health status. Moreover, there's a significant relationship between the educational level of mothers, the children's teeth-brushing behaviour as well as children cariogenic food consumption and the dmft score of the children, as well as children cariogenic food consumption and the dmft score of the children.

Table 3. Children's dmft score distribution according to selected characteristics

		Child dmft score								P value
		Caries free		Low caries		High caries		Total		
		N	%	N	%	N	%	N	%	
Child age	4 years	35	39.3	46	51.7	8	9.0	89	100	0.001
	5 years	22	27.5	39	48.8	19	23.8	80	100	
	6 years	18	19.6	38	41.3	36	39.1	92	100	
Number of children in the family	1 child	41	36.9	53	47.7	17	15.3	111	100	0.001
	2 children	29	25.7	56	49.6	28	24.8	113	100	
	3 children and above	5	13.5	14	37.8	18	48.6	37	100	
Mothers education level	Primary school	2	5.6	15	41.7	19	52.8	36	100	0.001
	Under-graduate education	42	25.8	86	52.8	35	21.5	163	100	
	Graduates and post-graduates	31	50.0	22	35.5	9	14.5	62	100	
Mother's working status	Worker	37	43.0	38	44.2	11	12.8	86	100	0.001
	Non-worker	38	21.7	85	48.6	52	29.7	175	100	
Child oral hygiene	Brushers	71	34.6	100	48.8	34	16.6	205	100	0.001
	Non-brushers	4	7.1	23	41.1	29	51.8	56	100	
Mother's role in their children oral hygiene behaviours	Observes and corrects	69	34.5	98	49.0	33	16.5	200	100	0.001
	Advices only	6	9.8	25	41.0	30	49.2	61	100	
Child consumption of cariogenic food	3 times or less	59	43.4	61	44.9	16	11.8	136	100	0.001
	4 times and above	16	12.8	62	49.6	47	37.6	125	100	
Fluoridated tooth paste usage	user	15	38.5	19	48.7	5	12.8	39	100	0.001
	Not-user	33	40.7	35	43.2	13	16.0	81	100	
	Don't know	27	19.1	69	48.9	45	31.9	141	100	
Child Frequency of visiting the oral health practitioner	Never had dental treatment	48	26.2	89	48.6	46	25.1	183	100	0.019
	Only for dental problems	9	20.5	23	52.3	12	27.3	44	100	
	Regular visitor	18	52.9	11	32.4	5	14.7	34	100	
Mothers dental visit frequency	For dental problems only	42	22.7	92	49.7	51	27.6	185	100	0.002
	Regular visitor (6 months or 1 year)	33	43.4	31	40.8	12	15.8	76	100	
Data collection place	Paediatrics policlinic	52	24.8	102	48.6	56	26.7	210	100	0.010
	Dental clinic	23	45.1	21	41.2	7	13.7	51	100	
Mother's oral health knowledge	Poor oral health knowledge	11	11.2	44	44.9	43	43.9	98	100	0.001
	Fair oral health knowledge	25	29.1	50	58.1	11	12.8	86	100	
	Good oral health knowledge	39	50.6	29	37.7	9	11.7	77	100	

Mothers' oral health knowledge status

Mothers cumulative oral and dental health knowledge is 4.24 ± 1.94. however, according to a study conducted in Kuwait, the mothers oral and dental health knowledge level was 4.68, while it was found as 7.32 in Taiwan (21,24). When we compared the results of oral and dental health knowledge of the mothers we found with another study conducted in

Table 4. Independent variables to mothers' oral health knowledge level logistic regression analysis*

Variable	β	S.E**	P	OR	%95 CI
Mother's education level					
Diploma, bachelors and above (reference)					
Middle school and high school					
Primary school	0.718	0.559	0.199	2.05	0.69-6.13
	2.900	0.905	**0.001**	18.18	3.09-107.09
Mother's work status					
Working (reference)					
Not Working	0.921	0.476	0.053	2.51	0.99-6.39
Visiting to the dentist frequency					
Regular visitor (reference)					
Non regular visitor	1.223	0.407	0.003	3.39	1.53-7.54
General doctors and practitioner advices towards oral health					
Had been advised (reference)					
Never advised					
	1.177	0.584	0.044	3.25	1.03-10.19
Constant	-3.059	0.694	0.000		

*Variables entered on step 1: Mothers education level, mothers work status, mothers visiting the dentist frequency, family doctors and general health practitioners' advices towards oral health and referral, mothers age group, examination place.
** S.E standard error

Nepal, in ours; 30% of mothers had moderate and 29% had good oral and dental health knowledge, however, 80% of Nepalese mothers had moderate level and 4% had good level of oral and dental health knowledge (25). When the factors affecting the level of oral and dental health knowledge of mothers in other systematic reviews, it showed that mother's education, working status, also, oral and dental health knowledge affects the children oral health status eventually (4,26,27). these results agree with our findings which manifested that the mothers with a high level of education had a significantly better level of oral and dental health knowledge than those with a lower level of education (4).

Preschool children oral health status

Three large studies in children in Turkey evaluated oral health status in 1988 and 2004. In 1988, dental caries was seen in 84% of 6-year-olds the average dmft score was found to be 4.4. These results are slightly higher than the 6 years old children dental caries prevalence (80.4%) with 3.2 mean dmft score we found (13).

In 2004, 70% of 5-year-old children had dental caries and the mean dmft score was 3.7 in comparison to 72.5% of 5-year-old children included in our study having a mean dmft score 2.3 (14).

There is a decrease in the mean dmft score in both age groups. This minor drop in the dmft value of children can be attributed to the increase in development in dental services and the awareness of society on this issue. In Turkey, despite the increased share of the national budget to be allocated to health services and preventive procedures in the past decade towards oral and dental health, the desired decrease in the value of the dmft score couldn't be achieved (15). These findings indicate that Turkey is lagging behind in the oral health target for the 21st century defined by the WHO and inadequate for continuous improvement of oral health (28).

On the other hand, in comparison to the countries in the same region of the world, our findings are relatively more desirable. The study in Kosovo found a dmft value of 5.8 and was twice as high as our findings (29). In a study conducted in Palestine, it was found that 76% of the children in the 4-5 age group had tooth decay and the mean dmft value was 2.46 (31). while in a study included 5 years old children in Athens children in Athens, Greece, the mean dmft value was found to be 1.77, which is considerably lower than our findings for the same age group (30). the oral health parameters in Northern European countries are substantially better when compared.

Table 5. Independent variables in relation to dmft score through logistic regression analysis*

Variable	β	S.E**	P	OR	%95 CI
Child age					
4 years old (reference)					
5 years old	1.551	0.672	0.021	4.72	1.26-17.60
6 years old	2.366	0.671	0.000	10.65	2.06-39.72
Mothers oral health knowledge score					
Good oral health knowledge (reference)					
Fair oral health knowledge					
Low oral health knowledge					
	0.285	0.604	0.637	1.33	0.41-4.34
	1.482	0.619	0.017	4.40	1.31-14.80
Teeth brushing frequency					
Regular brusher (reference)					
Non-regular brusher	2.094	0.720	0.004	8.11	1.98-33.28
Cariogenic food consumption frequency					
3 times or less per day (reference)					
4 times and above per day					
	1.636	0.516	0.002	5.14	1.87-14.11
Constant	-3.456	0.689	0.000		

*Variables entered on step 1: child age, number of children, teeth brushing frequency, bottle feeding usage, mothers oral health knowledge group, cariogenic food consumption frequency.
** S.E standard error

According to a research study investigating the prevalence of dental caries in 6-year-old children in Rotterdam, Netherlands, only 31.7% of children were found to have caries (32). also, in the city of Umea in Sweden, a comparative study of 4-year-old immigrants and indigenous children, concluded that 42% of migrant children had tooth decay, but only 15% of native Swedish children had tooth decay (33).

The impact of the mothers' oral health knowledge on preschool children oral health

Our study signified the mothers' role in their children's oral health and these results were like the reviews. Adding to that, our study stated that the mothers play a vital role in their children's dmft score which is considered in tandem with the finding of a study done in India (35).

Our results showed a significant direct relationship between the mothers' oral health knowledge and the children dmft score, which is also considered similar to the findings concluded in Iran, Tehran which similarly evaluated the influence of the mothers' oral health knowledge and attitude on their children oral health status (26). Likewise, the same was also concluded in another review in the United Kingdom emphasizing the parental knowledge, attitude and beliefs considering as a predictor of the children oral health status (27). The same study also discloses that the parental attitude and beliefs can have an influential role in the children nutritional and snacking behaviour as well as their oral hygiene behaviour (27). This interrelationship was not examined in detail in this study.

In the Netherlands, parents with low levels of education found to be increasing the dental caries morbidity in their children. Correspondingly in three studies, the level of education of mothers has shown a significant impact on oral health status (32,36,37). Schwendicke et al. stated that there was a relationship between socioeconomic status and tooth decay and attributed this to poor inadequate health information, poor nutrition, inadequate toothbrushing habits, and low health care (36).

Stecksen-Blicks et al.'s comparative study that included Swedish and immigrant children at 4 years of age examining the household influence on children oral health established that migrant families' children have lesser teeth brushing frequency and higher cryogenic foods consumption. (ice cream, sugar, chocolate, etc.). Hence, as a resultant, there was a higher prevalence of tooth decay among the migrants (33). This outcome is similar to our findings showing the effect of brushing habit and the consumption of cryogenic foods showing only that the mean dmft

score of the children who did not brush was 4.16 and the mean dmft of the brushers was 1.81. Add to that, 56.6% of the children consuming 3 times or less of the cryogenic food have tooth decay in comparison to 87.2% dental caries prevalence among children consuming 4 or more times cryogenic foods (33).

Another detailed comparative household research analysing the effect of the parents on pre-school children included Dutch, Turkish and Moroccan families showed that there was a significant difference in the oral health of the children as a reflection of the role of parents which is inter-related to their origin. The parents of the Dutch children had more internal locus of control and higher dental self-efficacy, and more frequent dental visits, which resulted in better oral health (38). This shows that the parents remain the main determinant of the children oral health status similarly to our results.

According to the logistic regression analysis we done two different models including both the mother's oral health knowledge score and their educational degree while in the other model the mother's educational status is not inserted. In the first model, the mothers' oral health knowledge score was excluded while in the second model it wasn't. this can be explained by the interrelationship between the mother's oral health knowledge and education level and showing that education remains of an important significance in oral health promotion.

Limitations and strengths of research

As the study was carried out at Dokuz Eylül University hospital, the results could not be generalized to the population. In addition, a standard method was not used in assessing the knowledge level of the mothers. The questionnaire for behaviour is open to recall and reporting bias.

On the other hand, the strengths of this study lie in assessing the mothers' oral health knowledge in relation to the preschool children oral health status conducted by dental examination that is performed by a single dentist which led to a standard assessment of oral health status. Since most studies in Turkey are conducted in school-aged children, this study also fills an information gap regarding preschool children.

CONCLUSION

The oral and dental health indices of the mothers in the study group are poorer than the developed countries and fall far below the 21st century WHO target. These results suggest that there is a need to increase the prevention services and oral and dental health promotion programs, especially for Turkish children and Turkish community in general, to raise the oral health standards.

For this purpose, it is necessary to develop policies and publicity programs for oral and dental health primarily in homes, kindergartens, and schools. Because the mothers remain the main influential factor of their children oral and dental health, promoting their oral and dental health information can play a direct role in the oral health prevention cycle.

We believe that this study can be an important step and guide in understanding the norms of the Turkish population and in improving the oral and dental health status of the society. Our study was carried out in a hospital in Izmir and there is a need for more studies from different regions of the country, and larger studies are needed at the national level.

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Author contributions: AM and GE designed the study, analyzed the data, and prepared the manuscript. AM and GK collected the data, GE guided article in the whole process from designing to writing. All listed authors meet the authorship criteria and that all authors are in agreement with the content of the manuscript.

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RESEARCH ARTICLE

PROMINENT CRISTA TERMINALIS MAGNETIC RESONANCE IMAGING FINDINGS

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ABSTRACT

Purpose: Prominent Crista Terminalis (PCT) is a frequent variation of the right atrium (RA) posterior wall with a pseudotumor image. This study aims to evaluate PCT image characteristics and cardiac functional effects with cardiac magnetic resonance imaging (CMR).
Material and Methods: Between 2016 and 2020, 140 patients (58 ±14 years) were evaluated retrospectively. PCT was measured in 2 planes with the longest thickness at the atrial end-diastole. Patients with crista terminalis thickness greater than 8 mm were evaluated. Patients were assessed by the RA, right ventricular (RV) end-diastolic diameter (ED), RV, left ventriculi (LV) ejection fraction (EF), and PCT diameter was included in the study. After the Kolmogorov-Smirnov normality test, cases were compared with the paired student t-test. The effect of the increase in PCT diameter on the RVEF, LVEF, and RAED, RVED was investigated with Pearson's correlation test.
Results: We did not find significant correlation (r<0,5) between PCT thickness and RVEF (r=0.49), LVEF (r=0,115), RAED (r=0.32), RVED (r=0.07). Fourteen patients (10%) with PCT had a history of arrhythmia. Arrhythmia was not observed in patients with PCT less than 10 mm. It was observed that the risk of arrhythmia increased with PCT thickness.
Conclusion: CMR image features provided reliable data for patient management in PCT diagnosis and follow-up. There was not detected a statically significant change in right and left heart functions in patients with PCT. It was observed that there was a relationship between arrhythmia incidence and PCT dimension in patients

Keywords: crista terminalis, right atrial mass, anatomical variants, ımaging pitfalls, cardiac magnetic resonance

INTRODUCTION

Crista terminalis is a fibromuscular structure that extends along the posterolateral free wall of the right atrium between the superior and vena cava inferior. Crista terminalis studies in the literature are echocardiography or cadaver studies (1,2). It has been reported that crista terminalis reaches up to 6 mm thickness in adolescents and adults (1). Crista terminalis thickness of more than 7 mm is considered as Prominent Crista Terminalis (PCT) (3-7). On echocardiography, PCT can be seen as a hyperintense misleading mass in the posterior wall of the right atrium (4). PCT is seen in a similar signal to the myocardium on cardiac magnetic resonance (CMR) (Fig. 1). Further examination with CMR is required for the differentiation of PCT and cardiac tumors.

Echocardiography is the primary imaging method in the evaluation of cardiac pathologies. Cardiac computed tomography angiography (CTA) or CMR cross-sectional imaging methods are also used in cardiovascular imaging (8). CMR is very important for morphological imaging of the heart and the differentiation of cardiac masses. PCT cross-sectional imaging findings in the literature are limited to case reports, and studies describing PCT cross-

Table 1. The distribution of the cases is shown. The cases are shown in the table according to crista terminalis thickness, sex, age, and right ventricular functions.

	Number of cases	Gender (K-E)	Age	RVEF (%)	RVSV (ml)
Group 1 (8-9 mm)	43	19-24	69	57	85
Group 2 (9-10 mm)	35	15-20	59	54	83
Group 3 (10-11 mm)	27	16-11	65	59	88
Group 4 (11-12 mm)	24	9-15	63	56	86
Group 5 (12-13 mm)	4	2-2	45	57	85
Group 6 (13-14 mm)	3	1-2	64	55	84
Group 7 (>15 mm)	2	1-1	49	52	88

sectional imaging features are few (3,9). PCT cross-sectional imaging findings were evaluated by CMR.

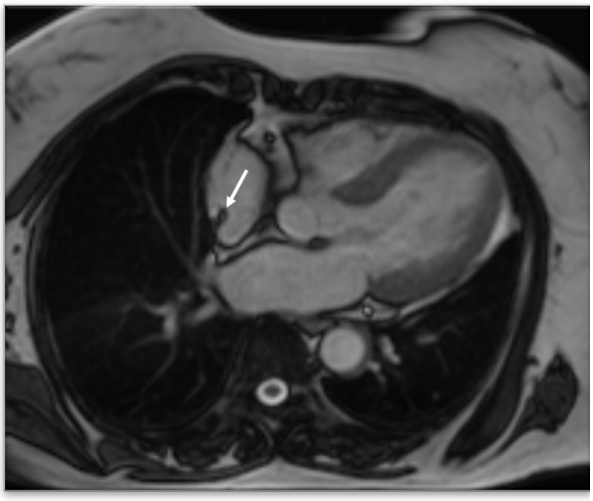

Figure 1. Cardiac MR white blood cine sequence (SSFP) four-chamber plane of 56 years old man. On the right posterolateral atrial wall extending into the atrium lumen, a 13 mm PCT (arrow) is seen in a similar signal to the myocardium.

Table 2. Shows the crista terminalis thickness and the number of patients.

Crista terminalis thickness	Number of cases
8-9 mm	43
9-10 mm	35
10-11 mm	27
11-12 mm	24
12-13 mm	4
13-14 mm	3
>15 mm	2

The purpose of this study is to evaluate the PCT image features, which can be defined as pseudo masses, by CMR, and to examine whether PCT dimensions are associated with right ventricular functions and the incidence of arrhythmia.

MATERIAL AND METHODS

Study Design

Ethical approval was obtained from the Izmir Katip Celebi University, Non-Interventional Clinical Studies Institutionel Review Board (Date 02.07.2020, No: 783). This study was designed as a single-center, retrospective study.

An observational cross-sectional study was conducted to evaluate CMR imaging findings in patients with PCT between 2016 and 2020. In the study, patients with a PCT over 8 millimeters in routine CMR were evaluated. Similar to the literature, cases with crista terminalis thickness less than 8 mm were not evaluated as prominent crista terminalis. Patients who had a history of thoracic surgery and inadequate images due to movement, metal artifact were not included in the study.

It was not included in the study because there was no crista terminalis thickness measurement in the echocardiography examinations.

CMR technique

CMR protocol with routine imaging was performed in all cases. CMR studies were applied with a 1.5 Tesla scanner (Aera®, Siemens Healthineers, Erlangen, Germany). Patients were scanned using 16-channel surface phased array body coils with the electrocardiogram triggering (ECG). After Standard localizer scan images, breath-hold cine images were

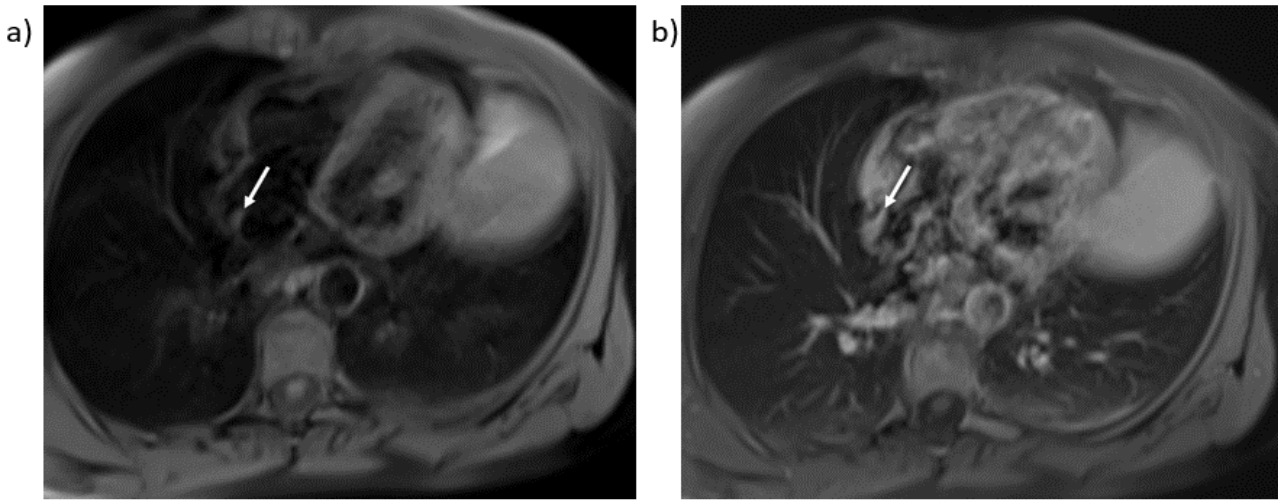

Figure 2. A 38-year-old woman, (a) four-chamber fat-suppressed T 1 and (b) PSIR sequence, in the right atrium posterior wall PCT (10 mm).

acquired in the 2-chamber and 4-chamber views for the heart. SSFP cine imaging was performed in a two-chamber multi-slice cine imaging view for biplanar assessment of right ventricular (RV) end-diastolic volume (RVEDV), and RV ejection fraction (RVEF). SSFP parameters were TE 1.23 ms, TR 33.35 ms, flip angle 55°, matrix minimum 192 x 156 mm, FOV maximum 340 mm, bandwidth 930 Hz, 30 phases per heart cycle, and iPAT GRAPPA acceleration factor 2. Contours were drawn automatically or manually before functional parameters were calculated automatically with Syngo. via for MRI.

We administered an intravenous injection of contrast agent into the antecubital vein at 0.2 mmol/kg (Magnevist; Schering, Berlin, Germany). The flow rate of 2 mL/sec was used. Minimum 10 minutes after contrast administration, IR inversion time scouting sequence was performed myocardial signal was suppressed for late gadolinium enhancement (LGE) imaging.

Image Review and Data Analysis

CMR cardiac examinations were evaluated by a board-certified radiologist who is more than 8 years of experience in cardiac imaging. On the Syngo.via MRI workstation, RV EF, LV EF, and RA ED, RV ED EF were calculated over functional sequences. The presence of right and left ventricular myocardial fibrosis was analyzed as present or absent in late gadolinium enhancement (LGE) images.

CT thickness measurements were performed in 4-chamber cine SSFP white blood sequences in the section with the maximum extension towards the lumen in the atrium end-diastolic phase. For the PCT measurement, 4-chamber multi-section sequences, sections perpendicular to the PCT plane were preferred to avoid the partial volume effect. The atrium wall was not included in the measurement. Atrial systolic phase measurements were not performed, as this may cause over measurement due to contraction. All images were evaluated together with functional CMR data at the workstation. Imaging findings and functional data were archived in picture archiving and communication systems (PACS).

Data were collected, including age, gender, CMR imaging features, and both ventricular morphological data. Data were evaluated as right and left heart functional data and PCT thickness. RV EF, LV EF, and RA ED, RV ED with PCT thickness were compared.

Statistical Evaluations

All statistical analyses were done with the help of SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Shapiro Wilk-W normality test was performed before performing a paired student t-test since the number of patients was (n >50). A paired student t-test was used to determine the significant differences between the variables of PCT cases. Mann-Whitney test was used for non-parametric variables. Pearson correlation coefficient was used for correlation between PCT diameter and RV ED, RA ED, RV EF, and LV EF. If the found r value is (-1), it is interpreted as a fully negative linear relationship, (+1) is a fully

positive linear relationship, and if r = 0 there is no linear relationship between the two variables. The closer the absolute value of the correlation coefficient is to the value of 1, the stronger is the linear association.

RESULTS

In patient selection, 140 patients (58 ± 14 years) with PCT of 8 millimeters or above based on the measurements made from the posterior wall of the right atrium between 2016 and 2020 were evaluated. 63 (45%) were women, 77 (55%) were men, and the mean age was 58 ± 14 years. The patients were grouped according to their PCT thickness (Table 1). Statistical analysis was made between PCT thickness groups. Thirty-four patients with a prediagnosis of mass in the posterior wall of the right atrium on echocardiography were accepted for CMR examination. (Fig. 2). PCT was detected incidentally in 106 patients.

The mean PCT thickness of the patient group was 9.12 mm. PCT thickness was measured 43 patient (8-9 mm), 35 patient (9-10 mm), 27 patient (10-11 mm), 24 patient (11-12 mm), 4 patient (12-13 mm), 3 patient (13-14 mm), 2 patient (14-15) mm and 2 patient (15 mm) (Table 2) (Fig 3). PCT showed polypoid extension towards the lumen in 13 patients. In patients with a preliminary diagnosis of a mass in the posterior wall of the right atrium in echocardiography examinations, PCT thickness was 20 patients (11-12 mm), 6 patients (12-13 mm), 5 patients (13-14 mm), 2 patient (14-15 mm) and 15 mm in one patient (Fig. 4). PCT contrast enhancement was not observed in patients with routine contrast and non-contrast fat suppression T1 sequences. EF values were within normal limits for both ventricles in patients with PCT (mean 60%; min 45%; max 72%).

Some additional findings were also observed in the CMR examination in PCT. For example, the fat thickness was <3 mm in the interatrial septum (IAS) in 95 patients. IAS fat thickness was 4-5 mm in 25 patients, 5-6 mm in 14 patients, and 6-8 mm in 3 patients based on the thickest measurements. Atrial septal lipomatosis hypertrophy (IAS fat thickness >8 mm) was observed in 3 patients (Fig. 5). In addition

Table 3. Table shows all Pearson correlation values between variables. Because the number of patients with a history of arrhythmia was low, the measurement could not be made.

	PCT	Arrhythmia	RV ED	RA ED	RV EF	LVEF
PCT	1	-	,070	-,342	,490	,115
Arrhythmia	.[a]	.[a]	.[a]	.[a]	.[a]	.[a]
RV ED	,412	.	1	,949	,088	-,185*
RA ED	,000	.	,949	1	,080	,157
RV EF	.490**	.[a]	.145	-.148	1	-.039

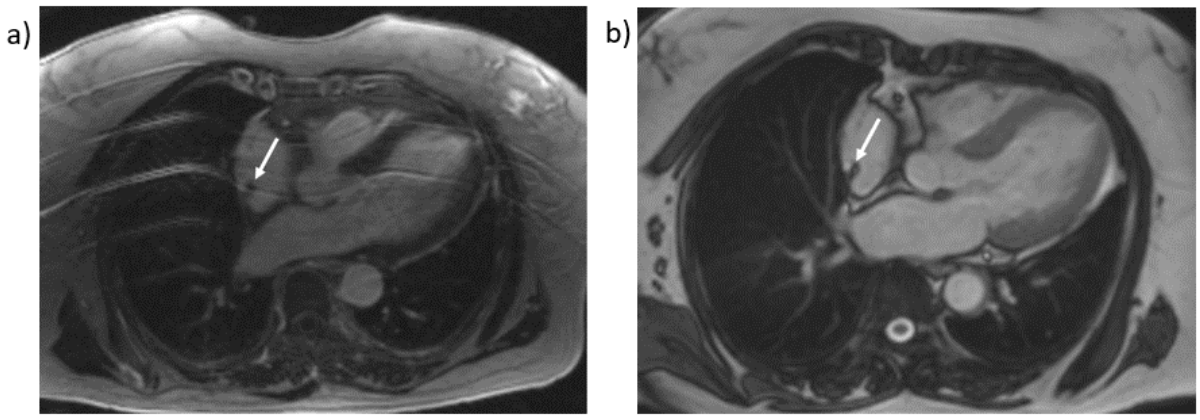

Figure 3. PCT in 40 y old man four-chamber PSIR (a) and cine SSFP (a) sequence seen 9 mm PCT (arrow).

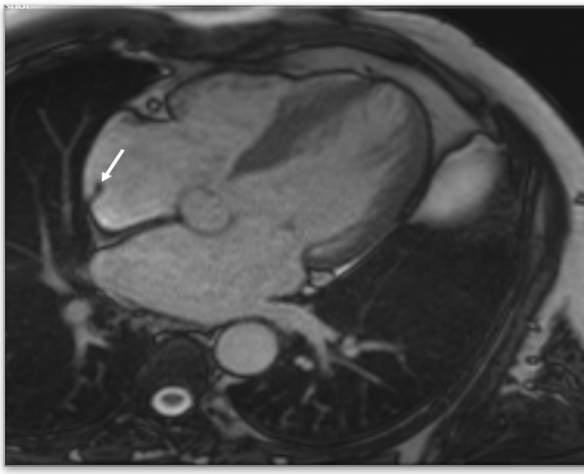

Figure 4. A 46 years old man who has PCT 13 mm on the right posterolateral atrial wall had a preliminary diagnosis of a mass in the posterior wall of the right atrium in echocardiography examination.

to right atrial PCT findings, 15 patients had pericardial effusion, 30 patients had left ventricular hypertrophic cardiomyopathy, 10 patients had pleural effusion, 5 patients had sigmoid septum, and 42 patients had ischemic viability losses in the myocardium. There was no free movement in CMR cine images.

14 (10%) of the patients defined the use of drugs for arrhythmia treatment on the CMR information and consent form. The hospital medical records of these patients were examined. 9 of these patients had atrial arrhythmia (5 premature atrial contractions, 3 atrial tachycardia, 1 supraventricular tachycardia) and 6 patients had a history of treatment for ventricular arrhythmia (4 patients' premature ventricular contractions, 1 patient ventricular tachycardia). PCT thickness in arrhythmia patients was 10-11 mm in 5 patients, 11-13 mm in 4 patients, 12-13 mm in 4 patients, and 15 mm in 1 patient. Arrhythmia was not observed in patients with PCT less than 10 mm. It was observed that the risk of arrhythmia increased with PCT thickness. However, a statistical study could not be done because the number of arrhythmia patients was few.

Signal enhancement was observed in 5 patients in right ventricular myocardial late gadolinium enhancement (LGE). PCT thickness was 9-10 mm in 2 patients, 10.7 mm in 1 patient, and 10-11 mm in 2 patients. LGE was detected in 12 patients in the LV myocardium. PCT thickness in these patients was 8-9 mm in 5 patients, 9-10 mm in 2 patients, 10-11 mm in 4 patients, and 13.4 mm in 1 patient. In 2 of these patients, a signal increase was observed in LGE in

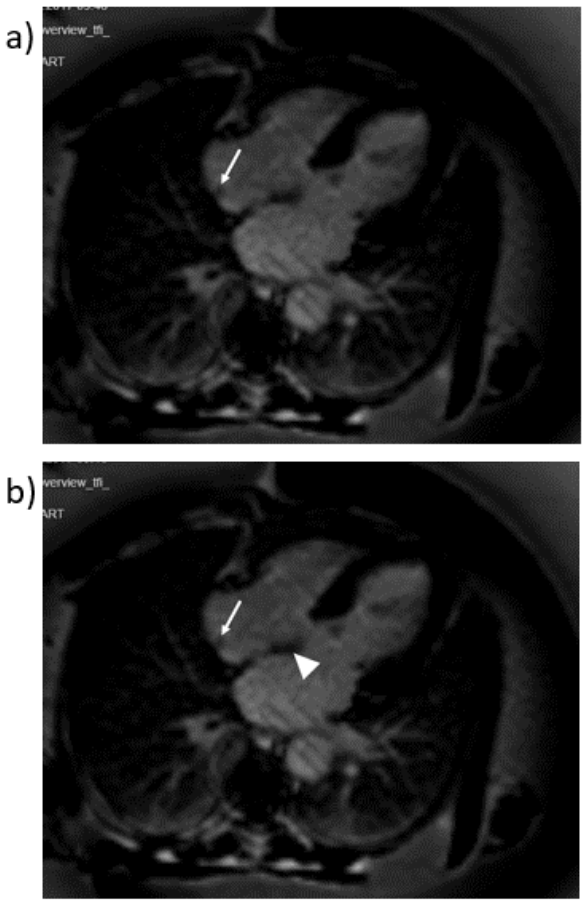

Figure 5. PCT in 40 y old man four-chamber PSIR (a) and cine SSFP (a) sequence seen 9 mm PCT (arrow).

the left ventricle. All patients had a history of ischemic heart disease. There was no significant correlation (r = 0.13) between left ventricular LGE signal increase and PCT thickness.

There was no significant correlation (r<0,5) PCT thickness and RVEF (r=0.49), LVEF (r=0,115), RAED (r=0.32), RVED (r = 0.07) [Table 3].

DISCUSSION

Prominent crista terminalis (PCT) is an anatomical variation in the posterior wall of the right atrium that causes a misleading mass in echocardiography. Finding of this study; PCT was observed as a non-contrast enhancing variation that did not contain significant heterogeneity and was not affected by RA systole in cardiac magnetic resonance imaging (CMR). Relationships between PCT and right, left heart functional data were examined in this study. There was no correlation between PCT thickness change and right ventricular (RV) end-diastolic diameter (ED) [Fig 6], right atrium (RA) ED [Fig 7],

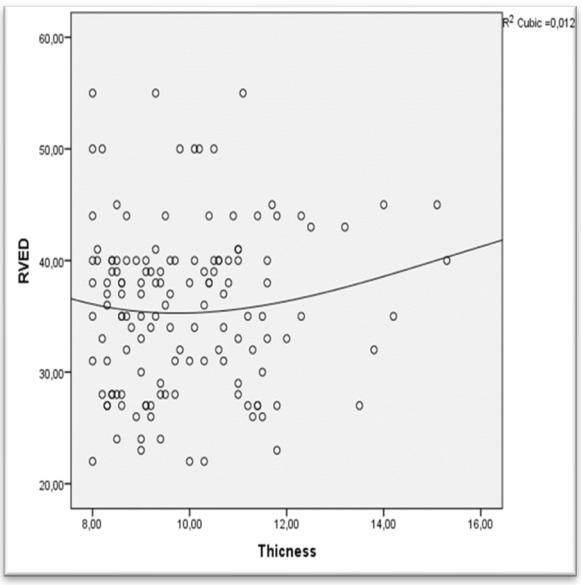

Figure 6. In this scatter plot graphic was observed that the change between PCT thickness and RV EF showed nominal distribution.

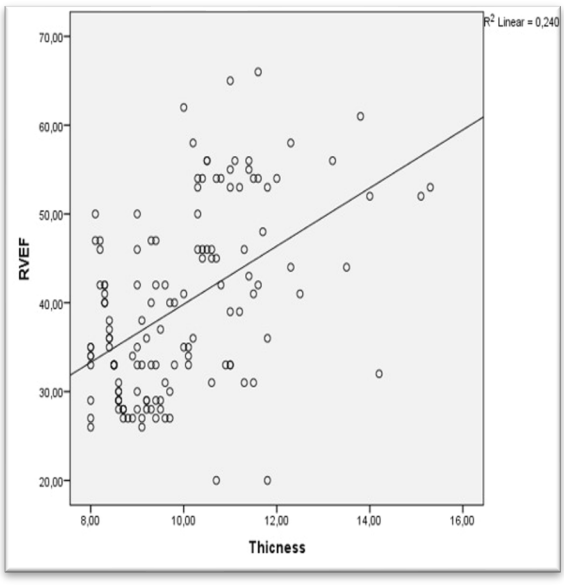

Figure 8. In this simple scatter plot graphic is seen that the change between PCT and RV EF showed nominal distribution.

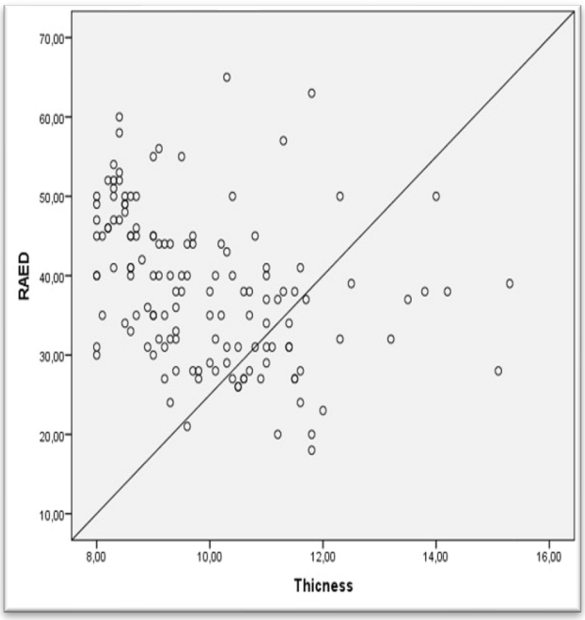

Figure 7. In this scatter plot graphic was observed that the change between PCT thickness and RV EF showed nominal distribution.

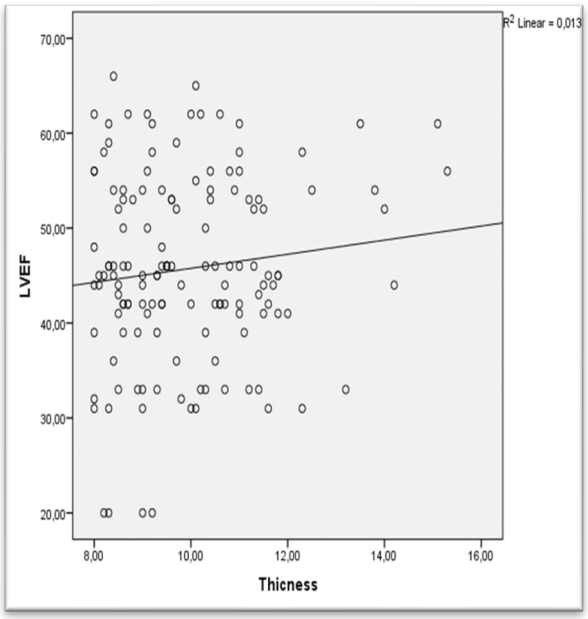

Figure 9. In this simple scatter plot graphic is seen that the change between PCT and RV EF showed nominal distribution.

right ventriculi (RV) ejection fraction (EF) [Fig 8], left ventriculi (LV) EF [Fig 9]. It was observed that the risk of arrhythmia increased with PCT thickness therefor PCT classification system has a clinical importance.

The benefits of using CMR in evaluating normal right atrial structures have been reported in the literature (2). Thebesian valve, persistent sinus venous, Eustachian valve, crista terminalis, and Chiari network are these structures. PCT imaging is difficult in echocardiography due to the right atrium posterior wall placement. Imaging is more difficult in some patients due to the chest structure. A posterior

angulation technique has been described to shorten the anterior ventricle in the apical four-chamber view for a clearer view of the CT. Confirming the diagnosis of PCT with 3D echocardiography methods, including TEE and transthoracic 3D imaging, may be insufficient (2). PCT is particularly confused with thrombus and myxoma. CMR image characteristics have been described in the literature for thrombus, rhabdomyoma, fibroma, and myxoma. Thrombus is observed as non-contrast enhancing intraluminal pathologies. Myxoma is the most common mass of the heart, which is generally pedunculated, can be contrast-enhancing, and can be heterogeneous in its internal structure, especially in the atrium (10). Examination of PCT CMR image characteristics is insufficient in the literature available to us. The incidence of arrhythmia with PCT (10%) was higher than in the literature (2). Crista terminalis arrhythmias are defined as "crystal tachycardia" (2,11).

Rastogi et al. examined the morphological pattern of crista terminalis (CT) in a cadaver study. In the study, all 80 specimens had CT. If CT was not visible in echocardiography and CMR examination, CT should be considered as thin. CMR represents a superior non-invasive modality to differentiate benign and malignant cardiac masses due to its high tissue contrast, higher spatial resolution, wider field of view, and unique ability for tissue characterization. Differentiation of PCT and real masses using CMR will provide very important clinical results. Standard CMR protocols for PCT assist in performing high-quality, diagnostic studies necessary to guide physician decisions regarding patient management, from initiating anticoagulation to attempting surgical resection (12,13).

Strengths and Limitations

This study has some limitations. The study is a single-center and retrospective study. A limitation is that there were no additional sequences for PCT imaging. The exclusion of the patients' echocardiography details in the study was accepted as a limitation. Another limitation was the absence of a pathological or surgical diagnosis in the patients.

CONCLUSION

In conclusion, CT is an anatomical fibromuscular structure in the posterior wall of the right atrium. CMR imaging characteristics should be well known, as PCT can be confused with mass and thrombus. In this study, CMR imaging characteristics of PCT patients were examined. This study should be expanded in a multi-cantered manner with studies that evaluate echocardiography findings together.

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RESEARCH ARTICLE

THE EFFECTS OF VISION ON STAIR DESCENT: KINETIC AND KINEMATIC ANALYSIS

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ABSTRACT

Purpose: The purpose of this study was to examine the effects of vision on stair descent activity.
Material and Methods: Twenty healthy participants aged between 20-22 (21 years) were included in the study. The patients were asked to walk on a platform with a height of 15 cm from the ground and a length of 4 meters, get down on a 30*60 cm long force platform at the end of the platform and continue walking. Test was repeated with glasses that reduced the light by 90%. Kinetic data were obtained with the Kistler Force platform. The data collected from the first contact of the person's foot to the force platform until the contact of the same foot with the platform was recorded. Descriptive statistics are given as median. Wilcoxon signed-rank test with Bonferroni correction was used to compare within-group measurement values.
Results: There were significant differences in the Min region on X-axis, the second peak on the second axis, and the second peak on Y-axis ($p<0.025$). When the kinematic parameters were compared, it was found that there was a significant difference between the min peaks of the ankle, hip, and knee joints ($p<0.025$).
Conclusion: If the vision is disrupted, even the person tries to minimize the injury risk caused by the uncontrolled movement, he/she is not able to take control of the midstance and push-off phase of the related lower extremity. It is necessary to also assess the kinetic and kinematic parameters of the contralateral lower extremity in order to broadly analyze the stair descent activity.

Keywords: Stair Descent, Vision, Kinetic, Kinematic

INTRODUCTION

During activities of daily living, the human body interacts with many internal and external forces most of which are repetitive in nature. Such forces include but not limited to forces of muscles during different phases of gait, joint reaction forces, ground reaction forces and pertubation forces from other individuals. One example is gait, as several forces act on different parts of the body depending on the phase of the gait cycle (1, 2). Muscles, articular cartilage, menisci, and ligaments, the contractile and non-contractile structures of the body, absorb some of the internal and external forces during gait. During the process of force absorption, the aforementioned contractile and non-contractile structures form a movement-specific stiffness. Proper movement-specific stiffness can

Figure 1. Instrumented staircase was used in this study. Height of wooden platform from ground = 0,15 m, length = 4 m. Force platform length = 0,6 m, width = 0,4 m.

only be achieved by the interaction of musculoskeletal and central nervous systems (3, 4). It is obvious that the stiffness coefficient of the muscular system may be altered by the neuromuscular mechanisms during the movement (5). Neuromuscular mechanisms (such as short-latency stretch reflex) function to prevent injuries in addition to providing a smooth movement. Short latency reflexes are generated just before the dissipation of the shockwave that is caused by the force in action (6). Thus, the muscle responses to shockwaves are generated (7). Through proprioceptive feedback, the body makes preparations for movements via anticipatory reactions. The data obtained by the golgi tendon organ, Pacinian capsules, and Ruffini corpuscles generate information about the position of the lower extremity. If there are any problems or alterations in this integration the reaction may not be performed correctly, and injuries may occur (8).

There are numerous studies that cover many aspects of stair ascent and descent in the literature (9-12). There are studies about kinetic and kinematic parameters of stair ascent and descent related to not only the different age groups but also the different types of stairs (9, 13, 14). According to Schick et al. and Speechley&Tinetti, stair activities, which pose no threats to adults, take an important part of the fall injuries (15, 16). There may be deviations from the normal movement pattern in stair descent related to the physiological alterations due to aging (17, 18). As a result of a prolonged double limb support phase, increased amount of support, and decreased movement velocity a safer pattern is chosen. These adaptations may be indicated as a result of muscle strength loss, moreover, in marathon runners, the more difficult stair descent activity may be performed backward after fatigue. But as it was reported in the previous studies, the stair descent activity may be negatively affected by muscle strength loss, cardiovascular disorders, poor vision, proprioception loss, and balance problems (19). First and foremost, the integration of vision, balance, and protective reactions is of utmost importance. It is known that with poor or disrupted vision, the balance and anticipatory reactions are also disrupted. Vision helps to maintain balance by working with the somatosensory system and vestibular system and also works as a crucial and reliable data source. Postural control problems may occur during the activities of daily living, with impaired vision or in a short moment of absence of mind (20-22). The proof in literature is scarce during stair descent activity, the disruption of the information, which is provided by the vision. The aim of this study was to investigate the possible alterations in kinetic and kinematic parameters related to stair descent activity with impaired vision.

Table 1. Demographic characteristics of participants

	Participants (n:20) Median – (IQR)
Age *(years)*	21 – (19.00 – 24.50)
Gender	12 male – 8 female
Body Height *(cm)*	167.5 - (164.25 – 176.50)
Body Weight *(kg)*	67.00 - (53.50 – 77.00)
BMI *(kg/m^2)*	22.18 – (20.07 – 24.65)

IQR: Interquartile Ratio

MATERIAL AND METHODS

The study was conducted between May 2016 and August 2016 at the Dokuz Eylul University School of Physical Therapy and Rehabilitation. Ethics committee approval was obtained from the Dokuz Eylul University Non-Interventional Ethics Committee Commission (Date: 30.07.2015, Decision Number: 2015 / 18-30). Inclusion criteria; 1 – Able to stand or walk without pain, 2- Being between the ages of 18-35. Exclusion criteria was having any history of orthopedic surgery.

The participants wore no clothes other than minimalistic undergarments, which enabled precise

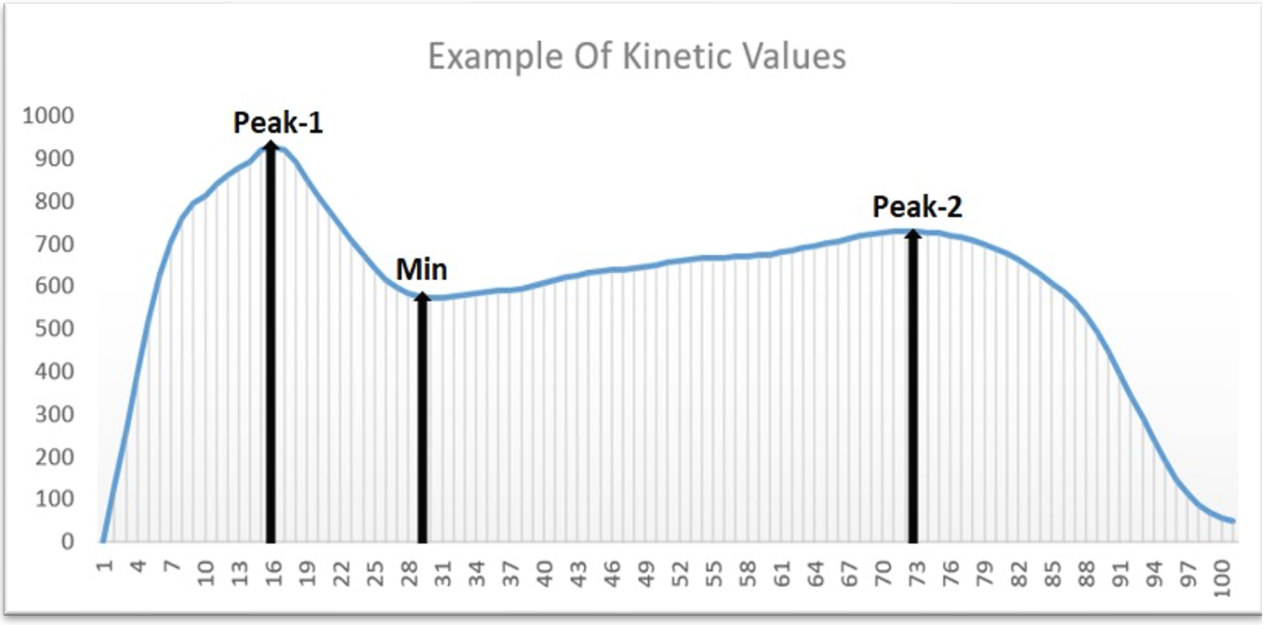

Figure 2. Example of Kinetic Values

marker placement and were barefoot during the evaluations. Demographics of the participants were recorded before starting the study protocol. After recording demographics, to conduct motion analysis; 1- ankle diameter measurement, 2-knee joint diameter, 3- pelvic diameter, 4- pelvic height, 5- lower extremity length measurements were performed respectively. The participants were asked to walk at a comfortable speed they prefered on a previously prepared wooden platform and to descend on the 30 * 60 cm long platform (force plate) at the end of the platform (Figure 1). The height of the wooden platform is 15 cm and its length is 4 meters. Before the assessment, participants were asked to repeat the activity at least 5 times as trials. After completion of trials, participants were asked to perform the same activity 2 more times; 1 without goggles and 1 with goggles, which reduces incoming light rays by 90%. Starting position on the wooden platform was selected so that the participants were able to complete the activity regardless of their step length. In both cases (with and without goggles), kinetic and kinematic data were obtained. Kinematic data were obtained by BTS™ motion analysis system with marker placement according to Helen Hayes protocol and kinetic data were obtained by the Kistler™ platform.

Reference kinetic values were determined for the data to be taken just before the assessment with the motion analysis (Figure 2). From the moment the person's foot first contacted the force platform, the data was collected until the same foot was removed from the platform. The collected data was transformed into a 100-frame sequence. After the sequence separation, the force platform data were analyzed in three sections according to the graph below (Figure 2). The first highest data obtained from the force platform (Peak-1), the lowest data following this data (Min) and, the next highest data (Peak-2) have been examined in three sections (Figure 2). Related to this data, lower extremity joints' range of motion, which were converted into 100-frame sequences, were selected for their corresponding degrees for statistical analysis.

Statistical analysis was performed using Statistical Package for Social Sciences 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) program. Descriptive analyzes were presented as mean±standard deviation. The Wilcoxon Signed-Rank test was used to compare the kinetic and kinematic data obtained according to both test conditions. Bonferroni correction was used ($p < 0.025$).

RESULTS

Demographic characteristics of the participants are given in Table 1. The study included 20 participants (12 male, 8 female).

The times of the participants' completion of the step-stroke activity and the kinetic and kinematic

Table 2. Kinetic and kinematic parameters during stair descent

	Eyes Open Tests Mean (SD)	**Eyes Closed Tests** Mean (SD)	***p***
X-P1 (N/m)	-85,0669 (48,82)	-33,5844 (120,34)	0.102
X-Min (N/m)	19,0055 (24,43)	-22,5217 (76,90)	**0.011***
X-P2 (N/m)	97,4075 (59,84)	42,6134 (65,02)	**0.020***
Y-P1 (N/m)	1148,6610 (269,21)	1363,9350 (448,43)	0.031
Y-Min (N/m)	516,2985 (125,73)	649,4260 (284,20)	0.064
Y-P2 (N/m)	684,7400 (195,34)	840,1770 (327,46	**0.024***
Z-P1 (N/m)	-14,2709 (61,25)	-4,6049 (56,29)	0.647
Z-Min (N/m)	-7,1203 (33,23)	-6,4119 (54,52	0.968
Z-P2 (N/m)	-8,9046 (48,04)	-12,2751 (62,27)	0.968
Ankle-P1 (deg)	0-,3440 (13,64)	-,9357 (16,02)	0.601
Ankle-Min (deg)	-1,3898 (12,23)	-4,4987 (11,50)	0.550
Ankle-P2 (deg)	5,0800 (9,39)	-6,0859 (12,70)	**0.007***
Knee-P1 (deg)	4,1356 (5,23)	8,3401 (13,98)	0.433
Knee-Min (deg)	3,7895 (5,06)	13,2903 (16,27)	**0.021***
Knee-P2 (deg)	3,7006 (3,23)	14,6074 (17,40)	0.030
Hip-P1 (deg)	8,1122 (7,52)	8,4012 (9,56)	0.970
Hip-Min (deg)	0,5163 (9,53)	6,2215 (7,83)	**0.007***
Hip-P2 (deg)	0,1042 (12,33)	3,6931 (10,85)	0.204

(*=p<0.025) Wilcoxon Signed Rank Test, p values were corrected with Bonferroni correction. X-P1: Kinetic 1st peak of X-axis, X-Min: Minimum Kinetic of X-Axis, X-P2: 2nd peak of X-Axis. Ankle-P1: 1st peak degree of ankle joint movement in the sagittal plane. (-) values refer to dorsiflexion of the ankle, hyperextension of the knee, and extension of the hip joint. (+) values refer to plantarflexion of the ankle, flexion of the knee, and flexion of the hip joint.

parameters shown during this activity are shown in Table 2 in both conditions with the eyes open and eyes closed.

As shown in Table 2, there were significant differences in the Min region on X-axis, the second peak on the second axis, and the second peak on Y-axis (p<0.025). When the kinematic parameters were compared, it was found that there was a significant difference between the min peaks of the ankle, hip, and knee joints (p<0.025).

DISCUSSION

The purpose of this study was to investigate the alterations in kinetic and kinematic parameters during stair descent activity with disrupted vision. Kinetic parameters were examined related to the foot initially contacted the force platform whereas kinematic parameters were examined related to the foot and lower extremity. There was not any study on this topic in the literature to our knowledge. In our study, with the disruption of vision, we found that the ground reaction force was increased and, the excessive energy (load), normally absorbed by related muscles and joints, could not be absorbed thus, the force required for push-off could not be generated.

In the literature, there are studies in which kinetic and kinematic analyzes are performed during stair ascent and descent activity (9, 12, 23). There are also publications on the importance of vision during stair descent (23, 24). In a study by Buckley et al., kinetic parameters during blurred vision were examined. According to the results of the study, participants tried to take a safe step until the somatosensory sense of the foot, which initially contacts the ground, perceived. It was determined that the participants tried to descend the steps cautiously (23). In our study, the sense of vision was blocked and it was tried to prevent them from developing a safe strategy. Therefore, the results of our study are different from the results of Buckley et al.'s study. However, similarly, it was found in our study that body control was tried to be achieved during step descent by

providing ground contact. In the study of Hamel et al., the relationship between decreased vision during stair descent activity and falling was tried to be defined with parameters related to the foot's contact with the ground (24). The results of the study showed that vision is important when the foot is in contact with the ground. In the study of Brinker et al., it was found that the markers set to support the sense of vision have beneficial effects (25).

The results of stair descent activity with minimal vision are somewhat similar to the results of functional drop landing activity. During drop landing activity, the body follows the specific pattern and, the related structures of the body try to absorb the shockwave. During undisrupted vision, when initial contact is performed with the forefoot, lower extremity joints move within a greater range of motion to reduce the velocity of the body. The greater range of motion enables eccentric control of the muscles and absorption of the shockwave. It is known that if the range of motion is not between optimal range, injuries may occur. It was indicated that a greater hip and knee joint range of motion may prevent ACL injuries (26). The human body reacts to increased ankle dorsiflexion range or velocity of the body by increasing the hip and knee joint range of motion (26). We also found similar results in our study. Participants completed the activity with an increased average flexion range of motion during minimal vision from initial contact to push-off phase including the midstance phase. The shockwave caused by the ongoing uncontrolled activity was tried to be eliminated by the flexion posture just before initial contact and in the y axis, the person was able to absorb shockwave as soon as initial contact occurs. In addition to flexion posture throughout the movement, the significant difference in flexion posture in the knee and hip joints was seen at the “min” area, in which the shockwave is trying to be absorbed. However, during the remaining part of the movement –push-off phase-, ankle dorsiflexion continued to increase. Thus, the ankle joint was not able to generate the required force for the push-off phase. The data of decreased kinetic parameters at the “x” axis confirms this hypothesis.

As the kinetic data were examined it was identified that the data significantly deviated from the normal values. The deviation was only not significant at the “z” axis. This effect indicates that the medial-lateral stability of the lower extremity presents similar results under both conditions. As the data of the “y” axis were examined, it was indicated that the aforementioned greater flexion posture was effective in neutralizing shockwaves during initial contact and absorption phases. The force influencing the “y” axis was detected to be increased during movement however, a significant effect was seen in the P2 area. Increased “y” axis force indicates the contralateral extremity was not able to transfer body weight under control. But during the increase in P2 area, it was indicated that the lower extremity was still trying to eliminate the shockwave and not able to generate the moment for propulsion.

Our study has two limitations. The former is that we only examined the kinematic parameters of the lower extremity in the sagittal plane, not axial rotation. Thus, it is not known that the alterations may or may not influence the results. The latter is that we were not able to analyze the contralateral lower extremity due to the limitations of our motion analysis system. We were not able to gather kinetic and kinematic parameters related to the contralateral lower extremity.

CONCLUSION

During the stair descent activity, vision is one of the most important parameters for the correct postural control. If the vision is disrupted, even a healthy individual tries to minimize the injury risk caused by the uncontrolled movement, he/she is not able to take control of the midstance and push-off phase of the related lower extremity. We believe further studies should also include the assessment of the kinetic and kinematic parameters of the contralateral lower extremity to broadly analyze the stair descent activity.

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RESEARCH ARTICLE

DETERMINATION OF ANXIETY LEVELS AND KNOWLEDGE LEVELS ABOUT COVID-19 DURING THE COVID-19 OUTBREAK OF PREGNANTS: SURVEY IN TURKEY

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ABSTRACT

Purpose: To determine the anxiety and knowledge levels of pregnant women about outbreaks during the COVID-19 pandemic.
Material and Methods: This study was conducted as a descriptive study with 276 pregnant women presenting to obstetrics and gynecology outpatient clinics of hospitals in eastern Turkey. The data were collected using a personal information form, a form for assessing the knowledge levels of the participants about COVID-19, and the COVID-19 Anxiety Scale.
Results: It was found that 75.4% of the participants were worried that they would catch COVID-19 in the hospital during or after childbirth. The mean COVID-19 Anxiety Scale score of the participants was 6.7±2.4 (min: 5, max: 14). The anxiety levels of the participants who were in the last trimester of pregnancy, those who did not receive information about COVID-19, those who changed their mode of delivery due to the pandemic, those who received inadequate prenatal care, those whose social support decreased, and those who felt vulnerable were significantly higher.
Conclusion: The results of this study revealed that anxiety in pregnant women is affected by various factors. It is important to provide care and support for these groups.

Keywords: pregnancy, COVID-19, anxiety.

INTRODUCTION

The novel coronavirus disease 2019 (COVID-19) first appeared in the Wuhan city in the Hubei province of China in December 2019. It spread rapidly around the world, and the World Health Organization (WHO) declared it a pandemic on 11 March 2020 (1). COVID–19 has been one of the most devastating outbreaks the world has faced this century, with cases exceeding 21 million and deaths reaching 761,779 (1).

This pandemic has significantly affected the daily lives of millions of people worldwide (2). Governments have had to take strict measures to prevent the spread of the virus and recommended that people stay at home (3). Both because of the COVID–19 pandemic itself and because of

Table 1. Distribution of pregnant women by socio-demographic and congenital characteristics (n=276)

Features	n	%
Education Status		
Non-Literate	36	13.0
Literate	24	8.7
Primary School	44	15.9
Secondary School	64	23.2
High School	52	18.8
University-College	56	20.3
Working Status		
Yes	24	8.7
No	252	91.3
Economic Situation		
Profit, less than spending	100	36.2
Profit equals spending	140	50.7
Profit, more than spending	36	13.0
Chronic Disease		
Has	44	15.9
Doesn't have	232	84.1
Assessment of health status		
Well	112	40.6
Moderate	144	52.2
Bad	20	7.2
Pregnancy trimestiria		
1. trimestiri	44	15.9
2. trimestiri	28	10.1
3. trimestiri	204	73.9
Regular medication using		
Yes	108	39.1
No	168	60.9

restrictions in countries, people's anxiety and fear levels have increased (4). In the literature, epidemics and pandemic such as COVID-19 have been shown to have effects on mental health such as high stress levels, anxiety, and depression (5). Pregnancy can be stressful enough in itself; for example, many women may feel fear regarding the protection of their health and that of their babies (4, 6, 7). In addition to this already existing pressure on the mental health of current or expecting mothers, the COVID–19 pandemic may increase the stress and anxiety levels of pregnant women (6, 8). In studies conducted in pregnant women during the COVID–19 pandemic period, the prevalence of anxiety was shown to be between 63% and 68% (9, 10). A qualitative study demonstrated that women experienced increased levels of fear for their own and their baby's health and safety, especially due to fear of infection, and COVID-19 appeared to have contributed to symptoms of anxiety in women already predisposed to anxiety in the prenatal period (11). High levels of stress during pregnancy, anxiety and depression, an increase in blood pressure, premature childbirth, and low birth weight can cause serious health problems such as postpartum depression (6, 8, 12). In fact, it was found that pregnant women skip hospital visits due to the risk of infection and do not receive adequate prenatal care (13). However, the antenatal care manual published by the World Health Organization in 2016 stated that pregnant women should be monitored at least eight times in the prenatal period (14). Lebel et al. (2020) found more prevalent symptoms of depression and anxiety to be associated with concerns about the threats of COVID-19 to the life of the mother and the baby, as well as concerns about not getting the necessary prenatal care, relationship tensions, and social isolation due to COVID-19 (15). The anxiety levels of pregnant women regarding COVID-19 infection can be affected by factors such as their education level, quality of life, occupation, income level, and social support. In addition to all these factors, pregnant women's knowledge levels about COVID-19 can also affect their anxiety and fear of COVID-19 infection (16). However, there is a limited number of studies in the literature that examined pregnant women's fears, anxiety levels, and knowledge levels regarding COVID-19 infection (8). Therefore, the aim of this study is to determine the anxiety and knowledge levels of pregnant women regarding COVID-19 infection.

MATERIAL AND METHODS

This cross-sectional descriptive study was conducted between 16 June 2021 and 8 July 2021 at a University Hospital in eastern Turkey, and the population of the study consisted of pregnant women who presented to the obstetrics and gynecology outpatient clinics of the hospital. The minimum required sample size of the study was calculated as 212 in a 95% confidence interval and with an error margin of 5% using the G*Power program (version 3.1.9.4). The study was completed with 276 pregnant women who met the inclusion criteria and volunteered to participate in the study. The inclusion criteria of the study were determined as being voluntary, being pregnant, not having a known and diagnosed psychiatric illness, having no communication problems, and having no complications in pregnancy. The potential participants were asked whether they had undergone any psychiatric evaluation before participating in the study. Whether the women who had undergone psychiatric evaluations were diagnosed with any psychiatric disease was evaluated. Those with a psychiatric diagnosis were not included in the study.

Table 2. Distribution of pregnant women according to their thoughts on the pandemic and pregnancy process (n=276)

Features	n	%
Thinking about changing the method of birth due to the pandemic		
Yes	112	40.6
No	164	59.4
Preferred birth method due to pandemic		
Vaginal Birth	188	68.1
Cesarean	88	31.9
Feeling vulnerable because you are pregnant during the pandemic		
Yes	176	63.8
No	100	36.2
Lack of prenatal care due to pandemic		
Yes	164	59.4
No	112	40.6
Decreased social support during pregnancy due to pandemic		
Yes	180	65.2
No	164	59.4
Fears she may catch coronavirus during childbirth		
Yes	208	75.4
No	68	24.6
Worry that the baby may catch coronavirus during or after birth		
Yes	188	65.1
No	88	31.9
Status of receiving information on COVID-19		
Yes	52	18.8
No	224	81.2
Sources of information*		
Web	160	58.0
Social media	148	53.6
The Ministry Of Health(Government)	100	36.2
Family-Parents	60	21.7
Discussion programs(TV shows,Realty shows)	20	7.2

*More than one source of information was preferred.

All participants who were interviewed were COVID-19-negative during the data collection process. Before starting the study, ethical approval was obtained from Bingol University, Scientific Research and Publications Ethics Board (Date: 7/04/2021, Number: E11707).

Data Collection Tools

The data were collected using a personal information form, a form on the knowledge levels of the participants about COVID-19, and the COVID-19 Anxiety Scale.

Personal Information Form

The form consisted of 16 questions on the sociodemographic and obstetric characteristics of the participants, and it was prepared by the researchers based on the relevant literature (16, 17, 18).

COVID-19 Knowledge Assessment Form: The form was prepared by the researchers based on the relevant literature, and it consisted of 18 questions designed to determine the knowledge levels, information sources, and attitudes of the participants regarding COVID-19 (17, 18, 19, 20). Each item in the form was presented with "true", "false", and "don't know" response options. The percentages of the “true” and “false” responses of the participants for the items were calculated to measure their knowledge levels (Table 3).

COVID-19 Anxiety Scale-Short Form: The scale was developed by Lee et al. (2020) to identify dysfunctional anxiety associated with the COVID-19 pandemic. The validity and reliability studies of the scale in Turkey were conducted by Biçer et al. (2020). The scale is a Likert-type scale consisting of 5 items (21, 22). The response options of each item are “0” Never, “1” Rarely, less than one or two days, “2” a few days, “3” more than 7 days, and “4” almost every day in the last two weeks. The lowest and highest possible scores on the scale are 0 and 20. Higher scores indicate higher levels of anxiety about the COVID-19 pandemic. The Cronbach’s alpha coefficient of the scale was found by Biçer et al. (2020) as 0.83. In this study, the Cronbach’s alpha value of the scale was found to be 0.83.

Data Collection

The data were collected by the researchers using the face-to-face interview technique by taking protective measures for COVID-19. The participants were informed about the study and given the necessary explanations, and then, their consent was obtained.

Data Analysis

All statistical analyses were performed using IBM SPSS Statistics version 23.0 (IBM Inc., Armonk, NY, USA). Percentage and frequency analyses, independent-samples t-test, and one-way analysis of variance (ANOVA) were used to analyze the collected data. The results were evaluated in a 95% confidence interval, and the level of statistical significance was accepted as $p<0.05$.

Table 3. Information of pregnant women about the covid-19 pandemic (n=276)

	Correct Answers		Wrong Answers	
Information Questions	**n**	**%**	**n**	**%**
Covid-19 is a respiratory infection caused by a new type of coronavirus. (T)	232	84.1	44	15.9
Pregnant women are as much at risk of contracting covid-19 as anyone else. (T)	176	63.8	100	36.2
The elderly and those with chronic disease are as at risk of contracting Covid-19 as anyone else. (T)	256	92.8	20	7.2
Covid-19 is transmitted by respiratory droplets such as coughing and sneezing. (T)	244	88.4	32	11.6
Covid-19 virus is transmitted by touching contaminated objects or surfaces through direct contact with infected persons. (T)	236	85.5	40	14.5
Covid - 19 is transmitted by touching the nose, eyes and mouth with dirty hands. (T)	232	84.1	44	15.9
Hands should be washed frequently with soap and water to avoid Covid-19. (T)	256	92.8	20	7.2
A surgical mask should be worn to protect against Covid-19. (T)	244	88.4	32	11.6
Social distance should be considered to protect from Covid-19. (T)	260	94.2	16	5.8
To avoid Covid-19, it is necessary not to touch the face and mouth with dirty hands. (T)	264	95.7	12	4.3
Alcoholic disinfectants can be used for disinfection during the covid-19 outbreak. (T)	264	95.7	12	4.3
There is no harm in breastfeeding while the covid-19 outbreak continues. (T)	216	78.3	60	21.7
A mother infected with the Covid-19 virus should breastfeed her baby. (T)	176	63.8	100	36.2
Anomalies occur in the baby of a pregnant woman infected with the Covid-19 virus. (F)	100	36.2	176	63.8
A mother infected with the covid-19 virus has a risk of premature birth in her baby. (T)	100	36.2	176	63.8
A pregnant baby infected with the Covid-19 virus is also born with the Covid-19 infection. (F)	56	20.3	220	79.7
Common symptoms of Covid-19 include fever, cough, and shortness of breath, but nausea and diarrhea have rarely been reported. (T)	224	81.2	52	18.8
The diagnosis of Covid-19 can be diagnosed by PCR testing on samples collected from nasopharyngeal and oropharyngeal discharge or sputum and bronchial Flushing. (T)	184	66.7	92	33.3

Ethical Aspects of the Study

This study was approved by the Bingol University Scientific Research and Publication Ethics Committee (Approval date: 07/04/2021, Number: E11707). Permission has been obtained from the Republic of Turkey Ministry of Health regarding the execution of COVID-19 studies (Dated:06.06.2021). Furthermore, the women who participated in the study were given a brief description of the study, and consent was received from those who agreed to participate in the study.

RESULTS

In the study, the mean age of the participants was 28.3±5.8 (min: 17, max: 46), all participants were married, and the mean duration of their marriages was 6.0±5.4 years (min: 1; max: 26). The mean gestational week of the participants was 28.1±10.8 (min: 5, max: 40), and the mean total number of their pregnancies was 2.3±1.3 (min: 1, max: 6). It was found that 23.2% of the participants had completed secondary school, and 8.7% worked in income-generating jobs. According to their self-reports, 40.6% of the participants had a “good” overall health status. The rate of the participants who were using medication regularly was 39.1% (Table 1).

It was found that 40.6% of the participants changed their preference of mode of delivery during the pandemic period. Of the participants, 68.1% said they preferred vaginal delivery. While 59.4% of the participants stated that they did not get enough prenatal care because they had skipped their prenatal follow-ups due to the pandemic, 65.2% stated that their social support during pregnancy decreased due to the pandemic. It was found that 75.4% of the participants were worried that they would contract COVID-19 in the hospital during or after childbirth. The vast majority of the participants (81.2%) stated

Table 4. Distribution of covid-19 Anxiety Scale scores according to socio-demographic and congenital characteristics of pregnant women (n=276)

Features	COVID-10 Anxiety Scale Score	Test* and pValue	
Education Status			
Non-Literate	8.6±3.6[1]	F=8.099	**p=0.001**
Literate	6.6±2.6	2<1	
Primary School	7.1±3.2[2]		
Secondary School	5.6±0.9[2]		
High School	6.4±1.4[2]		
University-College	6.7±2.0[2]		
Working Status			
Yes	6.1±1.0	t=-2.401	**p=0.020**
No	6.8±2.5		
Economic Situation			
Profit, less than spending	7.4±3.0[1]	F=9.784	**p=0.001**
Profit equals spending	6.1±1.7[2]	2<1	
Profit, more than spending	7.3±2.3[1]		
Chronic Disease			
Has	7.2±3.1	t=1.197	p=0.237
Doesn't have	6.6±2.2		
Assessment of health status			
Well	6.5±1.7	F=2.859	p=0.059
Moderate	7.0±2.9		
Bad	6.0±0.9		
Pregnancy trimestiria			
1. trimestir	5.3±0.4[1]	F=15.664	**p=0.001**
2. trimestir	5.5±0.9[1]	1<2	
3. trimestir	7.2±2.6[2]		
Regular medication using			
Yes	6.2±2.2	t=-2.788	**p=0.006**
No	7.0±2.5		

* F: ANOVA test, t: Independent-samples t-test.

that they had not received information about COVID-19 (Table 2).

It was found that most participants marked the option "true" regarding their use of substances related to protection from COVID-19. To the statement "COVID-19 is also seen in the baby of the mother who is infected", the vast majority of the participants responded as "false". The rates of the participants who responded as "true" to the statements "anomalies are observed in the baby of the mother who is infected with COVID-19" and "the mother who is infected with COVID-19 has a risk of premature childbirth" were both 36.2% (Table 3).

The mean COVID-19 Anxiety Scale score of the participants was 6.7±2.4 (min: 5, max: 14). There was a statistically significant difference between the mean COVID-19 Anxiety Scale scores of the participants who were illiterate (8.6±3.6) and the participants who were university graduates (6.7±2.0) ($p<0.05$). The COVID-19 Anxiety Scale scores of the participants who were not working, those who expressed their income as less than their expenses, those who were in the last trimester of pregnancy, and those who did not take regular medication were significantly higher. No significant relationship was found between the presence of chronic diseases and the overall health status assessment variables of the participants and their COVID-19 Anxiety Scale scores (Table 4).

The mean COVID-19 Anxiety Scale score of the participants who considered changing their mode of delivery was 8.2±2.8, while the mean score of those who did not consider this was 5.7±1.4 ($p<0.05$). The

Table 5. Distribution of COVID-19 Anxiety Scale score averages according to pregnant women's thoughts on the pandemic and pregnancy process

Features	COVID-19 Anxiety Scale Score Average	Test and P Value
Thinking about changing the method of birth due to the pandemic		
Yes	8.2±2.8	t=8.560 **p=0.001**
No	5.7±1.4	
Preferred birth method due to pandemic		
Vaginal Birth	6.4±2.3	t=-1.664 p=0.097
Cesarean	6.9±2.5	
Feeling vulnerable because you are pregnant during the pandemic		
Yes	7.5±2.8	t=8.729 **p=0.001**
No	5.5±0.7	
Lack of prenatal care due to pandemic		
Yes	7.1±2.4	t=3.350 **p=0.001**
No	6.1±2.3	
Decreased social support during pregnancy due to pandemic		
Yes	7.1±2.6	t=3.883 **p=0.001**
No	6.0±1.7	
Fears she may catch coronavirus during childbirth		
Yes	7.2±2.6	t=9.497 **p=0.001**
No	5.3±0.5	
Worry that the baby may catch coronavirus during or after birth		
Yes	7.0±2.5	t=3.481 **p=0.001**
No	6.0±2.0	
Status of receiving information on COVID-19		
Yes	6.3±2.0	t=-4.285 **p=0.001**
No	8.4±3.3	

mean COVID-19 Anxiety Scale scores of those who felt vulnerable because they were pregnant during the pandemic and those who expressed decreased social support due to the pandemic were found to be significantly higher ($p<0.05$). The mean COVID-19 Anxiety Scale score of the participants who were concerned that they or their baby would contract COVID-19 in the hospital during childbirth was significantly higher (Table 5).

DISCUSSION

Pregnancy is a period when women are emotionally sensitive and prone to anxiety due to hormonal and biopsychosocial changes, as well as physical changes. During this period, women often experience various concerns about themselves, their baby, their healthcare experience, childbirth, and parenting skills. The consideration of maternal-fetal risks and social isolation in addition to these concerns associated with being infected with COVID-19 due to the need to receive regular prenatal care increases anxiety in pregnant women, although research on the effects of this infection during pregnancy is insufficient (23, 24, 25, 26). In this study, the participants had low levels of COVID-19 anxiety (mean scale score: 6.7±2.4). A study conducted during the COVID-19 pandemic similarly found that 44.6% of pregnant women had anxiety (27). In a qualitative study conducted during the Zika outbreak, pregnant women were reported to feel fear, helplessness, and sadness (28). A meta-analysis published in 2017 reported a prevalence of 15.2% for any anxiety disorder and a rate of 22.9% for anxiety symptoms during pregnancy without any chronic diseases or pandemic (29). In another meta-analysis study, in which 15 studies conducted worldwide covering 11187 pregnant women in total were included, it was revealed that the rate of depression was 30%, and the rate of anxiety was 34% during the COVID-19 pandemic period (30). It is observed that the anxiety levels of pregnant women have increased during the COVID-19 pandemic period compared to the period before COVID-19. In this study, it was found that the participants responded to the items

about the effects of COVID-19 on their baby at a high rate of the option “true”. The inaccurate knowledge of pregnant women regarding the health of their children in the context of COVID-19 may be an important factor in their anxiety.

As in Turkey, women are disadvantaged in education and work environments due to the gender discrimination they experience in most societies, and unemployment in the process of conception and a pandemic fuel this situation for women. Low education and low socio-economic status among pregnant women are factors that affect their health-related behaviors and awareness levels (31, 32). In this study, it was found that the participants who were illiterate, those who were not working, and those who had less income than their expenses had significantly higher levels of COVID-19 anxiety. The lack of safe health-seeking behaviors among these pregnant women, their limited access to healthcare, and their limited knowledge of COVID-19 may have led to their anxiety due to uncertainty. Additionally, the participants of this study who had not received any information about COVID-19 had significantly higher levels of COVID-19 anxiety. It is believed that this situation may be related to the crisis environment caused by the pandemic and the fear of the unknown. Pregnant women around the world have been identified as among the most at-risk groups for the psychological outcomes of the COVID-19 pandemic (33). In this study, the participants who were in the last trimester of pregnancy and those who were not using regular medication (e.g., additional vitamins, minerals) had significantly higher levels of COVID-19 anxiety. This result was not surprising given the health risks brought about by the pandemic, as it is known that during the last trimester of pregnancy, women are more concerned about their child's health, they have fears about childbirth, and risky situations increase their anxiety about themselves and their baby (24). A similar conclusion was reached in the study conducted by Demir and Kılıç (2020) (27). Likewise, the Turkish Society of Obstetrics and Gynecology organized information meetings and published written documents related to prenatal monitoring and childbirth management to reduce anxiety in pregnant women (34).

It is important that nurses and midwives observe pregnant women more frequently during the pandemic period, especially toward the last gestational weeks, evaluate their feelings and thoughts, and take evidence-based initiatives to reduce negative emotions and ill-advised practices among these women. It has been reported that most pregnant women who have planned their childbirth before the pandemic are left alone due to transport problems and the risk of transmission to their families during pregnancy and childbirth due to mandatory restrictions, their birth planning is disrupted, and they are worried about these issues (10, 23, 25). In this study, it was observed that the participants who were considering changing their mode of delivery due to the pandemic had significantly higher levels of anxiety about COVID-19. In a systematic review, it was seen that 76.8% of 137 pregnant women preferred cesarean delivery during the COVID-19 pandemic period (35). It has even been reported that pregnant women want to start childbirth early or give birth by cesarean section due to the anxiety and stress they experience (23). It was argued that during the COVID-19 pandemic period, some pregnant women take precautions to protect themselves and their babies from this infection, which has a potential of mortality and a high risk of transmission (36). Considering that these conditions have a similar rationale, studies have also shown that pregnant women with concerns about being infected with COVID-19 prefer private medical institutions and cesarean section deliveries, which they find safer in terms of the risk of transmission at childbirth, so the number of vaginal births decreases (36, 37). This may lead to maternal and fetal health risks that pregnant women may face due to surgery when trying to avoid danger, as well as worsening the course of the disease in case of transmission (37).

Failure to provide the necessary social support in crisis periods such as the COVID-19 pandemic sets the stage for the anxiety of pregnant women who may not feel safe and could become lonely (38). In this study, it was found that the participants who felt vulnerable during the pandemic and those whose social support decreased had significantly higher levels of COVID-19 anxiety. Similarly, it has been reported that due to the pandemic, pregnant women do not feel social support because their relatives are not allowed in the maternity ward and due to the possibility of not being close to their family at the time of childbirth (23, 27, 38). It may be for this reason that the concerns of pregnant women about the process of childbirth are increasing (23, 27, 38). Linde and Siqueira (2018) stated that pregnant women are unable to control their lives, and they feel under pressure during the pandemic period (28). As seen

here, needs for healthcare and social support increase due to the growing concerns and problems that pregnant women experience during pregnancy and during the pandemic (25, 26, 39). According to the guidelines of WHO published in 2020, the incidence of COVID-19 in pregnant women is low, while pregnant women are closely monitored and supported by holistic care practices during the pandemic period, and the Association of Obstetrics and Gynecology recommends that the number of pregnancy follow-ups be limited to 6 between the 16th and 40th weeks of gestation (38, 40). However, most pregnant women delay routine health checks or even do not attend them unless they must, because they fear that they will contract COVID-19 on their way to or at a medical facility (10, 23, 25). In this study, it was found that the participants who received insufficient prenatal care had significantly higher levels of COVID-19 anxiety. It is believed that this condition occurs due to the physical and mental effects of the pandemic on pregnancy, as well as the insufficient satisfaction of the growing needs of women and neglect. This result highlights the importance for healthcare professionals to regularly monitor the health of pregnant women and their babies during prenatal care, inform women about the methods and effects of COVID-19 prevention, monitor their anxiety levels, and provide psychosocial support (24, 25, 26, 41). Due to concerns about the safety of pregnant women and their children, the constant use of alcoholic disinfectants and various antiseptics has posed a risk of poisoning. Additionally, some pregnant women have reported concerns that the pandemic could affect childbirth, postpartum breastfeeding, and infant care (23, 25, 26). In this study, it was determined that the participants who were worried that they or their child would contract COVID-19 during/after childbirth had significantly higher levels of COVID-19 anxiety. Demir and Kılıç (2020) reported that pregnant women's fears of dying due to COVID-19 were associated with high levels of anxiety (27). Considering the negative maternal, fetal, and neonatal consequences of anxiety during pregnancy, the importance of careful and adequate prenatal care and psychosocial support needs to be emphasized.

Limitations

A limitation of this study was that it was conducted in one of the eastern provinces of Turkey. Another limitation was that the study was conducted only in one health center.

CONCLUSION

As a result of this research, it was found that the variables such as education level, not using regular medication, income level, employment status, month of pregnancy, presence of social support systems, thinking that oneself or her baby will get Covid 19 infection during birth, and wanting to change the way of delivery preference affect the average score. In addition, it was determined that the presence of chronic disease did not affect the anxiety score.

In this study, anxiety levels were found to be higher in the participants who wanted to change their mode of delivery. For this reason, there is a need for studies to evaluate the mode of delivery preferences and delivery processes of women experiencing anxiety due to COVID-19. According to the results of this study, it may be recommended to provide training on COVID-19 to pregnant women and increase recommendations for the psychological health of pregnant women. Web-based training programs and web-based psychological support units can be established for pregnant women who cannot present to a health institution due to fear of infection.

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Author contributions: Study conception/design, critical revisions for important intellectual content, supervision, and data collection/analysis: ÖDY, FN, NB, MU; Drafting of the manuscript and statistical expertize: ÖDY, FN, NB, MU.

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RESEARCH ARTICLE

THE EFFECT OF HONEY THERAPY ON THE MANAGEMENT OF ORAL MUCOSITES IN HEAD AND NECK CANCER PATIENTS WITH CHEMORADIOTHERAPY: A RANDOMIZED CONTROLLED STUDY

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ABSTRACT

Purpose: The aim of our study is to examine the effect of honey treatment on oral mucositis management in patients with head and neck cancer receiving radiotherapy.
Material and Methods: The study was planned as a randomized controlled, single-blind, parallel group study. The study was conducted on 32 patients with 16 patients in each parallel group. Five data collection tools were used to collect the research data. Patient Identification Form , Researcher Mucositis Index, VAS- Pain, Honey Management Monitoring Chart (given to the patients in the treatment group). Oral Care Management Follow-up Form (given to the patients in the control group).
Results: The number of days with mucositis was similar in both parallel groups (Honey Group/Mean±SD: 14.88 ± 7.36, Bicarbonate Group / Mean ± SD: 14.38 ± 6.33). The average score of mucositis and score of pain between the groups is not statistically significant.
Conclusion: Honey application has not been found to be superior to bicarbonate mouthwash on the development and staging of oral mucositis.

Keywords: head and neck cancer , treatment – ınduced mucositis, pain and change in taste, honey

INTRODUCTION

Although head and neck cancers are not among the most important cancers in terms of epidemiological data, they are one of the complicated types of cancer that cause limitations in the daily lives of the patients depending on the disease process and the methods used in its treatment and negatively affect the quality of life (1). Head and Neck cancers were the seventh most common cancer worldwide, with approximately 930,000 new cases and 467,000 deaths annually, according to 2020 data from the GLOBOCAN study. Head and neck cancers are detected approximately three times more frequently in men than in women. The age-standardized incidence rates of head and neck cancers are 15.9 per 100,000 in men globally; it is 4.8 per hundred thousand in women (2). In our

Table 1. Baseline Characteristics at pretest between intervention and control groups

	Experiment: Honey (n=16)	**Control: Bicarbonate (n=16)**	**χ^2**	**P**
Age groups			3.529	0.060
45 years and under	5 (31.3)	1 (6.3)		
45 years and older	11 (68.8)	15 (93.8)		
Gender			1.689	0.194
Women	5 (31.3)	2 (12.5)		
Male	11 (68.8)	14 (87.5)		
Education level			0.613	0.736
Primary school	4 (25)	6 (37.5)		
Secondary School	8 (50)	7 (43.8)		
School / Faculty	4 (25)	3 (18.8)		
Body Mass Index (BMI)			2.032	0.154
18,5-24,9	9 (56.3)	5 (31.3)		
25 ve older	7 (43.8)	11 (68.8)		
Tumor area			3.639	0.162
Oral cavity	5 (31.3)	3 (18.8)		
Naso-oro-hypopharynx	10 (62.5)	8 (50)		
Larenx	1 (6.3)	5 (31.3)		
TNM phase			11.265	0.187
PT3N1	1 (6.3)	2 (12.5)		
T3N3AMx	3 (18.8)	3 (18.8)		
PT2N1	4 (25)	2 (12.5)		
T1N3M0	1 (6.3)	4 (25)		
Recurrence	0 (0)	1 (6.3)		
T2N2M0	3 (18.8)	0 (0)		
T1N0M0	1 (6.3)	0 (0)		
T1N2M0	0 (0)	1 (6.3)		
T4N1M0	3 (18.8)	3 (18.8)		
Systemic disease			1.412	0.235
Yes	3 (18.8)	6 (37.5)		
No	13 (81.3)	10 (62.5)		
Systemic disease classification			0.000	1.000
Hypertension	2 (12.5)	2 (12.5)		
COPD	2 (12.5)	2 (12.5)		
Diabetes Mellitus			7.863	**0.001***
Yes	0 (0)	5 (31.3)		
No	16 (100)	11 (68.8)		
The presence of a prosthesis			0.000	1.000
Yes	1 (6.3)	1 (6.3)		
No	15 (93.8)	15 (93.8)		
Smoking			0.000	1.000
Uses	3 (18.8)	3 (18.8)		
Not using	13 (81.3)	13 (81.3)		
Alcohol use			0.834	0.361
Uses	4 (25)	2 (12.5)		
Not using	12 (75)	14 (87.5)		
Dry mouth			0.000	1.000
Uses	6 (37.5)	6 (37.5)		
Not using	10 (62.5)	10 (62.5)		
Decreased taste			6.578	**0.010***
Uses	1 (6.3)	7 (43.8)		
Not using	15 (93.8)	9 (56.3)		

Table 1. Continue

Nutritional support			0.000	1.000
Uses	3 (18.8)	3 (18.8)		
Not using	13 (81.3)	13 (81.3)		
Fluid consumption			0.238	0.625
1000 -2000ml	2 (12.5)	3 (18.8)		
More than 2000 ml	14 (87.5)	13 (81.3)		
	Mean±SS	**Mean±SS**	**Z**	**P**
Age	55.38 ± 15.75	59.06 ± 9.57	-1.095	0.287
BMI	24.31 ± 4.22	27.5 ± 4.47	-1.929	0.056
Daily radiation dose	2.04 ± 0.05	2.06 ± 0.05	-1.046	0.381
Total radiation Dose	67.38 ± 3.77	65.06 ± 4.3	-1.529	0.149
Peformance point	87.5 ± 4.47	89.38 ± 4.43	-1.153	0.423

age-standardized incidence rates of head and neck cancers are 14.7 per hundred thousand in men; in women, it was found to be 3.1 per hundred thousand (3).

Patients receive radiation therapy involving the head and neck region for six weeks, thus the mucous membranes in mouth are affected. As oral, pharyngeal and laryngeal mucosa are exposed to ionizing radiation, in the second or third week, ulceration occurs in the epithelial tissue, oral mucosa swells, mouth-throat area aches and dries. Its incidence among patients receiving chemotherapy and radiotherapy reaches 80%.5 50% of the patients who receive radiotherapy treatment to the head and neck area experience 3rd stage mucositis (4-5).

Ulcers caused by damage to the oral mucosa pose a serious risk for bacterial contamination and systemic infection (6). It is very painful, makes speech difficult, affects chewing, swallowing, and oral intake of medicines. Additionally, oral mucositis increases the patient's hospital stay, treatment costs, use of narcotics to control pain, and parenteral nutrition as well, while worsening the quality of life of the patient. The correct management of oral mucositis means to take preventive approaches in a timely manner and to minimize the patient's distress by providing pain assessment and management (7). In addition to the granulocyte monocyte colony stimulating factor, topical corticosteroids used in mucositis management, honey is reported to be an effective approach to prevent oral mucositis (6, 8-12). Honey has been used since the Egyptian civilization, it is used in modern medicine for burn wounds, oral infections and surgical wound healing. It has antibacterial properties and accelerates the wound healing by increasing epithelization (5). The reason for using honey to manage radiation mucositis is its rapid epithelization effect in tissue injuries (5-6,13). The use of honey to manage radiation mucositis is its rapid epithelializing effect in tissue injuries. Bergman et al. he observed accelerated wound healing when unboiled honey was applied topically and theorized that this effect might be due to its energy generating properties, hygroscopic effect on the wound and bacteriostatic effect. There are studies in the literature stating that honey does not prevent mucositis, but reduces the severity of mucositis (8, 14-15). In a meta-analysis study, it is stated that it reduces the development of mucositis by 80% (8). Therefore, the aim of this study is to investigate the effect of honey therapy on oral mucositis management in patients with head and neck cancer receiving radiotherapy.

Study hypotheses

This trial was designed to test the following hypotheses:

1. Regular oral care with a standard oral care protocol (oral care solution with sodium bicarbonate) influences the healing of oral mucositis in patients with head and neck cancer receiving radiotherapy treatment.
2. Honey administration influences healing of oral mucositis in patients with head and neck cancer receiving radiotherapy treatment.

MATERIAL AND METHODS

Study Design

The study was conducted as a randomized single-blind parallel group study in patients with head and neck cancer.

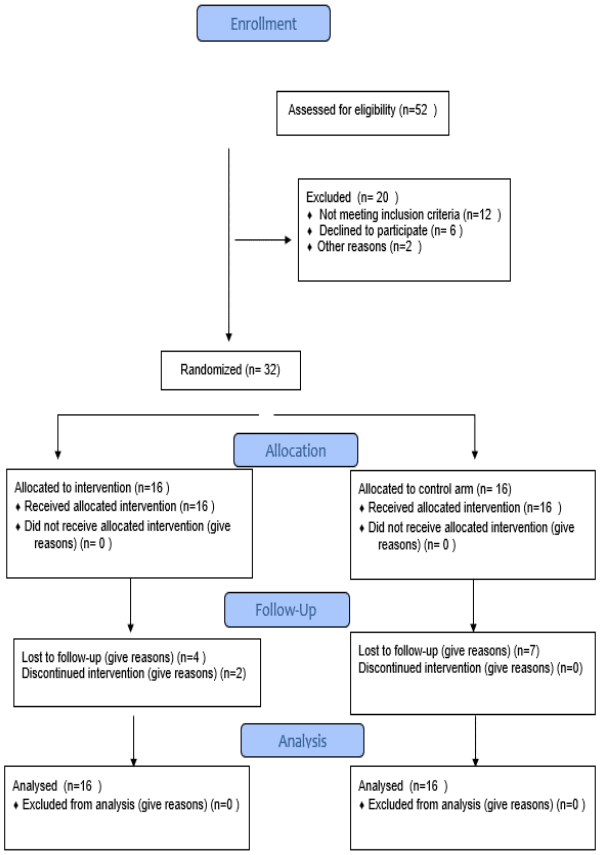

Figure 1. The flow Consort 2010 diagram of the study

Setting

The research was conducted a University Radiation Oncology Outpatient Clinic between February 2018 and March 2020. Head and neck cancer patients received radiation therapy at the clinic throughout the week except for Saturdays and Sundays, and their controls continued since the beginning of the treatment and throughout the process.

Recruiting, Randomisation and Masking

Patients were recruited by the consultants in radiation oncology based on predetermined inclusion and exclusion criteria. The patients included in the study were randomized by considering gender, age, smoking, primary tumor area, general health and radiotherapy dose, number of chemotherapy cycles (16-18). Consultants also obtained the informed consent by the eligible patients. The patients were randomised from the beginning of the treatment to either the intervention or the control arm by implementing simple randomisation using the envelope method. Based on this method, a pack of sealed envelopes including a card with either the word 'intervention arm' or 'control arm' written inside, was given to each patient after the agreement to participate to the study. Depending on which card was selected by the patients, they were allocated to the respective arm. He cares providers and those assessing outcomes were unaware of which arm the patient belonged to. In the study, it was planned to include 70 patients, 35 patients in each group, who met the selection criteria to reach 80% sampling power at a significance level of 5%.

Sample Size

Sample size calculation was performed by using G Power package version 3.1. A sample size of 32 (16 participants in each arm) was sufficient to identify an effect size of Cohen d= 1 with a statistical power 80% and 5% level of statistical significance (7-8). Data were collected over a 24-month period (February 2018 and March 2020).

Participants (Inclusion and Exclusion Criteria)

Selection criteria: Voluntary patients with head and neck cancer who had radical and/or adjuvant chemoradiotherapy indication, who were aged over 18, who were communicable, who had malignancy on oral cavity, pharynx (nasopharynx, oropharynx, hypopharynx) and larynx, who had TNM staging T 1-2 other than glottic laryngeal cancer, who had no hypersensitivity to bicarbonate oral care solution and honey, who had a Karnofsky performance scale of 70 and above, 22 who had a directly visible oral/oropharyngeal area in the area where the radiation is received (soft palate, tongue and mouth floor), who had normal liver and kidney functions, who had normal haematological values (hemoglobin>10 g/dl, thrombocyte>100.000mm3, leukocyte>3000 mm3), and who were mentally competent were selected to participate in the study (6).

Exclusion criteria: Patients with conditions such as unhealed wound in the oral cavity and oropharynx, sensitivity and poor oral hygiene, early stage glottic laryngeal cancer (T1-2), previously receiving chemotherapy or radiotherapy for upper respiratory tract, fasting blood glucose>150mg/dl, comorbidity such as diabetes or connective tissue diseases, were excluded from the sample (6, 18).

Intervention and Procedures

In the study, patients in the treatment group used honey; patients in the control group used sodium bicarbonate. All patients included in the study were

Table 2. Seven (7) weeks compared between groups of received measurements mucositis

	Experiment: Honey (n=16)	**Control: Bicarbonate (n=16)**	**χ^2**	**P**
Week - 1			1.588	0.452
No mucositis	13 (81.3)	13 (81.3)		
Painless ulcers, mild pain	2 (12.5)	3 (18.7)		
Edema, ulcers, can eat	1 (6.2)	0 (0)		
Week - 2			0.431	0.806
No mucositis	9 (56.3)	9 (56.3)		
Painless ulcers, mild pain	6 (37.5)	5 (31.3)		
Edema, ulcers, can eat	1 (6.2)	2 (12.4)		
Week - 3			9.874	**0.020***
No mucositis	1 (6.3)	8 (50)		
Painless ulcers, mild pain	10 (62.5)	4 (25)		
Edema, ulcers, can eat	4 (25)	2 (12.5)		
Erythema, edema, ulcers cannot eat	1 (6.2)	2 (12.5)		
Week - 4			0.840	0.840
No mucositis	3 (18.8)	5 (31.3)		
Painless ulcers, mild pain	7 (43.8)	5 (31.3)		
Edema, ulcers, can eat	4 (25)	4 (25)		
Erythema, edema, ulcers cannot eat	2 (12.4)	2 (12.4)		
Week - 5			3.430	0.330
No mucositis	2 (12.5)	5 (31.3)		
Painless ulcers, mild pain	4 (25)	6 (37.5)		
Edema, ulcers, can eat	8 (50)	4 (25)		
Erythema, edema, ulcers cannot eat	2 (12.5)	1 (6.2)		
Week - 6			2.076	0.557
No mucositis	4 (25)	6 (37.5)		
Painless ulcers, mild pain	3 (18.8)	5 (31.3)		
Edema, ulcers, can eat	7 (43.8)	4 (25)		
Erythema, edema, ulcers cannot eat	2 (12.4)	1 (6.2)		
Week - 7			1.322	0.516
No mucositis	4 (25)	7 (43.8)		
Painless ulcers, mild pain	6 (37.5)	5 (31.2)		
Edema, ulcers, can eat	6 (37.5)	4 (25.0)		
	Mean±SS	**Mean±SS**	**Z**	**P**
Number of days with mucositis	14.88 ± 7.36	14.38 ± 6.63	-0.133	0.894

* Significant at the 0.05 level; Likelihood ratio test.

instructed to rinse with mouthwash solutions recommended by the clinic for 1 minute, 4 times a day, every 6 hours (4x1), after each meal. In both groups, detailed information was given on adequate fluid intake, high protein dietary intake, avoidance of alcohol, spicy and acidic foods, and the importance of oral care. In parallel groups in the study, patients were admitted at the same time, the patient selection was planned appropriately and randomly assigned to the groups. Since the study is a single blind study, the nurse who evaluated the mucositis did not have information about which group the patient was in. Patients in the control group were instructed to perform oral care with 20 ml of bicarbonate oral care solution given in addition to the mouthwash solutions recommended by the clinic before and after the treatment and before going to bed. The patients in the treatment group receiving honey therapy received 20 ml honey for using it 15 minutes before and after radiotherapy treatment and 6 hours (before going to bed at night) to sweep the entire oropharyngel mucosa for an average of 2 minutes and swallow slowly (Biswal et al., protocol).

This practice was continued as long as radiotherapy continued (6-7 weeks) (5-6, 18, 20). At other times, it was reminded to continue oral care with the oral care solution recommended by the clinic. It was explained in detail to the person that the oral care with honey

Table 3. Comparison of pain, taste and weight change mucositis measurements within and between groups

	Experiment: Honey (n=16)		Control: Bicarbonate (n=16)		Comparison between groups	
	Mean±SS	**Median (%25-%75)**	**Mean±SS**	**Median (%25-%75)**	**Z**	**P**
Pain						
Week - 1	1.44 ± 2.22	1 (0 -1.5)	0.5 ± 1.1	0 (0 -0,5)	-1,728	0,128
Week - 2	2.06 ± 1.95	2 (0 -3)	0.38 ± 0.72	0 (0 -0,5)	-2,880	**0,007***
Week - 3	2 ± 1.63	2 (1 -3)	1.25 ± 1.34	1 (0 -2)	-1,318	0,210
Week - 4	2.25 ± 1.88	3 (0 -4)	1.63 ± 2.03	0,5 (0 -3)	-1,060	0,323
Week - 5	2.63 ± 2.03	3.5 (0 -4)	1.5 ± 2.13	0 (0 -3)	-1,685	0,110
Week - 6	2.69 ± 2.6	3 (0 -4.5)	1.44 ± 1.79	1 (0 -2,5)	-1,381	0,184
Week - 7	2.69 ± 2.36	2 (1 -4)	1.31 ± 1.78	0,5 (0 -2)	-1,938	0,061
Intragroup comparison	χ^2=10.587. P=0.102		χ^2=12.923. P=**0.044***			
Taste						
Week - 1	1.63 ± 1.45	1 (1 -1)	1.25 ± 0.58	1 (1 -1)	-0,221	0,897
Week - 2	1.88 ± 1.36	1 (1 -2)	2.06 ± 1.06	2 (1 -3)	-0,908	0,402
Week - 3	3 ± 1.46	3 (1.5 -4)	2.69 ± 1.54	2,5 (1 -4)	-0,599	0,564
Week - 4	3.31 ± 1.35	3.5 (3 -4)	3.06 ± 1.44	3 (2 -4)	-0,484	0,642
Week - 5	3.69 ± 1.35	4 (3 -5)	3.19 ± 1.52	3,5 (2 -4,5)	-0,913	0,381
Week - 6	3.44 ± 1.31	3.5 (3 -4.5)	3 ± 1.63	3 (1 -4,5)	-0,697	0,515
Week - 7	3.13 ± 1.15	3 (3 -4)	2.5 ± 1.46	2,5 (1 -3,5)	-1,332	0,210
Intragroup comparison	χ^2=36.389. P=0.001		χ^2=35.685. P=0.001			
Weight change						
Before treatment	70.94 ± 13.39		80.19 ± 14.94		-1.644	
After treatment	66.56 ± 12.88		75.56 ± 13.97		-1.622	
Intragroup comparison	Z: -3.550. p: 0.001*		Z: -3.530. p: 0.001*			

* Significant at the 0.05 level; Comparison between groups Mann Whitney u test. Intragroup comparison Wilcoxon test, SS: Standard deviation.

should be applied only on the days of radiotherapy and continued for 6-7 weeks during the treatment.

Questionnaire description

The data in the study were collected by five data total tools, including Patient Identification Form, Researcher Mucositis Index, VAS- Pain, Honey Management Monitoring Chart (given to the patients in the treatment group), Oral Care Management Follow-up Form (given to the patients in the control group).

Patient Identification Form; prepared based on literature includes the sociodemographic data of the patient and the data related to the patient's health diagnosis (The patient's diagnosis, systemic diseases, oral prosthesis, decayed teeth, periodontal diseases, regular tooth brushing habits, regular oral examination habits, dry mouth and taste. condition, oral hygiene status, daily fluid consumption) (5-6).

Karnofsky Performance Scale; is used to evaluate the general well-being of cancer patients. The condition of the individual is evaluated between 0-100 points. A score of 100 indicates very good health and a score of 0 indicates death. In 1949, Dr. Joseph H. Burchenal and Dr. David A. Karnofsky designed a scale according to which individuals with score 70 or higher are considered to have sufficient functional capacity (21). Patients with Karnofsky performance score of 70 and above were included in our study. Questionnaire Form for Assessing Mucositis, Pain and Nutrition Status of the Patient; In the study, the World Health Organization's Common Toxicity Criteria (CTC) mucositis grading system was used in the evaluation of mucositis.

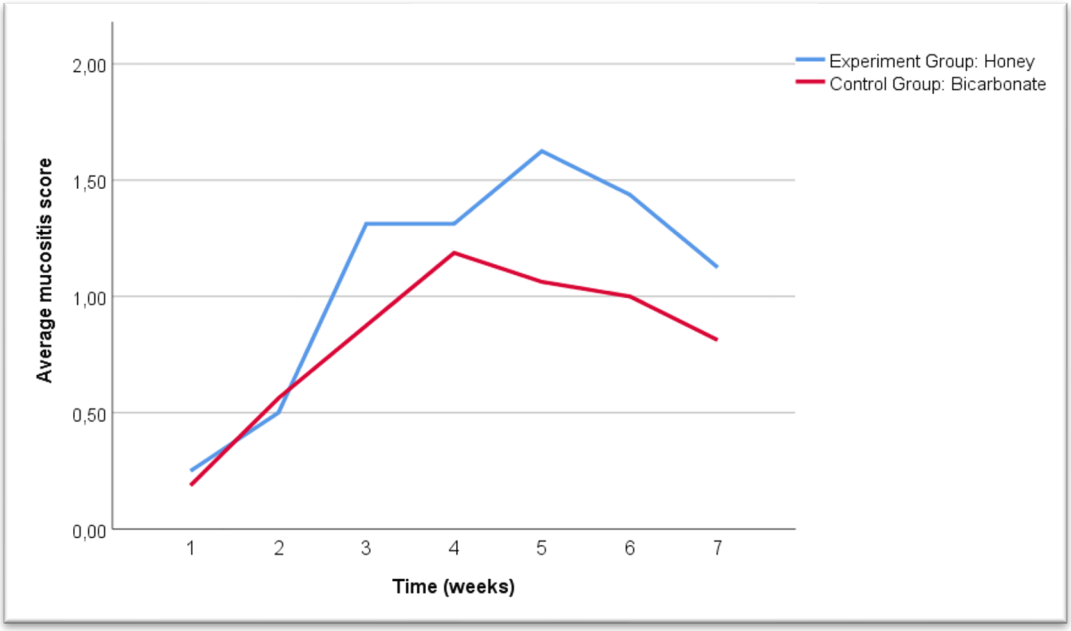

Figure 2. Line graph for variation of mean Mucositis score over time and groups

The scale, measurements wereas follows: 0 indicated no mucositis, 1 slight degree of mucositis, 2 moderate degree of mucositis, 3–4 indicated severe mucositis. WHO MAIis widely used at clinics for cancer patients to assess the degree of mucositis. Evaluation of the oral mucosa was performed by the investigator once a week, usually on Thursdays, when the patient came to the radiotherapy session. Since the total treatment period of patients was 6-7 weeks, a total of 7 measurement values were obtained for one patient. In case of intolerable mucositis, the number of days in which treatment could not be received was calculated. In addition, the pain in the mouth due to the formation of mucositis was evaluated with a visual analogue scale between 0 and 10, and the taste status was evaluated between 0 and 5. Pain was evaluated as 0: No pain, 1-3: Mild pain, 4-6: Moderate pain, 7-10: Severe pain; the taste perception was evaluated as 1: Good, 2-3: Moderate, 4-5: Bad (21). The nutritional status of the patients was evaluated according to the solid / liquid food intake and the use of nutritional support in the last 24 hours.

Honey Management Monitoring form was prepared to control the honey intake during the days / weeks of radiotherapy in order for the patient to perform his own monitoring. It was used only in patients in the treatment group.

Oral Care Management Follow-up Form was prepared to control the oral care application during the days / weeks of radiotherapy in order for the patient to monitor himself. It was administered to patients in both the control and treatment groups.

Quality Control of Honey

The chemical composition, pH, density and viscosity analysis of the honey to be used in the treatment of the patients were examined and assistance was received from Ege University Drug Development and Pharmacokinetics Research Application Center Research Clinic for chemical analysis. Before the study, it was planned to conduct aerobic cultures and candida colonization tests from the areas where infection was detected to examine the anti-microbial effect of honey on the oral mucosa of the patients, but no infected oral mucosa was encountered during the research process.

Application of Data Collection Tools

The data were collected face to face by the researchers. The researchers evaluated the patient's mouth in terms of oral mucosal tissue, color and moistness, formation of mucositis signals, pain in the oral mucosa, sense of taste and nutritional status.

Data Analysis

Compliance of numerical data with normal distribution was evaluated using the Shaphiro Wilk test. Mann Whitney U test was used to evaluate non-normally

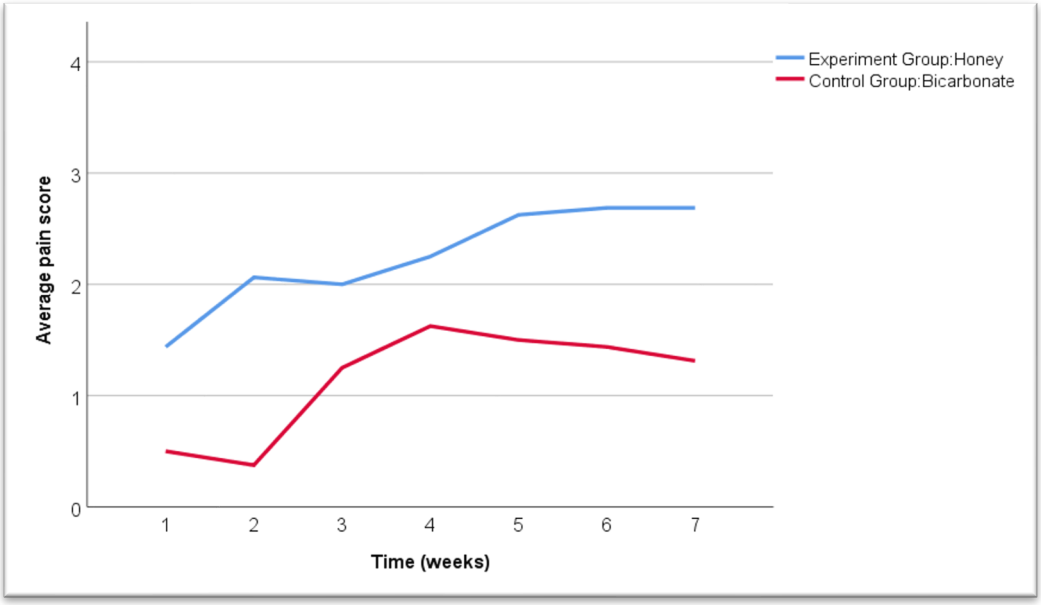

Figure 3. Line graph for the variation of the average Pain score over time and groups

distributed variables, and Freidman and Dunn multiple comparison tests were used to evaluate changes at 7 different times. Mean±standard deviation values were given for numerical variables, numbers and percentages were given for categorical variables. SPSS windows version 24 was used in the analyzes and a p value less than 0.05 was considered significant.

Ethical Considerations

During the planning of the study, necessary permissions were obtained from a Dokuz Eylul University Research and Application Hospital, and Department of Radiation Oncology where the study was carried out. The study was approved by Dokuz Eylul University, Clinical Research Ethics Committee (Date: 28.12.2017, Decision No: 2017/22-03). Written and verbal consent of the individuals included in the study was taken.

RESULTS

The sample was consisted of 26 men and 7 women with an age range from 32 to 87 years. Patients were diagnosed with various types of cancer in head and neck region including laryngeal, nasopharyngeal, hypopharyngeal, oral cavity. No statistically significant difference in relation to the cancer type of individuals in both arms was found. The 32 patients were randomized equally in the two arms (Fig. 1). Diabetes Mellitus was found in 27 patients in the study. Of the patients who meet the selection criteria, 26 interventions and 11 are used in the control group. Table 1 showed the good randomization between the two arms regarding clinical and demografic charecteristics of the partipicipants. A significant difference was observed between the experimental and control groups in terms of the presence of diabetes and decreased taste. In the control group, both the frequency of patients with diabetes and the frequency of patients with decreased sense of taste were found to be significantly higher. The groups show a balanced distribution in terms of other variables. When compared numerically, no significant difference was found between groups in terms of age and BMI. The daily, total radiation dose and performance scores were similar in the groups.

Except for the mucositis measurement taken at the 3rd week, there was no significant difference between the groups. No significant difference was observed between the groups in terms of the number of days with mucositis (Table 2).

While the pain measurements obtained in the second week were significantly higher in the experimental group (P = 0.007), there was no significant difference in the measurements in the other weeks and in the weekly measurements within the group. It was found that taste measurements increased as time progressed, but there was no significant difference between the groups in terms of measurements. Significant reduction in weight was observed in both

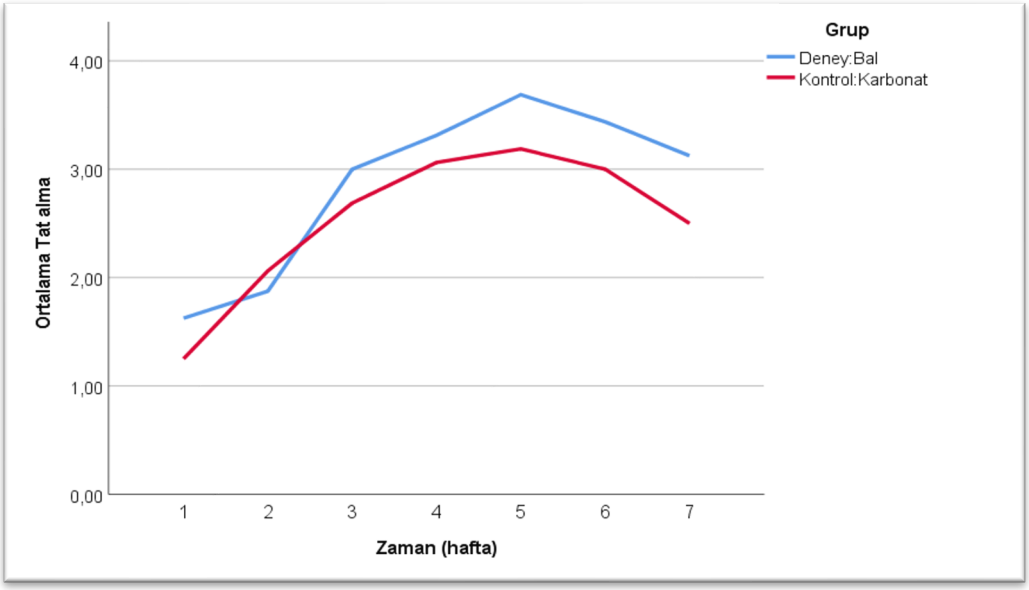

Figure 3. Line graph for the variation of the average Taste Score over time and groups

experimental and control groups after treatment. However, there was no significant difference between the groups before and after the treatment. This shows that the weight change is similar between the 2 groups (Table 3).

Below average mucositis, line charts for the change in pain score and take time to enjoy and groups are given.

- The average score of mucositis between the groups is not statistically significant (p> 0.05, Figure 2).
- The average pain score between the groups is not statistically significant (p> 0.05, Figure 3)
- The average taste score between the groups is not statistically significant (p> 0.05, Figure 4)

DISCUSSION

In our study we planned to evaluate the effect of honey on the healing process of oral mucositis due to radiation; the use of honey in oral care for oral mucositis management was not found superior to bicarbonate. In this context, the H1 hypothesis, which is one of our research hypotheses, "Regular oral care with a standard oral care protocol (oral care solution with sodium bicarbonate) has an effect on the healing of oral mucositis in patients with head and neck cancer receiving radiotherapy treatment." is accepted. There are studies in the literature with similar results (22-25). In MASCC / ISOO guidelines, patients are recommended to use a soft toothbrush as well as mouthwash with sodium bicarbonate and saline in oral care (25). In clinical practice, 0.9% saline solution, sodium bicarbonate and saline + sodium bicarbonate mixture (1 teaspoon of salt and 1 teaspoon of sodium bicarbonate in a glass of boiled cooled water) are cheap and easy-to-reach agents, so their use is recommended in oral care protocols (26). Maintaining good and regular oral hygiene is one of the main factors in reducing the reaction and severity of radiation on the mucosa (27). However, our result is not compatible with other studies that found the use of honey effective in the management of mucositis in patients with head and neck cancer, similar to our study (6-10, 14-15). This may be due to the small number of patients included in the study sample. Concordantly, one of our research hypotheses, H2 hypothesis, “Honey administration has an effect on healing of oral mucositis in patients with head and neck cancer receiving radiotherapy treatment.” is reject. In addition, the number of days with mucositis was similar in both groups, and the use of honey had no effect on the number of days with mucositis. However, in the study of Bulut & Tüfekçi (2016), it is stated that the use of oral care and honey together shortens the healing time of mucositis and reduces pain. In this context, the result of the study is incompatible with the literature (11).

The formation of oral mucositis may be affected by some variables. Age of the patient, poor oral hygiene, gender differences, genetic factors, alcohol & tobacco

use, renal and hepatic dysfunctions, oral care habits, body mass index, location of the tumor, hematological status, treatment plan and type, high dose chemotherapy and total body irradiation, dose and duration of treatment are among the factors affect the development of oral mucositis (9-10, 14). Factors that pose a risk and increase the susceptibility to bacterial colonization such as the patient's current oral conditions, dental caries, periodantal changes, pulpitis and xerostomia should be eliminated from the patient as much as possible during the treatment process (27). In our study, it was found that both groups showed a balanced distribution with regards to the above-mentioned variables. When compared numerically, there was no significant difference between the groups regarding age and BMI and the total daily radiation dose and performance scores were similar in the groups. In addition, it was observed that there was no significant difference in weight between the groups before and after the treatment, but a significant weight loss was experienced in both groups after the treatment. This shows that individuals receiving radiation therapy to the head and neck region should focus on the individuality and integrity of care. In the literature, malnutrition prevalence is observed in 44-88% of patients with head and neck cancer; It is stated that the eating problems that occur negatively affect the physical, psychological, social and existential structure of the person, and the importance of starting additional nutritional supplements and informing the patient and family on this issue is emphasized (28-29). It is included in the variables in which the difference was observed between the experimental and control groups in our study. In the control group, the frequency of patients with both diabetes and decreased sense of taste was found to be significantly higher. This may be due to the fact that patients with diabetes were included in the control group. At the same time, one of the long-term complications of diabetes is neuropathy. Besides, one of the long-term complications of diabetes is the development of neuropathies. Neuropathies in the nerves that transmit the sense of taste can cause taste disturbance in diabetic patients. In addition to diabetes, additional radiation therapy can cause salivary gland dysfunction and xerostomia, resulting in taste disturbance (30). In this context, it is important to carefully diagnose diabetic individuals who will receive radiation therapy to the head and neck region in terms of taste changes, loss of appetite (or anorexia) and weight loss, and management of this. In the current study, it was found that the analgesic use of the individuals in the treatment group and the pain measurements obtained in the second time measurement were significantly higher than the control group. However, since the groups are distributed in a balanced way in terms of variables, the exact reason for this is not known, and thought that it may be due to individual differences. According to literature, reasons such as decreased salivary secretion, decreased but concentrated salivary secretion, dry mouth and mucositis, decreased pharyngeal flexibility and peristalsis in patients with head and neck cancer who receive chemoradiotherapy trigger pain when swallowing and bring along increased use of analgesics (31). In this case, patients should be followed up in terms of late complications while the treatment process continues and in the following period. In our study, when the pain levels in all time intervals were checked, the differences occurred in the treatment and control groups at the same place at the 2nd and the 5th time. A borderline significance was also detected in the control group. Changes in these time intervals may occur due to the reason mentioned above. Oral mucositis usually begins in the second week of treatment in patients receiving radiotherapy. Chemotherapy combined with radiotherapy increases the release of nuclear factor -kB (NF-kB) known as pro-inflammatory responsible for mucosal toxicity. This causes the activation of tumor necrotic factor, interleukin 6, interleukin-beta, leading to destruction in the endothelial layer and connective tissue and disrupting of mucosal integrity. At the same time, the molecular pathway activates exacerbating mucosal destruction and ulcerations. Mucositis continues in a few weeks after the end of radiotherapy (26,31). This physiological process explains the cause of pain occurring in the 2nd and 5th time periods in both groups in our study. Kong et al. (2016) found that the use of honey delayed the onset of mucositis and decreased the pain score (22). However, no similar result could be reached in our study. The number of days with mucositis was similar in both groups and the use of honey did not have a significant effect on the number of days with mucositis.

Limitations of the Study

The limitation of the study is that it was conducted in a single hospital.

CONCLUSION

In our study, the use of honey was not found superior to the use of bicarbonate in head and neck cancer patients receiving radiotherapy in terms of the prevalence of mucositis and the grading of mucositis. In future studies, it may be suggested to increase the sample size and to conduct the study in a multi-centered manner.

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Analysis and/or interpretation: Ö.U, Literature Search: Ö.U., E.K., Writting: Ö.U, E.K, Critical Review: Ö.U, F.A.
Conflict of interests: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.
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RESEARCH ARTICLE

ARE THYROID AND SEX HORMONE RATIOS PREDICTIVE OF BREAST CANCER RISK? A PRELIMINARY STUDY AMONG A COHORT OF SRI LANKAN BREAST CANCER PATIENTS

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ABSTRACT

Purpose: The association of thyroid related diseases and sex hormones with breast cancer (BC) is reported with inconclusive results. The study was designed to analyse the thyroid/sex hormone ratios of BC patients.
Material and Methods: TSH, T3, T4, estrogen, progesterone and testosterone concentrations of newly diagnosed breast cancer patients (n=155) aged 30 to 75 years and age-matched normal controls (n=75) were analyzed. Thyroid: sex hormone ratios were calculated. Data on history of thyroid related diseases were collected.
Results: History of thyroid related diseases was significantly higher ($p<0.05$) in breast cancer patients compared to controls. Among the remaining, subclinical hyperthyroidism was found in 14%, but only 7% in healthy women. Significantly higher ($p<0.05$) mean T3 and T4 values and lower TSH levels were observed in patients with breast cancer when compared to healthy. Serum testosterone was significantly low among BC patients. Considering the thyroid to sex hormones ratios among postmenopausal women, T3/testosterone, T4/testosterone, T3/estrogen, T4/ estrogen, ratios were significantly different compared to healthy and the highest significance was found with T3/testosterone. Cutoff values studied from receiver operative characteristic curves indicated that a woman having T3/testosterone above 7.47 showed 12.5 times odds ($p=0.000$) of being diagnosed with BC.
Conclusion: The present study concludes that the incidence of thyroid related diseases is higher among Sri Lankan BC patients and elevation of T3/testosterone ratio is indicative of BC.

Keywords: breast cancer, sex hormones, thyroid hormones, thyroid/sex hormone ratios

INTRODUCTION

The impact of hyper and hypothyroidism on breast cancer (BC) is researched with inconclusive results. Some studies disclose profound effects of hyperthyroidism on BC cell proliferation (1). Some portray association between hypothyroidism and BC (2). The thyroid disease incidence is higher among BC patients when compared to apparently healthy individuals. Significantly high mean T3 and T4 and low TSH values in postmenopausal BC patients when

compared to controls implicate an association of hyperthyroidism and BC (3). Free T3 and T4 concentrations were higher in BC patients when compared to controls and benign breast tumors [4]. A dose-response positive association of T3 with the risk of BC exists with no such association between TSH and BC in postmenopausal women (5). In addition, T3 levels positively associate with invasive BC (6). In contrast, hypothyroidism and low-normal T4 are related with an increased risk of BC in post-menopausal women (2). In contrast to both above observations, some studies report unaltered thyroid profiles in BC women (7). Thyroid disorders such as hypothyroidism, hyperthyroidism or autoimmune thyroiditis did not have a higher incidence in BC patients or patients with benign breast tumors [4]. A negative correlation between TSH and T3 is seen in early BC but not in advanced BC (8). Thus, the exact impact of thyroid hormones in BC development and progression is not recognized (5).

Substantial changes in the expression of thyroid hormone receptors suggest a possible deregulation that could trigger BC development (9). Estrogen like effects of thyroid hormones are suspected to be impacting BC development (10). T3 is believed to promote BC cell proliferation and increase the effect of estrogen on cell proliferation in some BC cell lines indicating the role of T3 in BC development and progression (11). Similarly postmenopausal BC patients have significantly increased thyroid hormone/ estrogen ratios suggesting a possible tumor growth promoting effect due to the misbalance of the hormones (3). However, data on distribution of thyroid to sex hormones of BC patients is not reported.

Thus, this study was designed to analyze the incidence of thyroid related diseases and to analyze the thyroid profiles (TSH, T3 and T4), sex hormones of BC patients and compare with apparently healthy females. Attempts will be made to assess any significant associations with thyroid hormone / sex hormone levels in developing BC among Sri Lankan BC patients.

MATERIAL AND METHODS

Study Sample

The research is a cross-sectional study. Newly diagnosed female BC patients (n=155) who have not had any treatment for breast cancer (surgery, chemotherapy, radiotherapy) were identified from Apeksha Hospital (National Cancer Institute, Maharagama). Age matched apparently healthy females (n=75) were selected for the comparative study. Informed written consent was obtained from all participants before engaging in the study. Data on history of thyroid related diseases, menopausal status, hormonal contraceptive usage and hormone replacement therapies for any clinical condition were collected using an interviewer administered questionnaire.

Thyroid Profile

Venous blood samples from patients who have not undergone treatment for cancer or who have not had hormonal contraceptives/ any hormonal treatments six months before the diagnosis of carcinoma were collected. Blood samples of apparently healthy age matched females those who were not on any hormonal treatment were collected. Thyroid profile (T3, T4 and TSH) was analyzed using an enzyme immunoassay method with final fluorescent detection using MINI VIDAS analyzer (Biomerieux, France) using the separated serum.

Thyroid Stimulating Hormone (TSH)

Serum (200 µL) was introduced to sample well in the strip containing alkaline phosphatase-labeled monoclonal anti-TSH immunoglobulins [mouse], wash buffer [tris, NaCl, tween and sodium azide and substrate [4-methyl-umbelliferyl-phosphate, diethanolamine and sodium azide] and SPR coated with monoclonal anti-TSH immunoglobulins (mouse) were used for the detection.

Free Triiodothyronine (FT3) and Free Tetraiodothyronine (FT4)

Serum (100 µL) was introduced to the sample well. The reagent wells contained alkaline phosphatase labeled T3 derivative or T4 derivative and similar components as for TSH. The SPR had anti-T3 antibodies [rabbit] or anti T4 antibodies [rabbit]. The conjugate enzyme catalyse hydrolysis of substrate in to 4-methyl-umbelliferone of which the fluorescence was measured at 450 nm.

Sex Hormones and Ratios of Hormones

Serum estrogen, progesterone and testosterone levels of the same study sample were measured using MINI VIDAS immune analyzer (Biomerix, France) and thyroid/sex hormone ratios were calculated (12).

Table 1. Thyroid profile of breast cancer patients and apparently healthy females

Test		BC (n= 139) Mean± SD	AHW (n=75) Mean± SD	Reference ranges[1]
TSH (mIU/L)	Premenopausal	2.39 ± 1.87[a]	3.31 ± 1.98[a]	0.4-4.5
	Postmenopausal	2.34 ± 2.30[a]	3.03 ± 2.65[a]	
	All	2.38 ± 1.88[a]	3.19 ± 2.65[a]	
FT3 (pg/mL)	Premenopausal	2.64 ± 0.43[b]	2.47 ± 0.47[c]	2.08-6.74
	Postmenopausal	2.59 ± 0.41[b]	2.32 ± 0.43[c]	
	All	2.61 ± 0.41[b]	2.35 ± 0.33[c]	
FT4 (ng/dL)	Premenopausal	1.18 ± 0.30[d]	1.00 ± 0.37[f]	0.8-2.3
	Postmenopausal	1.13 ± 0.28[d]	0.97 ± 0.41[f]	
	All	1.16 ± 0.25[d]	0.99 ± 0.25[f]	

BC: Patients with breast cancer, AHW: apparently healthy women. Different superscripts in each row indicate significant differences ($p<0.05$) among hormones at each phase among breast cancer and apparently healthy females; TSH- serum thyroid stimulating hormone 3rd generation; FT3- serum free triiodothyronine; FT4- serum free tetraiodothyronine; 1Manual on Standard operation procedure, sample collection and reference range for clinical chemistry, World Health Organization, Ministry of Health and the Department of Biochemistry, Medical Research Institute, Sri Lanka

Statistical Analysis

Statistical data analysis was carried out using SPSS version 16.0 (2007, SPSS for Windows, SPSS Inc., Chicago, IL, USA) package. The quantitative data with skewed distribution were presented as median (Inter quartile range). The qualitative data were expressed by calculating the frequency and percentage. P value of less than 0.05 ($p<0.05$) was considered significant. Non-parametric significances were analysed by Mann-whitney U test. Correlations of parametric and non-parametric data were analysed by Pearson and Spearman test respectively. Receiver operative characteristic (ROC) curve was plotted for determination of cut off values of some selected biochemical parameters.

Ethical Approval and Informed Consent

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical clearance for the study was obtained from Ethics Review Committee, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka (Date: 07.11.2012, Number: 651/12/02; Date: 02.08.2014, Number: 28/14). The approval for registering patients and accessing histopathology data were obtained from the Director of National Cancer Institute, Maharagama, Sri Lanka. Informed written consent was obtained prior to enrolling participants.

RESULTS

Incidence of Thyroid-Related Diseases

Among breast cancer patient's majority were (63%) postmenopausal women with an average age of 63±7 years at the diagnosis of the carcinoma. Among the patients 10% (n=16) reported a history of thyroid related diseases and 6 were on medication for different thyroid related disorders. BC patients with known thyroid dysfunctions and the patients who were on hormonal contraceptives within the past six months before the diagnosis of carcinoma were excluded from the study. Serum TSH, T3 and T4 levels of remaining patients and of apparently healthy age matched females were analyzed (Table 1). Subclinical hypothyroidism was observed to be 14%

Table 2. Thyroid hormone/sex hormone ratios of postmenopausal breast cancer and apparently healthy women

Ratio	BC (n=97) Mean ± SD	AHW (n=45) Mean ± SD
T3/ Estrogen	0.20 ± 0.11[a]	0.15 ± 0.05[b]
T4/ Estrogen	0.08 ± 0.04[c]	0.06 ± 0.02[d]
T3/ Testosterone	25.52 ± 48.93[e]	5.14 ± 3.31[f]
T4/Testosterone	6.97 ± 4.38[g]	1.92 ± 1.00[h]
T3/Progesterone	11.38 ± 5.23[i]	10.03 ± 6.73[j]
T4/Progesterone	4.22 ± 2.11[k]	3.82 ± 2.22[k]

BC: Patients with breast cancer, AHW: apparently healthy women. Different superscripts in a row indicate significant differences ($p<0.005$) in hormones among breast cancer and apparently healthy women.

among the remaining BC patients, and only 7% of females categorized as apparently healthy had subclinical hypothyroidism. When compared with apparently healthy females a woman with thyroid disorders had a relative risk of 1.3 (CI 1.04-1.13) of having BC.

Thyroid Profile

The mean serum TSH of apparently healthy individuals was not significantly different when compared with women with BC even though serum TSH of BC patients was noticeably lower ($p>0.05$). Serum TSH was also not significantly different according to the menopausal status. However, serum T3 and T4 concentrations of BC patients were significantly higher ($p<0.05$) when compared with healthy females irrespective of the menopausal status.

Sex Hormone Concentrations of BC Patients

Among the study sample 37% of BC patients (n=57) were premenopausal. Serum estrogen and progesterone concentrations at each phase among premenopausal BC patients were not significantly different ($p> 0.05$) when compared with age matched controls. Serum testosterone concentrations of premenopausal BC patients were significantly lower ($p=0.001$) than apparently healthy females (12). However, since the number of premenopausal BC patients in each menstrual phase is comparatively less, and the hormone concentrations significantly varied according to each phase, the comparative statistical analysis was conducted with the sex hormone levels of postmenopausal BC patients and apparently healthy age matched postmenopausal women.

Serum estrogen and progesterone concentrations of postmenopausal BC patients were not significantly different to that of apparently healthy women. However, serum estrogen of these BC patients was noticeably lower. When compared with premenopausal women, postmenopausal women had significantly lower ($p=0.000$) serum estrogen and progesterone concentrations. Median (Inter quartile range) testosterone concentrations of postmenopausal BC and healthy women were 0.16(0.18) ng/mL and 0.21 (0.22) ng/mL respectively. Serum testosterone concentrations of BC patients were significantly low ($p=0.001$) irrespective of menopausal status when compared with healthy women (12).

Thyroid Hormones to/Sex Hormone Ratios

Considering the thyroid profile of the studied BC patients, even though the mean concentrations of thyroid hormones were within the normal reference range, significantly elevated levels of T3 and T4 concentrations were observed among BC patients when compared to apparently healthy. Among the studied sex hormones, serum testosterone was significantly low ($p<0.05$) and a considerable difference in the estrogen concentrations was observed though not significant ($p>0.05$). Thus, to study the possible risk associations with respect to thyroid and sex hormones, the ratio of thyroid hormones to sex hormones were studied and compared with apparently healthy women (Table 2).

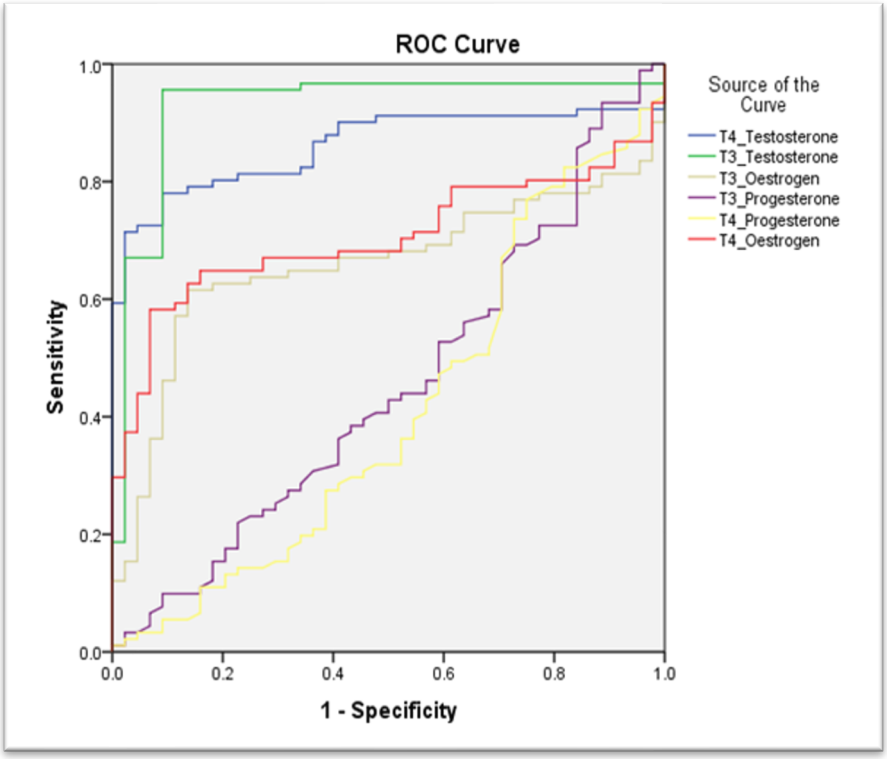

Figure 1. Receiver Operative Characteristic (ROC) Curves to predict the cutoff values

Significant differences in T3/estrogen, T4/ estrogen were found among the two groups and T3/testosterone and T4/ testosterone ratios indicated a high significance (p=0.000). Thus, ROC curves were used (Figure 1) to identify a possible predictor of BC risk and to find a cutoff value with a higher sensitivity and specificity. According to the figure 01, among all studied thyroid/sex hormone ratios, T3/ testosterone ratio showed the highest sensitivity and specificity with highest area under the curve being 93% indicating the possibility of using it as a predictor of risk compared to other studied parameters in BC diagnosis. According to the ROC curve the cutoff value was calculated as 7.47. Thus T3/ testosterone value above 7.47 was identified as a predictive indicator of identifying BC risk. T3/ progesterone or T4/ progesterone ratios were not significant in the study sample.

DISCUSSION

The effect of the changes in the daily lives of female thyroid and sex hormones have been implicated in mammary tumorigenesis and development. Effects of estrogen represent an increase in biological activities and therefore, in conjunction with T3 can act directly on mammary tissue by promoting differentiation (13). Due to these multiple hormonal interactions as well as the ubiquitous role that thyroid hormones play in the body's overall metabolism, the role that thyroid hormones may play in establishing and maintaining BC is exactly not known. Studies have established a direct action of thyroid hormones on the development of the normal mammary gland. But whether an alteration in thyroid status affects mammary tumor risk as well as development and growth are not entirely clear and needs to be studied further.

Among the BC patients in the present study sample, a considerable number of BC patients (n=16) reported a history of thyroid related diseases and among the remaining BC patients, the incidence of subclinical hypothyroidism was twice as high as among apparently healthy individuals. Studies reveal increased risk of BC in women with hyperthyroidism (14). Indicating an association between level of thyroid function and BC risk and the present study confirms the same for the first time in Sri Lanka.

Among the BC patients even though serum TSH levels were noticeably lower, serum T3 and T4 levels were significantly elevated indicating a possible impact of these on tumor development or progression. Cell line studies reveal that T3 can promote BC cell proliferation and increase the effect

of estrogen on cell proliferation. Thus, T3 may play a role in BC development and progression (11).

Circulating estrogens and androgens are found to be positively associated with the risk for BC in premenopausal women (15). However, previous findings indicate non-significant difference in serum estrogen and progesterone levels in BC patients and significant low levels of testosterone (12). The higher bioavailability of testosterone counteracts the proliferative effects of estrogen on mammary tissue and thereby exert a protective role to the breast, inhibiting cancer development and/or tumour growth (16) which might be a considerable stakeholder in the study group. Also, majority (75%) of the BC patients in the present study were either obese or overweight (17) and thus the impact of adiposity related secretions of androgens on BC cannot be undermined (18). A study reveals a synergistic response between T3 and high carbohydrate meals (19) whereas the BC patients in the present study were not regularly consuming balanced meals but were on frequent carbohydrate rich meals (unpublished observations). Thus the diet, the sedentary lifestyle and being either overweight or obese might have contributed to the present observations.

Lipid-soluble hormones in the blood are bound to hormone-specific transport proteins, while a smaller portion is bound to serum albumin. Testosterone-estrogen-binding globulin (SHBG) is a sex hormone-binding globulin that binds to testosterone and estradiol in the blood. Other known steroid-binding globulins are transcortin, primarily associated with progesterone and thyroxine-binding globulin (TBG), for transporting T4. Increased estrogen concentrations increase TBG concentrations. The rise in TBG is paralleled by a T4 increase to maintain a physiological concentration of free T4. Besides the effects on TBG concentrations, sex hormones also affect deiodinase activity which might together contribute to BC development [20].

In vitro studies reveal direct stimulatory effects of T3 on basal production of testosterone and estradiol (21) and according to the present study T3/testosterone above 7.47 indicated the highest risk. In other words, while elevated T3 contribute to BC cell proliferation, lower testosterone concentrations might have reduced the anti-proliferative and pro-apoptotic effect of testosterone on BC. Thus, the present study identifies that T3/ testosterone ratio can predict BC with higher odds when compared with other studied thyroid hormone/sex hormone ratios in identifying BC risk. The imbalance of thyroid hormones causes the dysfunction of the reproductive system (22) which might also impact on the concentrations of sex hormones.

Interestingly testosterone sometimes functions via conversion to estradiol [23] and lower testosterone in females might impact on obesity and poor glucose control. Considering the HbA1c levels 20% of BC patients showed values above 7% after excluding 13% of BC patients who were already on glycemic control drugs at the time of enrolment to the study. However further studies are needed to confirm the exact impact of lower serum testosterone and elevated T3 on developing BC as research on molecular mechanisms involving androgenic pathways in BC is still in their infancy.

CONCLUSION

Thyroid related diseases are significantly higher among BC patients and BC patients showed significantly elevated serum T3 and T4 levels than controls indicating the possible impact of hyperthyroidism in BC. Considering the thyroid hormone/sex hormone levels, significantly increased serum T3/ estrogen, T3/testosterone ratios among postmenopausal BC women implies the impact on hormone imbalance on BC development. Considering the Thyroid hormone/sex hormone ratios, serum T3/testosterone above 7 was identified as a potent marker in identifying BC risk among the study sample.

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Author contributions: H.M.K.A conducted the study and drafted the manuscript; S.E. supervised the study and reviewed the manuscript; K.S. supervised the study.

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RESEARCH ARTICLE

THE RELATIONSHIP BETWEEN THE LIFE QUALITY BASED ON PREGNANCY COMPLAINTS AND MATERNITY ROLE AND ACCEPTANCE OF PREGNANCY

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ABSTRACT

Purpose: The purpose of this study was to determine the relationship between life quality based on pregnancy complaints and maternity role and pregnancy acceptance.
Material and Methods: The sampling for the research featuring a cross-sectional design comprised 284 pregnant women who applied to the pregnant training class of a state hospital. Data were collected by "Personal Information Form", "Acceptance of Maternity Role" and "Acceptance of Pregnancy" sub-dimensions of the Prenatal Self-evaluation Scale and "Scale for Pregnancy Complaints and Their Impact on the Life Quality (SPCILQ)". Descriptive statistics and Pearson Relationship Analysis were used in the analysis of the data.
Results: The age average of pregnant women is 28.27±5.14, it was found that 33.8% of the pregnant women are high-school graduates, 79.8% are housewife, 86.6% have a moderate economic status, 84.2% have elementary family. The average pregnancy week of the pregnant is 31.98±8.16, the average pregnancy number is 1.60±0.48. It was determined that 78.2% of the pregnant women have a desired/planned pregnancy, 45.4% get information from physician, 41.5% get information from midwife in the prenatal controls regarding the complaints experienced in the pregnancy. The point average which the pregnant women took from the sub-dimension of the Acceptance of Maternity Role is 37.72±4.07; the point average they took from the sub-dimension of the Acceptance of Pregnancy is 40.14±4.34; the point average they took from Scale on Complaints in Pregnancy and Its Impact on the Life Quality is 72.29±28.10. A statistically positive-way weak relationship was detected between the point average of Scale for Pregnancy Complaints and Their Impact on the Life Quality (SPCILQ) and point averages of maternity role (r=0.209, p=0.000). No statistical significance was detected between point average of SPCILQ and point averages of the acceptance of the pregnancy (p>0.05).
Conclusion: As the impact of the pregnancy-based complaints on the life quality increases, a decrease is seen in the adaptation to the maternity role.

Keywords: maternity role, adaptation to pregnancy, pregnancy, pregnancy complaints, life quality

INTRODUCTION

Pregnancy is an important period when a set of anatomic, physiological and emotional changes are experienced in the maternal organism (1-3). While these changes vary by trimesters, the complaints caused by the pregnancy affect the daily life activities and thus, the life-quality of the pregnancy is also affected (4-7). Once the complaints which women

experience during the pregnancy, periods are examined; they experience such complaints as nausea, vomiting, nasal congestion, fatigue, thamuria, urinary tract infection, breast tenderness, pithiatism, increase in the vaginal secretion in the early period, they experience such complaints as increased appetite, edema, varicose, constipation, hemorrhoid, gas, back pain, muscle cramps, Brakston Hicks contractions, thamuria, fatigue, skin problems and lack of sleep (1). While the most common complaints of women in the early period are specified as fatigue, nausea and thamuria in the studies of the literature (4-8), the most common complaints experienced in the later period are generally specified as fatigue, constipation, edema, sleep problems (9,10).

While the complaints experienced during the pregnancy form for the purpose of maintaining the health of pregnant women and fetus, covering the metabolic needs and preparing the body for vaginal delivery, they stand out by differing in every woman (11-13). All complaints continuing during the process create a milestone in the life of woman and require adaptation to the maternity and new roles (2). The biggest role which the pregnant women will take in the future is inevitably maternity role. Identification with this role starts before the pregnancy and realizes within a year following the birth (14,15). The maternity role is defined as a process of learning the maternity behaviors (16). The formation of maternity identity of any woman realizes through the attachment, acceptance and participation in the new identity (15). The factors affecting the pregnant woman's acceptance of her maternity role are generally identified in the literature as to whether the pregnancy is planned or not, the number of births, age, educational level, working status, social support, etc. (14,17,18). Also, it is addressed in the studies conducted that the life quality impaired depending on the pregnancy complaints is affecting the psycho-social health adversely in the pregnancy (19-21). It was considered that the life quality that is based on the pregnancy complaints may also affect the maternity role and acceptance of the pregnancy by starting from the fact that the adaptation to the pregnancy and maternity role is affected by the psychosocial factors (14,17). There is no study in the literature where the impact of the pregnancy complaints on the life quality and the impact on the maternity role and acceptance of the pregnancy are examined. Not accepting the pregnancy and maternity role may lead the mother not to seek adequate care prior to the delivery, malnourishment in the pregnancy and problems in the attachment process between the mother and fetus. This situation may lead to impairment in the maternal self-reliance, reduction in the life satisfaction and even postpartum depression as well as the negative interactions between the mother and infant in the postpartum period (14,22). For this reason, as noted in the literature, women having difficulty in accepting the pregnancy have difficulty in adapting to the pregnancy and maternity (14). It is essential to determine the pregnant woman's life quality that is based on pregnancy complaints and to know its impact on the role and adaptation processes of the woman to prevent such and similar adverse circumstances without experiencing. The results of the research investigating the relationship between the life quality that is based on the pregnancy complaints and the maternity role and acceptance of the pregnancy will contribute to the midwifes to develop either the approaches which will provide the women to cope with the complaints they experience in the pregnancy or the interventions related with the acceptance of maternity role and acceptance of the pregnancy.

MATERIAL AND METHODS

This research designed in cross-sectional qualification was conducted for the purpose of establishing the relationship between the life quality based on the pregnancy complaints and the maternity role and acceptance of the pregnancy. The research population consisted of pregnant women who applied to a pregnant training class at a state hospital in the Malatya province. In the calculation made by using power analysis, the sampling of the research was determined as minimum 284 pregnant women with a level of significance of 0.05, a confidence interval of 95% and the ability to represent the population at 80%. Women who applied to the pregnant training class of the related hospital and meeting the criteria of being included in the research were elected with improbable random sampling method until the determined sampling group was reached. The healthy pregnant women who could communicate verbally, have no psychiatric problem and whose pregnancy realizes without using assisted reproductive techniques, were included in the research.

Table 1. Distribution of the Introductory Characteristics of Pregnant Women (n=284)

Descriptive Properties	n	%
Educational level		
Illiterate	9	3.2
Primary school graduate	55	19.3
Secondary school graduate	51	18.0
High school graduate	96	33.8
Graduated from a university	73	25.7
Working status		
Working	58	20.4
Not working	226	79.6
Income status		
Low	16	5.6
Middle	246	86.6
High	22	7.8
Family structure		
Nuclear Family	239	84.2
Traditional Family	45	15.8
Relationship with the spouse		
Negative	10	3.5
Neither positive nor negative	15	5.3
Positive	259	91.2
Relationship with family and environment		
Negative	3	1.1
Neither positive nor negative	16	5.6
Negative	265	93.3
Desired-Planned Pregnancy Status		
Yes	222	78.2
No	62	21.8
Status of Access to the Information in case of Experiencing Complaint		
I did not receive information.	25	8.8
The midwife informed me.	118	41.5
The doctor informed me.	129	45.5
I was informed via the Internet.	7	2.5
Other*	5	1.7
Total	**284**	**100**
Age of pregnant women (years) (mean±SD): 28.27±5.14 (min: 17; max: 44)		
Number of pregnancies (mean±SD): 1.60±0.48		
Gestation period (weeks) (mean±SD): 31.98±8.16		

* I got information from people around me.

Table 2. Distribution of the Lowest and Highest Points and Point Averages which the Pregnant Women Took from the Sub-dimensions of the Prenatal Self-Evaluation Questionnaire and Total and Sub-dimensions of the Scale for Pregnancy Complaints and Their Impact on the Life Quality (n=284)

Scales	The lowest and highest scores that can be obtained	The lowest and the highest scores obtained	Mean of the scores obtained (Mean±SD)
PSEQ-Acceptance of Pregnancy	14-56	23-48	40.14 ± 4.34
PSEQ-Acceptance of the Maternal Role	15-60	24-47	35.72 ± 4.07
SPCILQ	0-210	16-149	72.29±28.10

PSEQ: Prenatal Self-Evaluation Questionnaire
SPCILQ: Scale for Pregnancy Complaints and Their Impact on Life Quality

Data Collection Tools
"Personal Information Form", "Acceptance of Maternity Role" and "Acceptance of Pregnancy" sub-dimensions of the Prenatal Self-evaluation Scale and "Scale for Pregnancy Complaints and Their Impact on the Life Quality (SPCILQ)" were used in the collection of data.

Personal Information Form
There are 11 questions in the form prepared by the researchers pertaining to the individual (age, educational level, working status, spouse and family-environment relations, etc.) and obstetric characteristics of pregnant women (number of pregnancy, pregnancy week, whether the pregnancy is desired/planned or not).

Prenatal Self-Evaluation Questionnaire (PSEQ)
This questionnaire was developed by Lederman in 1979 for evaluating the adaptation of pregnant women to the pregnancy and maternity role (23). Turkish validity confidence study was conducted by Beydag and Mete in 2006 (24). "Acceptance of the Pregnancy" comprised 14 items and "Acceptance of maternity role" comprised 15 items, among the sub-dimensions of the questionnaire having 7 sub-dimensions, were used in this study.

- Items in the sub-dimension of the acceptance of pregnancy; 1, 3, 5, 7, 9, 17, 18, 19, 20, 22, 24, 26, 27, 29;
- Items in the sub-dimension of the acceptance of maternity role; 2, 4, 6, 8, 10, 11, 12, 13, 14, 15, 16, 21, 23, 25, 28.
- Reverse items; 1, 2, 3, 4, 6, 7, 9, 10, 15, 18, 23, 24, 25, 28, 29.

Every item in the questionnaire is measured in an evaluation of 4-point Likert type (4: Full describes, 3: partially describes, 2: Slightly describes, 1: Never describes). In the reverse items, the scoring is made vice versa. On the sub-scale of the acceptance of the pregnancy, pregnant women can take minimum 14, maximum 56 points; in the sub-scale of the acceptance of the maternity role, they can take minimum 15, maximum of 60 points. Low points show that the adaptation to the pregnancy is high. The Cronbach's alpha reliability coefficient of the scale is 0.81, the Cronbach's alpha reliability coefficients of the sub-dimensions of the "Acceptance of Pregnancy" and "Acceptance of maternity role" are 0.72 and 0.85, respectively. In this research, The Cronbach's alpha reliability coefficient of the sub-dimension of the "Acceptance of Pregnancy" was determined as 0.71, the Cronbach's alpha reliability coefficient of the sub-dimension of the "Acceptance of maternity role" as 0.78.

Scale for Pregnancy Complaints and Their Impact on the Life Quality (SPCILQ)
This scale was developed by Foxcroft K.F. et al., in Australia in 2008 for measuring the pregnancy complaints and their impact on the life quality (25).

Table 3. The Relationship between the Total Point Averages the Pregnant Women took from the Sub-dimensions of the Prenatal Self-Evaluation Questionnaire and Scale for the Pregnancy Complaints and Their Impact on the Life Quality (n=284)

	SPCILQ	
PSEQ-Acceptance of Pregnancy	r= -0.083	r= 0.161
PSEQ-Acceptance of the Maternal Role	p= 0.209	p= 0.000*

PSEQ: Prenatal Self-Evaluation Questionnaire
SPCILQ: Scale for Pregnancy Complaints and Their Impact on Life Quality
r: Pearson Correlation Analyze
*: p<0.05

Turkish validity reliability study was conducted by Gur and Pasinlioglu in 2016 (2). There are 42 items on the scale, and it is consisted of two parts. In the first part, it is assessed that how often the pregnant women experience the pregnancy complaints within the last one month, this part is a 4-point Likert type scale and it is coded as “Never” (0), “Rare” (1), “Sometimes” (2), “Often” (3). If it is marked between 1-3 for any complaint in the first part, it is proceeded to the second part of the scale. In the second part, it is a 3-point Likert type scale measuring how the complaints affect the Daily life activity and it is marked as “Never restricts (0)”, “slightly restricts (1)”, “excessively restricts (2)”. The scale has no break point. The rising of total point taken from the scale points out the bad/weak/low maternal and fetal outcomes. The Cronbach’s alpha reliability coefficient of the scale is 0.91. In this study, the Cronbach’s alpha reliability coefficient was found as 0.86.

Data Collection

Data were collected by using face-to-face interview method at weekdays with the pregnant women who applied to pregnant women training class of the related state hospital. These interviews lasted for 10 minutes on average.

Evaluation of Data

Coding and evaluation of data were performed in the computer environment by using SPSS 25.0 package program. In the statistical evaluation, percentage distribution, arithmetical mean, standard deviation, Cronbach alpha and Pearson correlation analysis were used. The results were evaluated at a confidence interval of 95% and at a significance level of p<0.05.

Ethical Arrangements

Ethical approval was taken from the İnönü University Scientific Research and Publication Ethics Committee (Health Sciences Non-Interventional Clinical Research Ethics Committee) to implement the research (Date: 17.07.2018; Decision number: 2018/15-22). At the same time, institutional permission was obtained from the institution where the research would be conducted. Verbal consents of all pregnant women were taken and all pregnant women had the “Informed Consent Form” signed before starting the research. Researchers informed the pregnant women about that the data obtained will be published for scientific purposes without using

personal information and they can leave the study at any time they want.

Limitedness of the Study

This research is limited to the pregnant women who applied to the pregnant women training class of a state hospital located in the east of Turkey.

RESULTS

Distribution of the introductory characteristics of the pregnant women was given in Table 1. The age average of pregnant women is 28.27±5.14 (minimum:17; maximum:44). The mean pregnancy numbers of pregnant women were found as 1.60±0.48 and the mean of pregnancy week as 31.98±8.16. 33.8% of the pregnant women are high-school graduates, 79.8% are housewife, 86.6% have a moderate economic status. 84.2% of pregnant women have an elementary family, 91.2% have a positive spouse relationship and 93.3% have a positive family-environment relationship. Also, 78.2%

have a planned pregnancy and 41.5% acquired access to the information by the midwife and 45.4% acquired access by the physician once they experienced pregnancy complaint.

The distribution of the lowest and highest points and point averages which the pregnant women took from the sub-dimensions of prenatal self-evaluation questionnaire and total and sub-dimensions of the scale for pregnancy complaints and their impact on the life quality was given in Table 2.

It was determined that pregnant women took minimum 23 and maximum 48 points from the sub-dimension of the acceptance of the pregnancy, minimum 24 and maximum 47 points from the sub-dimension of the acceptance of the maternity role in the prenatal self-evaluation questionnaire, they took minimum 16 and maximum 149 points from the scale for the pregnancy complaints and their impact on the life quality.

The total point average which the pregnant women took from the sub-dimension of the "Acceptance of the pregnancy" was found as 40.14±4.34, the total point average which the pregnant women took from the sub-dimension of the "Acceptance of maternity role" was found as 35.72±4.07. Also, the total point average which the pregnant women took from the scale for the pregnancy complaints and their impact on the life quality was determined as 72.29±28.10.

The relationship between the total point averages which the pregnant women took from the sub-dimensions of prenatal self-evaluation questionnaire and scale for the pregnancy complaints and their impact on the life quality was given in Table 3.

It was found that there is no statistically significant relationship between the point average of the sub-dimension of the acceptance of pregnancy and the point average of scale for the pregnancy complaints and their impact on the life quality (r=-0.083; p= 0.161).

It was found that there is a statistically positive-way weak significant relationship between the point average of the sub-dimension of the acceptance of the maternity role and the point average of the scale for the pregnancy complaints and their impact on the life quality and as the impact of the pregnancy-based complaints on the life quality increases, a decrease is seen in the adaptation to the maternity role (r=0.209; p= 0.000).

DISCUSSION

Learning of the pregnancy will be an important milestone of the woman's life and they will experience changes in their roles. It is considered that pregnancy-specific complaints will affect the acceptance process of the pregnancy and acquisition of the maternity role (14). In this part, the results of the study conducted for the purpose of establishing the relationship between life quality based on pregnancy complaints, maternity roles, and acceptance of the pregnancy are discussed in the related literature.

In this research, the total point average which the pregnant women took from the sub-dimension of the "Acceptance of Pregnancy" in the Prenatal Self-Evaluation Questionnaire was determined as 40.14±4.34, the total point average from the sub-dimension of the "Acceptance of the maternity role" was determined as 35.72±4.07. Once the point averages taken were examined, it was found that the adaptation of pregnant women to the pregnancy and maternity role was at a moderate level. Once the literature is reviewed, there are studies showing that the adaptation to the pregnancy is at moderate level, like our finding (21,26-32). As the pregnancy progresses, the psychological reactions of the pregnant woman will change, and her interest in herself in the first trimester will change direction as her infant and the welfare of her infant change over time. This direction change is an indicator that the adaptation to the pregnancy is realized. Hence, the studies conducted show that the pregnancy adaptation of pregnant women increases in the next pregnancy week (21,27,29,32-35). The pregnancy week of the pregnant women who were included within the scope of this study was 31.98±8.16 and this demonstrates that this finding is compatible with the literature. It is an expected finding that the pregnancy adaptation of pregnant women who are in the last trimester is at the moderate level. Also, it was found that the pregnancies of most pregnant women who were taken into the scope of this study were desired or planned (78.2%). In the literature review performed, it was found that being a planned pregnancy facilitates the adaptation to the pregnancy (14,21,26,27,29,36-45). Starting from these findings; it can be said that women who become pregnant willfully can adapt to the changes experienced in the

pregnancy more easily, particularly the women who become pregnant by planning with their husband can overcome the demanding process experienced in the pregnancy more easily.

In this research, the total point average which pregnant women took from the scale for pregnancy complaints and their impact on the life quality was found as 72.29±28.10. The highest point to be taken from the scale is 210 and once this finding was examined, it was found that the total point average taken was low, the pregnancy complaints have an adverse/negative impact on the life quality. It was determined in the literature review performed, there are similar findings to our finding and as the complaints which women experience increase, the life quality is affected adversely (12,19,46-57). It is also known that women experience physical and psychosocial problems as well as the changes emerging in the pregnancy and complaints experienced (11). Once these problems are combined with some high-risk factors emerged depending on the pregnancy and/or that have been already existed, the life quality of woman is negatively affected, in such case, the mortality and morbidity probability of mother and infant increases (5,8,20,46). Also, the literature review shows that the pregnancy complaints experienced in this period significantly decrease with the training and care support provided to the pregnant women (1,58-61). In the light of these findings, it can be said that as the complaints decrease, the negative impact on the life quality also decreases.

In this research, it was found that there is a statistically positive-way weak significant relationship between the point average of the sub-dimension of the acceptance of the maternity role and the point average of the scale for the pregnancy complaints and their impact on the life quality and as the impact of the pregnancy-based complaints on the life quality increases, a decrease is seen in the adaptation to the maternity role ($p<0.05$). The process of women to learn the maternity behaviors is called a maternity role. This process will be completed within a year, starting prior to pregnancy and following the birth (15,16,62-64). The process of transition to maternity and acquisition of maternity role is one of the most common life transition processes women experience and it usually points out a big failure period (19). Once the literature was reviewed, it was determined in the study performed by Stevens-Simon et al. (2005) that almost half of the pregnant women (32-46%) considered that being a mother would affect their life negatively. Once the characteristics of the pregnant women who were included in the same study were examined, it was found that being primiparous and feeling fear for being a mother are associated with this case (65). In addition to all these, the process of maternity acceptance may be adversely affected with the addition of pregnancy complaint. Once the literature was reviewed, it was also encountered with studies demonstrating that severe vomiting and nausea affected the acceptance of the pregnancy and thus, the acceptance of maternity was negative (16,29,66). Also, the pregnancy acceptance process of the expectant mothers who have difficulty in acquiring the maternity role in the prenatal period also delays. Depending on the emerging physical complaints, it should be known that expectant mothers can acquire a negative attitude towards the pregnancy and infant (21,67-69). From these findings, it was determined that as the negative impact of the emerging complaints based on the pregnancy on the life quality increases, a decrease is seen in the adaptation to the maternity role.

CONCLUSION

In this research, it was determined that as the negative impact of the emerging complaints based on the pregnancy on the life quality increases, a decrease is seen in the adaptation to the maternity role. Also, no significant relationship was detected between the negative impact of the pregnancy complaints on the life quality and the acceptance of the pregnancy. From these results, it should be determined what the pregnancy complaints are, the reasons for these complaints and the impacts on the mother and infant. The women should be supported with regard to these complaints and consulting should be properly provided. The pregnancy complaints should be examined by the midwife and other health professionals, training and seminars which will provide the complaints to decrease and support the increase in life quality of individuals should be organized. Also, an awareness should be raised in the expectant mothers by the midwifes in regard that these pregnancy complaints are temporary.

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RESEARCH ARTICLE

CARRIAGE OF ENTEROTOXIGENIC *STAPHYLOCOCCUS AUREUS* AND HYGIENE PRACTICES OF FOOD WORKERS

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ABSTRACT

Purpose: To determine the enterotoxigenic *Staphylococcus aureus* carriage rates and personal hygiene practices a total of 300 food workers participated, with 228 working in food businesses and 72 in hospital kitchens in Canakkale, Turkey.
Material and Methods: Participants completed a questionnaire about sociodemographic characteristics, hygiene practices, and food safety. Hand/nasal swabs were collected from the food workers. Inoculums were inoculated on Baird Parker Agar. Multiplex PCR and ELISA methods were used.
Results: The enterotoxigenic *S. aureus* carriage rate was 14% of food workers. Out of the 125 *S. aureus* strains, 42 (33.6%) were positive for one or more SE genes. Furthermore, *sea, seb, sec, sed*, and *sea+sed* were found in 16.0%, 6.4%, 9.6%, 6.4%, and 4.8% respectively. SEA, SEB, SEC, SED, and SEE were found at rates of 14.4%, 7.2%, 12.8%, 11.2%, and 20.8%. It was determined that as the education level of food workers increased, the *S. aureus* carriage rate decreased. The carriage rate was found to be higher in those who use gloves than those who do not. Hand carriers were determined more in nasal carriers ($p<0.05$).
Conclusion: Food workers who are carriers of enterotoxigenic *S. aureus* are a risk factor for food contamination. Training food workers on personal hygiene can be effective in preventing food poisoning.

Keywords: Enterotoxin, food workers, hygiene practices, *Staphylococcus aureus* carriage.

INTRODUCTION

Transference of *Staphylococcus aureus*, which is increasingly reported worldwide, is one of the most important known risk factors for *Staphylococcus* infection (1). Strains present in the nose can generally come into contact with hands, fingers, and the face, and therefore, nasal carriers can easily become skin carriers (2).

Staphylococcal food poisoning (SFP) caused by enterotoxin-producing *Staphylococcus* species is an important foodborne disease in many countries. Enterotoxigenic *S. aureus* can be present on the hands of food handlers and can easily contaminate food during processing (3). Lack of proper hygienic measures during preparation of food is a major risk of contamination, and staphylococcal food poisoning is often associated with manually prepared food (4). The transfer of enterotoxigenic microorganisms that can be present in the nose or skin of food handlers to cooked and especially protein-rich foods, as well as not keeping these foods refrigerated, are factors associated with enterotoxin poisoning (5).

Individuals working in food preparation and food services play an important role in spreading

foodborne diseases and epidemics due to poor personal hygiene, cross contamination, and a lack of food safety practices. This study was performed to determine certain demographic characteristics, personal hygiene practices, food safety practices and enterotoxigenic *S. aureus* carriage rates, of food workers in food businesses and hospitals in Çanakkale, Turkey.

MATERIAL AND METHODS

In the study, three-hundred food workers from 9 hospitals and 17 food businesses (such as diners, restaurants, and food factories) in Canakkale (Turkey) participated during 2014-2015. A multiple-choice questionnaire consisting of 12 questions was completed by 72 kitchen personnel working at the hospital and 228 working at food businesses. The questionnaire asked participants about their demographic characteristics, personal hygiene practices, and food safety behaviors. Participants were asked about age, gender, educational background, job title, and the number of years in the sector to determine their demographic characteristics. The frequency of hand washing and showering as well as glove and mask use were investigated to determine personal hygiene practices. Food workers were also asked if they regularly had nasal culture tests and received food safety training. Enterotoxigenic properties of 125 *S. aureus* isolates obtained from these individuals were tested using the PCR and ELISA methods.

Sampling, Isolation and Identification of *S. aureus*

Samples were collected from both nostrils, left and right hands (palm, interdigital folds, and wrists) using separate sterile swabs (6). Inoculums transferred to 5 ml Brain Heart Infusion Broth (Merck, Germany) were inoculated onto Baird Parker Agar medium (Merck 1.05406) containing egg yolk tellurite emulsion (Merck 1.03785). Isolates were identified using gram staining, catalase, coagulase, biochemical tests, and Latex agglutination tests (Slidex Staph-Kit, Biomerieux, France).

NCTC 10652 FDA 196E (*sea*), NCTC 10654 FDA 243 (*seb*), NCTC 10656 494 (*sed*) (National Collection of Type Cultures Public Health Laboratory Service, London), 1229/93 (*sec*), and FRI 918 (*see*) (National Reference Laboratory for Staphylococci, Robert-Koch-Institute, Wernigerode, Germany) S. aureus reference strains were used to search for staphylococcal enterotoxin genes.

Table 1. Staphylococcal enterotoxin primers

Primers	Oligonucleotide sequence (5'-3')	Product size (bp)	Reference	Multiplex PCR mix no
sea forward	GCA GGG AAC AGC TTT AGG C	520	(8)	1
sea reverse	GTT CTG TAG AAG TAT GAA ACA CG			
seb forward	ACA TGT AAT TTT GAT ATT CGC ACT G	667	(7)	1
seb reverse	TGC AGG CAT CAT GTC ATA CCA			
sec forward	CTT GTA TGT ATG GAG GAA TAA CAA	283	(8)	1
sec reverse	TGC AGG CAT CAT ATC ATA CCA			
sed forward	GTG GTG AAA TAG ATA GGA CTG C	384	(8)	2
sed reverse	ATA TGA AGG TGC TCT GTG G			
see forward	TAC CAA TTA ACT TGT GGA TAG AC	170	(8)	2
see reverse	CTC TTT GCA CCT TAC CGC			

DNA Extraction

Bacteria were boiled in lysis buffer solution and then centrifuged. Lysis buffer solution consisting of 925 µl H20, 25 µl sodium dodecyl sulfate, and 50 µl NaOH (2M) was prepared. Several *S. aureus* colonies were added and mixed in 50 µl Lysis buffer solution. Tubes were maintained in heating blocks at 100°C for 10 minutes to perform bacterial lysis. Fifty microliters of Tris EDTA buffer was added to the tubes, and centrifugation was performed at 13000 xg for 10 minutes. Forty microliters was transferred to 150 µl Tris EDTA buffer.

Detection of Staphylococcal Enterotoxin Genes by Multiplex PCR

A multiplex PCR method was used in the identification of staphylococcal enterotoxin genes (*sea, seb, sec, sed, see*). *Sea, seb*, and *sec* genes were investigated in the first tube, and *sed* and *see* genes in the second tube (Lovseth, et al., 2004) (Table 1).

For the PCR reaction, 20 µl mixtures consisting of 10 µl 2X ExPrime Taq premix (GenetBio, Korea), 1 µl (10 pmol/µl) forward primer, 1 µl (10 pmol/µl) reverse primer, pure water, and 1,5 µl bacterial DNA sample were prepared. Multiplex PCR protocol was set as: initial denaturation at 94°C for 3 minutes, 30 cycles; and final elongation at 94°C for 1 minute, at 53°C for 45 seconds, at 72°C for 1 minute and at 72°C for 5 minutes.

Detection of Staphylococcal Enterotoxins by ELISA

A RIDASCREEN SET A, B, C, D, E (R-Biopharm, Darmstadt, Germany) kit was used to identify SEA, SEB, SEC, SED, and SEE toxins by ELISA method. The testing procedure was carried out in the following order.

100 µl of supernatants and control solution was transferred to the wells. The cassette containing the strips was left for 1 hour incubation at 37 °C. The first washing of the strips was carried out with washing buffer (0.1% Thimerosal) in 5 replicates in an ELISA washing device (Biotek ELx50). 100 µl of conjugate *(1)* solution was added to the washed wells and left for 1 hour incubation at 37 °C. The second washing process was carried out as mentioned above. 100 µl of conjugate *(2)* solution was added to each well and left for 30 minutes incubation at 37 °C. The third washing process was carried out as mentioned above. 100 µl substrate/chromogen solution was added to each well and left for 15 minutes of incubation at 37 °C in the dark environment. The reaction was stopped by adding 100 µl stop solution to each well. The absorbance value at 450 nm wavelength within 5-10 minutes was performed using an ELISA reader (Biotek ELx800).

The cutoff value was calculated for each sample by adding 0.15 to the arithmetic mean of the negative controls on the studied strip. The toxins in the samples with an absorbance value above the cutoff value were determined as "positive".

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) software, version19.0, was used for the statistical analysis of data. Some sociodemographic characteristics, levels of knowledge about hygiene and food safety of food workers participating in the study were determined by applying a face-to-face questionnaire. The relationship between this information and *S. aureus* carriage was evaluated by Chi-square test. The significance test of the difference between the two averages (T-test) was used in comparing the statistical data of food workers employed in food businesses and hospital kitchens. The frequency table was used to evaluate the distribution of *S. aureus* strains that produce enterotoxin and the specified spa types to the workplaces. $p< 0.05$ was considered statistically significant.

Ethical Approval

The study was conducted using a protocol approved by the Local Ethics Committee of Clinical Research (Date: No: 050.99-214), and written informed consent was obtained from all participants.

RESULTS

S. aureus were isolated from the nose and/or hands of 125 (41.7%) food workers out of a total of 300. Ninety (30%) of these individuals had nasal, and 84 (28%) had hand carriage. *S. aureus* were also isolated from the hands of 49 (54.4%) nasal carriers. *S. aureus* hand carriage occurred at an increased rate in nasal carriers ($p < 0.05$). Among 300 food workers, ages ranged from 15 to 65 years, and the mean age was 33.9. Among these individuals, 164 (54.7%) were between the ages of 19-35 years; 193 (64.3%) of the participants were male. Among 294 individuals who answered the question about educational background, 104 (35.4%) were primary

school graduates, and 43 (14.6%) were college graduates. The carriage rates in primary school, secondary school, high school, and college graduates were 46.2%, 50.8%, 37.8%, and 25.6%, respectively. The percentage of carriers was inversely related to educational level ($p < 0.05$). (Table 2).

Among the 299 individuals who answered the question about the frequency of hand washing, 278 (93.0%) indicated that they washed their hands regularly and frequently, and 11 (3.7%) said that they washed their hands when they got dirty. In addition, 259 (86.6%) participants out of 299 said that they took a shower every day, and 31 (10.4%) indicated that they showered three days a week. One-hundred and twenty out of 299 participants (40.1%) said that they always used gloves, while 54 (18.1%) said that they did not use gloves while working. Sixty (50.0%) individuals of the 120 participants who always used gloves were carriers of *S. aureus*, whereas the remaining 60 (50.0%) did not carry *S. aureus*. Fifteen (27.8%) of the 54 individuals who did not use gloves carried *S. aureus*, whereas 39 (72.2%) did not. The rate of carriage in glove users was found to be significantly higher than the rate of carriage in those who did not use gloves ($p < 0.05$).

One-hundred and ninety-eight of 263 individuals (75.3%) stated that they changed their gloves when they got dirty, whereas 19 (7.2%) said that they never changed gloves. The rate of carrier was found to be higher in those who stated that they changed their gloves more frequently ($p <0.05$). Among 295 individuals, 120 (40.7%) indicated that they didn't use masks while working. One hundred and three (34.1%) out of 300 individuals stated that they had nasal culture tests once a year. Among 289 individuals, 153 (52.9%) indicated that they did not receive such training. There was no significant relationship between mask use, having regular nasal culture tests, or receiving food safety training in food workers and carrier rates ($p > 0.05$) (Table 3).

Among 125 *S. aureus* isolates, 20 (16%) had the sea, 8 (6.4%) had seb, 12 (9.6%) had sec, 8 (6.4%) had sed genes, and none of the isolates had the *see* gene. Six of the strains that had the *sed* gene also had the *sea* gene. From a total of 125 *S. aureus* isolates, 42 (33.6%) carried at least one of the enterotoxin genes. The enterotoxigenic *S. aureus* carriage rate was 14% of food workers. Thirty-one (33.3%) of these isolates were obtained from food businesses, and 11 (34.4%) from hospital food workers. There was no statistically significant difference when comparing workplace types in terms of the percentage of isolates that carry a toxin gene ($p > 0.05$). The *sea* (no:3,4,6,8,15), *seb* (no:7), *sec* (no:14) multiplex PCR gel appearance of *S. aureus* isolates is shown in Figure 1. In 42 *S. aureus* isolates that carried an enterotoxin gene, the presence of A, B, C, D, and E staphylococcal enterotoxins was investigated. There was A, B, C, D, and E toxin production in 18, 9, 16, 14, and 26 of the *S. aureus* isolates, respectively. Nine of the 42 isolates were found to be compatible with gene and toxin positivity. The *see* gene was not detected in any of the isolates with the PCR method, whereas the ELISA method revealed that 25 isolates contained the E toxin. Although the *sea* gene (n=4) and the *sed* gene (n=2) were detected in some strains, there was no toxin positivity according to the ELISA method. Twenty-seven isolates were found to carry one or two more different toxins according to the ELISA method in addition to the gene(s) detected by the PCR method (Table 4). The manufacturer reported that there might be antibody/toxin cross-reactivity for the RIDASCREEN SET A, B, C, D, E test kit (A/E, E/A, B/C, and C/B), and cross-reactions might be seen at a rate of 10–20%. In our study, the percentage of cross-reactions (60.4%) of such results was higher than what was reported by manufacturer. Similar results were also obtained in another study on this subject (9). The PCR method used in our study for enterotoxin detection was cheaper, faster, and more reliable than ELISA.

DISCUSSION

The percentage of nasal carriage in 47 individuals working in the food business in Brazil and 64 individuals working at the same job in Malaysia was found to be 30% and 24.3%, respectively. According to the results obtained from these studies, nasal carriage percentages were not higher than in our study (10). Among 200 food workers that were included in a study from Botswana, 115 (57.5%) were found to be *S. aureus* carriers. *S. aureus* carriage was found to be higher than our study (11). Carriage was detected in 93 (40.8%) of 228 individuals working in food businesses, and in 32 (44.4%) of 72 individuals working in hospital kitchens. The difference between the workers in food businesses and hospital kitchens was not statistically significant in terms of *S. aureus* carriage ($p > 0.05$). The relationship between age, gender, task in workplace, years of employment for food workers, and *S. aureus* carriage rates was not

Table 2. Distribution of demographic characteristics by workplace type and the relationship with *S. aureus* carriage rates.

Demographic characteristics		Workplace type		Total n (%)	*S. aureus* carrier rate		Total n (%)	*p* value
		Food business n (%)	Hospital n (%)		Pos. n (%)	Neg. n (%)		
Age	14-18	13 (5.7)	0 (0)	13 (4.3)	4 (30.8)	9 (69.2)	13 (100)	> 0,05
	19-35	140 (61.4)	24 (33.3)	164 (54.7)	69 (42.1)	95 (57.9)	164 (100)	
	36-50	54 (23.7)	44 (61.1)	98 (32.7)	42 (42.9)	56 (57.1)	98 (100)	
	51-65	21 (9.2)	4 (5.6)	25 (8.3)	10 (40.0)	15 (60.0)	25 (100)	
Total n (%)		228 (100)	72 (100)	300 (100)	125 (41.7)	175 (58.3)	300 (100)	
Gender	Female	64 (28.1)	43 (59.7)	107 (35.7)	42 (39.3)	65 (60.7)	107 (100)	> 0.05
	Male	164 (71.9)	29 (40.3)	193 (64.3)	83 (43.0)	110 (57.0)	193 (100)	
Total n (%)		228 (100)	72 (100)	300 (100)	125 (41.7)	175 (58.3)	300 (100)	
Educational background	Primary school	65 (29.3)	39 (54.2)	104 (35.4)	48 (46.2)	56 (53.8)	104 (100)	< 0.05
	Secondary school	44 (19.8)	21 (29.2)	65 (22.1)	33 (50.8)	32 (49.2)	65 (100)	
	High school	70 (31.5)	12 (16.6)	82 (27.9)	31 (37.8)	51 (62.2)	82 (100)	
	College	43 (19.4)	0	43 (14.6)	11 (25.6)	32 (74.4)	43 (100)	
Total n (%)		222 (100)	72 (100)	294 (100)	123 (41.8)	171 (58.2)	294 (100)	
Task in workplace	Cook	61 (27.7)	9 (12.5)	70 (24.0)	33 (47.1)	37 (52.9)	70 (100)	> 0.05
	Assistant cook	24 (10.9)	15 (20.8)	39 (13.3)	22 (56.4)	17 (43.6)	39 (100)	
	Kitchen cleaning personnel	34 (15.5)	13 (18.1)	47 (16.1)	16 (34.0)	31 (66.0)	47 (100)	
	Service personnel	101 (45.9)	35 (48.6)	136 (46.6)	49 (36.0)	87 (64.0)	136 (100)	
Total n (%)		220 (100)	72 (100)	292 (100)	120 (41.1)	172 (58.9)	292 (100)	
Years of employment	0–1 year	58 (25.8)	10 (13.9)	68 (22.9)	24 (35.3)	44 (64.7)	68 (100)	> 0.05
	1–4 years	56 (24.9)	15 (20.8)	71 (23.9)	32 (45.1)	39 (54.9)	71 (100)	
	4–10 years	50 (22.2)	24 (33.3)	74 (24.9)	31 (41.9)	43 (58.1)	74 (100)	
	> 10 years	61 (27.1)	23 (31.9)	84 (28.3)	37 (44.0)	47 (56.0)	84 (100)	
Total n (%)		225 (100)	72 (100)	297 (100)	124 (41.8)	173 (100)	297 (100)	

statistically significant (p>0.05) (Table 2). In other studies conducted in Ethiopia and Egypt, the relationship between sociodemographic characteristics of food handlers and *S. aureus* carriage rates was not statistically significant. In a similar study on hand washing practices, 179 (89.5%) food handlers had a habit of hand washing after toilet, while 21(10.5%) of food handlers had no habit of hand washing after toilet. In this study, as in our study, there was no significant relationship between food workers (5). Using gloves is of utmost importance in preventing the contamination of food. In addition, gloves should be changed at certain intervals, such as while moving on to other work and after touching raw fruits and vegetables. The ambiance under gloves provides a favorable condition for the growth of microorganisms if the glove is punctured or torn. It is well known that foodborne diseases due to contamination will not be reduced unless the habit of using gloves is completely adopted.

If, in fact, they have used gloves for a long time or if they have not changed or changed rarely, it may have been possible. Individuals who always use gloves and never or rarely change them seem to play a greater role in transferring pathogens to food than those who work with clean bare hands. A study conducted in the USA investigated the effect of glove use by food processing personnel in fast food restaurants on the microbial load in foods, and it was thought that the use of the same gloves for an extended period, as well as less frequent hand washing, increased bacterial contamination (12). The percentage of individuals who did not receive food safety training (52.6%) was extremely high in our study and is similar to the percentage 47.8% found (13). Lack of personal hygiene among workers in the food industry is an important factor in the development of foodborne diseases. These individuals may transfer pathogens to food from their hands during the production and distribution processes, which can lead to food poisoning (14).

In a prior study analyzing swab samples obtained from the nose and hands of 82 food workers, it was found that 20 (24.3%) workers had *S. aureus*, and 19 (95%) of those isolates contained one or more enterotoxin genes (6). Forty percent of the *S. aureus* strains (n = 99) obtained from food workers working at 5 different workplaces contained enterotoxin genes. The most frequently detected genes in the study were *sea* (20%) and *seb* (11%). Eight of the

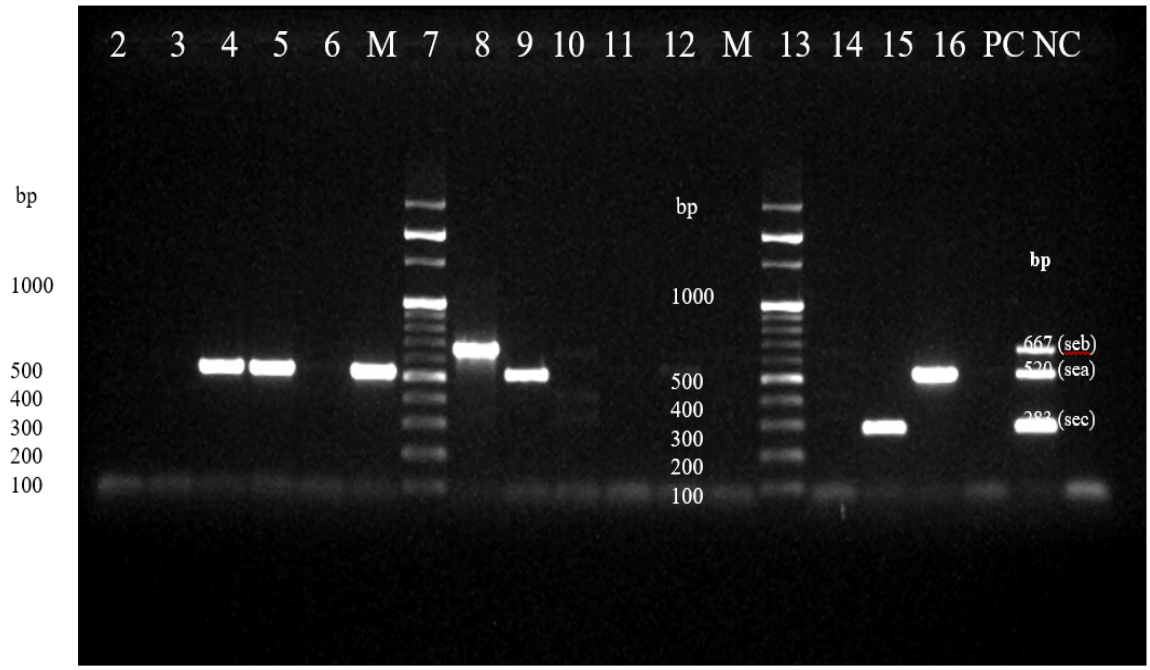

Figure 1. The *sea*+*seb*+*sec* multiplex PCR gel appearance of *S. aureus* isolates.

Table 3. Distribution of personal hygiene/food safety practices and the relationship with *S. aureus* carriage.

Questions	Answers	Total n (%)	*S. aureus* carriage		*p* = 0.05
			Positive n (%)	Negative n (%)	
How often do you wash your hands?	After going to the bathroom	7 (2.3)	2 (28.6)	5 (71.4)	> 0.05
	Before preparing food	3 (1.0)	2 (66.7)	1 (33.3)	
	As my hands get dirty	11 (3.7)	4 (36.4)	7 (63.6)	
	Regularly often	278 (93.0)	116 (41.7)	162 (58.3)	
Total n (%)		299 (100)	124 (41.5)	175 (58.5)	
How often do you take a shower?	Once a week	2 (0.7)	1 (50.0)	1 (50.0)	> 0.05
	Twice a week	7 (2.3)	0 (0)	7 (100)	
	Three times a week	31 (10.4)	13 (41.9)	18 (58.1)	
	Every day	259 (86.6)	111 (42.9)	148 (57.1)	
Total n (%)		299 (100)	125 (41.8)	174 (58.2)	
Do you use gloves?	No, I don't	54 (18.1)	15 (27.8)	39 (72.2)	< 0.05
	Sometimes	69 (23.1)	29 (42.0)	40 (58.0)	
	Frequently	56 (18.7)	20 (35.7)	36 (64.3)	
	Always	120 (40.1)	60 (50.0)	60 (50.0)	
Total n (%)		299 (100)	124 (41.5)	175 (58.5)	
How often do you change gloves?	I don't	19 (7.2)	3 (15.8)	16 (84.2)	< 0.05
	1-2 times a day	19 (7.2)	5 (26.3)	14 (73.7)	
	5-6 times a day	27 (10.3)	11 (40.7)	16 (59.3)	
	As they get dirty	198 (75.3)	95 (48.0)	103 (52.0)	
Total n (%)		263 (100)	114 (43.3)	149 (56.7)	
Do you use a mask?	No, I don't	120 (40.7)	45 (37.5)	75 (62.5)	> 0.05
	Sometimes	62 (21.0)	29 (46.8)	33 (53.2)	
	Frequently	39 (13.2)	16 (41.0)	23 (59.0)	
	Always	74 (25.1)	32 (43.2)	42 (56.8)	
Total n (%)		295 (100)	122 (41.4)	173 (58.6)	
Do you have a nasal culture test regularly (once a year)?	I never had	70 (23.4)	22 (31.4)	48 (68.6)	> 0.05
	I have the test irregularly	27 (9.1)	12 (44.4)	15 (55.6)	
	Yes	103 (34.1)	47 (45.6)	56 (54.4)	
	No	100 (33.4)	44 (44.0)	56 (56.0)	
Total n (%)		300 (100)	125 (41.7)	175 (58.3)	
Did you receive food safety training?	Yes	136 (47.1)	61 (44.9)	75 (58.3)	> 0.05
	No	153 (52.9)	60 (39.2)	93 (55.1)	
Total n (%)		289 (100)	121 (41.9)	168 (58.8)	

Table 4. Staphylococcal enterotoxin types in *S. aureus* isolates obtained from the PCR and ELISA methods.

Isolate number	SE genes	SE
1	*sec*	C,E
2	*sea*	A,D,E
3	*seb*	B,C,E
4	*seb*	B,C,E
5	*seb*	B,C,E
6	*sec*	C
7	*seb*	B,C,E
8	*sec*	C
9	*seb*	B,C,E
10	*seb*	B,E
11	*sec*	B,C,E
12	*sea*	A,D,E
13	*sea*	A,D,E
14	*sea, sed*	A,D,E
15	*seb*	B
16	*sea*	A,D,E
17	*sed*	Neg
18	*sec*	A,C,E
19	*sea, sed*	A,D,E
20	*sea*	A,D,E
21	*sea*	Neg
22	*sea*	A,D,E
23	*sea, sed*	A,D,E
24	*sea, sed*	A,D,E
25	*sec*	A,B,C
26	*seb*	B
27	*sec*	C
28	*sea*	Neg
29	*sea, sed*	A,D,E
30	*sea*	Neg
31	*sea*	Neg
32	*sec*	C
33	*sea*	A,D,E
34	*sea*	A,D,E
35	*sec*	C
36	*sea*	A,E
37	*sea*	A,E
38	*sec*	B,C
39	*sec*	C
40	*sea, sed*	A,D,E
41	*sed*	Neg
42	*sec*	C

A: SEA, B :SEB, C: SEC, D: SED, E: SEE

isolates (8%) carried more than one toxin gene (15). In another study including 332 food workers, 100 (30.1%) were carriers, 38 (38%) carried one or more enterotoxin genes, and *sea, seb, sec, sed*, and *see* genes were detected in 16%, 18%, 8%, 6%, and 8% of cases, respectively (16). In our study, the overall rate of enterotoxigenic *S. aureus* carriage in food workers in hospitals and food businesses was 14%, with a rate of 13.6% in hospital workers and 15.3% in workers from food businesses.

It was reported that 86.6% of *S. aureus* strains obtained from the employees of the city restaurants in Kuwait produced enterotoxin, and their distribution was 28% SEA, 28.5% SEB, 16.4% SEC, and 3.5% SED (17). In another study conducted in Botswana, 43 (21%) of the 204 isolates obtained from the nose, hands, and samples of 200 food workers were found to be enterotoxigenic, and the most common type of enterotoxin was SEA (34.9%) (11). *S. aureus* was isolated in 35 of the 102 food workers (34.3%) of the 19 restaurants serving in Santiago, and 19 (54%) of these strains were found to produce enterotoxin. The most frequently detected enterotoxin was the type A (12/19) (18).

CONCLUSION

The demographic characteristics, education levels, and hygiene practices of people working in food processing, preparation, and service are different. It was determined that as the education level of food workers increased, the *S. aureus* carrier rate decreased. Training food workers in personal hygiene and food safety practices can be effective in preventing food poisoning due to staphylococcal enterotoxins. Effective, periodically repeated trainings given by experts on food safety can reduce the attitudes and behaviors of these people that may pose microbiological risks. Food workers should be taught the importance of hand washing to reduce the transport of microorganisms and prevent contamination of the work environment (tools, equipment, etc.). It is also necessary to increase the knowledge and responsibilities of employers on food safety, workplace, and personnel hygiene.

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RESEARCH ARTICLE

COMPARING THE EFFECTS OF ERGONOMIC AND STANDARD OFFICE CHAIRS ON TRUNK MUSCLE ACTIVATION

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ABSTRACT

Purpose: Musculoskeletal disorders are one of the most common health problems faced by individuals who sit for prolonged periods. The sitting design of office chairs has recently become an important aspect in preventing the musculoskeletal disorders. The aim of this study is to determine the effect of different chair types on trunk muscle activation.
Material and Methods: Fifteen healthy participants (age 22.92 ± 3.40 years) were included in the study. Participants' muscle activations were assessed with the surface electromyography device while sitting and typing on the computer for 1 hour. These muscles were Thoracic Erector Spinae, Transversus Abdominus/Internal Oblique, and Upper Trapezius.
Results: When two different types of chairs were compared, in the first 10 minutes, % Maximum Voluntary Isometric Contraction difference was observed only in the Thoracic Erector Spinae ($p<0.05$). Also, % Maximum Voluntary Isometric Contraction difference was found only in the Transversus Abdominus/Internal Oblique ($p<0.05$) during the last 10 minutes. No significant difference was identified in two chair types in terms of activation of Upper Trapezius ($p>0.05$).
Conclusion: It should be considered that chair type may change the activation of trunk muscles in individuals working in a long-term sitting posture. Therefore, the use of ergonomic chairs suitable for the physiological needs of individuals should be recommended in order to encourage increased trunk muscle activation during prolonged sitting.

Keywords: Electromyography, ergonomics, muscle activation, office chairs.

INTRODUCTION

Musculoskeletal disorders (MSD), one of the most common health problems faced by office workers during work activity, are neuromuscular diseases that affect nerves, tendons, muscles, ligaments, and skeletal structure of the body (1,2,3). The most common MSD among office workers is neck and low back pain. The causes of these diseases include a sedentary lifestyle, prolonged sitting at a desk, and adaptation to sitting postures characterized by increased flexion and rotation in the neck and low back area among office workers (4). Many studies examining the impacts of parameters like furniture design at the office, working chair and desk design as well as prolonged sitting in front of computer and posture disorders of office workers indicated that ergonomic deficiency is a major risk factor for the work-related MSD (5,6,7). Any disproportion in chair dimensions may disrupt the ability of postural muscles to support the body, as well as causing pain and a feeling of discomfort by straining neuromuscular system unnaturally. A chair that satisfies ergonomic needs can reduce the incidence of musculoskeletal system symptoms and contribute

to the prevention of spinal problems (7). Thus, sitting comfort and design of office chairs has recently become an important aspect in preventing the MSD (8,9).

Many studies exist examining the changes in trunk muscular activation in sitting postures by using different chairs or surfaces (10-16). As a result of some studies, changes of chair or surface altered (increased or decreased) trunk muscle activations (11,14,15,16), while in some studies these changes did not have any effect on trunk muscle activations (10,12,13). Office workers usually need to sit for long hours to perform their duties. However, studies using EMG in their evaluations performed their measurements in short sitting periods (13,14,15). Studies evaluating long sitting periods (from 1 hour to 3 hours) focused only on the activations of Upper Trapezius (UT), and Erector Spinae (ES) muscles (10, 12). The Transversus Abdominus (TrA) and Internal Oblique (IO) muscles work as a local system that balances the compressive forces acting on the upper lumbar segments of the spine and increases lumbar stability through intra-abdominal pressure control (16). Therefore, the inclusion of IO/TrA muscles in studies examining the effects of chairs on trunk muscle activation is of great importance in terms of interpreting the results. Thus, the aim of this study designed with surface electromyography (sEMG) was to identify changes in UT, Thoracic Erector Spinae (TES) and IO/TrA muscles activation while using two different types of chairs in healthy participants in 1 hour.

MATERIAL AND METHODS

Fifteen healthy participants (9 males and 6 females) who worked sitting for at least 2 hours a day were included in this study. Demographic characteristics are given in Table 1. Exclusion criteria included having a deformity that may prevent sitting, having low back-neck problem in the last 12 months and still suffering from pain in this area, having a neurological or systemic disease, being pregnant, and having a body mass index below 18.5 or above 30. First, the participants' history and demographic information were collected. A segmental body composition analyser (Tanita Corp., BC418, Tokyo, Japan) was used to assess body mass index. Ethical approval was obtained from a local university ethics commission (Date: 06.02.2018, Number: 14574941-199-178316, Research Code Number: 2018-25). All the participants were informed about the study, and they signed an "Informed Consent Form" stating that they volunteered to take part in the study.

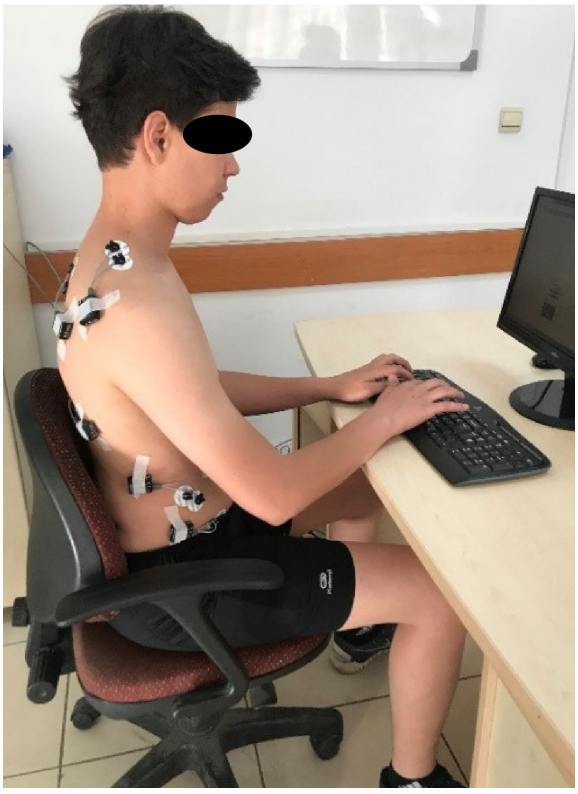

Figure 1. Standard office chair

Figure 2. Ergonomic office chair

The research was designed as a single group, repeated measures study. A sEMG device (Noraxon, USA, Inc, Scottsdale, AZ) was used to assess the activation of muscles. The assessments were conducted with the sEMG for 2 days and on two types of chairs while the participants were performing predetermined activities. Before starting the measurement, the subjects were shown the chair settings. One of the chairs was a non-ergonomic, non-adjustable standard office chair with backrest (see Fig. 1). As for the other chair, its seat depth, back hardness, lumbar support, armrest height, the width and angle of arm support, and angle and height of neck support were adjustable while it could support particularly spinal curves ergonomically. With the backrest applying resistance to the user, this chair could also be inclined 8 degrees forward and reclined 25 degrees and locked in four different positions (see Fig 2).

A randomization program was used to determine on which chair each participant would start the trial. The participants were asked to perform a single office task (typing on the computer desk) for 1 hour in their usual working posture. Over this 1 hour period, EMG signals were recorded. The second assessment was conducted after 7 days.

In collecting data, Noraxon's Mini DTS 8-channel EMG system (Noraxon, USA, Inc, Scottsdale, AZ) was used to measure signals obtained from the muscles. To record the EMG signals, the study used disposable, self-adhesive Ag/AgCl electrodes (Noraxon Dual EMG Electrode, USA), which are only intended for surface EMG applications.

Table 1. Demographic characteristics of participants.

	Participants (n=15) (mean±SD)
Age (years)	22.92 ± 3.40
Weight (kg)	63.02 ± 12.65
Height (cm)	174.78 ± 11.59
BMI (kg/m^2)	20.52 ± 2.96

SD: Standard Deviation, BMI: Body Mass Index

Since the previous sEMG study demonstrated there was no significant difference in muscle activation on the right and left sides of the body in healthy participants during relatively static tasks, only the muscles on the right side of the body were analysed (15). These muscles were TES, IO/TrA, and UT. Electrodes were placed at a distance of 20 mm, the diameter of the two circular adhesive areas was 1 cm, and dimensions of the figure 8-shaped adhesive were 4 cm x 2.2 cm (1.56 x 0.87 inch) (17). Before placing the electrodes, the area was shaved and lightly abraded with cotton soaked in alcohol to decrease the skin impedance below 5 kΩ (18). The electrodes were placed in parallel orientation to the determined muscle fibers as recommended by Surface Electromyography for the Non-Invasive Assessments of Muscles (SENIAM) (18). As TrA is positioned below the IO muscle fibers, the electrode determined for the IO also captures electrical signals for the TrA (17). Therefore, the data on these two muscles were assessed and interpreted together. The first 10 minutes and the last 10 minutes were included in the electromyographic analysis. Raw EMG signals were first checked visually for possible electrocardiographic artefact. Then, 10 Hz, IIR, Butterworth High-Pass and 500 Hz, IIR, Butterworth Low-Pass movement artefact and EKG filter were applied, and the Root Mean Square (RMS) values were computed by using the raw EMG data within sequential time windows (time windows: 0.1 s) to assess the EMG signals. After chair trials, Maximum Voluntary Isometric Contraction (MVIC) was induced for each muscle to normalize the EMG data, and EMG amplitudes were recorded.

Statistical Analysis

For statistical analyses, Statistical Package for Social Sciences (SPSS), Version 22.0 (SPSS inc., Chicago, IL, USA) was used. Visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/ Shapiro-Wilk Tests) were used to check whether the data were normally distributed, visual. Non-normal variables were indicated by using median (IRQ) while categorical variables were identified by using frequency and percentage (%). Wilcoxon Test was performed to determine the difference between the two chair types. For statistical significance, type 1 error level was set at 5%.

Table 2. Comparison of EMG values for both chair types in the first 10 minutes of the measurement

	Standard Office Chair	Ergonomic Office Chair	p
	Median (IQR)	Median (IQR)	
Upper Trapezius (MVIC%)	3.05 (1.48/9.26)	3.26 (1.02/6.55)	0.394
Thoracic Erector Spinae (MVIC%)	4.49 (3.96/7.74)	5.88 (4.09/12.98)	**0.047***
Transversus Abdominis/ Internal Oblique (MVIC%)	2.03 (1.37/4.54)	2.43 (1.08/4.00)	0.394

*p < 0.05. EMG: Electromyography, MVIC: Maximum Voluntary Isometric Contraction, IQR: Interquartile Range

Ethical Approval

Ethical approval was obtained from Gazi University Ethics Committee (Date: 06.02.2018, Number: E.25915, Research Code Number: 2018-25).

RESULTS

The comparison of the EMG activity on both chair types in the first 10 minutes of the 1 hour record indicated that there was a difference in MVIC% in the TES ($p<0.05$) while there was no significant difference between the chairs in other muscles ($p>0.05$, Table 2). According to the analysis result, it was found that muscular activation of the TES on the ergonomic chair was higher than the standard chair; however, the activation levels of other muscles were similar on both chairs.

Comparison of the EMG activity on the chairs in the last 10 minutes displayed a difference in MVIC% in the IO/TrA ($p<0.05$), whereas no significant difference was observed between the chairs in other muscles ($p>0.05$, Table 3). This result showed that the activation level of the IO/TrA in the ergonomic chair was higher than the standard chair while the activation levels of other muscles on both chairs were similar.

DISCUSSION

In this study, UT, TES, and IO/TrA muscle activation changes of individuals who perform typing tasks on the computer for 1 hour in 2 different chairs were examined. We found that the activation of the TES muscle in the first 10 minutes and the activation of the IO/TrA muscles in the last 10 minutes were higher in the ergonomic chair compared to the standard chair. No significant difference was identified between the two chair types regarding the activation of UT muscle. Office workers spend about 82% of their working time in a sitting position. Office work typically involves a prolonged static work posture, repetitive movements, and inappropriate hand and spine positions during work (19,20). For this reason, musculoskeletal disorders are very common among office workers (8, 9, 19). It has been reported that a chair that meets ergonomic requirements can be beneficial in reducing musculoskeletal symptoms and preventing spinal problems (7). Therefore, an increased number of studies are investigating the need for chairs that can support physiological curvatures ergonomically and reduce the inactivation of the trunk muscles in individuals who work in prolonged sitting postures and different types of chairs (10, 14, 15, 16). In their study on surgeons, Dalager et al. (2018) compared the effects of two custom-built ergonomic chairs with different and adjustable backrests, and a regular office chair on the muscle activation of the trapezius and ES (12). The study concluded that the ergonomic chair had no impact on the activation of the trapezius and the ES muscles. The authors claimed that

Table 3. Comparison of EMG values for both chair types in the last 10 minutes of the measurement

	Standard Office Chair	Ergonomic Office Chair	p
	Median (IQR)	Median (IQR)	
Upper Trapezius (MVIC%)	3.26 (1.90/8.15)	5.32 (1.81/8.76)	0.691
Thoracic Erector Spinae (MVIC%)	4.61 (2.51/8.60)	6.81 (4.33/10.12)	0.191
Transversus Abdominis/ Internal Oblique (MVIC%)	1.66 (1.30/2.54)	2.21 (1.71/4.23)	**0.031***

*p < 0.05. EMG: Electromyography, MVIC: Maximum voluntary isometric contraction, IQR: Interquartile Range

conducting the study using an occupational group that focused on patient safety and required intense concentration might have affected adaptation to the chair (12). Ellegast et al. (2012) investigated the effects of a standard office chair and four specific dynamic office chairs on the muscle activation of the TES and UT. The study reported no significant difference in muscle activation between the chairs. It was concluded that although the participants were shown how to use the chairs as a result of the fieldwork, their behaviour was difficult to control. Also, the participants were not accustomed to the chair, which may have affected the results (21). Neck disorders are very prevalent among office workers because of prolonged computer use. Ergonomic studies conducted on pain-free subjects asserted that a high level of muscle activation in the neck and shoulder area is a major risk factor for the development of a MSD (22). In our study, it was assumed that the muscle activation of the UT on the ergonomic office chair would decline significantly compared to the standard chair owing to its neck support with adjustable height and angle, armrest, and arm support. However, similar to the literature, there was no difference between the chairs. This may be due to the large standard deviation in UT and the fact that the participants could not adapt to the chair adequately because they were using the chairs for the first time during the measurement. Several studies have shown that a well-adjustable ergonomic chair increases productivity and reduces musculoskeletal complaints (19,21). For this reason, before the measurements, the participants were shown the adjustments of the chair. They were asked to adjust their chairs according to their comfort and sit in the position they felt comfortable. Thus, they may not have been able to use the neck and arm support of the chair effectively. For this reason, there may not be a difference between the chairs in terms of UT muscle activations.

According to the literature, the muscle activation by the TES was not affected by the chair type, but strongly affected by the diversity of office tasks performed (10). On the contrary, we found that the activation of the TES muscle in the first 10 minutes were higher with the ergonomic chair compared with the standard chair. The ergonomic office chair used in the present study can be adjusted in every aspect. It was considered that the chair could change the activation levels of the muscles by creating a push effect on the user because of its sensitive backrest. In addition, in a study investigating how TES muscle activation is affected by postural changes, it was observed that switching from sitting upright to slump sitting reduced the activation of the TES muscle by 3% maximal voluntary isometric contraction (15). Although we did not make postural assessment in our study, the reason for the increase in TES activation can be considered as the chair facilitating the upright sitting posture. As expected, TES muscle activation was higher in the ergonomic chair in the first 10 minutes.

The TrA and IO muscles function as a local system to counterbalance compressive forces on the upper lumbar segment of the spine and increase lumbar stability by controlling intra-abdominal pressure (16).

Analysis of the relevant literature did not reveal a similar study comparing the muscle activation of IO/TrA while performing computer typing tasks during prolonged sitting in ergonomic and standard chairs. The duration of the studies investigating the effects of different chairs on the activation of the IO/TrA muscles is 10 minutes or less. Besides, the studies compared standard office chairs without backrests with dynamic chairs (13,14). These studies found that IO/TrA muscle activation was not affected by the chair type. These results may be because of short evaluation times and the comparison of chairs with and without backrests. We found that the activation of the IO/TrA in the last 10 minutes was higher on the ergonomic chair compared with the standard chair. Rasouli et al. confirmed the association between slump posture and low activity of the TrA. (23). This result may be due to the fact that the ergonomic chair supports physiological curvatures and induces sitting upright with lumbar support. Although the sitting posture was not evaluated in our study, according to our clinical observation during the one-hour EMG measurement, the participants were urged to sit upright on the ergonomic chair using its adjustable lumbar support and applying resistance to the backrest. This posture resulted in, as expected, an increase in the muscle activation of the TES and IO/TrA.

In the literature, studies comparing the effects of different seat types on the activations of the muscles generally made short-term evaluations (30 min and below). However, longer-term evaluations should be preferred to interpret the results of the evaluations made in individuals who worked sitting for long hours, more effectively. In this study, EMG recordings were obtained for 1 hour while the participants performed the task of writing on the computer. By analysing the first and last 10 minutes of the one-hour recording, in addition to the acute responses, we wanted to get information about whether these muscles are different regarding their activation by the two-seat types after 1 hour.

Strengths and Limitations

The first limitations of this study were that the participants were not accustomed to the chairs used and thus, they might have failed to adapt to them. The second, the study was laboratory research. Although subjects were asked to maintain their natural sitting postures during the evaluation, they may not have been able to perform the usual natural sitting postures due to the placement of the EMG electrodes. The third limitation is postural evaluation was not performed on the participants during the EMG evaluation. The final limitation was the inclusion of healthy participants who worked in a sitting position for at least 2 hours a day instead of office workers.

CONCLUSION

Comparing the difference in UT, TES, IO/TrA muscles activation on ergonomic and standard office chairs in individuals working sitting for a prolonged time, this study concluded that the muscle activation of the TES was higher in the first 10 minutes on the ergonomic chair compared to the standard chair. On the ergonomic chair, the muscle activation of the IO/TrA was higher than the standard chair in the first 10 minutes. The increase in activation of the TES and IO/TrA muscles while sitting in an ergonomic chair can reduce the stress on passive structures such as joints and ligaments, and this may prevent the development of musculoskeletal problems. For this reason, it should be considered that chair type can change the activation of trunk muscles in individuals working in a long-term sitting position, and the chairs should be adjusted in accordance with the physiological needs of the individuals. Further research is needed for the long-term assessments of office workers evaluated with their own chairs in their own working environment.

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Conflict of interests: The authors report no conflict of interest.

Ethical approval: Ethical approval was obtained from a Gazi University Ethics Committee (Date: 06.02.2018, Number: E.25915, Research Code Number: 2018-25).

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RESEARCH ARTICLE

RESOLVIN D1 (RvD1) REGULATES *PORPHYROMONAS GINGIVALIS* LIPOPOLYSACCHARIDE-INDUCED Del-1 AND CYTOKINE EXPRESSIONS IN HUMAN GINGIVAL FIBROBLASTS

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ABSTRACT

Purpose: To detect the effect of Resolvin D1 (RvD1) on Developmental endothelial locus-1 (Del-1) and cytokine expressions of human gingival fibroblast cells exposed to *Porphyromonas gingivalis* lipopolysaccharide (*P. gingivalis*-LPS).
Material and Methods: The effect of RvD1 on cell viability of human gingival fibroblasts exposed to *P. gingivalis*-LPS was determined by MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay. Meanwhile, the effect of RvD1 on Del-1 and cytokine (IL-1β, IL-6, IL-8, IL-10, IL-17) expressions of human gingival fibroblasts exposed to *P. gingivalis*-LPS (1000 ng/mL) were studied by real-time PCR experiment, statistical analysis was performed using GraphPad Prism version 5 for Windows.
Results: Cell viability assay results demonstrated that RvD1 concentrations upregulated cell number compared to control group at 24 and at 72 h. While RvD1 reduced the IL-6, IL-8, and IL-17 mRNA expressions, the IL-10 and Del-1 mRNA expressions increased in a time- and dose-dependent manner. Also, IL-1β was not affected by RvD1 treatments.
Conclusion: The increased expression of Del-1 and IL-10 by RvD1 down-regulated the pro-inflammatory cytokine expressions induced by *P. gingivalis*-LPS in gingival fibroblast. Resolvin D1displayed regulatory effects on gingival inflammation in *P. gingivalis* LPS-induced cell culture experiment. In particular, results of this study show that Del-1 induced by RvD1 may have therapeutic potential to modulate periodontal inflammation.

Keywords: Cytokine, Del-1, gingival fibroblast, resolvin D1.

INTRODUCTION

Inflammation resolution is an active, well-coordinated mechanism that recovers tissue integrity and function, rather than the passive termination of inflammatory reactions by specialized pro-resolving lipid mediators (1,2). Lipoxins generated from arachidonic acid and resolvins and protectins derived from omega-3 polyunsaturated fatty acids are two examples of specific pro-resolving agonists (3). Docosahexaenoic acid (DHA) has a remarkable anti-inflammatory effect, which is attributed largely to its oxidation products such as resolvin, maresin, and

protectin (4). Resolvin D (RvD) is a group of lipoxygenase metabolites derived from DHA, with RvD1 and RvD2 receiving the most attention (5). The anti-inflammatory extracellular matrix protein known as Developmental Endothelial Locus-1 (Del-1) is released by endothelial cells and reduces inflammation in a range of organs, including the periodontium, brain, and lungs (6). Developmental endothelial locus-1 (Del-1) is an anti-inflammatory 52 kDa protein that is secreted by endothelial cells. It has three repeats that resemble epidermal growth factor (-EGF-) at the N-terminus (E1, E2, and E3) followed by two discoidin I-like domains (C1 and C2), or discoidin I-like domain 3 (EDIL3) (6). Furthermore, Del-1 specifically inhibits the expression of IL-17, which in turn inhibits the recruitment of neutrophils to the periodontium, reducing inflammation and bone loss. Del-1 also interacts with leukocyte 2 integrins, preventing the adhesion of ICAM-1 and lymphocyte function-associated antigen-1 (LFA-1, αLβ2, and CD11a/CD18) to inflammatory cells (7). The regulator role of Del-1 was displayed using young Del1 knocked-out (Edil3 -/-) mouse models, and the results show that Del-1 deficiency is associated with spontaneously high neutrophil infiltration and increased disease severity (8). Periodontal disease has been associated to gram-negative bacteria including Tannerella forsythia, Treponema denticola andPorphyromonas gingivalis. *Porphyromonas gingivalis* Lipopolysaccharide (*P. gingivalis*-LPS) is a crucial virulence factor and is critical in the onset and advancement of periodontal diseases. Moreover, *P. gingivalis*-LPS induces the expression of pro-inflammatory cytokines including tumor necrosis factor alpha (TNF-α), ınterleukin (IL)-1beta (β), and IL-6 in periodontal tissues (9,10). Del-1 deficiency caused severe inflammation and alveolar bone loss in animal periodontitis models, whereas local therapy with recombinant Del-1 reduced neutrophil infiltration and bone resorption (11). The expression of Del-1 is inhibited by the pro-inflammatory cytokine IL-17. Moreover, Del-1 is a necessary modulator of specialized pro-resolving mediators (SPMs)-dependent inflammation resolution that is essential for efficient synthesis of at least some key SPMs (RvD1 and RvE1).

In mouse models of periodontitis, genetic Del-1 loss promotes not only increased neutrophil infiltration but also IL-17-reliant inflammation-related tissue destruction. In contrast, deactivating of IL-17 signaling in Del-1-deficient animals, that is, mice with combined Del-1 and IL-17 receptor impairment, cures the Del-1 deficiency-related inflammatory diseases (12,13). Existing literature shows that RvD1 provides protection against IL-17-driven periodontal bone resorption in a Del-1-dependent manner via GSK-3b- and C/EBPb mechanism, whereas RvD1 disrupt this inhibitory pathway at the GSK-3b level by activating PI3K/Akt signalling (14).

The aim of this study was to clarify whether RvD1 affects cytokine and Del-1 mRNA expressions in human gingival fibroblasts. We hypothesized that RvD1 modulates the inflammatory response of P gingivalis LPS-induced HGF cells through cytokine and Del-1 expression.

MATERIAL AND METHODS

Cell Culture

Human gingival fibroblasts are the primary cell of gingival tissues and are involved in inflammation and immune responses as well as the synthesis and breakdown of connective tissue. Study was approved by Nigde Omer Halisdemir University, Non-Invasive Clinical Research Ethics Committee (Date: 24.03.2022, Decision Number: 2022/36).

Human gingival fibroblast (HGF) cells were thawed from our cell stock in cell culture media (DMEM; Gibco; Grand Island, NY, USA), 10% fetal bovine serum (FBS; Gibco), L-glutamine (600 mg/mL; Gibco;), penicillin (100 U/mL; Gibco), streptomycin (125 mg/mL; Gibco). Then, we maintained the cells in cell culture carbon dioxide incubator and observed the Hgf cells can be proliferation under inverted microscope. Cell line passage 3 (Hgf ǂ3) was used in the cell viability assay and the total RNA isolation experiments.

Experiments were performed twice in triplicate for each experiment for RNA isolation and three times in triplicate for cell viability.

Resolvin D1 (RvD1) Preparation

RvD1 was purchased from Cayman Chemicals (Ann Arbor, MI, USA). In line with previous studies on the effective dose of RvD1, a full range of RvD1 concentrations [Control (C), 1, 10, 100 ng/mL] was prepared, and added to the DMEM with 5% FBS (15,16).

Preparation of *Porphyromonas gingivalis* Lipopolysaccharide

Porphyromonas gingivalis Lipopolysaccharide product that is available for purchase was utilized in

its purest form (tlrl-ppglps-InvivoGen, SanDiego, USA). 1000 ng/mL of *P. gingivalis*-LPS was produced for use in cell viability and mRNA expression studies. Our earlier research revealed that cementoblasts and human gingival fibroblasts greatly reacted to *P. gingivalis*-LPS concentrations of 1000 ng/mL (9, 10).

Design of Study Groups

In order to determine the effect of RvD1 on *P. gingivalis*-LPS-induced cell viability and mRNA expression (cytokines, Del-1) of HGFs 5 study groups were planned including control (C), only 1000 ng/mL *P. gingivalis*-LPS (LPS) and 1 ng/mL of RvD1 combined with 1000 ng/mL *P. gingivalis*-LPS (LPS+R1), 10 ng/mL of RvD1 combined with 1000 ng/mL *P. gingivalis*-LPS (LPS+R10), 100 ng/mL of RvD1 combined with 1000 ng/mL *P. gingivalis*-LPS (LPS+R100) .

Cell Viability Assay

The 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyl tetrazolium bromide (MTT) (Sigma, St. Louis, MO, USA) test was used to demonstrate the impact of RvD1 on cell viability at 24 and 72 hours of *P. gingivalis* LPS-induced HGFs (Sigma, St. Louis, MO, USA). In this experiment, third passage HGF cells were trypsinized, and 200 µL cell solution containing $2X10^4$ cells was added to each well. Following a 24-hour incubation period, HGFs were treated with only 1000 ng/mL *P. gingivalis* LPS (LPS), and [Control (C), 1 ng/mL RvD1 (LPS+R1), 10 ng/mL RvD1 (LPS+R10), 100 ng/mL RvD1 (LPS+R100)] ng/mL of RvD1 combined with 1000 ng/mL *P. gingivalis*-LPS. Resolvin D1 or *P. gingivalis*-LPS were not administered to the controls. Following the RvD1/*P. gingivalis* LPS treatment, MTT was applied to the wells and incubated for two hours. 200 µL of dimethyl sulfoxide were added to each well after incubation to obtain blue formazan, whose optical density was determined at 540 nm. Cell viability at 72 hours was also determined using this procedure.

Real-time Polymerase Chain Reaction (RT-PCR)

To determine the mRNA expressions of pro-/anti-inflammatory cytokines, total RNA from HGF cells was collected 24 or 72 hours following treatment with varied doses of RvD1 and 1000 ng/mL *P. gingivalis* - LPS. The EZ-RNA Total RNA Isolation Kit's recommended methodology for RNA extraction was followed (Kibbutz BeikHaemek, Israel). The A260/280 ratio, as determined by spectrophotometry, was maintained above 1.8 utilizing a complementary DNA (cDNA) synthesis kit, first-strand complementary DNA was produced from 1.0 µg of total RNA (Applied Biosystems High-Capacity RNA-to-cDNA kit, Foster City, USA). Using the Brilliant SYBR Green Q-PCR Master Mix (2X) (Thermo Scientific, Massachusetts, USA), real-time PCR was carried out using 1.0 µL of cDNA for a total volume of 25 µL.

In order to ascertain whether any nonspecific PCR amplifications were generated, melting curve investigations of the PCR products were carried out. The reference gene for normalization was GAPDH, which was unaffected by the research treatments.

Statistical analysis

Statistical analysis was performed using GraphPad Prism version 5 for Windows. mRNA expression, by calculating the ΔCt (Ct housekeeping gene - Ct gene

Table 1. Synthetic gene-specific oligonucleotide primers used in this research. All sequences are from human and listed 5'–3'

Primer	Forward	Reverse
IL-1β	CTGATGGCCCTAAACAGATGAA	TCGGAGATTCGTAGCTGGAT
IL-6	GGTACATCCTCGACGGCATCT	GTGCCTCTTTGCTGCTTTCAC
IL-8	ACTGAGAGTGATTGAGAGTGGAC	AACCCTCTGCACCCAGTTTTC
IL-10	CATCGATTTCTTCCCTGTGAA	TCTTGGAGCTTATTAAAGGCATTC
IL-17	CCCAGGGACCTCTCTCTAATC	ATGGGCTACAGGCTTGTCACT
Del-1	CCTGTGAGATAAGCGAAGC	GAGACTCGGTGAGTAGATG
GAPDH	ACCACAGTCCATGCCATCAC	TCCACCACCCTGTTGCTGTA

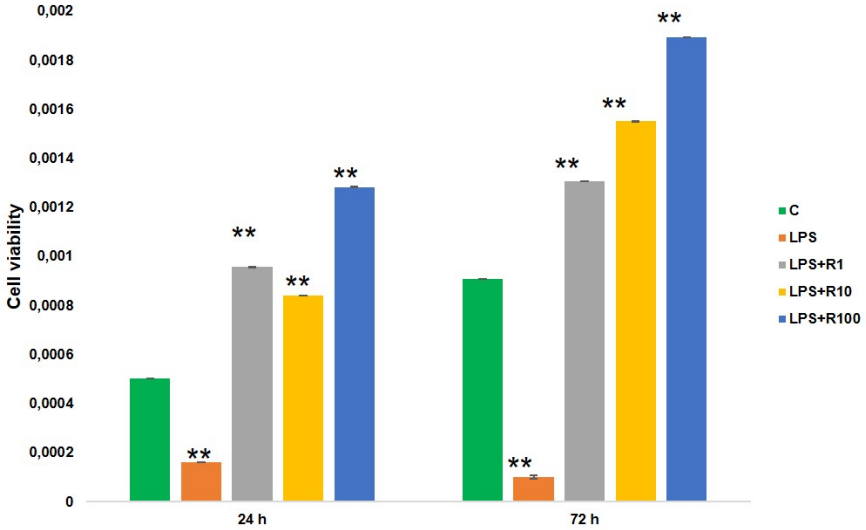

Figure 1. The effect of RvD1 on the *P. gingivalis*-LPS-induced cell viability in HGFs. The HGFs were treated with only 1000 ng/mL *P. gingivalis*-LPS and the combination of 1000 ng/mL *P. gingivalis*-LPS and 1 ng/mL RvD1 (LPS+R1), 10 ng/mL RvD1 (LPS+R10), 100 ng/mL RvD1(LPS+100) at 24 h and 72 h. *p<0.05, compared with the control (C).

of interest), and the expressions of different genes were expressed as 2-ΔCt. Triplicates were performed for each experimental point.The comparative Ct method was used for Q-PCR results (17). A one-way analysis of variance (ANOVA) with Dunnett's test and Tukey's HSD test was used to assess the cell viability and RT-PCR results. Differences between groups were considered significant when the confidence interval exceeded 95 % (P < 0.05).

RESULTS

RvD1 Effects on Viability of *P. gingivalis*-LPS Treated HGF Cells

Only 1000 ng/mL *P. gingivalis*-LPS (LPS)significantly decreased HGF cell viability (p<0.05) in a time-dependent manner compared to the control group (C) (Figure 1). Resolvin D1 counteracted the detrimental effects of *P. gingivalis*-LPS on cell viability when 1000 ng/mL *P. gingivalis* LPS and RvD1 were administered concurrently. Treatments with 1, 10 and 100 ng/mL RvD1 completely recovered the viability in a time- and dose-dependent manner compared to the levels found with 1000 ng/mL *P. gingivalis*-LPS alone (p<0.05). The highest increase in *P. gingivalis*-LPS-stimulated cell viability was achieved with 100 ng/mL RvD1, and it was 94% of the control after 24 and 72 hours (p<0.005) (Figure 1).

RvD1 Effects on HGFs Cytokines and DEL-1 Expressions Linked to Inflammation

Only 1000 ng/mL *P. gingivalis*-LPS (LPS) application, when compared to the control group (C), importantly improved the pro-inflammatory cytokine expressions (IL-1β, IL-6, IL-8, and IL-17) and reduced the anti-inflammatory cytokine expression (IL-10) at 24 and 72 h (p<0.05) (Figure 2). Additionally, 1000 ng/mL *P. gingivalis*-LPS combined with 1, 10, and 100 ng/mL RvD1 concentrations (LPS+R1, LPS+R10, LPS+R100) did not affect the expression of IL-1β compared to the control group at 24 and 72 hours (p>0.05). Conversely, treating cells with 1000 ng/mL *P. gingivalis* LPS and RvD1 concentrations (1, 10, and 100 ng/mL), when compared to the control group(C), reduced the expression of IL-6, IL-8, and IL-17 mRNA levels at both time periods (p<0.05). Resolvin D1 administration at 1, 10, 100 ng/mL dramatically upregulated the anti-inflammatory cytokine IL-10 in comparison to the control group (p<0.05). Additionally, the treatment with all RvD1 applications enhanced the expression of IL-10 that is suppressed by *P. gingivalis*-LPS to levels higher than those of the control group (p<0.05), with the rise becoming more noticeable at 72 h (Figure 2). The Del-1 mRNA expression levels between the HGF control and RvD1-treated groups displayed a important difference in RT-PCR results (p<0.05).

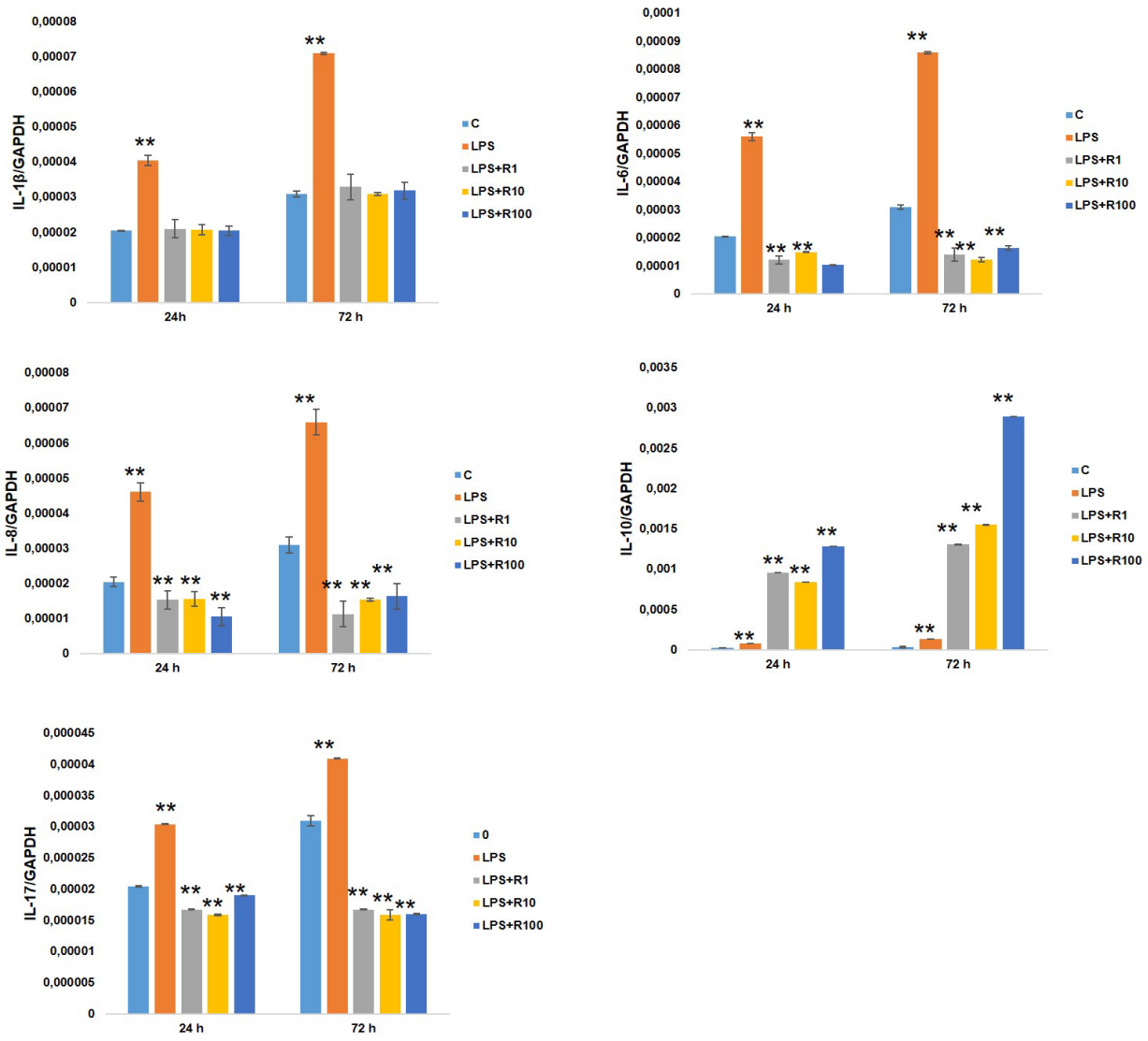

Figure 2. RvD1 affected the mRNA expressions of pro/anti-inflammatory cytokines of *P. gingivalis*-LPS-treated HGFs. The expression of pro/anti-inflammatory cytokines in HGFs from each group detected by quantitative RT-PCR (target genes were normalized to the housekeeping gene GAPDH). The cells were treated with only 1000 ng/mL *P. gingivalis*-LPS (LPS) and the combination of 1000 ng/mL *P. gingivalis*-LPS and 1 ng/mL RvD1(LPS+R1), 10 ng/mL RvD1 (LPS+R10), 100 ng/mL RvD1 (LPS+R100) at 24 h and 72 h. A.IL-1β, B. IL-6, C. IL-8, D. IL-10, E. IL-17 mRNA expressions of HGFs applied by only *P. gingivalis*-LPS, and the combination of *P. gingivalis*-LPS and RvD1. *p <0.05, compared with the control (C).

HGFcells induced by *P. gingivalis* LPS were treated with RvD1 concentrations (1, 10, 100 ng/mL) and total RNA was isolated from HGFs at 24 and 72 h with or without RvD1 concentrationsto determine the effects of RvD1 on Del-1 mRNA expression levels. Figure 3 shows that after the application of RvD1, the expression levels of Del-1 in the HGFs were significantly increased in a time- and dose-dependent manner at 24 and 72 h ($p<0.05$). as compared to the control group.

DISCUSSION

Resolvin D1, an omega-3 polyunsaturated fatty acid metabolite, has been demonstrated to reduce inflammation in vivo and decrease polymorphonuclear neutrophil (PMN) accumulation in tissue by preventing human PMN transendothelial migration and improving macrophages potential to phagocytose PMNs (16). We demonstrated earlier that *P. gingivalis* LPS-induced modification of phenotypic and inflammatory characteristics in HGF

could potentially be a pathogenic mechanism underlying tissue destruction. Therefore, we hypothesized that RvD1 modulates the inflammatory response of *P. gingivalis* LPS-induced HGF cells through cytokine and Del-1 expressions.

The results of this study demonstrate that RvD1 modulates cell viability and pro-/anti-inflammatory cytokine profiles andDel-1 expression of *P. gingivalis*-LPS-induced in HGFs. We used optimum dosage (1000 ng/mL) of *P. gingivalis*-LPS according to our previous studies (9,10. Resolvin D1reduced the pro-inflammatory cytokine expressions, whereas anti-inflammatory and Del-1 expressions increased in a time- and dose-dependent manner. In our previous study, *P. gingivalis*-LPS suppresses cell viability and proliferation in HGFs (9). Additionally, report we reported in our earlier study that 1000 ng/mL *P. gingivalis*-LPS significantly reduced cell viability in cementoblasts (10). In the literature we found another study performed by Khaled et al., in which they analyzed the effects of RvD1 using different concentrations (0- 1000 ng/mL) on HGFs and they determined that RvD1 both had no cytotoxic effects and importantly supressed the toxic effects of 13.5% (v/v) *P. gingivalis* supernatant on HGFs (16). Our findings are consistent with the findings of the Khaled et al. study. Cao et al. reported that RvD1 (50, 100, and 200 nM) human osteoblastic osteosarcoma cell line (MG-63) cell viability did not affect, but cell viability importantly decreased by 1000 ng/mL Escherichia coli-LPS application, and these reductions were significantly reversed by RvD1 treatment (18). Also, another study revealed that high-dose *P. gingivalis* LPS (≥ 50 µg/mL) importantly suppressed cell viability, while low-dose *P. gingivalis* LPS (≤ 10 µg/mL) did not importantly affect HGF viability (19).

Gingival fibroblasts are abundant in gingival tissue and have been reported to contribute in immune response and inflammatory events (20). Additionally, the cells react to different inflammatory cytokines and growth hormones (21). Cytokines are essential for regulating the inflammatory system. In addition to immune cells including lymphocytes, monocytes, macrophages, and granulocytes, they are also generated by epithelial, endothelial, and fibroblast cells. We analyzed the pro-/anti-inflammatory cytokine expressions of HGFs induced with 1000 ng/mL *P. gingivalis*-LPS and incubated with control, 1, 10, 100 ng/mL RvD1 at 24 and 72 h. Also, we applied to HGFs only 1000 ng/mL *P. gingivalis*-LPS for cytokine expressions at 24 and 72 h. As compared to the control, no significant difference in the IL-1β mRNA expression of *P. gingivalis*-LPS-induced-HGFs treated with any of RvD1 but only *P. gingivalis* LPS treated HGFs significantly increased IL-1β mRNA expression at 24 and 72 h . When cells were stimulated with only *P. gingivalis*-LPS IL-6, IL-8, and

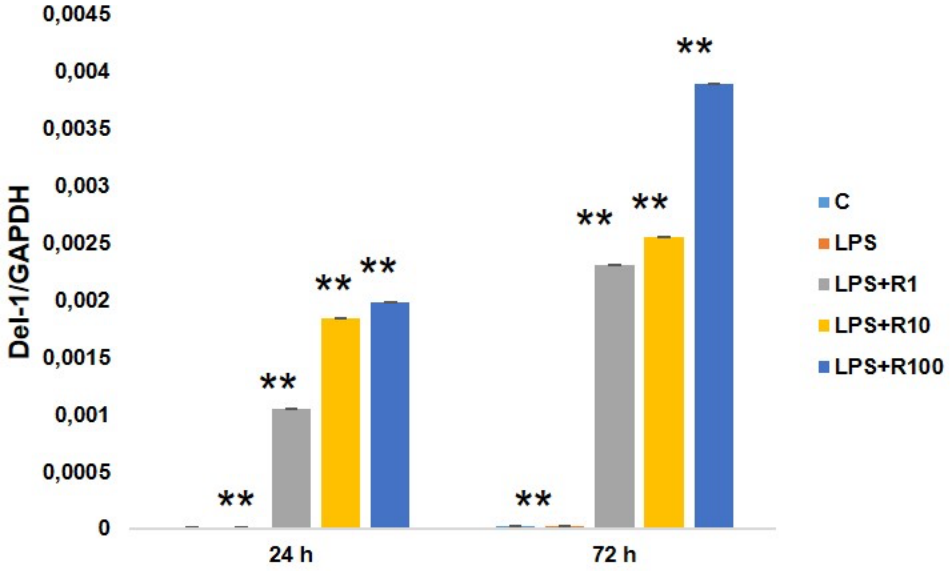

Figure 3. Demonstration of the effects of only *P. gingivalis*-LPS and the combination of 1000 ng/mL *P. gingivalis*-LPS (LPS) and 1 ng/mL RvD1 (LPS+R1), 10 ng/mL RvD1 (LPS+R100), 100 ng/mL RvD1 (LPS+R100) on Del-1 expression in HGFs at 24 h and 72h. *p <0.05, compared with the control (C).

IL-17 mRNA expressions dramatically increased, but RvD1 administration following *P. gingivalis*-LPS stimulation significantly decreased IL-6, IL-8, and IL-17 levels compared to the control group in a time- and dose-dependent manner. Our previous study demonstrated that higher concentrations (1000 and 3000 ng/mL) of *P. gingivalis*-LPS importantly stimulated IL-6 and IL-8 mRNA expressions of HGFs on days 3 and 8 (9). Another one of our studies had previously revealed that 1000 ng *P. gingivalis*-LPS dramatically increased the expression of IL-1β, IL-8, and IL-17 mRNA expression of cementoblasts at 16 and 24 hours. However, IL-8 and IL-17 expressions were decreased in the cementoblast cells induced with 1000 ng/mL *P. gingivalis*-LPS at 72 h. (10). The differences in the results between these studies may be due to the different origins of the cementoblast/HGF and the induction of both cells by *P. gingivalis*-LPS may result in different cytokine response in a time-dependent manner. Khaled et al. investigated the impact of RvD1 on *P. gingivalis* treatment on HGF expression of cytokines and they demonstrated that supernatant of *P. gingivalis* dramatically upregulated the mRNA expression of IL-6, IL-5, IL-17, IL-10, IL-8, monocyte chemoattractant protein (MCP)-1, MCP-2, and MCP-3. Also, the combination of *P. gingivalis* supernatant and RvD1 on HGFs showed that RvD1 significantly improved the TGF-β1 and importantly decreased MCP-1 and IL-6 levels (14). Our pro-inflammatory cytokine results in general are consistent with the literature (16). As reported in this study RvD1 dose-dependently increased IL-10 expression of *P. gingivalis*-LPS-induced HGFs at 24 and 72 h. The effects of 1000 ng/mL *P.gingivalis*-LPS on the expression of IL-10 mRNA expression was revealed in cementoblasts by our earlier study and our results demonstrated that 1000 ng/mL *P. gingivalis*-LPS increased the production of IL-10 in cementoblasts (10). Similarly, Khaled et al. reported that only *P. gingivalis* supernatant application to HGFs stimulated IL-10 mRNA expression (16). In this study, RvD1 concentrations significantly increased IL-10 expression in *P. gingivalis*-LPS-induced HGFs in a time- and dose-dependent manner.

Developmental endothelial locus-1 (Del-1) has been discovered as a new antagonist of the leukocyte LFA-1 integrin (CD11a/CD18), which restricts the movement of human neutrophils through endothelial cells (22). It modulates neutrophil recruitment to the periodontium and prevents inflammation and bone loss. Moreover, Del-1 prevents periodontal inflammation by inhibiting LFA-1 integrin-dependent neutrophil recruitment and IL17-mediated inflammation (7). In the present study, Del-1 expression was inhibited by only *P. gingivalis*-LPS, whereas IL-17 expression was upregulated by only *P. gingivalis*-LPS. While the level of Del-1 was increased by the combination of *P. gingivalis*-LPS and RvD1 as a time and dose-dependent manner, IL-17 expression was decreased in similar *in vitro* experiment conditions. Interleukin-17 is a pro-inflammatory cytokine that stimulates granulopoiesis and regulates neutrophil function, survival, and recruitment (23) andIL-17 suppresses the expression of Del-1 (12). When compared to young mice, the periodontium of old mice exhibits lower levels of Del-1 expression, which is correlated with high neutrophil recruitment and inflammatory bone loss that is IL17A-dependent in old mice in vivo models (12). Inonu et al. compared that salivary IL-17, LFA-1, and Del-1 were measured in individuals having gingivitis (G), chronic periodontitis (CP), and generalized aggressive periodontitis (GAP). It was determined that the CP and GAP groups had higher amounts of IL-17 and lower levels of Del-1 than the G and H groups (24). In addition, Maekawa et al. reported that IL-17 decreases Del-1 expression in human umbilical vein endothelial cells (HUVEC) by the GSK-3b- and C/EBPb-dependent pathway. Additionally, RvD1 reverses IL-17-stimulated Del-1 downregulation in vivo (14). Our results support an inverse relationship between Del-1 expression and IL-17 expression resulting from RvD1 in HGFs. Indeed, the periodontal tissue production of IL-17 is inhibited by Del-1, which is act as a gatekeeper of leukocyte recruitment and inflammation.

The lack of evaluation of Del-1 and cytokines (IL-1β, IL-6, IL-8, IL-10, and IL-17) protein levels was a limitation of this study. Quantification of protein levels would substantially improve our data and confirm the changes in mRNA expression in the HGF cells treated with a combination of *P. gingivalis*-LPS and RvD1.

CONCLUSION

Based on the findings of this study, *P. gingivalis*-LPS stimulates pro-inflammatory cytokines production in HGFs. Furthermore, combination of RvD1 and *P. gingivalis*-LPS decreased the pro-inflammatory cytokine expressions, while upregulating the anti-inflammatory cytokine expression and Del-1 levels in

a time- and dose-dependent manner. These findings seem to be consistent with the hypothesis that RvD1 modulates the gingival fibroblast from the *P.gingivalis*-LPS-stimulated inflammation by acting on pro-/anti-inflammatory cytokines of this damage. Also, RvD1 differentially affected IL-17 and Del-1 expressions in *P. gingivalis*-LPS-stimulated HGFs. RvD1 can thus provide a promising platform for IL-17-driven pathological inflammation including periodontal disease in a Del-1-dependent manner.

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Author contributions: SBB: Conception, design and finansman for research, literature review, writing and critical review for manuscript. SSH: Conception, design, supervision, critical review for manuscript.

Conflict of interests: No conflicting relationship exists for any author in this study.

Ethical approval: Study was approved by Nigde Omer Halisdemir University, Non-Invasive Clinical Research Ethics Committee (Date: 24.03.2022, Decision Number: 2022/36).

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RESEARCH ARTICLE

GENDER-BASED APPROACH IN FAMILY PLANNING IN PRACTICES IN TURKEY'S MOST FERTILE PROVINCE: SECONDARY ANALYSIS OF MIX METHOD TWO STUDIES

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ABSTRACT

Purpose: To determine the gender-based family planning approaches in the province in Turkey with the highest fertility rate.
Material and Methods: This study was carried out with the secondary analysis of the quantitative data on family planning from two different studies that the researchers conducted with in the same region, the same method and close to each other.
Results: In total, 56.7% of the women stated that they used any available family planning method, whereas 80.4% chose the method with their spouse. According to their responses, family planning methods used by women were intrauterine devices (41.2%) and withdrawal (28.9%). Furthermore, 10.5% of the men reported using any available family planning method, whereas 91.0% used the method decided by their spouse. According to the responses obtained from the male participants, the family planning methods used were pills (45.5%), intrauterine devices (18.2%), and male condom (18.2%). Women with a higher age, duration of marriage and the average number of living children had higher levels of using FP methods; The level of using FP method is lower in men who have not completed any education level, perceive their income level as "good", have health insurance, and men with a higher average age.
Conclusion: The study outcomes revealed that there was gender-based differences between women and men about the use of FP methods; furthermore, men took less responsibility for using FP methods and women-specific methods are generally used.

Keywords: Family planning, gender, men, Turkey, women.

INTRODUCTION

Maternal and infant mortality rates are still high in developing countries owing to the presence of high fertility rates, risky pregnancies, and complicated deliveries. According to the World Health Organization, 810 women die every day and 295 000 women every year due to pregnancy and childbirth. In 2017, it is stated that the maternal mortality rate was as high as 462 per 100.000 live births in developing countries and 11 per 100.000 live births in developed countries (1). In Turkey, the maternal mortality rate was 13.6 per 100.000 live births, which was marginally higher than that in developed countries (2).

To reduce the maternal mortality rate, it is imperative to provide uninterrupted and qualified services for all

women in need of family planning (FP), prenatal care, safe delivery, and postnatal care. Globally, the FP needs of approximately 214 million women of reproductive age are currently unmet (3). However, the use of modern FP methods in many parts of the world is not at a desired level. According to the latest estimates, the usage of modern FP methods by married women (age, 15–49 years) in developing countries has increased from 55.0% to 57.1% between 2000 and 2019. Reasons for this gradual increase include limitations in method diversity, lack of access, fear of side effects, inadequate service quality, negative impact of religion and culture, and gender-based obstacles (3).

Men have the potential to facilitate and hindrance the use of contraceptive methods to a considerable degree. Therefore, the lack of participation by men is an important factor responsible for obstructing the increase in the usage of FP methods (4). In many countries, FP services are traditionally perceived and offered as a service for women. Although most of the men in developing countries accept that FP is the mutual responsibility of couples, they do not actively contribute in selecting the pertinent contraception method with their partners (5,6). Certain cultural components of the traditional Turkish family structures prevent the spread of awareness related to the use of FP methods and services. And also, as in all other matters, the authoritarian and patriarchal structure in domestic relations requires the approval of the men to use the relevant FP method (7).

In Turkey, it is particularly important to have children for lineage continuity, especially in the culture of the Eastern regions. The province where the study was conducted, i.e., Şanlıurfa, has the highest fertility rate (total fertility rate, 3.89) in Turkey, and it is a province where maternal–infant mortality rates have consistently been high (8). In a region with a high fertility rate, conducting studies on factors that will affect the access and provision of FP services and planning appropriate interventions will make a significant contribution to protecting maternal–infant health.

This study aims to determine the gender-based family planning (FP) approaches in the province in Turkey with the highest fertility rate.

MATERIAL AND METHODS

Study Type

This is a cross-sectional study.

Study Population and Sample

Based on data of the Turkish Statistical Institute Population Registration System, the study population included 206.118 women aged 15–49 years and 246.653 men of reproductive age, who reside in the city center of Şanlıurfa (9).

The research was carried out with the secondary analysis of the quantitative data on family planning from two different studies (references will be added after article acceptance) that the researchers conducted with in the same region, the same method and close to each other. In the previous two studies, the use of family planning method was used only as a prevalence and other details were not included. In this study, descriptive statistics about FP were used. The data of 382 individuals, 172 married women and 210 married men, who were expected to use the method, were included in the study.

Data Collection

The data were collected through face-to-face interviews and using the Data Collection Form developed by the researchers. In this study, variables related to socio-demographic characteristics of the men and women (age, educational background, employment status, age of spouse, educational background of spouse, working status of spouse, language most spoken, income status, health insurance, family type, and duration of marriage) and characteristics of the FP methods used (method use status, method used, reason for choosing the method used, reason to not use a method, person who decided the method, and state of getting information about the method) were included.

Evaluation of Data

The data were analyzed using the IBM Statistical Package for Social Sciences (SPSS) for Windows 26.0 statistical package program (IBM, Armonk, NY, USA). Descriptive statistics, chi-square, and t test from univariate analysis methods were used for data evaluation. Fisher's exact test was used when chi-square assumptions are not satisfied. Statistical alpha level $p<0.05$ was considered significant.

Ethical Dimension of the Study

Ethical approval was obtained from the Ethics Committee of Koç University (Decision number 2016.004.IRB3.003, dated 27.01.2016; dated 27.07.2016 and numbered 2016.157.IRB3.088) for both studies whose data were used. Verbal consent

Table 1. Distribution of Some Socio-Demographic Characteristics of Women and Men by FP Method Use

	FP Method Use												
	Women[$]							Men					
	Using		Not using					Using		Not using			
	Number	%*	Number	%*	%**	X^2	P	Number	%*	Number	%*	%**	X^2	P
Educational Background														
No education[$$]	37	67.3	18	32.7	32.2	3.73	0.15	0	0.0	63	100.0	30.0	**13.2**	**0.001**
Primary school	26	53.1	23	46.9	28.7			14	19.2	59	80.8	34.8		
Secondary school and above	34	50.7	33	49.3	39.2			8	10.8	66	89.5	35.2		
Spoken Language														
Turkish	69	59.5	47	40.5	68.0	2.61	0.27	16	12.5	112	87.5	61.0	1.57	0.45
Kurdish	19	57.6	14	42.4	19.2			4	6.6	57	93.4	29.0		
Arabic	9	40.9	13	59.1	12.8			2	9.5	19	90.5	10.0		
Employment Status														
Working	25	56.8	19	43.2	26.2	1.00	0.56	19	10.2	168	89.8	89.0	***	0.71
Not working	72	56.7	55	43.3	73.8			3	13.0	20	87.0	11.0		
Perceived Income Status														
Good	14	48.3	15	51.7	17.4	1.22	0.54	4	4.7	82	95.3	40.9	**6.40**	**0.04**
Middle	66	59.5	45	40.5	64.5			15	13.5	96	86.5	52.9		
Bad	17	54.8	14	45.2	18.0			3	23.1	10	76.9	6.2		
Health Insurance														
Yes	73	56.6	56	43.4	75.6	1.00	0.54	14	8.2	156	91.8	81.0	***	**0.04**
No	24	57.1	18	42.9	24.4			8	20.0	32	80.0	19.0		
Educational Background of the Spouse														
No education	9	69.2	4	30.8	7.6	1.03	0.59	7	6.5	100	93.5	51.0	4.15	0.12
Primary school	27	58.7	19	41.3	27.1			11	16.2	57	83.8	32.3		
Secondary school and above	61	55.0	50	45.0	65.3			4	11.4	31	88.6	16.7		
Employment Status of the Spouse														
Working	90	58.4	64	41.6	92.3	1.22	0.13	2	18.2	9	81.8	5.2	***	0.32
Not working	5	38.5	8	61.5	7.7			20	10.1	179	89.9	94.8		

*Percentage of rows, ** Percentage of columns, *** Fisher's Exact Test, [$] Individuals who did not answer all questions in the female group, [$$] The group with significant difference.

was obtained from the men and women who agreed to participate in the study.

RESULTS

The mean age of the women and men was 32.2 ± 8.5 and 40.4 ± 12.0, respectively. In total, 32.2% women had had no formal education and 32.0% spoke a language other than Turkish at home. Only 26.2% of women were employed in an income generating job, 64.5% perceived their income level as “medium,” and 24.4% did not have health insurance. Furthermore, 65.3% of the spouses of the women had an educational background of secondary school and above and 92.3% worked in an income generating job. However, 30.0% of men had had no formal education and 39.0% spoke a language other than Turkish at home. In total, 89.0% of men worked in an income generating job, 52.9% perceived their income level as “medium,” and 19.0% did not have health insurance. Alternatively, 51.0% of the spouses of the men did not have any educational qualifications and 94.8% did not have an income generating job (Table 1).

The mean duration of marriage was 12.1 ± 9.4 years, and the mean number of living children was 3.1 ± 2.2 as reported by the women included in this study. The mean duration of marriage was 15.8 ± 12.4 years, and the mean number of living children was 3.1 ± 2.0 as reported by the men included in this study.

A total of 56.7% of the women reported that they used any of the available FP methods, among which the most used methods include are intrauterine devices (IUD, 41.2%) and withdrawal (28.9%). The desired FP method in 80.4% of the women was decided with their spouses. The most common reasons for preferring the FP method used were satisfaction (56.2%) and suggestions by health personnel (19.3%), whereas most common reasons for not using FP methods were pregnancy (14.5%) and the desire to conceive (7.0%). A total of, 48.3% of the women had a history of using an FP method other than the FP method they currently use. Only 29.1% of the women reported that they had received training on FP methods, and the most common source of training was nurses/midwives (70.0%) (Table 3).

According to the socio-demographic characteristics of the women, there was no difference among them in terms of using FP methods (Table 1). However, women with a higher mean age (p=0.04), duration of marriage (p<0.001), and number of living children (p<0.001) used FP methods to a significantly higher degree (Table 2).

In total, 10.5% of the men reported that they used any of the FP methods available. Pill (45.5%), IUD (18.2%), and male condom (18.2%) were among the most used methods. Furthermore, 91.0% of the men stated that their spouse decided on the FP method used. The most common reasons for why the men did not use FP methods were that their spouse did not want them to use (40.7%) and that they desired to have a child (22.5%). Other than the FP methods they currently used, 86.4% of the men reported not using any other FP methods. Only 8.1% of the men reported that they had received training on FP methods, and the most common sources of training were nurses/midwives (47.0%) and doctors (41.2%) (Table 3).

The level of using FP method is lower in men who do not have any formal education (p=0.001), perceive their income level as "good" (p=0.04) and have health

Table 2. Distribution of Some Characteristics of Women and Men by FP Method Use

	FP Method Use							
	Women				**Men**			
	Using	Not using			Using	Not using		
Characteristics	Mean ± SD	Mean ± SD	t	p	Mean ± SD	Mean ± SD	t	p
Age	33.3 ± 7.7	30.6 ± 9.3	**2.04**	**0.04**	34.5 ± 10.9	41.2 ± 11.9	**−2.48**	**0.01**
Duration of Marriage	14.3 ± 8.7	9.2 ± 9.6	**3.56**	**<0.001**	14.2 ± 14.3	16.0 ± 12.2	−0.64	0.52
Number of Children Living	3.7 ± 2.0	2.3 ± 2.3	**4.37**	**<0.001**	3.1 ± 1.9	3.1 ± 2.0	−0.14	0.88

insurance (p=0.04), and men with a higher average age (p=0.01), and this difference is statistically significant. However, there is no difference between use of FP method in men according to the most spoken language at home (p=0.45), employment status (p=0.71), education level of spouse (p=0.12), working status of spouse (p=0.32), duration of marriage and average number of living children (Table 1).

DISCUSSION

In this study, the secondary analysis of data on FP methods reported in two prior studies containing similar data on men and women was used. Study outcomes revealed that the socio-demographic information given by the women for themselves, and their spouses was very similar to that provided by the men for themselves and their spouses. Particularly, the number of living children is nearly identical in both groups. Conversely, there were remarkable intergroup differences in terms of the answers provided on the use of FP methods.

Accurate comparison of the data was limited by the fact that only a small number of men stated that they used any FP method. Although the female and male populations herein live in the same region and community, female reports were more compatible with the literature, whereas the male reports were considerably different from that reported in the literature. This could be attributable to the inability of men to express themselves comfortably about reproductive health and sexual issues, or due to the lack of sufficient interest.

In total, 56.7% of women and only 10.5% of men stated that they used FP methods. Furthermore, there were great differences between the answers of men and women in terms of the details of the method used. This thought-provoking result may be due to the following reasons: men continue to not take responsibility for using FP method, men do not mutually share this responsibility with their wives, or women must hide the methods they use from their spouses. In Şanlıurfa, having many children is accepted as a social norm, which subsequently generates social pressure and teachings. For this reason, couples may attempt to hide the fact that they use an FP method from their surroundings and in some cases even from each other. As a matter of fact, Eroğlu et al. reported in their study performed in the same region that women secretly use the FP methods and hide this fact from their spouses (10).

The most used methods reported in this study were IUD, withdrawal, and tubal ligation for women and pills, IUD, and male condom for men. Notably, women reported that they preferred the withdrawal method with limited effectiveness twice as much as the tubal ligation method. According to the Turkey Population and Health Research 2018 (TPHR 2018), which represents the entirety of Turkey, the most used methods were withdrawal (20%), male condom (19%) and IUD (14%) (12). In the present study, approximately 60% of the FP methods used are female-specific methods. This suggests that men take less responsibility in selecting and using an FP method, or they leave the decision to their spouses because they do not want to be involved in the decision-making process. Similarly, although men are in a decision-making position on many issues in the family, they reportedly do not use these roles in to avoid being involved in the responsibility for selecting the FP method (13).

In the current study, women stated that they mostly decided with their spouses on the method they used, whereas men stated that their spouses were more decisive in this issue. This result supports the result of the TPHR 2018 survey (12); furthermore, it may also suggest that men take less responsibility by leaving the decision on selecting the FP method to women.

In the study, the most prefer reason among men and women as the reason for choosing the method is “prefer with the method used.” The reasons for choosing a specific FP method differ in the literature. To illustrate, Amin (2012) reported that efficiency (30.5%) and ease of availability (18.1%) are frequently stated as the reasons considered while choosing the FP method (14). However, Amran et al. (2019) report low cost, did not any side effects, and ease of use (15). Therefore, these findings reveal the necessity of deciding on a specific FP method for each couple when receiving counseling on the FP methods.

Regarding the reasons for not using FP method, our results showed that men and women generally expressed similar reasons. One of the most common reasons for not using or stopping the use of a method was “desire of having a child”. In the TPHR 2018 study, among the reasons for quitting a method of contraception, “desire of having conceive” (38%) was the most frequent reason (12). However, in our study, it is noteworthy that the answer of desire of having child and not wanting to use a method was higher in

Table 3: Distribution of the Characteristics of FP Method Use Among Women and Men

	Women*		Men *	
Characteristics	**Number**	**%**	**Number**	**%**
FP Method Use				
Using	97	56.7	22	10.5
IUD	40	41.2	4	18.2
Tubal ligation	12	12.4	-	-
Male condom	11	11.3	4	18.2
Pill	6	6.2	10	45.5
Needle	-	-	1	4.5
Withdrawal	28	28.9	3	13.6
Not using	74	43.3	188	89.5
The FP Method Used Decided By				
Mutually	78	80.4	1	4.5
Alone	9	9.3	1	4.5
Only the spouse	10	10.3	20	91.0
Reason for Prefer the Method Used				
Spouse's decision	3	3.0	2	9.0
Satisfaction	55	56.2	16	72.8
Ability to hide from spouse	1	1.0	-	-
Medical staff recommendation	15	19.3	-	-
No answer	24	24.5	4	18.2
Reasons for Not Using FP Method				
Pregnancy/Spouse being pregnant	25	14.5	21	11.2
Desire to conceive	12	7.0	42	22.5
Spouse does not want	10	5.8	76	40.7
The person’s own refusal	-	-	76	4.3
Being in menopause/Spouse being in menopause	10	5.8	18	9.6
Breastfeeding/Spouse breastfeeding	7	4.1	1	0.5
Health problems	5	2.9	-	-
Considering the methods as unhealthy	1	0.6	-	-
Reluctance to explain	-	-	21	11.2
FP Method Previously Used				
Yes	58	48.3	3	13.6
No	62	51.7	19	86.4
Previous Training About FP Methods				
Yes	50	29.1	17	8.1
From nurses/midwives	35	70.0	8	47.0
From doctors	11	22.0	7	41.2
From teachers	2	4.0	-	-
From pharmacists	-	-	1	5.9
From the internet	2	4.0	-	-
Not remembered	1	2.0	1	5.9
No	122	70.9	193	91.9

* Individuals who did not answer all questions in both the female group and the male group.

men than in women. This could be attributed to the unwillingness of men to answer this issue, which they perceive as protecting their privacy.

Majority of the women included in this study were part of a group who were poorly educated and were not employed but rate their economic level as was considered “medium.” This result is consistent with the Southeastern Anatolia Region data of the TPHR 2018 survey. Conversely, the group of men included in the study had a relatively higher education level and a higher rate of having an income generating job, as across the globe and Turkey. Certain socio-demographic characteristics, especially educational background, reportedly affect the use of FP method (16-18). In this study, the educational and income levels of men affected the usage of FP method. However, it is important to note that socio-demographic findings of women did not make any difference in terms of the FP method used. Like the literature, while the level of education in males increases, the level of FP use also increases; Unlike the literature, the level of FP usage decreased as the income level increased. It is thought that the tendency of low-income individuals to prefer FP use has increased due to the increase in the cost of childcare such as nutrition, education, and health services. This result may be important in terms of showing that the preferences have started to change. However, this result needs to be supported by other studies. Considering the fact that nearly one third of the women included in this study did not have any educational qualifications and the majority of the others have a low level of education, it can be inferred that the absence of educational qualifications does not have a positive effect on FP use.

In this study, it was observed increase in age, duration of marriage, and number of children resulted in a proportional increase in the degree to which FP methods were used. Considering the mean number of living children noted in this study, it is a probable that women attempt to limit their fertility as they reach the desired number of children. Several studies in the literature reported that as the age of women increases, their level of using FP method increases (19-21).

Strengths and Limitations

In Turkey, marriage is the beginning of the period when it is socially acceptable to become sexually active and conceive children. For this reason, since it was thought that unmarried individuals could not/may not answer the questions about FP method use, only the data of married women and men were included in the study.

CONCLUSION

In conclusion, there were gender-based differences between women and men with regard to the use of FP methods; furthermore, men took less responsibility for using FP methods and women-specific methods are generally used. In line with these findings, It is recommended to carry out studies in which gender attitudes are measured and monitored in the use of family planning methods, and qualitative studies that investigate the attitudes and barriers of men regarding their participation in family planning are recommended.

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RESEARCH ARTICLE

THE EFFECTS OF RESPIRATORY MUSCLE FUNCTIONS ON TRUNK MUSCLE ENDURANCE IN HEALTHY YOUNG ADULTS

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ABSTRACT

Purpose: Respiratory muscles play a dual role in breathing and trunk stability during activities. The relationship between respiratory muscle functions and trunk stability has not yet been clarified. The aim of the study was to examine the effects of respiratory muscle functions on trunk muscle endurance in healthy young adults.

Material and Methods: McGill's trunk muscle endurance tests, which consist of trunk flexion endurance test (FE), Sorensen test (ST) and Side Bridge test (SB), were used to evaluate the participants' trunk muscle endurance. Maximal inspiratory and expiratory pressures were measured to determine respiratory muscle strength. The respiratory muscle endurance test was performed with the incremental threshold load protocol using a threshold IMT device.

Results: A total of 51 healthy young adults, with a mean age of 21.8 ± 3.2 years, were evaluated. The results of the linear regression models were significantly explained 46% of the variance in the SB and 38% in the FE, (for SB Adj R2=0.46, F=21.40, p<0.001 and for FE Adj R2=0.38, F=15.65, p<0.001). Respiratory muscle endurance contributed 30% to the endurance of the trunk flexor muscles, while respiratory muscle strength contributed only 8%. Similarly, respiratory muscle endurance contributed 38% to the endurance of the trunk lateral flexor muscles, while respiratory muscle strength contributed only 8%.

Conclusion: Although respiratory muscle strength and respiratory muscle endurance were independent contributors to trunk muscle endurance, respiratory muscle endurance more affected trunk muscle endurance than respiratory muscle strength in healthy young adults.

Keywords: Endurance, respiratory muscles, strength, trunk muscles

INTRODUCTION

In the last decades, the number of studies investigating the importance of muscle endurance has increased. The terms of muscle strength and muscle endurance refer to different functions of the muscles. Muscle strength is the ability of a muscle or muscle group to withstand a resistance (1), however, the muscle endurance is defined as maintaining the muscle or muscle group's ability to sustain of withstanding applied resistance (2). In addition, the measurements of endurance are task-specific for each muscle. Muscle strength, one of the main

components of health and physical fitness, has an important role in the performance of many activities in daily life, while muscle endurance is related to the resistance of a muscle or muscle group to fatigue.

Respiration that is autonomous and rhythmic is one of the basic functions ensuring the continuity of life. It must be sustainable under all conditions, and therefore many muscles have to work in harmony (3). Respiratory muscles are classified according to the respiratory phase in which they are active. In the inspiratory phase of respiration, the diaphragm, external intercostal and scalene muscles are active. In the expiratory phase, the transversus abdominis (TrA) muscle, the internal oblique (IO) muscle, the external oblique (EO) muscle, the rectus abdominis (RA) muscle, and the internal intercostal muscles between the ribs are active. Respiratory muscle performance can be evaluated in terms of strength and endurance. Although respiratory muscle strength and endurance appear to be closely linked in many cases, endurance can't be accurately predicted from strength measurements (2). It has been shown that respiratory muscle strength is decreased while respiratory muscle endurance increases in patients with cystic fibrosis (4). Respiratory muscle strength has a positive effect on lung volumes and provides greater ventilation of the lungs. However, the endurance of the respiratory muscles is related to the fatigue of the respiratory muscles and allows the respiratory muscles to maintain their ability to do work (4, 5). Respiratory muscle strength and respiratory muscle endurance are parameters that can be improved with respiratory muscle training. Although respiratory muscle training increases respiratory muscle strength, the increase in respiratory muscle endurance better reflects clinical improvement than respiratory muscle strength (6, 7).

Respiratory muscles in humans play a dual role in breathing and trunk stability during activities. It has been shown that the diaphragm, the main inspiratory muscle, is also active during trunk activities. Although the diaphragm does not reveal direct action on the spine, it plays an important role in providing and maintaining core stability by increasing abdominal pressure. Besides, the diaphragm is stimulated before the muscles that initiate the limb movements, thereby playing a substantial role in core stability during limb movements (8). Even that the number of studies examining the effect of respiratory muscle training on trunk stability has increased recently (9-11), the relationship between respiratory muscle functions and the trunk stability has not yet clear. The aim of this study is to examine the effects of respiratory muscle functions on trunk muscle endurance in healthy young adults.

MATERIAL AND METHODS

Study Design and Participants

After the ethics committee's approval, a total of 51 healthy young participants with an age range of 18 to 25 years were included in this cross-sectional study. Since the lungs of healthy individuals between the ages of 18 to 25 years complete their physiological maturation and the lung tissue starts to deteriorate with age after this age range, our study includes only individuals in this age range (12). The inclusion criteria: not having any spine deformity such as scoliosis, not diagnosed with any orthopaedic, neurological, or cardiorespiratory diseases. Subjects were excluded if they have any previous spinal or abdominal surgeries, a previous or current pregnancy. Subjects were also excluded if they have regular exercise habit or smoking. Regular exercise habit; was defined as subjects that exercising for at least 45 minutes, 3 days a week for the last 6 months. In addition, participants were demanded not to consume caffeine, or eat any food in the 2 hours previous to the study. The respiratory functions, respiratory muscle strength and endurance, were measured for each participant at the same time of day.

Respiratory Muscle Strength

Respiratory muscle strength was evaluated by measuring intraoral maximal inspiratory pressure (MIP) and expiratory pressure (MEP) using an intraoral pressure meter device (Cosmed® Pony FX, Italy) according to the ATS/ERS testing protocol (13). MIP and MEP were measured from residual volume and total lung capacity; the tests were performed in the sitting position, wearing nose clips and using a standard mouthpiece during the maneuver. Measurements were repeated at least five times with one-breath intervals between each other, the highest value among the best three measurements without a difference of 10 cmH2O or 10% were recorded (14).

Respiratory Muscle Endurance

The respiratory muscle endurance test was performed using a Threshold IMT (Philips® Respironics, Inc) device with the incremental

threshold load protocol, which is repeatable, has less learning effect and clear results, according to ATS / ERS (13). During the test period, the participants were asked to maintain an upright position of the trunk. External load was provided by starting with 30-40% of the previously determined MIP value and increasing the MIP value by 5-10% every 2 minutes. The participant was asked to try to complete the test within 10 minutes by breathing through the mouth throughout the test. The last MIP value that the participant could tolerate for 2 minutes was accepted as the respiratory muscle endurance value (13, 15). Before starting the test, it was explained to the participants that if they felt too much dyspnea, palpitations and/or dizziness during the test, they could remove the device and the test would end (16). Measurements were made by a single physiotherapist using a standard chair.

Trunk Muscle Endurance Tests

McGill's trunk muscle endurance tests, which consist of trunk flexion endurance test, Sorensen test and side bridge test, were used to evaluate the participants' trunk muscle endurance (17). A trial test took a few seconds to show participants the position visually and learn the correct position. Participants were asked to take the test position after a 30-second rest, and the command to "start" was given after checking the correctness of the test position. Each test was repeated twice, with a maximum of two stimuli to ensure the correct test positions with 5 minutes of rest between tests. The maximum time in seconds that participants could stay in a static position during the test was recorded using a standard chronometer. The longest duration of the 2 tests that limited at 240 seconds was recorded. All trunk muscle endurance tests were measured by a single physiotherapist.

Trunk flexion endurance test (FE); the participants were positioned on a mat, with 90 degrees of hip and knee flexion in addition to 60 degrees of trunk flexion and also arms crossed over the trunk. The physiotherapist conducting the assessment supported the participant's feet and fixed his feet on the ground (18). The test was terminated when the participant could not maintain the position and time is recorded (17).

Sorensen test (ST); the participants were positioned in the prone position on an examination bed high above the ground. They were asked to keep their bodies outside of the bed with their pelvis, hips and knees on the bed until spina iliaca anterior superiors being at the edge of the bed. The participants were immobilized using a belt at the gluteal line level and supported by the physiotherapist at the ankles. In this position, the time that the arms crossed in front of the trunk and the trunk maintained its horizontal position was recorded. A chair was placed in front of the bed for safety and support when starting the test (17).

Side bridge test (SB); the participants were positioned on the dominant side on a mat in the lateral position with 90 degrees of shoulder abduction and 90 degrees of elbow flexion. The lower extremities were in extension and the upper foot was in front of the lower foot, while the humeral head, trochanter major and lateral malleolus were aligned. In this position, the participants were asked to lift their bodies on their forearms and sides of the feet. The test was terminated when the participants were unable to maintain a straight body position, or the hip fell down (17).

Statistical Analysis

All data were analyzed using SPSS 24.0 for Windows. Normally distributed data were presented as means and standard deviation. A partial correlation analysis was performed to investigate the relationship between the trunk muscle endurance tests and other variables. The multiple regression models were used to examine the effect of respiratory muscle strength and endurance to the contribution of trunk muscle endurance. Multicollinearity issues were verified using an interaction test. If the variation inflation factor (VIF) value was higher than five, it was considered as multicollinearity. The alpha level was set at .05 for all statistical analyses (19).

An a priori power analysis was conducted to determine the necessary number of participants G*Power (version 3.1; Universität Düsseldorf, Düsseldorf, Germany).(20) The required sample size was calculated using a power of 0.80, an effect size of 0.38 (determined from a pilot study based on the correlations between trunk muscle endurance and respiratory muscle endurance), and a 2-tailed design with an alpha value of 0.05. A total of 49 subjects were needed.

Ethical Consideration

Ethical approval was obtained from the Dokuz Eylül University, Non-Invasive Research Ethics Committee (with decision no: 2020/04-37, date: 17/02/2020). The

Table 1. Characteristics of Participants

Parameters	Participants (n=51)
Age, years	21.8 ± 3.2
Height, m	1.70 ± 0.09
Weight, kg	64.2 ± 14.6
BMI, kg/m^2	22.0 ± 3.9
Male / Female, n (%)	24 (47.1) / 27 (52.9)
MIP, cmH_2O	61.3 ± 24.1
MEP, cmH_2O	72.8 ± 23.1
RME, cmH_2O	28.8 ± 7.9
Trunk muscle endurance tests	
Trunk flexion endurance test, sec	44.9 ± 13.4
Sorensen test, sec	107.7 ± 38.5
Side Bridge test, sec	46.6 ± 10.9

Data are presented as mean (SD) or n (%). **BMI:** Body mass index; **MIP:** Maximal inspiratory pressure; **MEP:** Maximal expiratory pressure; **RME:** Respiratory muscle endurance; **sec:** seconds.

study was performed in accordance with the ethical standards as laid down in the 1965 Declaration of Helsinki and its later amendments. Informed consent was obtained from all individual participants included in the study.

An abstract of this study was presented at the International Congress of the European Respiratory Society, organized as a Virtual Congress, held on 5-8 September 2021, and published as a congress abstract in a supplement of the European Respiratory Journal.

RESULTS

The mean age and body mass index (BMI) of the participants were 21.8 ± 3.2 years, 22.0 ± 3.9 kg/m2 respectively. The characteristics of participants are presented in Table 1 and the study flow is presented in Figure 1.

The results of the multiple linear regression analysis for SB and FE are presented in Table 2. The best models with dependent variables SB and FE were significant (for both models, $P < 0.001$). The respiratory muscle endurance affected the R2 change in the model that SB was dependent variable by 38% ($\Delta R2 = 0.38$), while respiratory muscle strength affected 8% ($\Delta R2 = 0.08$). Besides, the respiratory muscle endurance affected the R2 change in the model that FE was dependent variable by 30% ($\Delta R2 = 0.30$), while respiratory muscle strength affected 8% ($\Delta R2 = 0.08$) (Table 2).

DISCUSSION

Previous studies have investigated the relationship between respiratory and trunk activations (9-11, 21-26). Although these studies revealed a relationship between respiratory muscle strength and trunk muscle endurance, there appear to be no studies that identify the relationship between trunk muscle endurance and respiratory muscle endurance. Therefore, this study was conducted to investigate the effects of respiratory muscle functions on trunk muscle endurance in healthy young adults. We showed that trunk muscle endurance is associated with both respiratory muscle strength and respiratory muscle endurance. Moreover, respiratory muscle

endurance more affected trunk muscle endurance than respiratory muscle strength.

Abdominal pressure increases to reduce the external load on the spine during trunk or extremity movements. If the diaphragm is in a relaxed position while the abdominal pressure increases, the pressure is transferred to the thoracic cavity, and this may cause adverse effects on hemodynamics and also the central nervous system. To prevent these complications, the diaphragm is active during trunk and limb movements so that the transmission of abdominal pressure to the thorax is minimized (23). Trunk muscles contract before limb movements begin and provide postural stability during limb movements. The diaphragm, which is the roof of the structure defined as the core region, contributes to trunk stability by increasing and maintaining abdominal pressure during its contraction (26). More importantly, to maintain postural stability, the diaphragm contracts simultaneously with the transversus abdominis, one of the most important trunk muscles, independently of respiration (27). It has been reported in many studies that respiratory muscles are also active during non-respiratory activities, and it has even been revealed that they can be trained with non-respiratory activities (22-25). In the literature, the relationships between respiratory and trunk muscle functions are mostly based on results from interventional studies. Strongoli et al. (25) measured transdiaphragmatic pressure (Pdi), which provides an estimate of diaphragm activity, during different thirteen core exercises using balloon catheters. They have found that core exercises cause a variety of Pdi and some of which sufficient to produce an inspiratory muscle training stimulus (25). In a study by Depalo et al. (23) to strengthen the diaphragm with non-respiratory exercise, they showed that the diaphragm can be activated and even trained by non-respiratory activities. Mustafaoğlu et al. (22) investigated the effects of core stabilization exercises on respiratory muscle strength. They have demonstrated that patients with substance use disorder, who participated in a 6-week core exercise training program combined with deep breathing, showed statistically significant improvements in MIP and MEP parameters compared with controls. In another study in which stroke patients were randomly divided into two groups, neurodevelopmental core exercises were applied to the one group and dynamic neuromuscular core exercises to the other group for four weeks. Significant increases in respiratory muscle strength were found in both groups after the four-week

Table 2: The Multiple Linear Regression Analysis for Side Bridge and Trunk Flexion Endurance Tests

	B	SE	β	t	p-values	VIF	ΔR^2
Dependent variable: SB[a], sec							
Constant	17.59	4.59		3.825	< 0.001		
RME, cmH_2O	0.71	0.16	0.51	4.553	< 0.001	1.15	0.38
MIP, cmH_2O	0.14	0.05	0.31	2.750	0.01	1.15	0.08
Dependent variable: FE[b], sec							
Constant	12.24	6.03		2.031	0.04		
RME, cmH_2O	0.75	0.21	0.44	3.685	0.001	1.15	0.30
MIP, cmH_2O	0.17	0.07	0.31	2.607	0.01	1.15	0.08

[a] Dependent variable: SB, Model: *Adj* R^2 = 0.46, F = 21.40, p< 0.001
[b] Dependent variable: FE, Model: *Adj* R^2 = 0.38, F = 15.65, p< 0.001
p< 0.05 was considered significant. **SB:** Side bridge; **RME:** Respiratory muscle endurance; **MIP:** Maximal inspiratory pressure; **MEP:** Maximal expiratory pressure; **FE:** Trunk flexion endurance; **B:** Unstandardized beta; **SE:** Standard error; **β:** Beta; t: Student's t test statistic; **VIF:** Variance inflation factor; Δ**R²:** Change of coefficient of determination; ***Adj:*** Adjusted; **sec:** seconds.

exercise program (24). In the relevant study, the researchers thought this was due to the involvement of the transversus abdominis, internal oblique, external oblique, and diaphragm as common muscles in respiratory and trunk stabilization. Therefore, the relationship between trunk muscles and respiratory muscles provides postural stability. In this study, we found a significant relationship between trunk muscle endurance and inspiratory muscle strength in healthy young adults. This effect has been demonstrated previously by diaphragm contractions during trunk activity, even supported by the improvement in diaphragm strength with core training programs (24-26). Not only trunk stabilization affects respiratory muscle strength, but also respiratory muscle strength also affects trunk stabilization, in other words, there is a mutual effect. Besides, there are studies examining the effect of respiratory muscle training on trunk stability (9-11). The more important task of the diaphragm, which is the most important muscle of respiration, than supporting the core stability is the inspiration phase of breathing (28). This dual task of the diaphragm has made the effect of respiratory muscle training on trunk muscles a topic of interest in the literature. Janssens et al. (9) investigated the effects of high-density inspiratory muscle training (IMT) versus low-density IMT on proprioceptive use during postural control in 28 individuals with low back pain (LBP). After 8 weeks of training, individuals trained high IMT have shown higher back proprioceptive signals during postural control and improvement in inspiratory muscle strength. In another study, Lee et al. (10) have investigated the effect of respiratory muscle training on trunk stability in 33 stroke patients. They applied expiratory muscle training (EMT), IMT and trunk stabilization exercises to one group and only trunk stabilization exercises to the other group. Although there was an increase in transversus abdominis thickness in both groups, this gain was significantly higher in the group, which applied EMT, IMT, and trunk stabilization exercises, than the other. Finta et al. (11) have demonstrated a significant increase in trunk stability in the group in which breathing exercises were combined with trunk exercises in patients with nonspecific low back pain.

To our knowledge, the relationship between respiratory muscle endurance and trunk muscle endurance has not been studied before. Moreover, this study is the first to examine the relationship between respiratory muscle endurance and trunk muscle endurance in this way. However, Shah et al. (29) have compared the maximal voluntary ventilation (MVV) values, which is a respiratory parameter associated with respiratory endurance, in individuals with and without chronic low back pain. They have found that MVV values were lower in individuals with low back pain than those without. They thought that this may be due to the synergistic activation of the diaphragm with the transversus abdominis muscle and the impairment of transversus abdominis activity in individuals with low back pain. In another study, Hackett (30) investigated at if there were any differences in lung function and respiratory muscle strength between individuals who exercised for strength versus endurance. When compared to the strength-trained group, the endurance-trained group generally performed better in terms of lung function and respiratory endurance. Hackett also showed the change in respiratory endurance with the change in MVV values like Shah et al. (29, 30). Yüksel et al. (31) examined the relationship between pulmonary function, respiratory muscle strength, and trunk muscle endurance. They found that pulmonary function and respiratory muscle strength are associated with the endurance of the trunk muscles. In previous studies (9, 21-23, 25, 30, 31), the relationship between trunk muscles and respiratory muscles was examined through trunk muscle activities and only respiratory muscle strength. For this reason, it was either examined how the respiratory muscle strength changed by giving trunk exercises, or core stabilization was evaluated by giving exercises to increase respiratory muscle strength. However, the strength and endurance are different functions for skeletal muscles and most importantly, respiratory muscles are also skeletal muscles (2, 3). The number of mitochondria is the determinant of endurance and studies have shown that muscle strength training and muscle endurance training are based on different mechanisms and their effects on mitochondrial activity are different (32, 33). These findings suggest that endurance may not be improved with strength training alone. In our study, trunk muscle endurance was related to both respiratory muscle strength and endurance. However, we found that respiratory muscle endurance was more contribute to trunk muscle endurance. Respiratory muscle endurance contributed 30% to the endurance of the trunk flexor muscles, while respiratory muscle strength contributed only 8%. Similarly, respiratory muscle endurance contributed 38% to the endurance of the

trunk lateral flexor muscles, while respiratory muscle strength contributed only 8%.

This study has some potential limitations. Firstly, dynamic trunk endurance may be more functional than static trunk endurance in healthy young adults. In this study, we only used static endurance tests to evaluate trunk muscle endurance. Secondly, although the relationship between trunk muscle endurance and respiratory muscle endurance was investigated in this study, the lack of measurements of trunk muscle strength limits the evaluation of the relationship with trunk muscle strength. Finally, since this study conducted on a certain age group, our results may not reflect all healthy population.

CONCLUSION

The results of this study show that although respiratory muscle strength and respiratory muscle endurance were independent contributors to trunk muscle endurance, respiratory muscle endurance more affected trunk muscle endurance than respiratory muscle strength in healthy young adults. In addition, we believe that this study will shed light on further studies on the trunk and respiratory muscles. Future studies are needed to investigate the relationship between respiratory muscles activities and trunk muscles activities.

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Ethical approval: Ethical approval was obtained from the Dokuz Eylül University, Non-Invasive Research Ethics Committee (with decision no: 2020/04-37, date: 17/02/2020). The study was performed in accordance with the ethical standards as laid down in the 1965 Declaration of Helsinki and its later amendments. Informed consent was obtained from all individual participants included in the study.

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RESEARCH ARTICLE

RELATIONSHIP BETWEEN THE PRESENCE OF CHRONIC PAIN AND ADHERENCE TO THE MEDITERRANEAN DIET IN UNIVERSITY STUDENTS

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ABSTRACT

Purpose: This study evaluated the presence of chronic pain and adherence to the Mediterranean diet and to examined the relationship between diet and pain among university students.
Material and Methods: This descriptive cross-sectional study was conducted with volunteer students from November-December 2019. Students' demographic and health information, nutritional habits were questioned, 24-hour retrospective food consumption was recorded, they were asked to fill in the pain assessment form, the Mediterranean diet adherence scale, and the international physical activity questionnaire, finally, their measurements (height, weight) were evaluated.
Results: The study included 595 students (87.2% female) with a mean age of 20.2±1.48 years. The prevalence of chronic pain was 37.8%. The majority of these students (58.7%) had moderate pain intensity (5-7 points). In the Mediterranean diet adherence score, 75% of students had <7 points. There was no significant association between chronic pain status and adherence to the Mediterranean diet.
Conclusion: This study was not significantly found the relationship between the presence of chronic pain and adherence to the Mediterranean diet. It is thought that, since the majority of students with chronic pain had poor adherence to the Mediterranean diet, observing a relationship between pain and compliance may have resulted in a negative result. To better understand the connection between chronic pain and diet, more research is needed.
Keywords: Chronic pain, mediterranean diet, university student, pain measurement.

INTRODUCTION

While pain is defined as an “unpleasant sensory or emotional experience with actual or potential tissue damage”, persistence of this pain for over 3 months is referred to as chronic pain (CP) and today, it is addressed as a disease per se rather than being considered a symptom (1). It has been observed that there is a worldwide lack of wide-ranging studies examining the prevalence of CP and that there are great differences from society to society. However, with increasing evidence, it has been reported that the prevalence of CP is gradually increasing in children, adolescents, and young adults (18-25 years of age) (2).

CP studies have generally focused on middle-aged and elderly adults. But it is important to determine the condition that the prevalence of CP in university students, who are quite immobile nowadays and spend most of their time in front of the computer. In a study carried on with young people, it was determined that pain affects daily life, academic success, and productivity (3). It has been shown in students that

studying for long hours in the same position often creates physical stress, and their efforts to achieve academic success create psychological stress and these stresses cause musculoskeletal pain (4). In another study, which reported that CP is common among university students, it was found that the students mostly experienced CP in the musculoskeletal system, with upper back pain in 49.2%, neck pain in 43.7%, and lower back pain in 40.2% (5).

Like most diseases, CP is often caused by a combination of multiple or a series of events. There are a number of factors that affect intensity, the duration, and effects (social, psychological, physical, and emotional) of CP, even if it is an accelerant event alone (e.g., injury) (6). Nutrition can be one of them. There are meta-analyses and systematic reviews showing that diet therapy can have beneficial effects on CP (7-9). In these studies, it was determined that supplementing the diet with certain foods such as vitamin B12, magnesium, omega-3, vitamin D can relieve pain. At the same time, an anti-inflammatory diet pattern (such as the Mediterranean-style diet), in which daily consumption of olive oil, oilseeds, fruits and vegetables, and legumes are high, and consumption of processed foods and meat is low, has been found to have potential benefits for CP patients, including reduced analgesic intake.

This study was carried out to assess CP status with adherence to the Mediterranean diet (AMD) and to investigate the relationship between diet and pain among university students, who are young adults.

MATERIAL AND METHODS

This descriptive cross-sectional study was carried out with students at University of Health Sciences. It was completed with 595 students between the ages of 18 and 27. The population of the faculty consisted of 2053 students enrolled in the 2019 fall semester.

The voluntary consent of the participating students was obtained. Pregnant or lactating students or those with psychiatric illnesses were excluded. In addition, the study's exclusion criteria were students who had undergone any surgery involving the musculoskeletal system.

Data Collection

The study data were collected face-to-face in November-December 2019. In total 608 students volunteered to participate in the study. Due to missing data and the exclusion criteria, 13 students were excluded. The study was thus conducted with 595 students.

The students' demographic and general health information, dietary habits, and 24-hour retrospective food consumption records were obtained through a questionnaire developed by the researchers. The height and body weight measurements of the students were recorded by the researchers with a portable stadiometer (Mesitaş®) and a portable digital scale (Tanita HD 366). “Body mass index (BMI) [body weight (kg)/height (m2)] was calculated according to the height and bodyweight of the students”. “The BMI values are classified in accordance with the The World Health Organization (WHO) <18.5 kg/m2 underweight; 18.5-24.9 kg/m2 normal; 25.0-29.9 kg/m2 overweight; ≥30.0 kg/m2 obese”.

Expert researchers recorded all students' 24-hour retrospective food intake. The Nutrition Information System (BeBIS 8.2®) program was used to calculate the energy and nutrient values.

With the pain assessment form, they were asked to mark the pain location on the pain area drawing, and they were questioned about the frequency and duration of the pain they experienced, whether they saw a physician due to pain and whether they had received a diagnosis. Pain intensity was evaluated with the “Numeric Pain Rating Scale (NPRS) scale with a score of 0-10 (no pain… unbearable pain)” (10). “Pain levels were classified as mild (1-3 score), moderate (4-6 score), and severe (7-10 score)” (11). The pain location and the information about the pain were reviewed and evaluated together with the physiotherapist. This is mentioned in the acknowledgments section.

AMD was determined by the “Mediterranean Diet Adherence Screener (MEDAS)”. The MEDAS consists of 14 questions. The total score is calculated by giving 1 or 0 points for each question asked according to the amount of consumption. “A total score of 7 or above shows acceptable AMD and 9 or above shows strict AMD”. The validity and reliability of the Turkish version of the scale were confirmed (12).

“The International Physical Activity Questionnaire (IPAQ-Short Form)” was used to determine the students' physical activity status (13). This form, which determines the level of physical activity, is answered for the last 7 days, and consists of 7 main questions. Three types of activities are identified. These are walking, moderate-intensity, vigorous-

Table 1: Descriptive features of the student (n=595)

	Mean ± SD or n (%)
Age (year)	20.2 ± 1.48
Gender	
Male	76 (12.8)
Female	519 (87.2)
Pain status	
No pain	333 (56.0)
Acute pain (≤3 month)	37 (6.2)
CP (>3 month)	225 (37.8)
Duration of chronic pain (month)	25.6 ± 25.27
NPRS for chronic pain	5.1 ± 1.85
Chronic pain intensity (n=225)	
Mild (1-4 point)	42 (18.7)
Moderate (5-7 point)	132 (58.7)
Severe (8-10 point)	51 (22.7)
Chronic pain location*	
Waist	72 (32.0)
Back	69 (30.7)
Neck	65 (28.9)
Knee	20 (8.9)
Leg	12 (5.3)
Shoulder	11 (4.9)
Thigh	6 (2.7)
Feet	6 (2.7)
Arm	4 (1.8)
Ankle	4 (1.8)
Hip	2 (0.9)
Calf	1 (0.4)
Forearms	1 (0.4)
Not musculoskeletal (head, pelvic, etc.)	47 (20.9)
BMI (kg/m^2)	21.6 ± 3.06
BMI classification	
Underweight (< 18.5 kg/m^2)	89 (15.0)
Normal (18.5-24.9 kg/m^2)	421 (70.8)
Overweight (25.0-29.9 kg/m^2)	80 (13.4)
Obese (≥ 30.0 kg/m^2)	5 (0.8)
MEDAS score	5.6 ± 1.82
Adherence to the Mediterranean diet	
Not adherence (< 7 point)	413 (69.4)
Acceptable adherence (7-8 point)	146 (24.5)
Strict adherence (≥ 9 point)	36 (6.1)

*Evaluation was made on more than one answer.

NPRS: Numerical Pain Rating Scale; MEDAS: Adherence to the Mediterranean diet Scale; BMI:Body Mass Index

intensity activity. The IPAQ technique was used to score physical activity (13). According to this technique, The Metabolic Equivalent Minutes (MET) value determined for the three types of activities is calculated by multiplying the frequency and duration of the activity.

"Total MET-min/week = (Walking METs*min*days) + (Moderate METs*min*days) + Vigorous METs*min*days)".

Students with a total score of "<600 MET on the physical activity scale were classified as sedentary, students with 600-3000 MET were classified as

moderate active, and students with >3000 MET were classified as very active"(13).

Statistical Analysis

Categorical variables were summarized by number and percentage, and numerical variables by mean and standard deviation. “Student's t test” was used for comparisons between pain groups. The “Mann-Whitney U test” was used for the continuous variable with a discrete structure. The “chi-square test and Fisher’s exact test” were used in the analysis of categorical data. “Pearson correlation coefficients” were calculated to examine the linear correlation between continuous variables. The data were analyzed using “SPSS 21 and the statistical significance level was set at 0.05”.

Ethical Consideration

The study was approved by the University of Health Sciences, Hamidiye Non-Interventional Research Ethics Committee on 08.11.2019 with decision number 19/145.

RESULTS

The study included 595 students (87.2% female). The prevalence of CP was 37.8%. The most painful areas of the students with CP were the waist (32.0%), back (30.7%), and neck (28.9%). Most of these students (58.7%) had moderate pain levels. Only 30.6% of all students adhered to the Mediterranean diet (MD) (Table 1).

Table 2 demonstrates that there is no significant difference in the mean age, BMI, MEDAS scores between students with and without CP. Looking at Table 2, it is seen that students with CP had lower MET scores than those without (p>0.05). MEDAS scores were similar for both groups (p>0.05) (Table 2).

As shown in Table 3, it was determined that students with CP received 1626.1 ± 604.85 kcal/day energy, and those without CP received 1643.8 ± 700.22 kcal/day energy (p>0.05). When the daily carbohydrate values were examined, it was seen that the students without CP have the higher mean of amount and percentage compared to the students with CP (p>0.05). The daily protein amount and percentages of students without CP were higher than those with CP, daily fat amount and percentages were found to be lower compared to those with. Fiber consumption means are similar in both student groups (p>0.05). When the mineral intake means of the students were examined, the sodium intake mean was found to be higher in the group without CP, and the iron intake mean was found to be similar in both groups. The mean intakes of other minerals were higher in the group with CP (p>0.05). The mean intake of fat-soluble vitamins A and D was higher in the student group without CP, and the mean of vitamin E and K intake was higher in those with CP (p>0.05). As for the water-soluble vitamins, the mean intake of thiamine, riboflavin, and pyridoxine vitamins was similar in both groups, and the mean intake of vitamin B12 and total folate was higher in students without CP (p>0.05) (Table 3).

It was determined that 30.9% of those without CP followed MD, and 29.8% of those with CP followed the MD (p>0.05). A significant relationship between the presence of CP and the level of physical activity was determined (p=0.024). While 37.8% of those with CP were sedentary, 30.3% of those without CP were sedentary. While the rate of very active students without pain is 19.5%, it is 11.6% for those with pain. In addition, of those with CP, 15.6% were underweight, 69.8% were normal weight, and 14.7% were more than normal BMI. Of the group without CP, 70.6% had a normal BMI. The association with the presence of CP between BMI groups was not significant (Table 4).

In Table 5, the comparison of the questions of AMD according to the presence of CP and the level of pain is presented. The proportion of those who consumed < 48 grams of olive oil per day was found to be higher in the group with and without CP than those who consumed >48 grams per day (p>0.05). Similarly, the proportion of those consuming < 3 or >3 servings of vegetables and < 2 or >2 servings of fruit per day did not differ significantly according to the presence of CP and the severity of CP. The proportion of students reporting >100 or <100 grams of red meat per day significantly differed by CP status, with lower consumption of red meat being more common in those with CP (p=0.004). When the daily consumption of red meat is examined according to the degree of CP, the proportion of students with mild, moderate, and severe CP who consume > 100 grams of meat per day was found to be higher than the students with mild, moderate, and severe CP who consume < 100 grams of meat per day (p>0.05). While the rate of the students who consumed < 3 servings of legumes per week was higher in those with CP, the proportion of those who consumed >3 servings was found to be higher in those without CP

Table 2: Comparison of the mean of continuous variables according to the presence of chronic pain

	Presence of chronic pain				
	No (n=333)		Yes (n=225)		p
	Mean ± SD	Min-Max (Median)	Mean ± SD	Min-Max (Median)	
Age (year)	20.2 ± 1.46	18-27 (20)	20.4 ± 1.49	18-26 (20)	0.086†
Height (m)	1.7 ± 0.08	1.5-1.87 (1.65)	1.7 ± 0.08	1.48-1.88 (1.65)	0.881†
Weight (kg)	59.7 ± 10.63	39-100 (58)	59.4 ± 11.17	39-95 (57)	0.753†
BMI (kg/m^2)	21.7 ± 3.05	15.63-35.43 (21.3)	21.6 ± 3.18	15.60-35.76 (20.98)	0.733†
MET score (min/week)	1693.5 ± 1653.27	49.5-6264.0 (1132.5)	1643.6 ± 1446.67	132-7011 (1113)	0.541‡
MEDAS score	5.6 ± 1.75	1-10 (6)	5.6 ± 1.93	1-11 (6)	0.753†
The amount of water (L/day)	1.4 ± 0.72	0-4 (1.4)	1.4 ± 0.67	0-3 (1.2)	0.569†
Number of main meals	2.5 ± 0.59	1-4 (3)	2.6 ± 0.56	1-4 (3)	0.055‡
Number of snacks	1.5 ± 0.87	0-5 (1)	1.5 ± 0.95	0-6 (2)	0.298‡

*p<0.05; †Student t test; ‡ Mann-Whitney U test

MET: Metabolic Equivalent Minutes; MEDAS: Adherence to the Mediterranean diet Scale; BMI:Body Mass Index

(p>0.05). The proportion of students consuming < 3 or ≥ 3 servings of fish or shellfish per week did not differ significantly by chronic presence but differed significantly by level of CP. Less fish or shellfish consumption was more common in those with moderate CP (p<0.05). The students who reported that they consumed cake, cookies, biscuits or pudding, pastries (not homemade) < 3 times a week were more common in those with CP (p>0.05). The rate of those who prefer white meat (chicken, turkey, fish) instead of red meat (beef, mutton, lamb, etc.) was higher in the CP group than in the non-group (p>0.05) (Table 5).

DISCUSSION

The present study determined the frequency of CP and the correlation between CP and AMD in university students. A significant relationship between the presence of CP and AMD was not found. In addition, among the two groups, among the MEDAS items, a significant difference was determined between the consumption of meat and those who consumed tomato or tomato paste with olive oil, onion, and garlic/leek sauce together with their meals. It is known in clinical practice that usually it is difficult to cope with chronic musculoskeletal pain. Integrating lifestyle factors into an individually designed treatment can be a promising strategy for these patients because research examining lifestyle factors such as obesity, unhealthy diet, and stress has shown that patients under the same biological conditions experience different pain experiences and report different pain results (14). Among these lifestyle factors, nutrition has received little attention in pain research thus far. However, it has a great potential to be a key factor in pain treatment. WHO explains and emphasizes the importance of diet regarding chronic disease management as follows: “Nutrition is coming to the fore as a major modifiable determinant of chronic disease, with scientific evidence increasingly supporting the view that alterations in diets have strong effects (both positive and negative) on health throughout life” (15). In addition, a study states that there is a versatile correlation between pain and nutrition (16).

The antioxidant content of foods and the vasodilators they contain; the effects of nutrition on inflammatory, biochemical, and oxidative pathways; and the neurophysiological roles of some nutrients in pain pathways are the main factors in the correlation between nutrition and pain (17). Studies examining the effect of diet on inflammatory markers have shown that diets rich in fiber, healthy fats, fruits, and vegetables and low in sugar, starchy carbohydrates, and unhealthy fats can decrease inflammation and pain (18, 19). The MD is a good example of this type of diet. This diet consists of fresh vegetables and fruits rich in antioxidant vitamins, fish rich in n-3 polyunsaturated fatty acids with anti-inflammatory characteristics, and olive oil rich in antioxidants such as oleic acid, vitamin E, carotenes, and flavonoids. It also contains red wine rich in polyphenolic compounds that have been found to have a protective effect on acute and chronic inflammation models.

Table 3: Comparison of the mean of energy and macro-micronutrients according to the presence of chronic pain

	Presence of chronic pain				
	No (n=333)		**Yes (n=225)**		
	Mean ± SD	**Min-Max (Median)**	**Mean ± SD**	**Min-Max (Median)**	**p**
Energy (kcal)	1643.8 ± 700.22	657.3-3745.3 (1545.9)	1626.1 ± 604.85	511.6-4088.9 (1688.5)	0.792†
Carbohydrate (g)	182.7 ± 94.77	59.7-457.4 (157.3)	178.3 ± 79.99	37.8-464.2 (169.9)	0.876†
Carbohydrate (%)	44.8 ± 8.90	24-62 (45)	44.1 ± 8.98	30-67 (44.0)	0.619†
Protein (g)	62.6 ± 30.32	21.2-146.4 (60.6)	61.9 ± 27.77	11.1-172.8 (60.3)	0.964†
Protein (%)	15.8 ± 5.14	8-29 (15)	15.7 ± 4.52	9-29 (15)	0.833†
Fat (g)	70.8 ± 31.69	20.1-157.8 (63.5)	72.7 ± 30.9	20.9-166.7 (66.2)	0.785†
Fat (%)	38.7 ± 8.13	17-54 (39.5)	40.1 ± 9.10	20-61 (39)	0.402‡
Alcohol (%)	0.67 ± 3.89	0-26 (0.0)	0±0	0-0 (0)	0.091†
Fiber (g)	18.5 ± 11.74	5.1-63.3 (15.4)	18.7 ± 10.29	3.7-64.9 (17.1)	0.566†
Cholesterol (mg)	290.6 ± 215.10	25.9-1156.7 (256.8)	279.1 ± 157.76	56.0-742.9 (243.2)	0.862†
PUFA (g)	13.3 ± 9.53	1.5-43.7 (10.1)	13.7 ± 8.02	3.4-42.6 (12.0)	0.405†
MUFA (g)	23.6 ± 11.95	6.7-56.3 (19.5)	25.3 ± 11.89	7.6-63.8 (22.9)	0.292†
Sodium (mg)	6161.9 ± 12510.74	859.9-55417.4 (2739.5)	4630.9 ± 8815.91	569.4-53124.1 (2836.8)	0.706†
Potassium (mg)	2003.4 ± 840.98	808.6-4904.3 (1726.6)	2065.9 ± 771.43	633.9-4692.9 (1983.6)	0.686‡
Calcium (mg)	603.0 ± 223.06	196.7-1159.1 (565.8)	640.6 ± 240.9	99.4-1194.6 (611.3)	0.406‡
Magnesium (mg)	257.3 ± 114.15	104.8-631.4 (218.4)	265.9 ± 118.85	62.3-832.8 (249.4)	0.409†
Phosphorus (mg)	1030.0 ± 498.57	440.3-2821.9 (934.4)	1040.2 ± 468.9	248.6-2972.9 (958.2)	0.624†
Iron (mg)	9.5 ± 4.97	2.6-23.9 (8.5)	9.5 ± 4.33	2.3-27.4 (9.6)	0.555†
Zinc (mg)	8.2 ± 4.36	1.7-26.5 (7.9)	8.8 ± 4.4	2.3-33.5 (8.1)	0.332†
Vitamin A (µg)	1584.7 ± 4211.78	130.0-25483.1 (732.5)	802.9 ± 536.81	160.4-3858.9 (679.7)	0.853†
Vitamin D (µg)	2.8 ± 7.70	0.1-53.4 (1.7)	2.5 ± 5.99	0.3-46.8 (1.6)	0.907†
Vitamin E (mg)	9.4 ± 7.39	1.5-38.0 (7.3)	10 ± 6.39	2.5-39.4 (8.6)	0.209†
Vitamin K (µg)	89.6 ± 88.30	7.9-408.6 (57.8)	92.3 ± 81.74	10.6-418.8 (60.3)	0.491†
Vitamin C (mg)	96.7 ± 73.67	0.8-276.2 (73.5)	76.2 ± 61.86	8.2-308.7 (62.8)	0.175†
Thiamine (mg)	0.8 ± 0.55	0.3-3.6 (0.7)	0.8 ± 0.41	0.2-2.8 (0.8)	0.528†
Riboflavin (mg)	1.3 ± 0.90	0.4-5.4 (1.2)	1.2 ± 0.46	0.2-2.8 (1.1)	0.774†
Pyridoxine (mg)	1.3 ± 0.91	0.3-5.9 (1.1)	1.1 ± 0.54	0.3-3.4 (1.0)	0.658†
Vitamin B12 (µg)	5.8 ± 15.34	0.1-91.9 (2.1)	3.2 ± 2.26	0.4-13.2 (2.8)	0.195†
Total Folate (µg)	290.8 ± 274.14	86.9-1695.5 (226.6)	245.1 ± 132.21	65.6-876.7 (222.2)	0.981†

*p<0.05; † Mann-Whitney U test; ‡ Student t test
PUFA: Polyunsaturated fatty acid; MUFA: Monounsaturated fatty acid

One intervention study found that herbal-based dietary intervention reduced pain and improved quality of life (20).

In Mediterranean countries (Italy, Spain, and Greece,), AMD among students was found to be 20-30% (21), > 40% (22), and > 70% (23), respectively. In our study, AMD was 30.6%. Today, there are studies indicating that young people are moving away from healthy lifestyle habits and tend to abandon the MD (24, 25). The reason for the lack of a correlation between the presence of pain and AMD in the present study may have been the low adherence to the diet. When the daily olive oil consumption of the students was evaluated, it was determined that 91.0% of the

Table 4. Comparison of adherence to the Mediterranean diet, body mass index, and physical activity according to chronic pain status

	Presence of chronic pain		
	No (n=333)	Yes (n=225)	
	n (%)	n (%)	p
The Mediterranean diet			
Not adherence	230 (69.1)	158 (70.2)	0.772
Adherence	103 (30.9)	67 (29.8)	
Physical activity level			
Sedentary (<600 MET)	101 (30.3)	85 (37.8)	
Moderate active (600-3000 MET)	167 (50.2)	114 (50.7)	0.024*
Very active	65 (19.5)	26 (11.6)	
BMI classification			
Underweight	50 (15.0)	35 (15.6)	
Normal	235 (70.6)	157 (69.8)	0.978
Overweight and obese	48 (14.4)	33 (14.7)	

*p<0.05. MET: Metabolic Equivalent Minutes; BMI:Body Mass Index

group without pain and 88.4% of the group with pain consumed less than 48 grams of olive oil (p>0.05). However, the rate of those who consumed tomatoes with olive oil, tomato paste, onion, and garlic/leek sauce in addition to vegetables, rice, pasta, and other dishes more than twice a week was higher in the group without CP, and the difference between the two groups was significant. It has been determined that olive oil polyphenols in the MD reduce inflammatory biomarkers, and plasma oxidative stress. Therefore, olive oil consumption in the MD has been shown to be an important factor in reducing oxidative stress and inflammation (26). Furthermore, extra virgin olive oil contains oleocanthal, a natural anti-inflammatory compound that inhibits cyclooxygenase enzymes, which are known to increase the production of prostaglandins, which are important in the inflammatory response and pain pathway in the prostaglandin biosynthesis pathway. This compound has been shown to be as effective as the nonsteroidal anti-inflammatory drug ibuprofen. 50 g of extra virgin olive oil contains 200 g/ml of oleocanthal, 60-90% of which is absorbed, equating to 9 mg per day. This amount is equivalent to 10% of the adult ibuprofen dosage for pain relief. This amount, however, may be beneficial because low-dose aspirin is also known to provide cardiovascular health benefits (27,28). Although Turkey is one of the leading countries in olive oil production, it is thought that the effects of olive oil on health are not fully understood by the public and this situation is reflected in consumption. However, it should be kept in mind that economic and cultural effects on nutrition affect food preferences.

Consumption of diets containing high animal protein and fat is common among students and these diets have been associated with inflammation and CP (29, 30). It is generally believed that people who stay away from these products might feel less pain. The prevalence of CP and inflammation is significantly lower in individuals who eat a plant-based diet than in those who eat an average American diet (29). In our study, lower consumption of red meat being more common in those with CP. There are many mechanisms by which a plant-based diet can reduce chronic skeletal muscular system pain. These include reduced exposure to inflammatory precursors, free radical neutralization, increased vascularization via lipid profile reduction, weight loss, and thus reduced mechanical load (20).

In the current study, majority of the students (70.8%) had a normal BMI, and CP did not significantly differ between the BMI groups. A study examining the correlation between obesity and pain reported that there was no direct correlation between BMI and pain; however, various factors such as inflammatory mediators, obesity-related structural changes, and lifestyle characteristics might have an effect (31). One of the most recent population-based studies documented a consistent association between obesity and CP (32). There is evidence that pain symptoms increase due to increases in BMI. In fact, it is not surprising that there is a strong association between obesity and pain, as obesity reflects a chronic systemic inflammatory state. In the presence

Table 5: Comparison of Mediterranean diet adherence questions according to pain level and the presence of chronic pain

		Presence of chronic pain			Level of chronic pain (*n*=225)			
		No (n=333)	Yes (n=225)	*p*	Mild (n=42)	Moderate (n=132)	Severe (n=51)	*p*
		n (%)	n (%)		n (%)	n (%)	n (%)	
1. Do you use olive oil as main culinary fat?	≤ 2 times/week	189 (56.8)	145 (64.4)	0.069	27 (64.3)	84 (63.6)	34 (66.7)	0.929
	> 2 times/week	144 (43.2)	80 (35.6)		15 (35.7)	48 (36.4)	17 (33.3)	
2. How much olive oil do you consume in a given day (including oil used for frying, salads, out-of-house meals, etc.)? (1 tbs. = 13.5 g)	< 48 g	303 (91.0)	199 (88.4)	0.326	36 (85.7)	117 (88.6)	46 (90.2)	0.793
	> 48 g	30 (9.0)	26 (11.6)		6 (14.3)	15 (11.4)	5 (9.8)	
3. How many vegetable servings do you consume per day? (1 portion: 200 g)	< 2 portions	238 (71.5)	160 (71.1)	0.926	33 (78.6)	93 (70.5)	34 (66.7)	0.437
	≥ 2 portions	95 (28.5)	65 (28.9)		9 (21.4)	39 (29.5)	17 (33.3)	
4. How many fruit units (including natural fruit juices) do you consume per day? 1 portion fruit = 80 g 1 portion fruit juice=100 mL	< 3 portions	269 (80.8)	183 (81.3)	0.870	38 (90.5)	106 (80.3)	39 (76.5)	0.202
	≥ 3 portions	64 (19.2)	42 (18.7)		4 (9.5)	26 (19.7)	12 (23.5)	
5. How many portions of red meat, do you consume per day?	> 100 g	130 (39.0)	61 (27.1)	0.004*	8 (19.0)	33 (25.0)	20 (39.2)	0.065
	< 100 g	203 (61.0)	164 (72.9) ‡		34 (81.0)	99 (75.0)	31 (60.8)	
6. How many servings of butter, margarine, or cream do you consume per day? (1 tbs. = 12 g)	> 1 portion	100 (30.0)	79 (35.1)	0.207	12 (28.6)	52 (39.4)	15 (29.4)	0.276
	< 1 portion	233 (70.0)	146 (64.9)		30 (71.4)	80 (60.6)	36 (70.6)	
7. How many sweetened and/or carbonated beverages do you drink per day? (1 tbs. = 100 mL)	> 1 portion	87 (26.1)	59 (26.2)	0.980	9 (21.4)	38 (28.8)	12 (23.5)	0.566
	< 1 portion	246 (73.9)	166 (73.8)		33 (78.6)	94 (71.2)	39 (76.5)	
8. How much wine do you drink per week? (1 glasses = 125 mL)	< 7 glasses	332 (99.7)	224 (99.6)	1.00†	42 (100.0)	131 (99.2)	51 (100.0)	0.702
	≥ 7 glasses	1 (0.3)	1 (0.4)		-	1 (0.8)	-	
9. How many portions of legumes do you consume per week? (1 portion = 150 g)	< 3 portions	206 (61.9)	145 (64.4)	0.536	30 (71.4)	85 (64.4)	30 (58.8)	0.450
	≥ 3 portions	127 (38.1)	80 (35.6)		12 (28.6)	47 (35.6)	21 (41.2)	
10. How many portions of fish or shellfish do you consume per week? (1 portion = 100-150 g)	< 3 portions	322 (96.7)	220 (97.8)	0.607†	39 (92.9)	132 (100.0)	49 (96.1)	0.015*
	≥ 3 portions	11 (3.3)	5 (2.2)		3 (7.1)	-	2 (3.9)	
11. How many times per week do you consume commercial sweets or pastries (not homemade), such as cakes, cookies, biscuits, or custard?	> 3 times	155 (46.5)	110 (48.9)	0.587	18 (42.9)	68 (51.5)	24 (47.1)	0.593
	< 3 times	178 (53.5)	115 (51.1)		24 (57.1)	64 (48.5)	27 (52.9)	
12. How many servings of nuts (including peanuts) do you consume per week? (1 portion = 30 g)	< 3 portions	200 (60.1)	129 (57.3)	0.521	28 (66.7)	75 (56.8)	26 (51.0)	0.309
	≥ 3 portions	133 (39.9)	96 (42.7)		14 (33.3)	57 (43.8)	25 (49.0)	
13. Do you preferentially consume chicken, turkey, or fish meat instead of beef, mutton, lamb?	White < red	159 (47.7)	95 (42.2)	0.199	20 (47.6)	52 (39.4)	23 (45.1)	0.575
	White > red	174 (52.3)	130 (57.8)		22 (52.4)	80 (60.6)	28 (54.9)	
14. How many times per week do you consume vegetables, pasta, rice, or other dishes seasoned with sofrito (sauce made with tomato and onion, leek or garlic and simmered with olive oil)?	< 2 times	101 (30.3)	88 (39.1)	0.032	16 (38.1)	51 (38.6)	21 (41.2)	0.941
	≥2 times	232 (69.7) ‡	137 (60.9)		26 (61.9)	81 (61.4)	30 (58.8)	

*p<0.05; †Fisher Exact test; ‡Refers to the higher ratio; tbs: tablespoon

of chronic pain, the body produces more C-reactive protein and proinflammatory mediators such as interleukin-6. Furthermore, adults with chronic pain were found to gain more weight due to changes in appetite, with leptin levels increasing over time. However, there is a lack of data on how obese and chronic pain patients respond to weight loss treatments (33). However, following bariatric surgery, it was discovered that the majority of patients with preoperative chronic pain experienced significant improvement (34). Despite studies indicating that the presence of chronic pain prevents individuals from losing weight, it should be aimed to provide positive benefits by adopting a more comprehensive, team-based approach that addresses both weight and pain management (35,36).

There was a significant relationship between the presence of CP and activity level. A lower proportion of students with CP were very active. Although we cannot infer cause and effect in this study, it can be predicted that CP may affect the activity level, which will be more negative for health in older ages.

Limitations

This is a cross-sectional study and cannot establish a cause-and-effect relationship. So, there is no way to know whether the dietary habits preceded the pain or vice versa. In addition, in this study, the presence, location, duration, and intensity of pain were entirely based on self-report. So, further studies can be planned in which clinical and biochemical findings are also evaluated, and advanced research should be planned in which we can establish a cause-and-effect relationship. On the other hand, the fact that fewer male students volunteered than female students limited the possibility of evaluating the difference between the sexes. Finally, AMD was very low among all students.

CONCLUSION

CP and especially musculoskeletal pain are quite common. Especially young adult university students are likely to experience a negative impact on their quality of life in the following years. However, the correlation between dietary patterns or dietary components and CP is not yet clear. Numerous studies including interventions testing the nutritional advice or support in populations with CP are needed.

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RESEARCH ARTICLE

PSYCHOMETRIC PROPERTIES OF THE CHRONIC LIVER DISEASE QUESTIONNAIRE IN PATIENTS WITH CHRONIC LIVER DISEASE

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ABSTRACT

Purpose: Chronic liver disease (CLD) is a major public health problem worldwide and it leads to increase in morbidity and mortality. This study aimed to evaluate the psychometric properties of Chronic Liver Disease Questionnaire (CLDQ) in Turkish patients with CLD.
Material and Methods: The study was conducted in the methodological research design. Using a convenience sampling method 235 patients with CLD in a Akdeniz University. The instrument's psychometric properties were examined to determine factor analysis, criterion-related validity, internal consistency, interrater reliability and construct validity.
Results: The patients average age was 55.48±12.02 years. Viral hepatitis was the most common etiology of CLD (53.6%). The total sample had a mean CLDQ score of 4.73±1.12.
The factor analysis revealed that the scale consists of six sub-dimensions. No item was removed from the original scale. Cronbach's alpha coefficient was found as 0.93. According to the results of the confirmatory factor analysis of the Turkish version of CLDQ, that six sub-dimensions consisting of 29 items was confirmed.
Conclusion: Valid and reliable measurement tools are needed to evaluate health related quality of life (HRQoL) in patients with liver disease. Chronic Liver Disease Questionnaire is a valid and reliable measurement instrument.
Keywords: Chronic liver disease, CLDQ, nursing care, reliability, validity.

INTRODUCTION

Chronic liver disease (CLD) is a major public health problem worldwide and it leads to increase in morbidity and mortality (1). Chronic liver disease which leads to fibrosis, cirrhosis, hepatocellular carcinoma, multiple organ failure, liver transplantation. Therefore, necessary preventive and therapeutic measures should be taken before chronic liver diseases progress until the end stage. Although the major causes of CLD are preventable and treatable, CLD account for approximately 2 million deaths per year worldwide (2, 3). Besides an increased risk of mortality, CLD can cause reduced health-related quality of life (HRQoL) (4). Patients with CLD have abdominal, muscle, and/or joint pain, lack of appetite, and complications related to liver cirrhosis, such as ascites, variceal bleeding, hepatic encephalopathy, and emotional problems (5). In her study, Fabrellas states that nurses have paid little attention to do research about quality of life of patients with liver diseases unfortunately, compared to other chronic diseases, especially diabetes mellitus, cardiovascular diseases, and chronic pulmonary diseases (6). Although patients with CLD are vulnerable and at risk of death, it is surprising that such little attention has been paid to describing their

symptom prevalence and HRQoL (7). Hence, reliable measurement tools are needed for nursing interventions and symptom management. In order to be able to use measurement tools reliably in symptom management, these measurement tools need to be adapted to the culture in question.

Assessment of HRQoL is important for patients with CLD. Across the worldwide, studies on HRQoL of patients with CLD have used generic and disease specific questionnaires. Generic questionnaires are applicable to all types of chronic diseases and provide a global assessment of HRQoL (8). Reliable and adapted to culture questionnaires are needed to evaluate HRQoL. Generic surveys enable comparisons between many chronic diseases, but they might not be sensitive enough to catch changes that are clinically significant due to the development of the disease or treatments for these ailments. Unlike generic questionnaires, disease specific questionnaires may be more responsive to disease-related changes and determine the effect of a disease's symptoms on a patient's health and the effects of therapy (9). Disease spesific questionnaires are potentially powerful tools for evaluating the functional, physical, psychological status, emotional, and cognitive functioning, presenting gains of treatment and reflecting patients' ability to return to a normal lifestyle in CLD patients (9, 10).

To the best of our knowledge, the Chronic Liver Disease Questionnaire (CLDQ) is the first disease specific HRQoL instrument developed for patients with CLD (11). The CLDQ is a simple and brief instrument with good responsiveness in several stages of liver disease (12). The questionnaire has already been adapted and validated for the Brazilian, Bengali, German, Japan, Persian, Sinhala, Swedish, Greek, and Spanish population (13-21) In addition, it has also been adapted to disease groups such as Hepatitis C, and NASH (22, 23). However, there was no reported translation or validation of the CLDQ to the Turkish language in the literature. Thus, this study aimed to evaluate HRQoL, and obtain the psychometric properties of the culturally adapted of Chronic Liver Disease Questionnaire (CLDQ) in Turkish patients with CLD.

MATERIAL AND METHODS

Translation and adaptation of the CLDQ

The translation-back-translation methodology was used for the adaptation following the Guidelines for Translating and Adapting Tests (24). First, three bilingual translators (proficient in English and Turkish) independently translated the English language version of CLDQ into Turkish. Then, two translators (proficient in English and Turkish) performed back-translations independently. The questionnaire was reviewed and modified by a team of 10 competent expert, whom of two of them gastroenterologist, others of them academic members in the nursing faculty, whether the translation had been suitably adjusted for the spesifics of the Turkish medical and caring systems and culture. After expert panel, a draft of the Turkish version of CLDQ was formulated. Experts evaluated each item of the final version of the CLDQ over 10 points. Then Kendall's w coefficient was calculated. The experts judgments showed that the correlation between the items on the questionnaire were quiet good ($p<0.05$) (25). As a result of the language adaptation, the Turkish version of the CLDQ was found to be comparable with the original version of the CLDQ. After the language translation stage, the questionnaire was applied to five patients with CLD to test its understandability. These patients were not included in the study. These patients did not give any suggestions or corrections about the questionnaire at this stage.

Design and Participants

According to studies on questionnaire adaptation, the sample size can be 5–10 times the number of items in the questionnaire (25). There are 29 items in this questionnaire, this questionnaire was applied to a total of 235 patients with CLD agreeing to participate in this study. The study was conducted in the gastroenterology inpatient clinic and the outpatient clinic of Akdeniz University, between November 24th, 2016, and April 5th, 2017. None of the patients had an adverse or side effect because of this study. The patients who had been diagnosed with CLD for at least 6 months, who were 18 years old or over, literate, had no other psychiatric or emotional problems, language or cognitive difficulties, and Child Turgotte Pugh Score A and B. We excluded the patients who have liver tumors, liver transplantation, and Child Turgotte Pugh Score C. The Child Turcotte Pugh Score was indicator of severity of liver disease. The Child Turgotte Pugh Score includes some variables like ascites, hepatic encephalopathy, INR, total bilirubin, and albumin. Each variable was three severity categories between 1-3 points in the Child Turcotte Pugh Scoring System. As the severity of the illness increasing, the Child Turcotte Pugh Score

increased. Received high scoring from this questionnaire was a bad indicator of quality of life (2). When the patients experience decompansation symptoms such as ascites, hepatic encephalopahy, their Child Turgotte Pugh score gets into C and their general status impaired. We thought patients who have impaired general status cannot answer the questionnaires properly. Furthermore, patients have liver tumors and/or liver transplantation need to complicate treatment methods like this chemotherapy, immunsupressive. Both these diseases and treatment methods inpaired general health status, emotional status, or other organ functions. Those who patients might have experience severity symptoms and cannot answer the questionnaires properly. For this reason, we excluded patients who have Child Turgotte Pugh score C, liver tumors and/or liver transplantation. It took approximately 10 minutes to fill out the questionnaire. Most of the patients easily filled out the questionnaire. It took approximately 10 minutes to fill out the questionnaire. Most of the patients easily filled out the questionnaire.

Data Collection

Data collected in face-to-face interviews using CLDQ, The Liver Disease Symptom Index 2.0, Socio-demographic and clinical data questionnaire at Akdeniz University Hospital.

Chronic Liver Disease Questionnaire

The CLDQ is the first disease specific HRQoL instrument developed for patients with CLD. It is a 29-item self-report questionnaire, consisting of six subdimension, which include abdominal symptoms, fatigue, systemic symptoms, activity, emotional function and anxiety. All items ask for the symptoms during the previous two weeks. The overall ICC value of original CLDQ is 0.59 (11).

The Liver Disease Symptom Index 2.0

The Liver Disease Symptom Index 2.0 (LDSI 2.0) was used to determine the validity of the CLDQ in this study. It was developed by Van Der Plas et al. (2004) (26) and adapted to the Turkish population by Eraydin et al. (2014) (27). All items ask for the symptoms during the previous week, and a lower score indicates a better HRQoL. The value of Cronbach's α is 0.91 (27).

Socio-Demographic and Clinical Data Questionnaire

The socio-demographic and clinical data questionnaire prepared by the researchers as a result of literature survey (14-16, 19). It evaluated socio-demographic information including age, gender, etiologies of the CLD, history of decompensation symptoms.

Statistical Methods

We performed all statistical analyzes after cleaning the extreme data. For continuous data, means and standard deviations were recorded; for categorical variables, frequencies and percentages were reported. Also, descriptive statistic was used including t-test and variation analysis. For factor analysis, the sample size should be adequate. For the evaluating sample adequate, Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy value and Bartlett's Test were performed to evaluate whether the sample was large enough. Determine whether the sample size is adequate for factor analysis using the KMO test. KMO should be more than 0.60. The null hypothesis must be rejected (p 0.05) if there is a strong chance that at least some of the variables in the correlation matrix are correlated. This is determined via Bartlett's test. If so, this means that there is a high correlation between the variables and the data set shows a multivariate normal distribution (25). These results indicate that the sample was adequate for factor analyses. In terms of the sampling adequacy, KMO value was found as 0.92, and Bartlett's Test of value was 6089.5 ($p<0.001$). The principal component analysis and direct oblimin rotation were used in factor analysis. To determine the internal consistency of reliability, Cronbach's alpha was used. Interrater reliability was calculated using the intraclass correlation coefficient (ICC). Agreement between CLDQ and LDSI 2.0 were assessed by calculating the Pearson correlation coefficient. To confirm of factor structure, we conducted confirmatory factor analysis (CFA). All analyses were performed using SPSS Statistic Software (v. 23.0; IBM Corporation, Armonk, NY, USA) and IBM SPSS AMOS (v. 21.0; IBM Corporation Software Group, Somers, NY, USA) and the significance level was set to 0.05.

Table 1. Socio-demographic and clinical data characteristics of all patients

Socio-demographic and clinical data characteristics (N=235)	Number (n)	Percentage (%)
Age in years ($\bar{X}$=55.48±12.02)		
≤44	49	20.9
45-59	89	37.9
≥60	97	**41.2**
Gender		
Male	119	**50.6**
Female	116	49.4
Duration of the CLD (months)		
6 -12	34	14.5
13 -24	28	11.9
25 and over	173	**73.6**
Etiologies of the CLD		
Viral hepatitis	126	**53.6**
Liver cirrhosis	105	**44.7**
Others	4	1.7
History of decompensation symptoms*		
Ascites		
Encephalopathy	119	**50.8**
Variceal bleeding	48	24.1
	32	16.1
CTP grade (in cirrhotic patients)		
A	21	20.0
B	84	80.0

*Calculated according to the percentage value
CLD, Chronic Liver Disease; CTP, Child Turcotte Pugh

Ethical considerations

Permission to translate and use the CLDQ in Turkish population was granted by authors of the questionnaire. The research was approved by the Akdeniz University, Clinical Research Ethics Committee (REDACTED) (2012 KAEK-20/20.07.2016-429) and director of the studied hospital in Akdeniz University (26708535-903.99). The participants were informed about the research, and their written consents were obtained prior to filling out the questionnaires. Every procedure was carried out in line with the Helsinki Declaration.

RESULTS

Sociodemographic data

A total of 235 patients with CLD were interviewed and consented to participate in this study. The patients average age was 55.48±12.02 years of age. The lowest age was 21 and highest age was 77. The majority of patients were male (50.6%). Viral hepatitis was the most common etiology of CLD (53.6%; Chronic hepatitis B (CHB) n=92, Chronic hepatitis C (CHC) n=34) while 44.7% of patients had liver cirrhosis. Patients with nonalcoholic steatohepatits and alcololic liver disease formed the other participants. The majority of the patients with CLD had previously experienced decompensation (ascites, hepatic encephalopathy, variceal bleeding); 50.8% of these patients had experienced ascites, 24.1% had experienced encephalopathy and 16.1% had experienced variceal bleeding. However, all patients were in a compensated state when the data were being gathered.

According to Child Turcotte Pugh Scoring, 20% of the cirrhotic patients were classified as Child A, while 80% of the cirrhotic patients were classified as Child B (Table 1). The total sample had a mean CLDQ score of 4.73±1.12. Patients without cirrhosis had the best quality of life ratings. In terms of quality of life, the Child A group outperformed the Child B group. We performed one-way Anova test to determine significance level. Qulity of life score has significant difference levels between the three groups ($p<0.001$) (Table 2).

Table 2. Quality of life scores of patients with CLD

	Non-cirrhotic patients	Patients in Child A group	Patients in Child B group	Total	F	p
Scoring from the CLDQ	5.34±0.9	4.28±0.19	3.91±0.8	4.73±1.12	2.64	p<0.001

CLD, Chronic Liver Disease; CLDQ, Chronic Liver Disease Questionnaire

Psychometric properties of CLDQ

Explaratory Factor Analysis

Explanatory Factor Analysis (EFA) revealed six factors with an eigenvalue of 1, which explained 73.14% of the cumulative variance. In addition, exploratory factor analysis was confirmed by Horn's parallel analysis. These analyses confirmed that the factor structure was the same as the original CLDQ. In most of the items, the highest factor loadings were on the original factors. The loading weights, obtained with the EFA, are shown in Table 3. As seen in Table 3, five items loaded on Factor 1 (fatigue), eight items loaded on Factor 2 (worry), three items loaded on Factor 3 (abdominal symptoms), six items loaded on Factor 4 (systemic symptoms), four items loaded on Factor 5 (emotional function), and three items loaded on Factor 6 (activity), and when any item is deleted, no increase in Cronbach's alpha value is observed.

Item 14 about having limited diet had almost equally higher loading on two subdimensions, namely the 5th subdimension (emotional function) and 6th subdimension (activity). As suggested in the studies of the principal component analysis, when the factor loadings are very close and stacked under multiple factors (Stevens, 2002), one needs to review the original questionnaire and its factor loadings to determine which subdimension the item should load on. As a result, the item 14 about having limited diet in the original questionnaire was included in the "activity" (6th) subdimension in the Turkish version of CLDQ. In the Turkish version of the CLDQ, "fatigue" subdimension is completely same as the original.

Items numbered 10 about feeling anxious, 12 about unhappy and 24 about depressed were grouped under the "anxiety" subdimension in the Turkish version of the CLDQ, while they were originally grouped under the "emotional function" subdimension in the original version of the CLDQ. The item 6 about having shortness of breath was in the "abdominal symptoms" subdimension in the Turkish version of the CLDQ, while it was under the "systemic symptoms" subdimension in the original CLDQ. The items 16 about having difficulty sleeping at night and 20 about falling asleep were grouped under the "systemic symptoms" subdimension in the Turkish version of the CLDQ, while they were under the "emotional function" subdimension in the original version of the CLDQ. The item 7 about not been able to eat as much as you would like was under the "emotional function" subdimension in the Turkish version of the CLDQ, while it was in the "activity" subdimension in the original version of the CLDQ. The item 5 about abdominal pain was under the "activity" subdimension in the Turkish version of the CLDQ, while it was under the "abdominal symptoms" subdimension in the original version of the CLDQ.

Criterion-related validity

Criterion-related validity was evaluated by correlation between Turkish CLDQ and LDSI 2.0. Pearson's correlation coefficient was used to correlate the scores with each other. All results were considered statistically meaningful at $p<0.05$ (Table 4).

Internal Consistency

Internal consistency was assessed through Cronbach's alpha scores. According to the statement, the reliability level anticipated for the research-useable measurement tools is 0.70 or higher (25, 28). Considering the internal consistency of the subdimension and reliability of the Turkish version of the CLDQ, the total Cronbach's alpha was 0.95. All subdimension, except the "activity" subdimension, met the minimum reliability criterion (>0.70) for the Cronbach's alpha coefficient. Cronbach's alpha values ranged from 0.53 to 0.93. Internal consistency was found to fulfill acceptable internal reliability standards for the sample (Table 5).

Table 3. Factor structure of the Turkish version of the CLDQ

Items	Items in the subdimensions of the Turkish version of the CLDQ						Corrected item total correlation	Cronbach's alpha if item deleted
	Factor 1 Fatigue	Factor 2 Worry	Factor 3 Abdominal symptoms	Factor 4 Systemic symptoms	Factor 5 Emotional function	Factor 6 Activity		
Item 4 (Feeling sleepy)	0.85						0.547	0.933
Item 2 (Tired)	0.74						0.739	0.931
Item 11 (Decreased energy)	0.58						0.716	0.931
Item 8 (Decreased strength)	0.55						0.742	0.931
Item 13 (Feeling drowsy)	0.49						0.613	0.932
Item 22 (Worrying about symptoms)		0.91					0.714	0.931
Item 10 (Feeling anxious)		0.88					0.625	0.932
Item18 (Worrying about family)		0.84					0.700	0.931
Item 25 (Worrying about health status)		0.83					0.665	0.932
Item 28 (Worrying about never feeling any better)		0.83					0.582	0.932
Item12 (Feeling unhappy)		0.78					0.689	0.931
Item 24 (Feeling depressed)		0.78					0.634	0.931
Item 29 (Concerning about liver transplant)		0.53					0.455	0.931
Item 1 (Feeling of abdominal bloating)			0.88				0.600	0.931
Item 17 (Feeling of abdominal discomfort)			0.85				0.648	0.932
Item 6 (Having shortness of breath)			0.66				0.494	0.931
Item 21 (Having muscle cramps)				0.70			0.533	0.930
Item 20 (Falling asleep)				0.50			0.597	0.931
Item 16 (Having dfficulty sleeping at night)				0.56			0.645	0.930
Item 23 (Having a dry mouth)				0.54			0.598	0.932
Item 3 (Having bodily pain)				0.48			0.576	0.931
Item 27 (Having itching)				0.41			0.300	0.932
Item 15 (Having be irritable)					0.66		0.45	0.931
Item 26 (Having concentrating problems)					0.65		0.597	0.932
Item 19 (Having swings mood)					0.61		0.612	0.930
Item 7 (Not been able to eat as much as you would like)					0.42		0.576	0.931
Item 5 (Abdominal pain)						0.68	0.398	0.930
Item 9 (Having trouble lifting or carrying heavy objects)						0.51	0.597	0.930
Item 14 (Having limited diet)						0.39	0.45	0.933
Variance Explanation Ratios (%)	47.09	8.27	5.09	4.76	4.19	3.70		

CLDQ, Chronic Liver Disease Questionnaire

Table 4. Correlations between the CLDQ, LDSI 2.0 and theirs subdimensions

CLDQ LDSI 2.0	Abdominal symptoms	Fatigue	Systemic symptoms	Activity	Emotional function	Anxiety	Totaly
Itch	-0.30**	-0.26**	-0.47**	-0.33**	-0.26**	-0.38**	-0.42**
Joint pain	-0.44**	-0.51**	-0.71**	-0.55**	-0.46**	-0.40**	-0.61**
Pain in right upper abdomen	-0.41**	-0.28**	-0.37**	-0.46**	-0.29**	-0.26**	-0.40**
Sleepiness during day	-0.41**	-0.75**	-0.42**	-0.49**	-0.48**	-0.39**	-0.59**
Worry about family situation	-0.46**	-0.50**	-0.42**	-0.47**	-0.47**	-0.77**	-0.66**
Decreased appetite	-0.68**	-0.49**	-0.36**	-0.57**	-0.45**	-0.40**	-0.57**
Depression	-0.54**	-0.62**	-0.52**	-0.53**	-0.54**	-0.77**	-0.74**
Jaundice	-0.28**	-0.26**	-0.26**	-0.29**	-0.28**	-0.31**	-0.34**
Extra items (six items)	-0.57**	-0.57**	-0.43**	-0.64**	-0.60**	-0.46**	-0.63**
Total	-0.72**	-0.75**	-0.69**	-0.76**	-0.69**	-0.74**	**-0.88****

** Correlation is significant at 0.001.
CLDQ, Chronic Liver Disease Questionnaire; LDSI, Liver Disease Symptom Index

Interrater reliability

Interrater reliability was evaluated with test-retest scores and ICC. For this purpose, the Turkish version of the CLDQ was re-applied to 60 patients. The test-retest of the Turkish CLDQ was performed after two to three weeks. The test-retest correlation coefficient average for the Turkish version of the CLDQ was 0.79 ($p<0.001$, Table 5). The test-retest correlation coefficient ranged from 0.48 to 0.89. Overall ICC of the Turkish version of the CLDQ was 0.88 ($p<0.001$). ICCs ranged from 0.65 to 0.94. Although the Cronbach's alpha of the "activity" subdimension was low (0.57), test-retest reproducibility was good according to an ICC of 0.79 and test-retest correlations ($r= 0.66$, $p<0.001$) (Table 5).

Construct validity

Confirmatory factor analysis was used to evaluate the construct validity. For the 29 items in the CLDQ's original form, CFA was conducted, and fit indices were assessed. The model fit indexes of CLDQ were calculated as $\chi2/df = 2.320$, GFI = 0.910, CFI = 0.961, RMSEA = 0.075, according to the analysis results (Table 6). As a result of the CFA, the model fit values of the 29 items in the Turkish form of CLDQ were at an acceptable level. Standardised coefficients of the CLDQ were presented in Figure 1. According to the results of the CFA of the Turkish version of CLDQ, that six sub-dimensions consisting of 29 items was confirmed.

DISCUSSION

According to the EFA, the final version of the Turkish CLDQ matched well with the original CLDQ. Specifically, EFA revealed that the Turkish version of the CLDQ is divided into six subdimensions, same as the original English version of the CLDQ. Recently, however, statistics studies suggested that items with factor loadings greater than 0.30 should not be removed from the questionnaire (29). In this study, each item had a factor loading greater than 0.30; therefore, none of the items were removed from the questionnaire. Other studies also found six subdimensions, namely the fatigue, emotional function, worry, abdominal symptoms, activity, and systemic symptoms (13, 15-21, 23). Unlike our findings, Mucci et al. (16) also found six subdimensions, but the sixth subdimensions was called preoccupation, instead of worry. However,

Table 5. Reliability analyses of the Turkish version of the CLDQ

	Mean	Standart deviation	Cronbach's alpha	Test-retest realibility		
				Corelation coefficient	P value*	ICC
Abdominal	5.41	1.64	0.86	0.52	<0.001	0.67
Fatigue	3.97	1.45	0.93	0.82	<0.001	0.90
Systemic Semptoms	4.99	1.31	0.81	0.67	<0.001	0.79
Activity	5.61	1.18	0.53	0.66	<0.001	0.79
Emotional Function	5.44	1.18	0.74	0.48	<0.001	0.65
Worry	4.08	1.35	0.95	0.89	<0.001	0.94
TOTAL	**4.73**	**1.12**	**0.93**	**0.79**	**<0.001**	**0.88**

***** Correlation is significant at 0.001.
CLDQ, Chronic Liver Disease Questionnaire; ICC, Intraclass Correlation Coefficient

Ferrer et al. (2006) (14) found seven subdimensions. The first six subdimensions were like the original version of the CLDQ, but their seventh subdimension was the sleep. Younossi et al. found four subdimensions covering 29 items (22).

There were other differences in the subdimension of the Turkish version compared to the original CLDQ. The question "How much of the time during the last two weeks has shortness of breath been a problem for you in your daily activities?" loaded on the systemic symptoms subdimension in the original version of the CLDQ, whereas it loaded on the abdominal symptoms subdimension in our study. This difference may be due to the percentage of the patients that have cirrhosis in our study and those who had experienced decompensation symptoms, particularly ascites, which can lead to shortness of breath. Ascites in patients with advanced liver disease can affect breathing, and patients with ascites can experience shortness of breath (30, 31).

Two other items "How much of the time during the last two weeks have you had difficulty sleeping at night?" and "How much of the time during the last two weeks have you been unable to fall asleep at night?" loaded on the emotional function subdimension in the original version of the CLDQ but loaded on the systemic symptoms subdimension in our study. Sleeping is perceived as an effective factor in maintaining homeostasis, which is necessary for growth in Turkish culture (32). We believe that sleeping problems loaded on the systemic symptoms subdimension due to this reason.

The question "How much of the time during the last two weeks have you experienced abdominal pain?" loaded on a different subdimension. This question loaded on the abdominal symptoms subdimension in the original version of the CLDQ but loaded on the activity subdimension in our study. This may be due to the perceived in Turkish patients with CLD and its effects on their activities of daily living. Patients who experienced abdominal pain have restricted activities and ability to move (33). Therefore, abdominal pain was grouped under the activity subdimension in our study. Finally, the question "How much of the time during the last two weeks have you not been able to eat as much as you would like?" loaded on the activity subdimension, in the original version of the CLDQ, but loaded on the emotional function subdimension in our study. We believe that this is also due to the cultural differences. In Turkish culture, eating is an important activity that gives pleasure to people, and food is served to celebrate the happy moments by organizing a dinner gathering with families and friends (34, 35). The fact that the patients who are not able to eat may feel unable to fully participate in these important family occasions may explain why this question is loaded on the emotional function subdimension. The correlations between the CLDQ

Table 6. CLDQ fit indices (36)

Fit indices	Perfect fit indices	Acceptable fit indices	Model value
χ2/df	χ2 /df < 2	2 < χ2/df < 5	**2.320**
GFI	0.95 ≤ GFI ≤1	0.90 ≤ GFI ≤0.95	**0.910**
CFI	0.95 ≤ CFI ≤1	0.95 ≤ CFI ≤0.90	**0.961**
RMSEA	0 ≤ RMSEA ≤0.05	0.05 ≤ RMSEA ≤0.08	**0.075**

subdimension and Turkish version of the LDSI 2.0 subdimensions were acceptable, which indicate the predictive validity of this questionnaire. The predictive validity of the CLDQ was also confirmed in other studies (11, 15, 19, 21).

Overall, the Cronbach's alpha was excellent at 0.93. However, the activity subdimension had the lowest Cronbach's alpha value of 0.53. It can be as a result of the few items (three) (25). This result may be due to the three item loadings on this subdimension; as suggested by Sipahi et al., (29) decreased number of items loaded on a factor leads to the lower reliability coefficient, which its acceptable lower limit is 0.60 (29). Ranawaka et al. (17) also found similar results, where the Cronbach's alpha value of the activity subdimension was 0.48 (17). In addition, Pappa et al. (20) stated in their study that the activity subdimension had the lowest Cronbach's alpha value of 0.74. Undeniably, however, this factor needs further exploration. Morever we analysed “cronbach’s alpha if item deleted” values of every item. When any item is deleted, no increase in Cronbach's alpha value is observed, and therefore we did not removed any item from original CLDQ.

The test-retest correlation coefficient was 0.79 in our study ($p<0.001$), with a test-retest correlation coefficient ranging from 0.48 to 0.89 per subdimensions. In this study, we found that the emotional functions subdimension had the lowest coefficient (0.48). This result is understandable, as emotional functions are unstable and easily affected by other environmental changes. Overall ICC of the Turkish version of the CLDQ was 0.88 ($p<0.001$). Mucci et al. (2013) (16) found slightly higher ICC than our results since the time between first and second application ranged from 1 to 15 days in their study. Their higher results may be due to the short time interval. Yet, our ICC results were higher than the original version of the CLDQ. In the original study, ICC analysis was carried out to test the reliability after six months of the original administration for test-retest analysis (11). In this study, test-retest analysis was carried out after two or three weeks. The time duration was a well-established interval since the progression of the disease is likely to remain stable during this interval. The optimal time frame is thought to be between two and four weeks in order to balance out any bias and inconsistencies brought on by the disease's course. Six-month period in the original study might be too long, which may cause lower results. In the Spanish version of the CLDQ, the retest was applied two weeks after the first test application (14). Their results (0.90) were similar to the results of this study. According to the reliability analysis results of our study, the questionnaire was found to be reliable.

CLD is causing the quality of life of the patients to be adversely affected for a long time. So that the symptoms experienced in the CLDQ are determined by reliable questionnaire and symptom management should done effectively. Interestingly, HRQoL scoring in the Turkish version of the CLDQ showed significant differences in terms of the Child-Turcotte-Pugh Scoring groups. Patients without cirrhosis had the best quality of life ratings. Child A group outperformed Child B group in terms of test scores. The results of Tanaka et al. (21) were similar to ours. The Child B group had the lowest scores in all participants (21). The previous studies also had similar results (13, 14, 17). In their study, Pappa et al. (20) reported that patients with Child A group had better HRQoL compared to the patients in Child B or C groups. However, our results were similar to that of reported by Tanaka et al., in which the Child B group had the lowest scores (21). Other researchers have also reported similar findings, suggesting that the Turkish version of the CLDQ measures HRQoL well within the cirrhotic-patient population (13, 14, 17).

In this study, we performed CFA to test the factor structure of the CLDQ. The model fit indexes of CLDQ

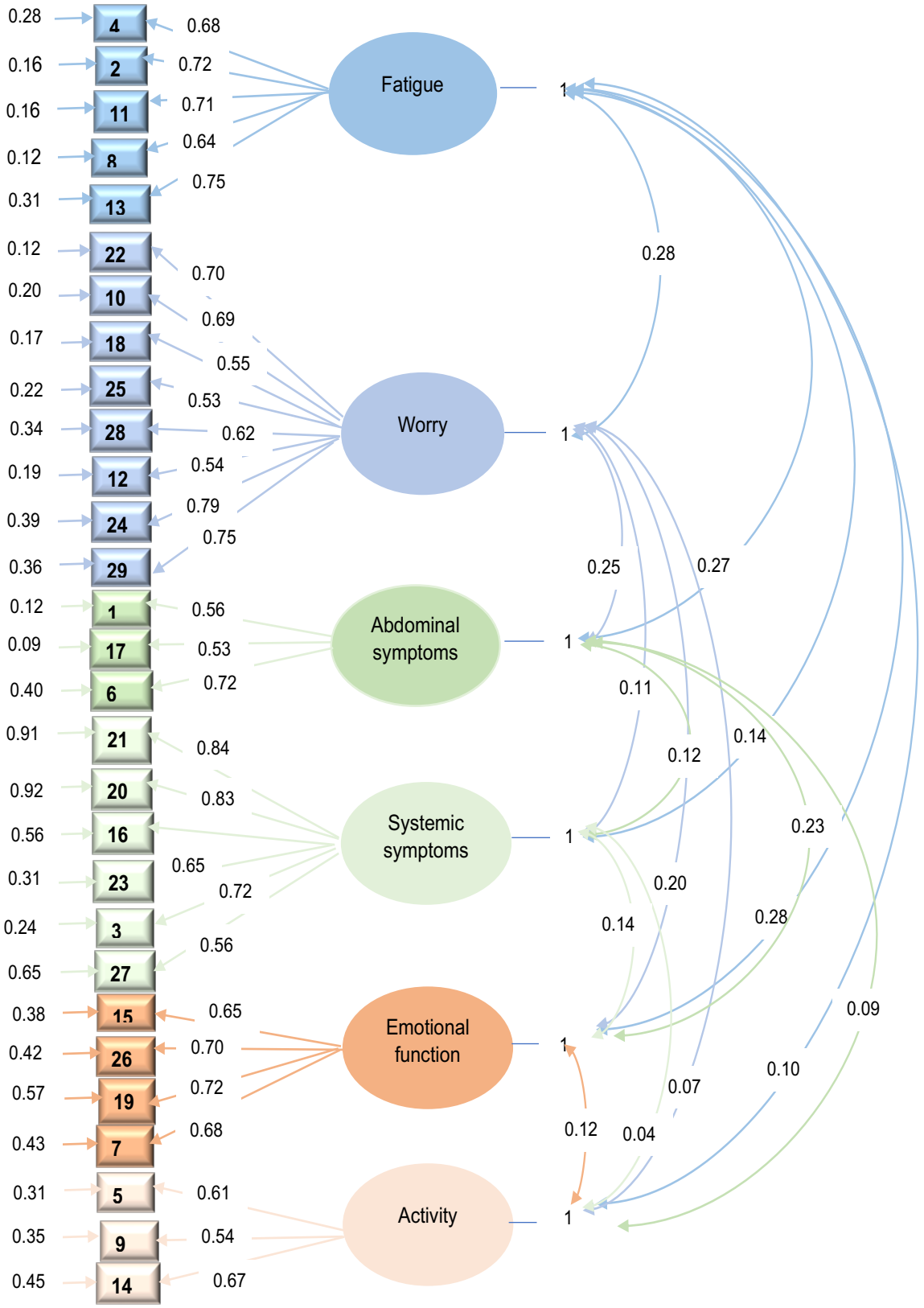

Figure 1. Standardised coefficients

were calculated as $\chi 2/df = 2.320$, GFI = 0.910, CFI = 0.961, RMSEA = 0.075, according to the analysis results. According to CFA results of the CLDQ, the models of fit indexes were adjusted acceptably (38). Since CFA was not performed in determining the psychometric properties of the original scale (11), no comparison was made. Moreover, the other studies in which to test reliability and validity of CLDQ have not reported CFA results (13, 14, 16, 18, 20, 22, 23). The CFA was not applied in the many studies and therefore, no comparisons could be made in this respect.

The study had a couple limitations. First limitation is that the cultural differences we suggested as the reasons why certain items loaded on different factors than the original CLDQ. Since lack of results of CFA of other studies, we could not compare our results of CFA. This was our last limitation.

CONCLUSION

In conclusion, the validity and reliability of the CLDQ were confirmed in the Turkish population, and it will be a useful HRQoL tool in assessing the effects of CLD. HRQoL of non-cirrhotic patients was better than patients with liver cirrhosis. Also, patients in the Child Turgotte Pugh Score A group had better HRQoL than patients with Child Turgotte Pugh Score B group. We recommend researcher should conduct trials to determine quality of life of patients with CLD. According to result of these trials, medical treatment and nursing care should be organized and individualized in accordance with the symptoms, using a multidisciplinary team approach and suitable instruments. In this study, some items loaded on different factors than the original CLDQ. Further studies are needed to confirm the differences we found, where several items loaded differently than the original CLDQ, which we believe is due to cultural differences. Furthermore, studies in which conduct CFA is needed to compare our results.

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Author contributions: Study Desing: FC, HB, ZY; DataCollection: FC; Data Analysis: FC, HB; ManuscriptWriting: FC, HB, ZY.

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

Ethical approval: The research was approved by the Akdeniz University, Clinical Research Ethics Committee (REDACTED) (2012 KAEK-20/20.07.2016-429) and director of the studied hospital located in Akdeniz University (26708535-903.99).

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RESEARCH ARTICLE

THE INVESTIGATION OF KINESIOPHOBIA, PAIN CATASTROPHIZING, PHYSICAL ACTIVITY, ANXIETY, AND DEPRESSION IN PATIENTS WITH OR WITHOUT MYOCARDIAL INFARCTION

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ABSTRACT

Purpose: The study aimed to investigate kinesiophobia, pain catastrophizing, physical activity, anxiety, and depression in patients with MI.
Material and Methods: A cross-sectional study was conducted with 100 participants (50 myocardial infarction, 50 age-sex matched controls). Participants were evaluated with the Tampa Scale of Kinesiophobia for Heart (TSK Heart), Pain Catastrophizing Scale (PCS), International Physical Activity Questionnaire-Short Form (IPAQ-SF), and Hospital Anxiety and Depression Scale (HAD).
Results: IPAQ-SF (except sitting time) was higher in the control group ($p<0.01$). PCS score ($p<0.01$), HAD-A ($p=0.001$) and HAD-D ($p=0.006$) scores were significantly higher in the MI group. TSK Heart was correlated with Sitting PA ($r=0.425$), Walking PA ($r=-0.574$), Moderate PA ($r=-0.632$), HAD-A ($r=0.641$) and HAD-D ($r=0.827$) ($p<0.01$). There was a relationship between HAD-A with Sitting PA, Walking PA and Moderate PA ($r_1=0.445$, $r_2=-0.485$, $r_3=-0.378$, $p<0.01$). Lastly, HAD-D was correlated with Sitting PA, Walking PA and Moderate PA ($r_1=0.475$, $r_2=-0.520$, $r_3=-0.578$, $p<0.01$).
Conclusion: The study results showed decreased physical activity, increased kinesiophobia, pain catastrophizing, depression and anxiety in patients with MI. In addition, kinesiophobia was related to mild-moderate physical activity and depression-anxiety.

Keywords: Aerobic exercise, fear of movement, MI, pain perception, psychosocial status

INTRODUCTION

Cardiovascular diseases (CVD) cause significant disability and death rates, burdening the health system and economy (1, 2). Various psychosocial parameters also additionally have a negative impact on public health. Myocardial infarction (MI) patients

Table 1. The baseline physical and clinical characteristics of the participants

	MI patients (n=50)	Control group (n=50)	p
Age (years, mean±SD)	61.9±11.9	62.5±10.2	0.514[a]
Gender (women/men, n)	11/39	13/37	0.640[b]
BMI (kg/m^2, mean±SD)	25.8±2.1	26.6±3.0	0.393[a]
Duration after MI (months, mean±SD)	4.9±3.8	n/a	n/a
Type of MI (STEMI/Non-STEMI, n)	25/25	n/a	n/a
Marital status (married/single, n)	47/3	44/6	0.295[b]
Occupation status (active/retired, n)	16/32	23/27	0.159[b]

SD: standard deviation, n: number of patients, BMI: Body Mass Index, MI: Myocardial Infarction, STEMI: ST-Elevation Myocardial Infarction, Non-STEMI: Non-ST-Elevation Myocardial Infarction, a: Mann–Whitney U test, b: Pearson Chi Square test

are prone to fear movement. Kinesiophobia indirectly leads to a sedentary lifestyle in MI patients. Accordingly, the symptoms of individuals with MI should be addressed comprehensively, including the psychological state (3, 4).

Previous studies reported that the risk of MI for depressed individuals is 2.9 times (5), and the risk of MI for individuals with anxiety is 2.5 times (6). Moreover, anxiety and depression are independent risk factors that increase cardiac morbidity and mortality (7). Fear and avoidance behavior develop in the acute period in individuals with MI. There is a possibility of developing kinesiophobia, in individuals who cannot control their fear (8). Increased anxiety in individuals with coronary artery diseases (CAD) affected kinesiophobia behaviours (9).

Studies have revealed that 21% of individuals develop kinesiophobia six months following the cardiac event (10). Physical inactivity and depression develop due to kinesiophobia and destructive thoughts, leading to avoidance behavior (11, 12). Individuals with CAD have been shown to avoid physical activity and exercise due to fear of movement (13, 14). In addition, activity areas such as fitness centers were suspended in many countries during the COVID-19 pandemic. Long-term quarantine practices have created a deficiency in staying physically active and affect people's quality of life (15). As a vicious circle, insufficient physical activity again causes negativities such as kinesiophobia and catastrophic thoughts. The importance of physical activity in the rehabilitation of MI patients is an undeniable fact (16).

The fact that there are studies for patients with acute MI, kinesiophobia levels of MI patients has not been demonstrated by cross-sectional studies, holistically (10, 14). Revealing kinesiophobia would be an essential contribution to the rehabilitation process of coronary artery disease. Crucial negative clinical variables caused by kinesiophobia on prognosis can be prevented. To our knowledge, no studies have focused on patients' perceptions of kinesiophobia after MI, holistically. The study aimed to investigate kinesiophobia, pain catastrophizing, physical activity, anxiety, and depression in patients with MI. Accordingly, the difference between the parameters of pain catastrophizing, physical activity, anxiety, and depression in individuals with and without MI was compared. The study questioned whether pain catastrophizing, physical activity, anxiety, and depression increase in patients with MI. We hypothesized that pain catastrophizing, physical activity, anxiety, and depression might be increased in patients with MI compared to healthy individuals. The secondary aim was to analyze the correlation degree between kinesiophobia, pain catastrophizing,

Table 2. The comparison of the scores between the groups

	MI patients (n=50)	Control group (n=50)	p
IPAQ - Total (MET min week−1)	598.9±383.4	5115.3±5870.4	**0.001[a]**
Sitting PA (MET min week−1)	355.6±429.4	381.5±369.4	0.498[a]
Walking PA (MET min week−1)	104.9±131.4	2031.3±2569.6	**0.001[a]**
Moderate PA (MET min week−1)	58.4±119.3	716.3±1554.5	**0.009[a]**
Vigorous PA (MET min week−1)	0.0±0.0	554.0±1665.0	**0.001[a]**
PCS	26.0±9.4	7.3±8.5	**0.001[a]**
HAD-A	9.0±2.7	4.7±3.0	**0.001[a]**
HAD-D	8.2±3.8	6.0±3.1	**0.006[a]**
TSK Heart	44.2±5.6	n/a	n/a

SD: standard deviation, n: number of patients, IPAQ: International Physical Activity Questionnaire-Short Form, PA: Physical activity, MET: Metabolic equivalent, PCS: Pain Catastrophizing Scale, HAD-A: Hospital Anxiety and Depression Scale-Anxiety Subscale, HAD-D: Hospital Anxiety and Depression Scale-Depression Subscale, TSK Heart: Tampa Scale for Kinesiophobia Heart, a: Mann–Whitney U test

physical activity, anxiety, and depression in individuals with MI.

MATERIAL AND METHODS

Study Design and Participants

A cross-sectional study was conducted between January and June 2022 with a total of 100 participants, 50 of whom were diagnosed with myocardial infarction by a cardiologist, and 50 were age and sex-matched control group without a history of myocardial infarction, in the Department of Cardiology at Muğla Sıtkı Koçman University. Inclusion criteria for the study; patients over 18 years of age, at least one month and maximum of one year after myocardial infarction, and who could speak Turkish were determined. The potential cases of MI and the control group with orthopaedic/neurologic diseases, severe psychiatric, somatic and pulmonary disorders, presence of comorbidities such as heart valve disease, cardiac shock and cardiomyopathy, patients with heart failure and physical activity limitation who scored three or worse according to the New York Heart Association Functional Classification (17), and individuals who did not sign the consent form were excluded from the study.

Procedure

The study was conducted following ethical principles and the Declaration of Helsinki. Participants were included in the study through a questionnaire-based assessment. Expert two cardiologists assessed the participants with a diagnosis of myocardial infarction. Informed voluntary consent was obtained from the participants before participating in the study. The study protocol was approved Ege University, Medical Research Ethics Committee (No:21-4.1T/63, Date: 15.04.2021).

Data Collection

Demographic and clinical characteristics (e.g., type of myocardial infarction, time elapsed after myocardial infarction) of all participants included in the study were recorded. All participants were evaluated with the Tampa Scale of Kinesiophobia for Heart (TSK Heart), International Physical Activity Questionnaire-Short Form (IPAQ-SF), Hospital Anxiety and Depression Scale (HAD), Hospital Anxiety and Depression Scale-Anxiety Subscore (HAD-D), The Pain Catastrophizing Scale (PCS).

Table 3. The relationship of kinesiophobia with other symptoms

n: 50	TSK Heart (r)	p
IPAQ - Total	0.112	0.438
Sitting PA	**0.425****	0.002
Walking PA	**-0574****	0.0001
Moderate PA	**-0.632****	0.0001
PCS	0.047	0.746
HAD-A	**0.641****	0.0001
HAD-D	**0.827****	0.0001

SD: standard deviation, n: number of patients, IPAQ: International Physical Activity Questionnaire-Short Form, PA: Physical activity, PCS: Pain Catastrophizing Scale, HAD-A: Hospital Anxiety and Depression Scale-Anxiety Subscale, HAD-D: Hospital Anxiety and Depression Scale-Depression Subscale, TSK Heart: Tampa Scale for Kinesiophobia Heart, r: Spearman correlation coefficient, **: p<0.001

Sample Size

The G-Power 3 software was used to conduct the research's power analysis (18). Even though no comparable studies were published, "Cohen's d" was utilized to calculate the "effect size". Considering the “medium effect size” (0.50) (19), 46 cases were anticipated to be adequate for MI and control groups (80% power and 95% confidence level were considered).

Tampa Scale of Kinesiophobia for Heart (TSK Heart)

The Tampa Kinesiophobia Scale (TSK) was developed by Kori et al. (20). TSK was adapted to cardiac diseases by Bäck et al. and named (TSK-H). The TSK-H was adapted in Turkish by Acar et al. TSK-H consists of 7 items and four sub-dimensions, and each item scores between 1 and 4 points. After reversing the 4th, 8th, 11th and 12th items, the total score is calculated. The scores obtained from the scale are in the range of 17-68 points. A high score on the scale indicates high kinesiophobia (21).

International Physical Activity Questionnaire-Short Form (IPAQ-S*)*

IPAQ-S was adapted in Turkish by Saglam et al. (22). The questionnaire, consisting of 7 questions, questions the frequency and duration of light, moderate and vigorous physical activities performed in the last seven days. According to the total score calculated, individuals' physical activity levels are classified as inactive, low, or adequate (23).

Hospital Anxiety and Depression Scale (HAD)

HAD was developed by Zigmond and Snaith (24). HAD was adapted in Turkish by Aydemir et al. The scale includes anxiety and depression sub-dimensions. The HAD scale contains 14 questions, half of which (odd numbers) measure anxiety and the other half (even numbers) depression. Questions in the scale are scored on a four-point Likert scale, each ranging from 0 to 3. A higher score indicates a worse condition (25).

The Pain Catastrophizing Scale (PCS)

PCS consists of 13 questions with a Likert-type scale scored between 0-4. A high score indicates an increased pain and fear of experiencing pain (27). PCS was developed by Sullivan et al. (26). PCS was adapted in Turkish by Suren et al.

Statistical Analysis

“SPSS software (Statistical Package for Social Sciences) was used for Windows v25.0 (SPSS Inc, IBM Corp, Armonk, New York). The variables were provided as mean, standard deviation (SD), and per cent). A statistical significance level of 0.05 was chosen. The normality of the variables was demonstrated using the one-sample Kolmogorov–Smirnov test and a Histogram. Because none of the data distributions was normal, the Mann-Whitney U test was used to compare case group differences. The discrepancies between the categorical variables were further checked using Pearson's chi-square test. The comparison of the parameters was also carried out with the Spearman correlation coefficient.”

RESULTS

The mean age of the MI group and control group were 61.9±11.9 years and 62.5±10.2 years, respectively. The STEMI and non-STEMI type of MI were equal (n:25/25). The mean duration after MI was 4.9±3.8

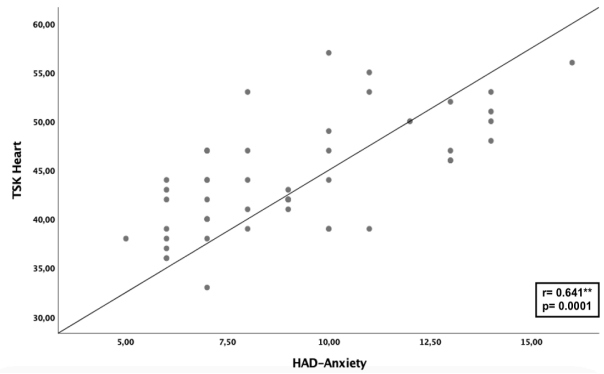

Figure 1. Scatter plot of the correlation between TSK Heart and HAD-Anxiety

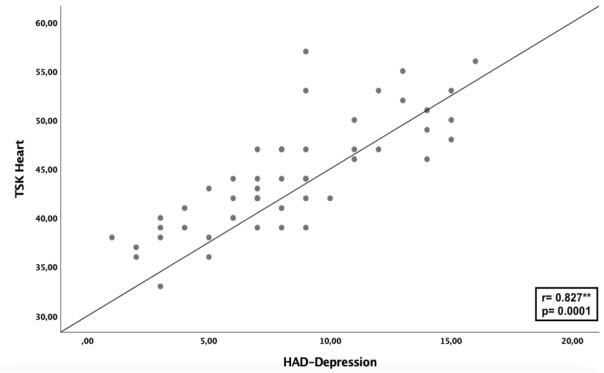

Figure 2. Scatter plot of the correlation between TSK Heart and HAD-Depression

months. The baseline physical, demographical and clinical characteristics of the two groups are presented in Table 1. There was no significant difference in the baseline data of the groups (p>0.05). The questionnaire-based assessment results from the comparison of the MI and control group patients are given in Table 2. There was a significant difference between the two groups in IPAQ - Total (MET min week−1), Walking PA (MET min week−1), Moderate PA (MET min week−1), and Vigorous PA (MET min week−1) (p<0.01). The control group were significantly more physically active. However, Sitting PA (MET min week−1) was not statically different between groups (p>0.05).

PCS score was higher in MI patients (p<0.01). On the other hand, HAD-A (p=0.001) and HAD-D (p=0.006) scores were significantly higher in the MI group. Since TSK Heart was developed to assess cardiac patients, the sex and age-matched control group could not fill out this questionnaire. Therefore, a comparison of the groups was unavailable for the TSK Hearth.

Correlational analysis was carried out to holistically observe the relationship between parameters in the MI group. First, PCS was not significantly correlated with any parameters (p>0.05). Second, TSK Heart was correlated with Sitting PA (r=0.425), Walking PA (r=-0.574), Moderate PA (r=-0.632), HAD-A (r=0.641) and HAD-D (r=0.827) (p<0.01) (Table 3) (Figure 1 and 2). Third, there was a relationship between HAD-A with Sitting PA, Walking PA and Moderate PA (r_1=0.445, r_2=-0.485, r_3=-0.378, p<0.01). Lastly, HAD-D was correlated with Sitting PA, Walking PA and Moderate PA (r_1=0.475, r_2=-0.520, r_3=-0.578, p<0.01) (Table 4).

DISCUSSION

The present study results revealed physical inactivity, increased kinesiophobia, pain catastrophizing, depression and anxiety in patients with or without myocardial infarction. Besides, kinesiophobia was demonstrated to be related to mild to moderate physical activity and depression-anxiety. On the other hand, depression and anxiety symptoms of the MI patients were also correlated with walking and moderate physical activities.

During to COVID-19 era, individuals were prone to stay at home for a long time without daily routines. Therefore, people's physical activity decreased daily (28). Individuals with MI have been more affected by quarantine measures as they are in the risk group due to their chronic diseases (29). Along with the decreased level of physical activity, there were also negative effects on the psychological state of individuals with MI (30). In this respect, neuropsychiatric parameters such as kinesiophobia and pain catastrophizing may be indirectly affected. The present study is unique in terms of the relevant psychosocial parameters. Furthermore, kinesiophobia in MI patients had not been adequately investigated. Various studies investigated kinesiophobia with cases of coronary artery disease (10, 13, 14, 31-34). However, to our knowledge, no other studies demonstrated kinesiophobia and pain catastrophizing specific to MI cases, and a comparative analysis was not conducted.

Only one qualitative study has performed an analysis based on the relationship of kinesiophobia to physical activity and exercise (35). The relationship between these two parameters, the cornerstones of cardiac rehabilitation, with fear of movement was investigated in patients who left 2-3 months after acute MI. The study's results emphasized that coping with the fear

Table 4. The relationship of depression-anxiety with other symptoms

n: 50	HAD-A (r / p)	HAD-D (r / p)
IPAQ - Total	0.254 / 0.075	0.200 / 0.163
Sitting PA	**0.445**** / 0.001	**0.475**** / 0.0001
Walking PA	**-0.485**** / 0.0001	**-0.520**** / 0.0001
Moderate PA	**-0.378**** / 0.007	**-0.578**** / 0.0001
PCS	0.272 / 0.056	0.050 / 0.732

SD: standard deviation, n: number of patients, IPAQ: International Physical Activity Questionnaire-Short Form, PA: Physical activity, PCS: Pain Catastrophizing Scale, HAD-A: Hospital Anxiety and Depression Scale-Anxiety Subscale, HAD-D: Hospital Anxiety and Depression Scale-Depression Subscale, r: Spearman correlation coefficient, **: p<0.001

of movement after myocardial infarction is a dynamic process that requires internal and external support. However, since there is no quantitative data, the relational analysis should have been emphasized at the statistical significance level and based on numerical data. The results of our study made an additional contribution to the literature in this respect. Since it is known that MI patients with high anxiety and depression have more pain perception (36), our study is valuable in terms of catastrophizing pain and associating it with kinesiophobia. In addition, the long-term depression-reducing effect of physical activity also indirectly affects kinesiophobia and pain catastrophe through psychosocial parameters (37).

The present research was a cross-sectional case-control study. The individuals with MI who left the first one-month acute period was compared with the age- and sex-matched control group. We also showed that some physical and demographic data were congruent in baseline assessment between the two groups. In this respect, it was observed that the selectivity of the study's exclusion criteria was well-accomplished. That is, the two groups were homogeneous in terms of socio-demographic data. Since the BMI, marital and occupational status of the patients were considered to affect their psychological and physical status, the groups' homogeneity had the utmost importance in controlling the analysis.

Our study mentioned that individuals with MI were more inactive in all physical activity parameters (except sitting time). It was also observed that individuals with MI had worse clinical conditions regarding pain catastrophe and anxiety depression. Kinesiophobia was associated with sitting and moderate physical activity levels. In other words, individuals who are active in walking and moderate physical activities have less fear of movement. As expected, it was concluded that individuals with low depression and anxiety levels also had low kinesiophobia. In addition, it has been revealed that those who do more walking and moderate-intensity activities have better psychosocial status.

It was already known that the psychosocial states of physically active individuals were better in patients with MI (30, 36). It is apprehended that aerobic exercises such as light-paced walking and moderate-intensity recreational activities, which are included in many cardiac rehabilitation programs and guidelines, are essential in reducing anxiety and depression symptoms (38). In parallel, we observed that kinesiophobia was low in these individuals. Individuals are more able to overcome their fear of movement with an active life. However, pain catastrophizing was not associated with any parameter. In other words, it is not possible to say that individuals who are physically active, have a low level of depression and do not have kinesiophobia are at a reasonable level in terms of pain catastrophizing. The relationship between the perception of pain and the psychological state is already distinguished (36). Though, we concluded that individuals maintain their pain perceptions independently of their movement and physical activity levels in the post-MI period. Considering the quantitative and qualitative studies that recommend following the fear of movement as a process (10), a more comprehensive study in pain catastrophizing, especially in patients who have passed one year after MI is recommended. Moreover, the positive effect of one-year physical activity and follow-up on psychiatric condition supports this situation (39).

Kinesiophobia and psychosocial status in coronary artery disease have been discussed in various studies in the literature (10, 13, 14, 31-34). Bäck et al. found kinesiophobia associated with physical activity level (moderate-high) and anxiety (13). Şahin et al. also emphasized the relationship betwleeen aerobic capacity, physical activity and kinesiophobia and claimed that cardiac rehabilitation reduces fear of movement (34). Knapik et al. suggested that kinesiophobia can be reduced by increasing physical

activity (31). These results also supported our results regarding physical activity and psychosocial level. On the other hand, several studies associated kinesiophobia with age, gender and education level in individuals with MI (10, 31, 40). Since we have strictly controlled our exclusion criteria, both groups were age, sex and other demographics matched. Therefore, the differences in age, gender or education would not affect the results of our study, presumably. According to another research report, it is also reported that individuals with kinesiophobia stay away from entering a cardiac rehabilitation program (14). Most cardiac rehabilitation program includes aerobic moderate physical activity pieces of advice (38). Therefore, also considering the results of our study, physical activity and kinesiophobia are thought to be entered a vicious circle in patients with MI. Yümin et al. emphasized that kinesiophobia reduces the quality of life in individuals with coronary artery disease (33). Since it is known that people with low physical activity have high levels of anxiety and depression, it can be predicted that the psychological dimension of quality of life may also be low in individuals with kinesiophobia.

Some limitations of the study should be emphasized. First, individuals could be evaluated in different periods from the beginning of the pandemic, and the results could be presented. In this way, the effect of psychological state and decrease in physical activity on kinesiophobia and pain catastrophizing could be observed more clearly. Second, a more comprehensive activity assessment would be possible if physical activity assessment was evaluated with sensor-based wearable health technologies such as a pedometer or an accelerometer. Third, analyzes could be replicated according to the education level and gender of the patients.

CONCLUSION

The study results showed decreased physical activity, increased kinesiophobia, pain catastrophizing, depression and anxiety in patients with MI. In addition, kinesiophobia was related to mild to moderate physical activity and depression-anxiety. Also, depression and anxiety symptoms of the MI patients were observed to be related to walking and moderate physical activities. Considering the relationship of kinesiophobia with mild to moderate physical activity, clinicians may have taken precautions against kinesiophobia by encouraging individuals with MI to engage in physical activity. Further studies should detail the relationship between physical activity and kinesiophobia in more comprehensive physical activity monitoring from MI patients with a pedometer or sensor-based devices.

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Conflict of interests: The authors declare that they have nocompeting interests.

Ethical approval: The study was carried out in accordance with the ethical principles and the Helsinki Declaration. The study protocol was approved by the Medical Ethics Committee of Ege University (No:21-4.1T/63, Date: 15.04.2021). Informed consent of the patients was obtained.

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RESEARCH ARTICLE

IMPORTANCE OF PHYSIOLOGY EDUCATION IN PHYSIOTHERAPY AND REHABILITATION

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ABSTRACT

Purpose: Physiology is an experimental science and is present in the fundamental education of medicine and health sciences. The study aimed to investigate the importance of physiology education in physiotherapy and rehabilitation (PT).
Material and Methods: The study retrieved the opinions of 249 participants (131 physiotherapists (PTs) and 118 PT students) on physiology education with an online questionnaire. The questionnaire included 30 items on the following subjects: physiology education, effects of physiology education on professional life, opinions on supplementary materials (laboratory brochures, books), and PT curriculum (lessons and lesson hours of physiology).
Results: Theoretical physiology education mainly employed PowerPoint or projection (66.4% of PTs and 55.1% of students), while practical education utilized supplementary materials in the laboratories of 40.5 % of PTs and 35.6 % of students. Nearly half of the participants (47.8%) declared the quality of the physiology education as moderate. A ratio of 41.2% of PTs and 44.9% of students neither agreed nor disagreed with receiving problem-focused physiology education. Participants considered that the most critical physiology course was exercise physiology. Furthermore, they stated that physiology education was essential in clinical practice and helpful in understanding other curriculum lessons.
Conclusion: Physiology education was critical in clinical lessons and professional life quality in PT. The results of the study recommend increasing and updating problem-based physiology education.

Keywords: Curriculum, education, human physiology, physiotherapy, students

INTRODUCTION

Human physiology is one of the fundamental sciences in the physical therapy curriculum, and it guides students and clinicians in learning clinical problem-solving skills (1). Moreover, physiology is an experimental scientific discipline. It is essential to the solid health education foundation. Many learning techniques for undergraduate students aim to teach the core principles of physiology: evaluation, ecosystems and environments, causal mechanisms, the cell, structure-function relationships, and levels of organization (2). The widespread teaching methods are online test skills, e-test animations and games, virtual labs, hand-held learning, and case-discussion studies (3). In 2001, the Nelson R. Mandela School of Medicine (NRMSM; Durban, South Africa) launched a problem-based curriculum in which physiology learning is integrated with relevant clinical scenarios. This curriculum expected students to understand physiology through self-research, in which certain aspects are addressed (4). Another study conducted with medical students concluded that physiology education was more crucial in the early years to master pathologies. However, this thought lost popularity because physiology is necessary to understand and interpret symptoms and laboratory results in more advanced classes (5).

Table 1. Demographic characteristics of the participants

Variables	Physiotherapists (n:131) Median (IQR)/ n(%)	students (n:118) Median (IQR)/ n(%)
Age, year median (IQR)	25(24-27)	22(21-22)
Gender Female, Male n(%)	86(65.6),45(34.4)	96(81.4),22(18.6)
Professional experience n(%)		-
0-1 years	26(19.8)	
<5 years	80(61.1)	
> 5years	25(19.1)	
Working place n(%)		-
University	11(8.4)	
Research hospitals	5(3.8)	
Hospital	18(13.8)	
Special education and rehabilitation center	48(36.6)	
Healthy Life Center	6(4.6)	
Public institutions	7(5.3)	
Physiotherapy center	36(27.5)	

IQR: Inter Quantile Ranging; n: number, %: percentage

Additional techniques, such as theoretical and practical training, can facilitate the teaching and learning process in different disciplines of knowledge (6, 7). This process is critical in health science education, such as PT, for understanding the physiological basis, essential for patient evaluation, and patient-specific treatment programs (8). Although physiotherapists conduct planning and implementing a personalized exercise program by considering the physiological effects of the treatment modalities they will apply, there is little information about physiology education in PT (9). Therefore, the current study aimed to investigate the significance of physiology education in PT according to PTs' and students' opinions.

MATERIAL AND METHODS

The study took place with volunteer PTs and PT students. The current research was conducted between January and March 2021 using a questionnaire delivered via Google Forms (Google, Mountain View, CA, USA).

Participants

The study enrolled 118 students and 131 PTs. All participants gave Informed consent to participate in the study. Individuals who received physiotherapy and rehabilitation undergraduate education and had a physiology course in their curriculum were in the study. On the other hand, individuals who did not complete the physiology course process and did not receive a passing grade from the university where they received physiotherapy and rehabilitation education, and have backgrounds in other health sciences or medical education were not in the study.

Questionnaire

Researchers developed a questionnaire with four parts inquiring about demographic data and 30 items on physiology education (about the curriculum, education, and clinical practice).

- The first-part items were about physiology education: the hours of the lesson, the title of the teaching instructor, the department of the teaching instructor, and theoretical and practical teaching methods.
- The second part consisted mainly of open-ended questions on Likert-type items (between 1 and 5). In the grading, the following expressions were given: 1 = "not effective," 2 = "slightly effective," 3 = "moderately effective," 4 = "very effective and 5 = "extremely effective." This section discussed the effects of physiology education on professional life and various PT lessons (general PT, orthopedics, cardiopulmonary, pediatric neurology, and neurological).
- The third part investigated the opinions of the participants via five-point Likert-type items "strongly disagree," "disagree," "undecided," "agree," and "strongly agree". Opinions on supplementary materials (laboratory brochures and books), curriculum, and the number of lesson hours were in this part.
- The fourth part discussed the advantages of physical therapy courses: Heat, Light, and

Hydrotherapy; Electro Physical Agents; Exercise Physiology; Basic Measurement and Evaluation in Physiotherapy; Manipulative Treatment Techniques; Principles of Treatment Movements; Neurophysiologic Approaches; Biomechanics and Kinesiology; Pediatric Rehabilitation; Orthotics, Prosthesis, and Rehabilitation; Orthopedic& Sports Rehabilitation; Pulmonary Rehabilitation; Cardiac Rehabilitation.

Table two contains all questionnaire items.

Validity of the Questionnaire

The Lawshe technique evaluated the content validity of the draft questionnaire (10). Within the scope of the Lawshe technique, a questionnaire was sent via email to three physiotherapists and two undergraduate PT students who were blind volunteers and clinically working on the prepared questionnaire. Coverage validity rates were based on the values by Ayre & Scally (11). For the answers of the five evaluators, the content validity ratio was at least 0.99 at the p=0.05 significance level. Cronbach's alpha determined the internal consistency of the validated questionnaire, and its value was 0.860.

Statistical Analysis

The Windows-based SPSS 20.0 statistical analysis program was used (Armonk, NY: IBM Corp). Data normality was tested with the Kolmogorov–Smirnov test. The survey results were expressed in percentages. The baseline characteristics of the participants were reported as median (IQR)/mean (SD). Chi-square and Fisher's exact tests analyzed categorical variables. The Mann–Whitney rank-sum test compared the ordinal data between the physiotherapist and students. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1 presents the baseline characteristics of the participants. Their mean age was 24.14 ±3.99 years. The clinical experience of the physiotherapists was generally less than five years (61.1%) (Figure 1). PTs mainly worked in special education, rehabilitation centers (36.6%), and PT centers (27.5%) (Figure 2).

Participants stated that weekly hours of the physiology course (Part I, Table 2) were mostly (PTs, 35.9% & students, 38.1%) four (two theoretical and two practical) for one semester. Most teaching members of the physiology course were from the faculty of medicine (PTs, 61.1%; students, 67.8%) and were professors (PTs, 50.4%; students, 33.1%). The practical education method was commonly computer/atlas (40.5%) in PTs versus laboratory (35.6%) in students. The theoretical teaching methods were mostly PowerPoint/projection (PTs, 66.4%, and students, 55.1%; Part I, Table 2).

Table 2 shows the participants' opinions on the effect of physiology education on PT in parts II, III, and IV. Opinions on the effectiveness of physiology education in clinical lessons in undergraduate education were mainly *very effective* (PTs, 32.8%, and students, 37.3%). The effectiveness of physiology education in the current clinical practice was mainly *moderately effective* according to the participants (PTs, 33.3%, and students, 37.5%). Therefore, the effectiveness of the physiology education in general PT (moderately effective), pediatric rehabilitation (moderately effective), neurological rehabilitation (very effective), orthopedic rehabilitation (moderately effective), and cardiopulmonary rehabilitation (very effective) lessons was graded differently (Part II, Table 2).

There were significant differences in some opinions between the physiotherapist and the students (Part III, Table 2). Unlike the students, PTs mostly

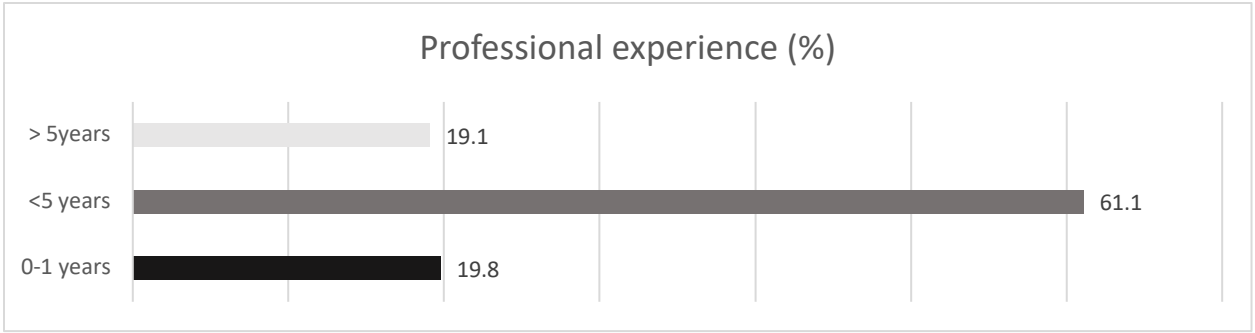

Figure 1. Professional's experience

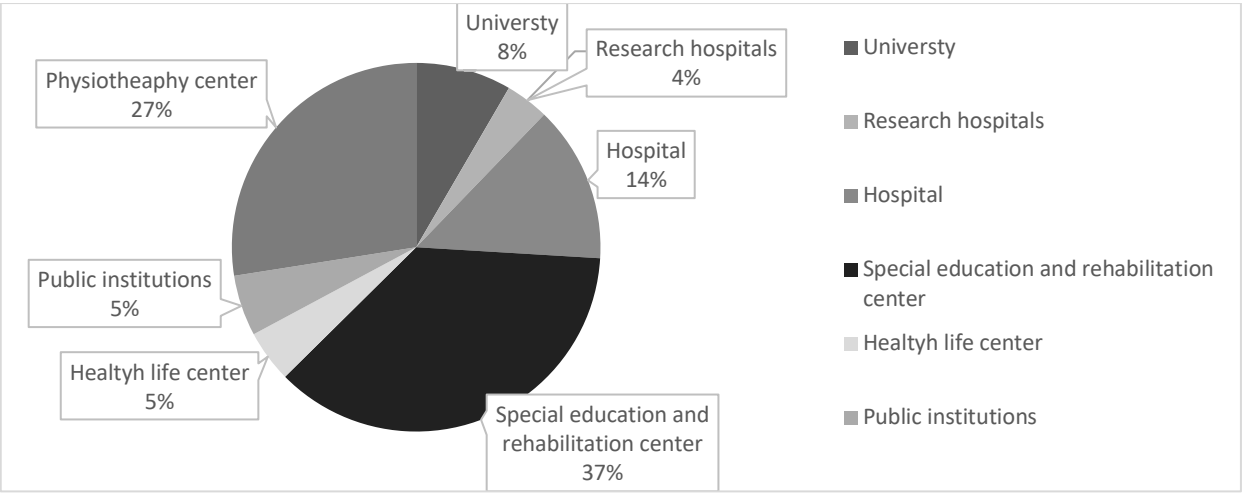

Figure 2. Professional's experience

disagreed with the opinion that the supplementary materials (laboratory leaflet and book) of practical training were sufficient (p = 0.025). Furthermore, they mostly agreed that an update in physiology education should take place in the PT's curriculum (p<0.001). PTs thought that physiology weekly course hours should increase (p = 0.002), contrary to the students' opinion. Approximately half of the participants (PTs, 49.6%, and students, 51.7%) agreed that continuity of physiology education was necessary for clinical practice after graduation. On the other hand, students mostly agreed that physiology education was essential for understanding a patient's signs and symptoms (p = 0.010). Students had difficulty in learning and reading any subject related to the physiology course (p = 0.015), contrary to the PTs.

PTs (49.5%) and students (51.7%) agreed that continuing physiology education is necessary for clinical practice after graduation. Participants (PTs, 61.1%; students, 59.3%) strongly agreed that physiotherapy and rehabilitation students should have physiology lessons made compulsory. Most participants (PTs, 43.5%, and students, 43.2%) wanted to take part in a physiology education other than undergraduate education. Most participants agreed with the following statements: regularly attending the physiology course is very beneficial for professional life (PTs, 53.4%, & students, 65.3%), practical training in human physiology lessons helps individuals gain skills (PTs, 45%, and students, 39%), and laboratory homework and quizzes after each practical training of the human physiology lessons contribute to learning (PTs, 42%, and students, 41.5%). Moreover, most participants agreed that *the practical training information was beneficial* and that *they use the physiology lesson notes and read them if they need for clinical practice.* PTs and students agreed with the following statements: they read evidence-based studies on the relevant search engines and checked the treatment program, they explained the physiological basis of the effects of the practice to the patients, and the physiology education helped to understand the other department lessons. Contrary to these opinions, they were indecisive about receiving problem-oriented education in physiology education (Part III, Table 2).

A standard answer to *How many lessons in the PT curriculum have you benefited from in physiology education?* was mostly one to four (PTs, 68.7%, and students, 61%). Nearly half of the participants (47.8%) stated that the quality of the physiology education was moderate. Participants answered the question "What is the necessary subject of physiology in PT education?" with exercise physiology (PTs, 45.8%, and students, 44.1%; Part IV, Table 2, Fig 3).

DISCUSSION

This study showed in detail the significance of physiology education in PT according to PTs' and students' perceptions. The important findings of the present study are as follows: 1) Physiology education was effective in PT, but the effectiveness graded on clinical lessons differed. 2) The supplementary materials (laboratory leaflet and book) used in the practical training and the tools and equipment were insufficient. 3) Physiology education was essential for understanding a patient's signs and symptoms.4) The requirement of continuing physiology education for clinical practice after postgraduate was generally

Table 2. Insights about curriculum and education

	Physiotherapist (n:131) %	**Students (n:118) %**
PART I		
Theoretical/practical Undergraduate Education Hours		
2T/2P	35.9	38.1
3T/2P	15.3	19.5
3T/3P	5.3	2.5
4T/3P	30.5	21.2
Other	13	18.6
Teaching Member		
Prof.	50.4	33.1
Associate Prof.	20.6	16.9
Asist. Professor	9.9	27.1
Lecturer	7.6	7.6
Others	11.5	15.3
Department of teaching instructor		
Physiotherapy	20.6	22
Veterinary medicine	0.8	1.7
Biology	11.5	6.8
Medicine	61.1	67.8
Other	6.1	1.7
Practical education method		
I. Experiment Animal	0	1.7
II. Laboratory	25.2	35.6
III. Simulation	1.5	0.8
IV. Computer / Atlas	40.5	26.3
IV. Other	24.4	22.9
II + IV	8.4	12.7
Theoretical education method		
I. Overhead projector	5.3	1.7
II. Writing board	3.1	4.2
III. Powerpoint /projection	66.4	55.1
IV.Other	3.8	0.8
I+II+III	2.3	4.2
II+III	19.1	33.9
PART II		
How would you evaluate the effect of your physiology education on clinical lessons in undergraduate education?		
Not effective at all	5.3	1.7
Slightly effective	21.4	16.9
Moderately effective	26.7	35.6
Very effective	32.8	37.3
Extremely effective	13.7	8.5
How would you evaluate the effect of the physiology education you on your practice in the professional life?		
Not effective at all	8.5	4.8
Slightly effective	19.4	15.4
Moderately effective	33.3	37.5
Very effective	24.8	35.6
Extremely effective	14	6.7
How would you evaluate the effect of your physiology education on General PT lessons?		
Not effective at all	3.8	1.7
Slightly effective	20.6	18.6
Moderately effective	32.1	37.3
Very effective	30.5	28
Extremely effective	13	14.4

Table 2. Continue

How would you evaluate the effect of your physiology education on Pediatric Rehabilitation lesson?		
Not effective at all	8.4	5.9
Slightly effective	23.7	23.7
Moderately effective	26.7	32.2
Very effective	25.2	22.9
Extremely effective	16	15.3
How would you evaluate the effect of your physiology education on Neurological Rehabilitation lesson?		
Not effective at all	4.6	3.4
Slightly effective	22.1	20.3
Moderately effective	26	26.3
Very effective	47	50
Extremely effective	0	0
How would you evaluate the effect of your physiology education on Orthopedic Rehabilitation lesson?		
Not effective at all	4.6	6.8
Slightly effective	19.1	25.4
Moderately effective	36.6	31.4
Very effective	28.2	19.5
Extremely effective	11.5	16.9
How would you evaluate the effect of your physiology education on Cardiopulmonary Rehabilitation lesson?		
Not effective at all	3.1	5.1
Slightly effective	16	15.3
Moderately effective	28.2	25.4
Very effective	28.2	30.5
Extremely effective	24.4	23.7
PART III		
Supplementary materials (laboratory leaflet and book) used in the practical training of the human physiology lesson are sufficient.		
Strongly disagree	20.6	22
Disagree	43.5	32.2
Neither agree nor disagree	24.4	20.3
Agree	11.5	25.4
I felt the insufficient of physiology education during the patient evaluation or treatment		
Strongly disagree	6.9	3.4
Disagree	23.7	16.1
Neither agree nor disagree	32.8	38.1
Agree	28.2	33.9
Strongly agree	8.4	8.5
An update on physiology education should be perform in the curriculum of the physiotherapy and rehabilitation department and more lesson hours should be added.		
Strongly disagree	4.6	0
Disagree	6.9	14.4
Neither agree nor disagree	15.3	28
Agree	45.8	39.8
Strongly agree	27.5	17.8
Continuity of physiology education is required in terms of clinical practice after graduation.		
Disagree	9.2	6.8
Neither agree nor disagree	22.1	20.3
Agree	49.6	51.7
Strongly agree	19.1	21.2

Table 2. Continue

Physiotherapy and rehabilitation students should have the physiology lesson education compulsory.		
Disagree	2.3	0.8
Neither agree nor disagree	6.9	5.9
Agree	29.8	33.9
Strongly agree	61.1	59.3
The physiology lessons I had in physiotherapy and rehabilitation education was sufficient.		
Strongly disagree	9.2	2.5
Disagree	24.4	17.8
Neither agree nor disagree	36.6	39.8
Agree	24.4	34.7
Strongly agree	5.3	5.1
I would like to take part in a physiology study other than undergraduate physiology education		
Strongly disagree	4.6	2.5
Disagree	13	6.8
Neither agree nor disagree	21.4	22
Agree	43.5	43.2
Strongly agree	17.6	25.4
Physiology education is important for understanding a patient's signs and symptoms		
Disagree	6.9	0
Neither agree nor disagree	9.2	7.6
Agree	42.7	56.8
Strongly agree	41.2	35.6
I have difficulty to learning while reading any subject related to physiology.		
Strongly disagree	5.3	4.2
Disagree	39.7	27.1
Neither agree nor disagree	26.7	21.2
Agree	19.8	39.8
Strongly agree	8.4	7.6
Attending physiology class regularly is very beneficial for my professional life.		
Disagree	4.6	0.8
Neither agree nor disagree	13.7	8.5
Agree	53.4	65.3
Strongly agree	28.2	25.4
The practical training of the human physiology lesson helped me gain skills.		
Strongly disagree	3.1	4.2
Disagree	9.9	6.8
Neither agree nor disagree	26.7	35.6
Agree	45	39
Strongly agree	15.3	14.4
The laboratory homework and quizzes after each practical training of the human physiology lessons contributed to my learning.		
Strongly disagree	4.6	5.9
Disagree	12.2	8.5
Neither agree nor disagree	32.8	30.5
Agree	42	41.5
Strongly agree	8.4	13.6
The tools and equipment used in the practical training of the human physiology lessons are sufficient.		
Strongly disagree	20.6	15.3
Disagree	35.9	41.5
Neither agree nor disagree	33.6	25.4
Agree	6.9	15.3
Strongly agree	3.1	2.5

Table 2. Continue

I can use the information I learned in the practical training of the human physiology lessons in my daily life.		
Strongly disagree	3.8	2.5
Disagree	12.2	11.9
Neither agree nor disagree	27.5	34.7
Agree	46.6	43.2
Strongly agree	9.9	7.6
When I need some physiological information during clinical practice, I open my physiology lessons notes and read it.		
Strongly disagree	1.5	1.7
Disagree	12.2	7.6
Neither agree nor disagree	20.6	15.3
Agree	52.7	59.3
Strongly agree	13	16.1
When I need some physiological information during clinical practice, I read evidence-based studies in relevant search motors and set the treatment programs.		
Strongly disagree	0.0	0.8
Disagree	9.9	6.8
Neither agree nor disagree	19.1	18.6
Agree	52.7	59.3
Strongly agree	18.3	14.4
I explain the physiological basis of the effects of the practices I apply in practical life to my patients.		
Disagree	9.2	9.3
Neither agree nor disagree	21.4	28.8
Agree	52.7	51.7
Strongly agree	16.8	10.2
I received a problem-oriented education in physiology education.		
Strongly disagree	9.2	5.1
Disagree	24.4	21.2
Neither agree nor disagree	41.2	44.9
Agree	19.8	22
Strongly agree	5.3	6.8
The physiology education helped me to understand other department lessons		
Disagree	6.1	4.2
Neither agree nor disagree	16.8	16.9
Agree	53.4	59.3
Strongly agree	23.7	19.5
PART IV		
How many lessons in the physiotherapy curriculum have you benefited from physiology education		
1-4 courses	68.7	61
5-9 courses	23.7	28
10 < courses	7.6	11
How do you evaluate the quality of your physiology education		
Bad	15.3	10.2
Moderately	51.1	44.1
Good	27.5	35.6
Very good	6.1	10.2
Which is the absolutely necessary subject of physiology in PT education		
Muscle contraction mechanism	31.3	30.5
Respiratory physiology	0.8	3.4
Circulatory physiology	4.6	2.5
Nerve physiology	17.6	19.5
Exercise physiology	45.8	44.1

Difficulty reading any physiology-related subject was mostly declared by students. 7) The most critical physiology subject was exercise physiology, and physiology education was more necessary in clinical practice and helped to understand other courses in the curriculum.

Physiology education, part of the core curriculum for all health science students, is essential for clinical application and multidisciplinary connections (12). A study showed that students' perception of their inter-professional competence improved after conducting an inter-professional education (IPE) experience during the renal physiology block of a graduate-level course (13). In the current study, most students and professionals declared that physiology education has practical impacts on clinical lessons, current professional life, and general PT lessons. Clinical physiology lessons should be added to the health sciences curriculum because of the effectiveness of active learning.

Physiology education is taught through PowerPoint presentations in most medical and health science schools (12). Poor results in traditional methods have led to research on novel teaching methods to encourage active learning and students' creativity (14). Novel learning methods and mediums in physiology education include animations, games, online homework, virtual laboratories, tactile learning, case studies, external resources, online testing (face-to-face), licensure exams, and social media. These techniques have helped to prepare students for the technologically advanced health profession workforce and study groups (3). In the current study, 64.1% of the participants in PTs and 54.2% of students stated that supplementary materials (laboratory leaflets and books) were insufficient in the practical teaching of human physiology lessons. Novel active learning methods should be blended with traditional methods in PT physiology education in line with technological advances.

Using animals in the practical teaching of physiology is still controversial. Appropriate approaches are therefore a constant subject of research. Studies comparing students' perceptions of animals to virtual (video/computer) laboratory courses in physiological sciences related to the effectiveness of the problem-based learning (PBL) hybrid curriculum are present in the literature (15). A study applied the PBL method as a hybrid curriculum with some lectures and hands-on lessons to support students' learning (16). Another study showed that students gave feedback as *helpful* and *incentivizing* after the introduction of integrated laboratory classes into their PBL curriculum (17). According to Goyal et al., radical changes are necessary for the practical physiology education of medical undergraduates. In the present study, 47.4% of students stated that reading any physiology-related subject was difficult. Both students and PTs were indecisive on whether they had received problem-oriented education in physiology (41.2% of PTs and 44.9% of students) (18). A study with physiotherapy students revealed varying applications of PBL-related skills in clinical practice. Further research would be useful to explore the factors that enable students to successfully put into practice the qualifications developed using a PBL approach (19).

Physiological information about practical skills is a guide in the clinic. A study indicated that nursing students learn the physiology content best when it directly relates to workplace experiences (20).

In clinical practice, many questions remain about the content and effects of physical rehabilitation interventions in children and youth with acquired brain injury. Therefore, it is crucial to identify gaps in the evidence to synthesize current knowledge about the impacts of physical rehabilitation interventions on functional recovery and daily functioning in children and youth with acquired brain injury and to guide future research. Knowing the physiological processes will contribute to this process (21).

Similar to previous study findings, most physiotherapists worked in special education and rehabilitation centers, and most participants stated that their physiotherapy education had a considerable impact on their professional lives. These clinics were where children and youth with acquired brain injury were trained, and although the effectiveness of physiology in neurological rehabilitation is mostly accepted, its impact on pediatric rehabilitation cannot be underestimated. Updating the human physiology curriculum with case studies related to practical skills in PT is recommended.

Bornman and Brend emphasized the need for more studies by health practitioners focusing on changes in clinical practice (22). Similar to the previous study, in the present study, most clinicians were willing to participate in a physiology study other than undergraduate physiology education in clinical practice.

PTs and students had differing opinions on some subjects, including the sufficiency of the supplementary materials (laboratory leaflet and book)

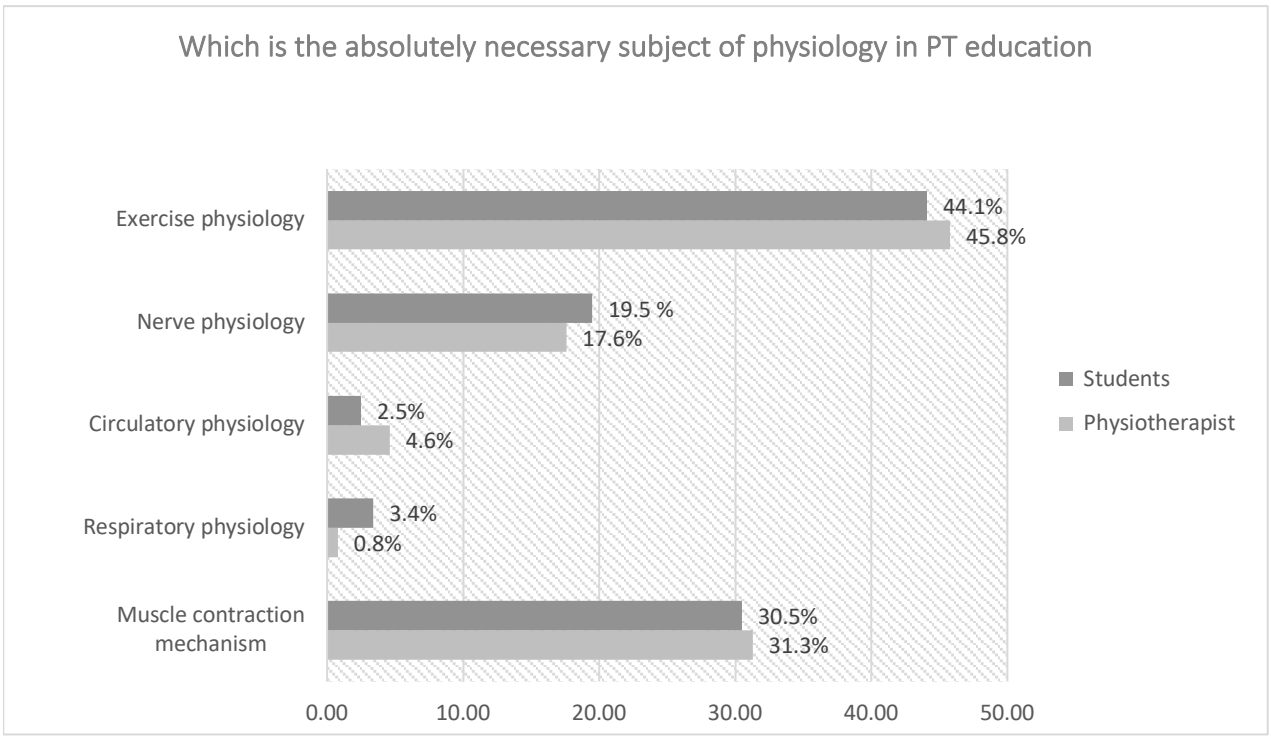

Figure 3. Which is the absolutely necessary subject of physiology in PT education

in practical training, whether an update on physiology education should be performed in the curriculum of the PT, the essentiality of physiology education for understanding a patient's signs and symptoms, and the difficulty in learning and reading any subject related to the physiology course. Although the students had difficulty reading and understanding physiology topics, they did not agree with the idea of adding additional courses. The differences in the developments in higher education according to the years may be due to the differences in thought, such as the difficulty of learning and reading any subject related to the physiology course (23). Additionally, the change in understanding with changes in years may also be related to the development of critical thinking skills, which is a way of thinking that consists of mental processes such as analysis and evaluation (24). In our previous study, the critical thinking levels of PT students who could get down to the core of their problems, evaluate the patient from every aspect in terms of rehabilitation, and offer different treatment methods were low in the training phase (25). It is recommended that training on problem-based learning and the physiological basis of these problems and treatment modalities should be higher in physiotherapy education.

This is the first study in Turkey on physiology education in physiotherapy and rehabilitation. It explored the significance of physiology education in practice and showed the differences in physiology education thought between students and clinicians. Nevertheless, there were some limitations in the study. The duration of clinical experience of the physiotherapists varied in the present study. A comparison of the perceptions of physiology education in PT according to the duration of clinical experience should be investigated. This could not be analyzed due to the heterogeneity of the clinical experience duration of PTs. Further studies with larger sample sizes are necessary to generalize the results. Most participants were from different universities, and the physiology curricula of these universities were not analyzed. Researchers should consider the differences in the physiology curricula at different universities.

CONCLUSION

This study showed the students' and PTs' opinions on the effectiveness of physiology education in PT. The supplementary materials (laboratory brochure and book) for the practical teaching of human physiology

lessons were insufficient. According to students, learning and reading about physiology were difficult. Attending a physiology course was very beneficial for PTs. Physiology education was essential to understand patients' signs and symptoms and explain to patients the physiological basis of the effects of PT applications. Although problem-oriented education was implied, physiology education, in general, helped to understand other PT courses. Exercise physiology was a necessary subject of physiology in PT education. Instead of PowerPoint/board, more simulation-based training or technology-supported physiology teaching can be practiced in PT education. Therefore, an update to the physiology education in the PT curriculum is necessary. Future research must investigate the significance of problem-based human physiology education for active learning in all health sciences.

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Author contribution: IH and NK came up with the project concept together. With the help of NK, IH gathered and analyzed the data. The authors made significant contributions to the manuscript's development. The final manuscript was examined and approved by IH and NK.

Conflict of interests: There is no declaration of interest.

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RESEARCH ARTICLE

VALIDITY AND RELIABILITY OF THE TURKISH VERSION OF THE PELVIC PAIN IMPACT QUESTIONNAIRE

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ABSTRACT

Purpose: The objective of this study was to assess the validity and reliability of the Pelvic Pain Impact Questionnaire's Turkish translation (PPIQ-T).
Material and Methods: This study was conducted with 110 female patients (mean age: 43.67±11.71 years), who were being treated as inpatients or outpatients in the Obstetrics and Gynecology Department. Necessary permission for PPIQ was obtained and translation procedures were applied in terms of cultural adaptation. Test-retest and internal consistency were used for reliability. The correlation between the McGill Pain Questionnaire (MPQ) and the Short Form-36(SF-36) was analyzed to determine the construct validity of the questionnaire. Additionally, exploratory factor analysis and confirmatory factor analysis were used to test the factorial validity of the PPIQ-T.
Results: Intraclass correlation coefficient (ICC) was 0.95, while the Cronbach alpha value was 0.92. A significant correlation was determined between PPIQ-T and SF-36 questionnaires (r= 0.62-0.78, p<0.001), and MPQ (r=0.85, p<0.001). The Kaiser-Meyer-Olkin coefficient was 0.87, according to exploratory factor analysis (EFA). Confirmatory Factor Analysis values were found Chi-Square as 31.142, df as 18, RMSEA as 0.08, and p<0.05.
Conclusion: The study's results indicated that the PPIQ-T can be utilized to evaluate patients with chronic pelvic pain in a variety of contexts and for treatment planning.

Keywords: Validity and reliability, pelvic pain, quality of life, women's health, pain, pelvis

INTRODUCTION

The European Association of Urology defines chronic pelvic pain (CPP) as long-lasting or persistent pain felt in parts of the male or female pelvis (1). CPP, which is seen at the rate of 5.7%-26.6% of women worldwide (2), includes the suprapubic region, inguinal, urethral, penile clitoral, perineal, rectal, and back region, hips, and thigh regions (3). The causes of CPP include gynecological reasons such as pelvic inflammatory diseases, pelvic adhesions, endometriosis, ovarian remnants, ovarian retention syndrome, pelvic congestion syndrome, and non-gynecological reasons such as irritable bowel syndrome, myofascial pain syndrome, and psychosocial factors (4). World Health Organization (WHO) reported that 14% of females experience CPP at least once during their lifetime (2).

Associated with the multiple etiological factors, many symptoms are seen in CPP (5). The most frequently seen psychological problems in women with CPP are depression, anxiety, multi-psychological disorders, and somatic disorders (6). In addition, quality of life

(QOL), emotional state, work, and family life are affected (7-10). Quality of life includes values, perspectives, satisfaction, living conditions, accomplishments, functionality, cultural contexts, and spirituality. At the same time, QOL is very important in health research, and QOL research involves a variety of patient groups and different research plans (11,12). Therefore, evaluation of women with CPP and raising awareness of this subject is of great importance in respect of taking the necessary precautions in the early stage and creating treatment programs.

With the literature in mind, Jane Chalmers et al. created the Pelvic Pain Impact Questionnaire (PPIQ) to close the knowledge gap and address evolutional flaws, divergent expert opinions, and challenges with pelvic pain diagnosis (13). There has been no research done on the Turkish validity, reliability, or cultural adaptability of this questionnaire. This study was conducted to assess the validity and reliability of the Turkish version of the PPIQ, which will be a fundamental component in the assessment of CPP and the planning of treatment.

MATERIAL AND METHODS

Participants

This study was conducted with 110 female patients, who were being treated as inpatients or outpatients in the Obstetrics and Gynecology Department of Adnan Menderes University Training and Research Hospital between April 2019 and October 2019.

The Izmir Demokrasi University's Scientific Research and Publication Ethics Committee approved this study (decision no:2019/05-01, dated:10.04.2019). The number of subjects was defined concerning literature stating that the sample size should be tenfold the number of items in a questionnaire (14). Therefore 110 individuals were recruited into the study. The inclusion criteria were determined as female gender, age of ≥18 years, being literate, and being diagnosed with a CPP problem. The exclusion criteria were determined as the inability to communicate verbally or having any cognitive or mental function disorder. The study was explained to the individuals who satisfied the requirements for

Table 1. The physical and clinical data of the patients

Variables (n=110)	Min-Max	Mean±SD
Age (years)	18-65	43.67±11.71
Height (cm)	150-172	160.20±4.71
Body Weight (kg)	45-110	71.52±13.29
BMI (kg/cm^2)	16.53-45.79	28.00±5.80
PPIQ-T	2-32	14.76±7.99
MPQ	24-88	47.70±17,34
SF-36		
Physical functioning	0-100	67.22±27.66
Role limitation	0-100	51.85±41.19
Role emotional	0-100	57.27±44.50
Vitality	0-75	45.40±18.17
Mental health	8-80	56.10±18.46
Social functioning	0-100	62.61±28.57
Bodily pain	10-100	53.56±24.18
General health	0-90	46.75±24.01

Min: Minimum, Max: Maximum, SD: Standard Deviation, BMI: Body Mass Index. SF-36: Short Form 36, MPQ: McGill-Melzack Pain Questionnaire. PPIQ-T: Turkish Pelvic Pain Impact Questionnaire

Table 2. Item mean scores, item-total correlations, and Cronbach's α coefficient if an item deleted from The PPIQ-T

The Pelvic Pain Impact Questionnaire	Mean (SD)	Item-total correlation	Cronbach's α if item deleted
In the past month, how much has your pelvic pain affected your:			
Energy Levels	2.61 (1.01)	0,768	0.90
Mood	2.51 (1.17)	0,766	0.91
Sleep	1.60(1.59)	0,746	0.90
Stomach and intestinal function	1.93 (1.19)	0,770	0.92
Ability to sit for longer than 20 minutes	1.62 (1.40)	0,758	0.91
Ability to perform and function normality at home/work/school/university	2.01 (1.13)	0,761	0.90
Ability to take part in physical activity (e.g. jogging, yoga, bicycling)	1.87 (1.21)	0,761	0.91
Ability to wear certain clothes (e.g. underwear, tight fitting clothes)	0.54 (1.12)	0,769	0.91

PPIQ-T: Turkish Pelvic Pain Impact Questionnaire

inclusion, and those who decided to participate obtained from whom an informed consent form. A record was made for each subject of demographic and descriptive data including age (years), height (cm), body weight (kg), and body mass index (BMI) (kg/m^2).

Translation Process and Procedure

The translation process and procedure were conducted according to Beaton et al. (15). Firstly, K. Jane Chalmers gave her consent for the requisite validity and reliability studies of the PPIQ to be conducted in Turkish. First, the Turkish cultural adaptation of the questionnaire was performed. The questionnaire was first translated from Turkish to English by 3 physiotherapists, each with a good level of English, independently of each other. The first Turkish questionnaire was prepared from these translations and was then examined by a committee of physiotherapists with a good knowledge of English to determine whether or not it matched the English original. A physiotherapist with a high level of English translated the questionnaire into a text that was mutually agreed upon, then the two versions were compared. The appropriateness of the Turkish was evaluated by a language specialist. The Turkish translation that was found to be consistent with the original was applied to a group of 10 patients for evaluation of the suitability of the Turkish language and compatibility with Turkish culture and society. Patients were asked for recommendations when questions that produced comprehension issues were observed. According to the results obtained, there was no requirement for any corrections such as additions, removals, or changes to the questionnaire, and so the final form was created, named the Pelvic Pain Impact Questionnaire- Turkish (PPIQ-T).

Reliability

The most popular method for determining reliability is to use Cronbach's coefficient. Reliability refers to the consistency and stability of the measurement tool. The internal consistency of the PPIQ-T was evaluated using Cronbach's α coefficient. It is commonly accepted that a Cronbach's rating >0.8 denotes high internal consistency (16). In this study, dependability was rated as acceptable for Cronbach's alpha values of 0.7, good for Cronbach's alpha values of 0.8, and outstanding for Cronbach's alpha values of 0.9. The most popular approach for assessing a scale's stability is test-retest reliability, and a correlation coefficient of >0.7 is typically assumed to mean that a scale is stable (17). The test-retest reliability was used in this study to assess the questionnaire's reliability. This evaluation is applied to subjects in the

Table 3. Correlation coefficient (r) between PPIQ-T and SF-36, McGill

Pelvic Pain Impact Questionnaire		
		Totally Point r (p)
SF-36		
Physical health	Physical functioning	-0.77 (<0.001)
	Role-physical	-0.62 (<0.001)
	Bodily pain	-0.78 (<0.001)
	General health	-0.73 (<0.001)
Mental health	Vitality	-0.72 (<0.001)
	Social functioning	-0.72 (<0.001)
	Role-emotional	-0.63 (<0.001)
	Mental health	-0.73 (<0.001)
MPQ		0.85 (<0.001)

r: Correlation Coefficient, SF-36: Short Form 36, MPQ: McGill-Melzack Pain Questionnaire, PPIQ-T: Turkish Pelvic Pain Impact Questionnaire

same situation at different times. Therefore, in this study, the questionnaire was applied twice at an

interval of one week. The second measurements were included in the study for patients who stated that their condition had not changed.

Validity

The McGill Pain Questionnaire (MPQ), which measures pain, and the Short Form-36 (SF-36), which measures the quality of life, were both utilized to test the construct validity of the questionnaire. The MPQ and SF-36 were chosen because the PPIQ-T contains items that examine pain and quality of life. Additionally, exploratory factor analysis and confirmatory factor analysis were used to assess the factorial validity of the PPIQ-T (18).

Instruments

Pelvic Pain Impact Questionnaire

The PPIQ, which evaluates chronic pelvic pain, is formed of 10 items, the first 8 of which are scored from 0-4 with Likert-type responses. These questions are about energy level, mood, sleep, stomach, and intestinal function, sitting duration, functionality, physical activity, and wearing clothes. Additionally, there are two supplementary questionnaires except for scoring. While question 9 is about tampon usage, question 10 is about sexual relationships. This questionnaire can be used for individuals or groups. The total points are obtained as the total of the points of each item, and the final two items are not included in the calculation. High points indicate high impact (13).

McGill Pain Questionnaire

The Turkish translation of the McGill Pain Questionnaire was used in this study to measure pain. The MPQ was developed by Melzack and Torgerson in 1971 and has been used in many studies since 1975 (19,20). It has been translated into more than ten languages and the Turkish version validity and reliability studies were conducted by Yazıcı, Eti-Aslan, and Olgun (21). The MPQ is formed of four sections, the first of which includes name, surname, age, medical diagnosis-problem, type and dose of analgesia if used, and the perceptions of the patient in respect of localization of the pain, characteristics, time associations, and severity (20).

Short Form 36

The SF-36 was used in this study to evaluate the quality of life. Koçyiğit et al. conducted the validity and reliability of the SF-36 Turkish version (22). One of the most used measures for gauging quality of life is the SF-36. The SF-36 comprises 36 items in 8 dimensions of physical function, role restrictions (related to physical and emotional problems), social function, mental health, vitality, and general perceptions of pain and health. This is a self-reported form that can be completed by the patient in a very

Table 4. Factor solution by principal axis factoring of items from the PPIQ-T

Items	Initial Eigenvalues			Extraction sums of squared loadings		
	Total	% Of Variance	Cumulative %	Total	% Of Variance	Cumulative %
Energy Levels	5.224	65.300	65.300	4.851	60.632	60.632
Mood	0.842	10.531	75.830			
Sleep	0.612	7.654	83.484			
Stomach and intestinal function	0.457	5.710	89.194			
Ability to sit for longer than 20 minutes	0.324	4.055	93.250			
Ability to perform and function normality at home/work/school/university	0.257	3.217	96.467			
Ability to take part in physical activity (e.g., jogging, yoga, bicycling)	0.155	1.940	98.407			
Ability to wear certain clothes (e.g., underwear, tight fitting clothes)	0.127	1.593	100.000			

PPIQ-T: Turkish Pelvic Pain Impact Questionnaire

short time (23). The advantages of the SF-36 are that it can be completed in a short time, it is sensitive, and the health status can be evaluated in both positive and negative aspects (24). Rather than providing a single total score, total points are given for each subscale separately, ranging from 0-100. A score of 100 points indicates good health, and a score of 0 indicates poor health status.

Statistical Analysis

The data obtained in the study were analyzed statistically using IBM SPSS vn. 24.0 software. The results were stated as number (n) percentage (%), mean ± standard deviation (SD), and minimum and maximum values. Cronbach α coefficient and ICC values were used for reliability. For the construct validity of the questionnaire, the correlation of the McGill Pain Questionnaire (MPQ) and the Short Form-36 (SF-36) was examined. The pearson correlation coefficient was used to evaluate the correlation. Also, the factorial validity of PPIQ-T was examined with exploratory factor analysis and confirmatory factor analysis. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The study included a total of 110 patients with pelvic pain. First, the data were recorded the age, height, weight, and BMI values of the patients. The physical and clinical data of the patients are shown in Table 1. The PPIQ-T total score was found to be 14.76 ± 7.99, the MPQ total score was 47.70 ± 17.34, the SF-36 subgroups were 67.22 ± 27.66 (physical functioning), 51.85 ± 41.19 (role-physical), 53.56 ± 24.18 (bodily pain), 46.75 ± 24.01 (general health), 45.40 ± 18.17 (vitality), 62.61 ± 28.57 (social functioning), 57.27 ± 44.50 (role-emotional) and 56.10 ± 18.46 (mental health).

Reliability

Cronbach α coefficient of the questionnaire was calculated as 0.92 for overall (8 items). The range of corrected item-total correlations, which show that the items were largely homogeneous, is 0.62-0.83. These

values are shown in Table 2. Also, the questionnaire was applied twice to the same subjects at an interval of one week, and the test-retest correlations were examined. ICC for test-retest reliability was 0.95 (95% confidence interval: 0.93-0.97). These values demonstrated good reliability. The questionnaire also includes two open-ended questions which are not included in the calculation. Some patients in Turkey may not wish to answer these questions. In this study, 78 subjects answered the first question and, 81 the second. Therefore, as in the original version of the questionnaire, these two questions were not included in the scoring or statistical analyses.

Validity

The SF-36 and MPQ, which are currently widely used, were used to evaluate the construct validity of the PPIQ-T. By examining the relationship between these questionnaires, the construct validity of the PPIQ-T for use in Turkey was investigated. A strong relationship was determined in all items of the questionnaire, and these were statistically significant in all the items ($r = 0.62$-0.85, $p < 0.001$). These data are shown in Table 3.

According to factorial validity results, EFA found that the KMO coefficient was 0.87, and Bartlett's test result was $X2 = 635.904$, $p < 0.001$. The factor with 5.22 eigenvalues was discovered using the factor analysis solution. The total variance of the questionnaire was obtained as 65.30%. The items' factor loads ranged from 0.636 to 0.874. Table 4 displays the results of an exploratory factor analysis of the PPIQ-T. Results of the CFA of PPIQ-T are shown in Fig. 1. CFA values were found Chi-Square as 31.142, df as 18, RMSEA as 0.08, and $p<0.05$.

DISCUSSION

This study's objective was to assess the validity and reliability of the Pelvic Pain Impact Questionnaire's Turkish translation, which was originally developed by Jane Chalmers et al. The study's results showed that the PPIQ-T is valid and reliable and can be utilized in the assessment of patients with CPP and in the formulation of treatment plans. Also, to our knowledge, this study is the first translation of the PPIQ to another language. Therefore, we think that it is so important in this field.

It is necessary to have a good understanding of CPP clinically and the reasons and the solutions required should be found from the starting point of the reasons. However, the diagnosis of CPP shows differences among clinicians. Clinical tests are generally focused on physiological problems and the association between an individual's health and functional level is ignored. Therefore, validity and reliability studies were made of the PPIQ, which was developed by Chalmers et al. (13), as the questionnaire is considered to have an important place in literature and clinically in respect of questioning the patient in all aspects. The PPIQ has the advantages of being able to be easily understood and completed by the patient and scoring can be easily applied (13).

For patients with CPP, pain is a significant part of life. Daily activities and the quality of life of women are affected, and there are negative effects on mental health, physical health, and sexual functions (25-29). Although chronic pain cannot always be improved, patients can continue functions at a normal or close to a normal level, and a better quality of life can be provided (30,31). In a community-based study in England by Zondervan et al. (29), it was reported that approximately 70% of women experienced moderate or severe pain, activities were restricted by the pain in 58%, and 33% could not go to work for at least one day because of pain in the previous 12 months. As seen in these studies, CPP has a negative effect on the life of the individual in different respects, and therefore, the necessary evaluations should be made, and treatments should be planned as early as possible.

The SF-36 and MPQ, which are currently widely used and are valid and reliable in Turkish, were used to evaluate the validity of the PPIQ-T in this study. The relationship between these questionnaires was examined. A high level of correlation was determined in all the subgroups of the questionnaires used in the study and the PPIQ-T, and these were statistically significant in all the sub-parameters. These results showed that the PPIQ-T was valid.

To determine the reliability of the questionnaire, it was applied twice after a one-week interval to the same participants who showed no change in symptoms. Subjects who showed abnormal symptom changes were excluded. The correlations between the items were determined to be at a good level and the general Cronbach alpha value was calculated as 0.92. In 3 separate cohort studies of a total of 1203 females diagnosed with CPP, Jane Chalmers et al (13) created a 10-item form by selecting appropriate questions and applied this to the participants. By applying the same questionnaire to the same participants after 7-10 days, the test-retest reliability

of the questionnaire was proven. The ICC for test-retest reliability was 0.95. Thus, the questionnaire was evaluated as having good reliability (13). The values obtained in this study of the PPIQ-T were similar to those results. The questionnaire also includes two open-ended questions which are not included in the calculation. Some patients in Turkey may not wish to answer these questions. In this study, 78 subjects answered the first question, and 81 the second. Therefore, as in the original version of the questionnaire, these two questions were not included in the scoring or statistical analyses.

CPP is seen as a common problem that severely affects the quality of life. Previous studies have shown that the normal daily living activities of women are affected by the tension created by the pain and their quality of life is significantly reduced (10). Therefore, a quality-of-life questionnaire was selected for this study. The PPIQ-T was compared with the SF-36 and there was determined to be a strong inverse correlation between the physical health and mental health subdimensions of the SF-36 and the PPIQ-T. In a study of 1160 women by Grace and Zondervan (10), it was reported that CPP had a negative effect on the general health status of the women. It has also been shown that patients with CPP experience sleep problems, daily activities are affected by pain in almost half, and activities (walking and moving) are restricted (14.3%) or cannot be undertaken (12.2%) without resting or taking analgesics (10).

The difficulties in diagnosis and the complex anatomy of the pelvic region were the limitations of this study. In addition, patients had trouble in expressing the complaints and symptoms experienced, they have prejudiced that they would be harmed by participation in the study or were unwilling to participate created difficulties in conducting the study. However, the increasing prevalence of CPP makes it a problem requiring early precautions to be taken. Therefore, it can be considered that this questionnaire will be widely used to determine individuals with this problem and form recommendations for solutions.

CONCLUSION

In conclusion, the Turkish version of the Pelvic Pain Impact Questionnaire was determined to be valid and reliable for the evaluation of patients with chronic pelvic pain in Turkey. It can be preferred for use in clinics as a short, comprehensible, and effective evaluation method, which allows the evaluation of chronic pelvic pain in many aspects.

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RESEARCH ARTICLE

CHANGES IN MULTIMORBIDITY PREVALENCE IN TURKEY (2008-2019)

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ABSTRACT

Purpose: To examine the 11-year change in the prevalence of multimorbidity according to age, gender, educational status and NUTS (Nomenclature of Territorial Units for Statistics) regions from 2008 to 2019 in Turkey.
Material and Methods: Data from the Turkiye Health Survey conducted by the Turkish Statistical Institute (TUIK) every 2 or 3 years from 2008 to 2019 were used. Descriptive statistics for multimorbidity were calculated according to gender, age groups, educational status, and IBBS regions. Absolute and relative changes in the prevalence of multimorbidity for 11-year period were examined in the EXCEL program.
Results: In the period between 2008 and 2019, the prevalence of multimorbidity increased by 77.0% in relative terms. The increase in the prevalence of multimorbidity was more evident in the female gender (9.7% to %5.5 in absolute terms), in the group with a low education level (11.4% in absolute, 94.2% in relative terms), in those living in the Eastern Anatolia Region (19.7% absolute, 226.4% relative), and in the aged group 75 years and above (17.8% in absolute terms).
Conclusion: Multimorbidity shows an increasing trend and it is a priority issue for our country.

Keywords: Multimorbidity, trends, change

INTRODUCTION

People with multimorbidity have been increasing globally, due to ageing of communities, demographic and epidemiologic transition, and unhealthy lifestyle (1,2). Multimorbidity is defined as the co-existence of two or more chronic conditions in an individual. Multimorbidity prevalence varies between 12.9% and 95.1% according to age groups (3).

In a study conducted in the Üsküdar region of Turkey, the prevalence of multimorbidity was 27.8% in the population aged 40 and over (4), in a telephone health survey in Germany the prevalence was 39.6% in the population aged 18 years and over (5), and in a representative study in Australia the prevalence as 32.6% (6). Age, socioeconomic deprivation, gender, education level, and unhealthy lifestyle are the most known determinants of multimorbidity (7,8).

As age and socioeconomic deprivation increase prevalence of multimorbidity increases (8). In a large-scale cross-sectional study conducted in Canada, it was found that social deprivation increased the risk of multimorbidity 3.7 times, and in another study conducted in England, there was a strong relationship between age and socioeconomic deprivation with multimorbidity (9,10). Similar to other studies, a study conducted in China showed that multimorbidity rises with age, it is more common in women, those with lower education levels, those without health insurance, and with unhealthy lifestyles (11). Multimorbidity is associated with polypharmacy, more hospitalization, high cost, and low quality of life and functionality closely (12). Multimorbidity increases disability and mortality in the elderly (12). This study aimed to describe trends

in the prevalence of multimorbidity in Turkey from 2008 to 2019.

MATERIAL AND METHODS

The current study was carried out using the data obtained from the Turkiye Health Survey, which was conducted every 2 or 3 years from 2008 to 2019 by TUIK (13,14,15,16,17,18). Turkey Health Survey is a cross-sectional study that examines the health status and health-related behaviors of the adult population over the age of 15. Institutional populations such as army, prisons, and care home residents were excluded. The study sample was selected using a stratified two-stage cluster sampling method. Urban-rural categorization was performed as external stratification criteria. Settlements that have a population between 20.000 and below were categorized as rural, while those having a population between 20.000 and above were categorized as urban. The first stage sampling unit is proportional to the size of randomly selected blocks from clusters (blocks) containing an average of 100 addresses; the second stage sampling unit is the household addresses randomly selected from each selected cluster (13). The number of households and respondents surveyed by the Turkey Health Survey was 14.655 from 6140 households in 2008, 14.447 people from 6551 households in 2010, 28.055 people from 12160 households in 2012, 26.075 people from 8634 households in 2014, 23.606 people from 8325 households in 2016, and 17.084 people from 8166 households in 2019.

Study variables

Dependent variables were the presence of chronic diseases and multimorbidity. In this study, multimorbidity was defined as the presence of two or more of the eight self-reported chronic conditions including hypertension, diabetes, coronary heart disease, asthma, chronic obstructive pulmonary disease, stroke, myocardial infarction, and depression). Presence of chronic diseases in 2008, 2010, 2012 TUIK Health Surveys were based on the responses of individuals on the questions; “Have you experienced the following health problems? Has this health problem been diagnosed by a physician? Have you lived this health problem in the last 12 months?”. In 2014, 2016, and 2019 surveys, the response of the participants to the question “did you experience the following health problems in the last 12 months?” was used to determine the existence of chronic disease.

Independent variables were age, sex, education level, and NUTS (Nomenclature of Territorial Units for Statistics) regions. Age groups were determined as 15-24, 25-34, 35-44, 44-54, 55-64, and 65-70. Participants were separated into three groups based on their education level (low, medium, and high). Those who graduated primary school and/or secondary school and illiterates were grouped as 'low education level', those who graduated high school or occupational high school as “medium education level’, and those achieved associate degree, undergraduate, and/or postgraduate degrees as 'high education level'. The twelve NUTS regions were regrouped into the seven geographical regions of the country for ease of comparison: Marmara, Aegean, Central Anatolia, Mediterranean, East Anatolia, Black Sea, and Southeast Anatolia. However, since the sampling number of the research in 2019 was not sufficient to give an estimate at the level of the Southeastern Anatolia Region, there is no available data for the Southeastern Anatolia Region in 2019.

Statistical Analysis

Descriptive statistics were calculated for multimorbidity according to age, sex, education level, and NUTS regions in every health survey database by using weights provided by TUIK. Subsequently, predicted prevalence of multimorbidity was calculated using simple linear regression equation between given years and prevalence of multimorbidity. The reason for forming the simple linear regression between multimorbidity and years was the presumption of multimorbidity change linearly according to years. When the data were examined, it was thought that the increase and decrease in the frequencies between years might be due to the sampling, the fact that the chronic conditions constituting multimorbidity were defined in different ways in the studies, and the data collection method.

To refine this ambiguity in the data, predicted multimorbidity prevalences were calculated. Absolute and relative changes in terms of multimorbidity in the 11-year period were investigated using the EXCEL program. The prevalence in 2019 was subtracted from the prevalence in 2008 to calculate absolute change.

Table 1. General Characteristics of Participants in Turkiye Health Surveys, 2008-2019

		2008		**2010**		**2012**		**2014**		**2016**		**2019**
	n	%	n	%	n	%	n	%	n	%	n	%
Gender												
Man	6662	45,5	6287	43,5	12925	46,1	8721	45,6	7668	44,5	7784	45,6
Woman	7993	54,5	8160	56,5	15130	53,9	10408	54,4	9574	55,5	9300	54,4
Age Group												
15-24	2878	19,6	2667	18,5	5119	18,2	3388	17,7	2905	16,8	2730	16
25-34	3311	22,6	2902	20,1	5605	20	3661	19,1	3006	17,4	3070	18
35-44	2888	19,7	2819	19,5	5555	19,8	3768	19,7	3444	20	3395	19,9
45-54	2429	16,6	2505	17,3	4921	17,5	3332	17,4	3007	17,4	2918	17,1
55-64	1609	11	1756	12,2	3459	12,3	2555	13,4	2368	13,7	2513	14,7
65-74	946	6,5	1115	7,7	2116	7,5	1498	7,8	1545	9	1589	9,3
75+	594	4,1	683	4,7	1280	4,6	927	4,8	967	5,6	869	5,1
NUTS												
Marmara Region	4746	32,4	5019	34,7	9172	32,7	4879	25,5	4922	28,5	6162	36,1
Aegean Region	472	3,2	367	2,5	735	2,6	1053	5,5	726	4,2	474	2,8
Central Anatolia Region	2564	17,5	2245	15,5	4185	14,9	3589	18,8	2598	15,1	2691	15,8
Mediterranean Region	1577	10,8	1417	9,8	2786	9,9	1612	8,4	1873	10,9	2080	12,2
Black Sea Region	3818	26,1	4144	28,7	8946	31,9	5475	28,6	5561	32,3	4781	28
Eastern Anatolia Region	776	5,3	897	6,2	1537	5,5	1607	8,4	1043	6	896	5,2
Southeastern Anatolia Region	702	4,8	358	2,5	694	2,5	914	4,8	519	3	-	-
Education Level												
Low	10919	74,5	10680	73,9	19747	70,4	13166	68,8	11572	67,1	10771	63
Middle	2457	16,8	2280	15,8	4937	17,6	3362	17,6	3106	18	3246	19
High	1279	8,7	1487	10,3	3371	12	2601	13,6	2564	14,9	3067	18
Total	**14655**	**100**	**14447**	**100**	**28055**	**100**	**19129**	**100**	**17242**	**100**	**17084**	**100**

Table 2. Prevalences of multimorbidity by gender, age groups, NUTS regions and educational status, Turkiye Health Surveys 2008-2019

	2008	2010	2012	2014	2016	2019	Absolute Change	Relative Change	Estimated Absolute Change	Estimated Relative Change
Gender	%	%	%	%	%	%	%	%	%	%
Man	7,2	7,8	7,6	12,2	11,8	12,7	5,5	76,4	6,4	92,8
Woman	12,3	12,3	12,3	21,8	20,8	22	9,7	78,9	12	106,2
Age Groups										
15-24	0,8	0,7	0,5	3,1	2,7	2,6	1,8	225	2,5	516,7
25-34	2,4	2,3	1	4,8	3,5	3,8	1,4	58,3	2,7	105
35-44	6,4	4,9	4,2	9,9	9	9,1	2,7	42,2	4,6	90,2
45-54	13,2	11,3	10,5	23,3	19,9	20,8	7,6	57,6	11	97,3
55-64	21,5	23,1	23,3	32,7	30,7	31,5	10	46,5	11,8	54,6
65-74	33,7	30,9	35,3	43,9	40,4	45,8	12,1	35,9	14,3	45,3
75+	31,2	35,5	35,5	46	47,7	49	17,8	57,1	19,6	62
NUTS										
Marmara Region	12,3	9,3	9,5	18,1	17,8	18,8	6,5	52,9	9,6	98
Aegean Region	8,6	4,5	14,4	16,1	19,1	16,1	7,5	87,2	11,7	153,9
Central Anatolia Region	8,4	10,9	12,5	16,8	14,1	17,5	9,1	108,3	8,7	93,5
Mediterrenian Region	9,6	9,8	9,5	16,1	16,8	14,8	5,2	54,2	7,6	82,6
Black Sea Region	9,1	12,6	8,6	17,7	15	15,9	6,8	74,7	7,2	73,5
Eastern Anatolia Region	8,7	7,8	18,7	17,9	21,9	28,4	19,7	226,4	20,5	268,4
Southeastern Anatolia Region	8,5	8,8	3,2	17,7	27,2	-	18,7	220	18,5	486,8
Education Level										
Low	12,1	12,5	12,7	21,7	21,6	23,5	11,4	94,2	13,5	122,7
Middle	3,3	3,7	4,3	9,1	7,9	8,5	5,2	157,6	6,2	193,75
High	4,7	5	4,2	6,6	5,9	7,2	2,5	53,2	2,6	59,1
Total	**10**	**10,4**	**10,1**	**17,4**	**16,8**	**17,7**	**7,7**	**77**	**9,4**	**101,1**

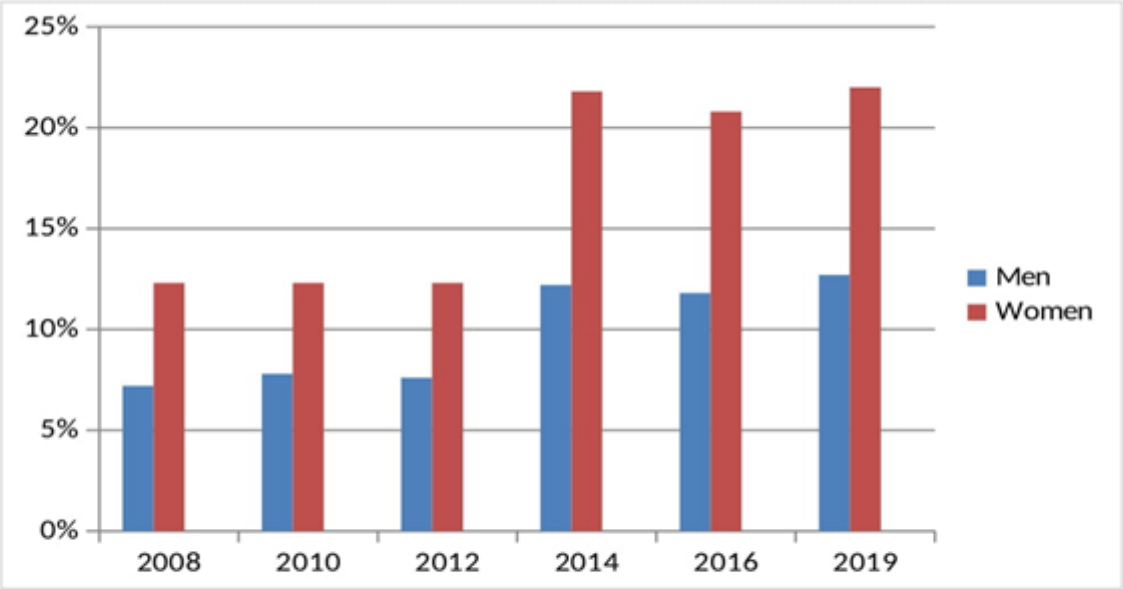

Figure 1. Prevalence of multimorbidity by gender and years

To calculate relative change, the prevalence in 2019 was subtracted from the prevalence in 2008, and the result was divided by the prevalence in 2008 again. To be able to carry out this study permission was taken from TUIK. Dokuz Eylul University, Non-Invasive Research Ethics Committee's approval was obtained with the decision dated 01.03.2021 and numbered 2021/07-33.

RESULTS

Descriptive characteristics of the study population were summarized in Table 1. Over the years, the proportion of women participating in the study ranged from 56.5% to 53.9%. In terms of age distribution, the proportion of participants in the 55-64, 65-74 and over 75 age groups increased between 2008 and 2019. On the other hand, the proportion of 15-24 age group decreased over the years. Considering the distribution of the people in the study group by NUTS regions, it can be said that the participation rates fluctuated over the years. Individuals participating in the study consisted mostly of low education level.

Multimorbidity prevalence was 10% in 2008 and 17.7% in 2019. In total, it was observed that the prevalence of multimorbidity increased by 7.7% in absolute terms and by 77% in relative terms between 2008 and 2019 (Table 2). A more pronounced increase was observed in women compared to men (9.7% and %5.5 in absolute terms respectively) (Figure 1, Table 2). Although there was a rise in multimorbidity in all age groups, the biggest increase (17.8% in absolute terms) was observed in elderly population (≥75). In terms of NUTS Regions the highest increase in the prevalence of multimorbidity was in the Eastern Anatolia Region (19.7% absolute, 226.4% relative), while the lowest increase was found in the Mediterranean Region (5.2% absolute, 54.2% relative) (Figure2, Table 2). In education level groups, the highest increase was in individuals with low education level (11.4% in absolute, 94.2% in relative terms); on the other hand, the lowest increase was in individuals with high education level (2.6% in absolute, 59,1 in relative) (Figure3, Table 2). In addition, absolute and relative changes calculated by using the frequencies estimated by linear regression analysis of the frequency of multimorbidity by years are presented in Table 2. The estimated frequency of multimorbidity increased by 9.4% in absolute terms and by 101.1% in relative terms between 2008 and 2019. Overall, it is evident that the estimated absolute differences in gender, age groups, regions, and educational status groups were higher than the actual differences.

DISCUSSION

In this study, absolute and relative changes in the prevalence of multimorbidity were estimated using the data obtained from Turkey Health Survey conducted by TUIK from 2008 until 2019 in the population aged 15 and over. In the period between 2008-2019, the prevalence of multimorbidity

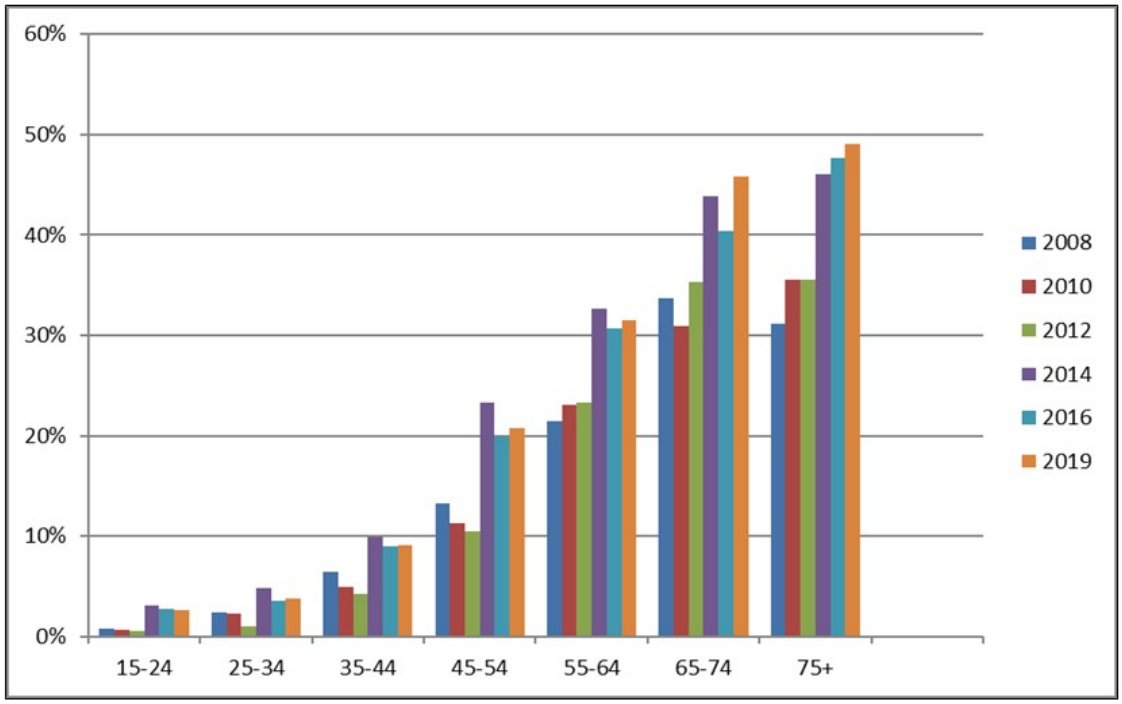

Figure 2. Prevalence of multimorbidity over the years by age groups

increased by 7.7% in absolute terms and by 77.0% in relative terms. According to estimated changes, in total, the prevalence of multimorbidity increased by 9.4% in absolute terms and by 101,1% in relative terms. The increase in the prevalence of multimorbidity was more evident in the female gender, in the group with a low education level, in those living in the Eastern Anatolia Region, and in the age group 75 years and above.

Part of this increase can be explained by an increase in diagnosis of chronic diseases as a result of an increase to access to health services over the years. In year 2002 average number of applying to a doctor was 3.1 and in 2019 this figure reached to 9.8 (18). Additionally, a series of reforms in Turkey within the framework of the Health Transformation Program (HTS) since 2003 has been carried out. One of the aims of HTS was strengthening the health care system, infrastructure, and surveillance system. These improvements in the health system might improved access to health services, outpatient diagnosis and facilitated treatment opportunities (23).

Although there have been many studies on the prevalence of multimorbidity in the literature, there is a limited number of studies on this subject in Turkey (3, 4).

In a study consisting of 15.688 participants in England, multimorbidity was defined as the co-existence of two or more chronic diseases/conditions in an individual. According to the study findings, multimorbidity prevalence was found to have increased over the years: in 2002/2003, the prevalence was 31.7% and as to 2012/2013, the prevalence was 43,1% (19). Similarly, our study also found that the prevalence of multimorbidity increased over time, the prevalence of multimorbidity was 10% in 2008, while it was 17.7% in 2019. The frequency of multimorbidity was found to be higher over time in the previously mentioned study compared to our study, which might have resulted from the fact that the former was conducted based on medical records using UK BIOBANK data, whose participants were aged 50 and over, and 16 chronic diseases/conditions were included in the study (19).

A cross-sectional study conducted in Canada between 1974 and 2014 found that the prevalence of multimorbidity increased from 19.4% to 32.1%, an increase of 12.4% when standardized to the population in 2014, and the prevalence of multimorbidity was higher in women than in men (20). The fact that the prevalence of multimorbidity was found to be higher in women compared to men is in line with the findings of the current study;

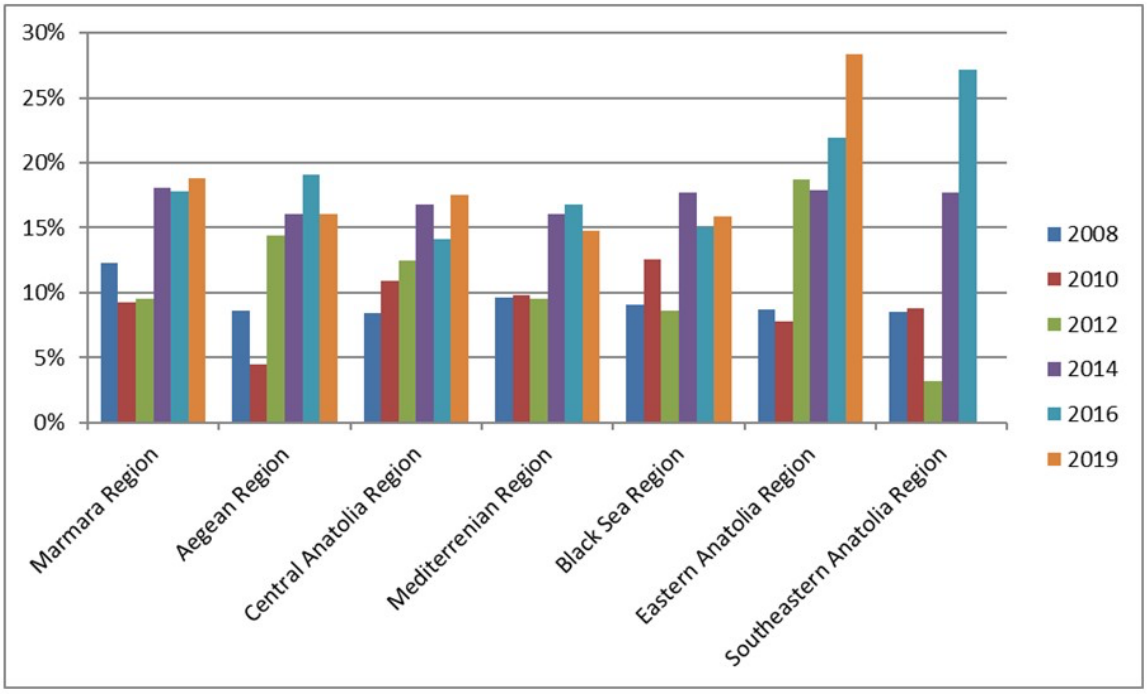

Figure 3. Prevalence of multimorbidity by NUTS and years

however, the fact that the frequency of multimorbidity was higher than that in our study may be due to the inclusion of 12 chronic health problems in the Canadian study.

In a study in the Netherlands, two data sources were used, including medical records of patients listed in a nationally representative network of general practices over the period 2002–2011 and national health interview surveys over the 11-year period. The prevalence of multimorbidity rose from 12.7% to %16.2 in the general practice network and from 14.3% to 17.5% based on the self-reported national health survey data; the estimated prevalence of multimorbidity had increased by 9.3%. Our study has found that the estimated prevalence of multimorbidity in total increased by 9.4% in absolute terms and by 101.1% in relative terms between 2008 and 2019 (21). Although 11 chronic conditions were included in the study mentioned above, the fact that the estimated prevalence of multimorbidity was found to have a similar ratio to the findings of our study may have arisen from the sampling of research and the population included in the study.

An observational study conducted using data from the Nijmegen Continuous Disease Registry, enrolling approximately 13,500 patients, found that increasing age, female gender, and low socioeconomic status are associated with an increase in the prevalence of multimorbidity in the period between 1985 and 2005, including those with four or more chronic diseases by a 300% increase (22). This result is coherent with the findings in our study, which found that the increase in the prevalence of multimorbidity was more evident in the elderly, women, and those with low educational levels.

In the literature, prevalence of multimorbidity increases groups with low socioeconomic status and those living in the deprivation areas (3). However, determinants of multimorbidity were not examined in detail in this study because of lack of data in the Health Surveys databases used in this study. The social determinants of multimorbidity in our country should be comprehensively addressed.

As it is evident from discussions here, multimorbidity was defined as the co-existence of two or more chronic conditions in our study as was done in other studies. On the other hand, differences in the number of diseases in the study and differences in the demographic characteristics of the research population complicate the comparison of results. For this reason, standardization is essential for the assessment and definition of multimorbidity. In other words, the number of chronic conditions to be included in the study and the general characteristics of the population to be studied should be clearly

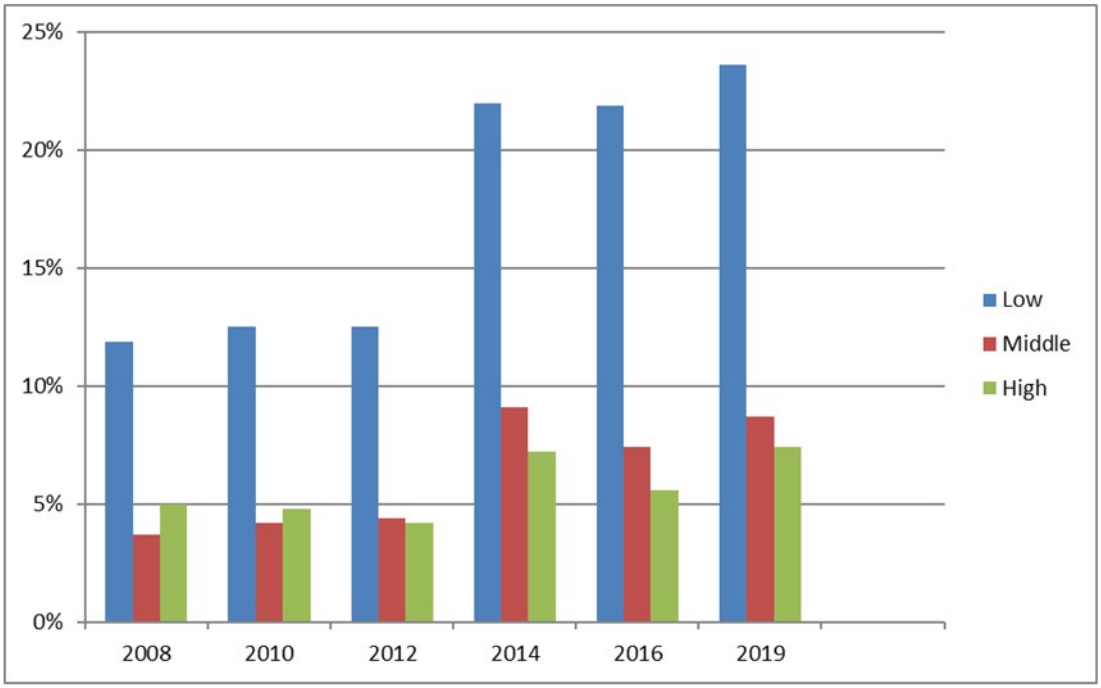

Figure 4. Prevalence of multimorbidity by years and education level

defined, and a precise definition of multimorbidity should be provided.

Understanding the epidemiology of these diseases is of great importance in terms of public health measures to be taken as individuals with chronic diseases and those with multimorbidity have poorer health outcomes aside from a higher risk of death compared to those without multimorbidity or chronic diseases. Likewise, it is of vital importance to organize health services in line with the needs of individuals with these diseases (3,4,8).

Strengths and Limitations of the Study

The key strength of this study is the use of large-scale nationally representative samples of the Turkey population by the statistical institution that produces statistics on chronic diseases, lifestyle, and sociodemographic characteristics and that it presents comparable data in terms of multimorbidity epidemiology.

The fact that the data is based on personal statements may have caused these diseases to be over-or underreported. However, since the data collection method is the same in all TUIK Health Surveys, the difference observed between the years cannot be explained simply by the difference in the statements of the individuals. Changes in the survey questions or the way how questions were used over the years may affect the prevalence. For example, while the frequencies in 2008, 2010 and 2012 were close to each other, it is noteworthy that there had been a marked increase in the frequency of some diseases and multimorbidity as of 2014; similarly, the frequencies in 2016 and 2019 were found close to each other. This finding suggests of a change in method rather than an actual increase in diseases. Having examined the trends in diseases one-by-one, the prevalence of depression has increased more than twice in 2014. The number of people included in the study and the distribution of people between age groups may have affected the frequency of both diseases and multimorbidity. The rate of patients aged 65 and over in the study group has increased since 2014 compared to previous years.

CONCLUSION

This study is the first study in our country using the national survey data and examining the change in the frequency of multimorbidity over time. The findings show that the prevalence of multimorbidity increased remarkably in 11 years. The increase in the prevalence of multimorbidity is more pronounced in the female gender, in the 75 and above age group, those with a low education level, and those living in the Eastern Anatolia Region. Decision-makers need to take these trends into account to improve public

health. Future disease prevention and control programs should consider multimorbidity.

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Peer-review: Externally peer-reviewed.

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RESEARCH ARTICLE

GENETIC DIFFERENCES IN PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR ALPHA GENE IN ENDURANCE ATHLETES (LONG DISTANCE RUNNERS) AND POWER/ENDURANCE ATHLETES (WRESTLERS, FOOTBALL PLAYERS)

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ABSTRACT

Purpose: Peroxisome proliferator-activated receptor alpha gene plays an important role in the expression of genes involved in fatty acid, glucose, and energy metabolism. *PPARα* intron 7 G/C polymorphism (rs4253778) is one of the genes associated with athletic performance. This study aimed to investigate the genotype distribution and allele frequencies of *PPARα* G/C of endurance-oriented athletes (long-distance runners) and power/endurance-oriented athletes (wrestlers and football players) and non-athletic individuals.
Material and Methods: The elite Turkish wrestlers (n=53), football players (n=71), long-distance runners (n=34), and non-athletic individuals (n=56) were involved in the study. The PPARα G/C polymorphism in intron 7 was analyzed using polymerase chain reaction (PCR) primers and restriction fragment length polymorphism method (RFLP). Genomic DNA was extracted by the phenol/chloroform method. Genotyping for the intron 7 G/C variant was performed by PCR and restriction enzyme digestion. The amplified fragment of 266 bp digested by *TaqI* restriction enzyme generated 216 bp and 50 bp in the presence of the CC genotype, and only 266 bp in the presence of the GG genotype.
Results: Genotypes and allele frequencies of *PPARα* intron 7 G/C were compared between endurance-oriented athletes (long-distance runners) and power/endurance-oriented athletes (wrestlers, and football players) categorized according to their sport disciplines. In addition, athletes were compared to non-athletic individuals. The genotype and allele frequencies of *PPARα* intron 7 G/C were similar in the groups of athletes and non-athletic individuals ($p>0.05$). There was no statistically significant association in genotype distribution and allele frequencies of the *PPARα* gene among endurance-oriented athletes, power/endurance-oriented athletes, and non-athletic individuals ($p>0.05$).
Conclusion: The *PPARα* gene polymorphism may not be considered as a distinctive genetic marker in endurance and mixed sport disciplines.

Keywords: Genetics, *PPARα*, rs4253778 polymorphism, sports

INTRODUCTION

It is now well established that genetic variations are associated with health and physical performance (1). The completion of the human genome project in 2003, in addition to revealing the number, structure, and physical maps of human genes also lead to an increasing interest in the genetic influence on athletic performance (2). Human athletic performance is a multifactorial phenomenon and influenced by environmental (physical training, diet, advances in equipment, technological help, etc.) and genetic factors (3). Such components of athletic performance as strength, power, endurance, muscle fiber size and composition, susceptibility of musculoskeletal injuries, and other phenotypes are significantly influenced by genetics (4). It has previously been observed that athlete status is a heritable trait: genetic factors account for nearly 66% of the variance in athlete status. The rest of the variance is owing to environmental factors (5). Therefore, identification of performance-associated polymorphisms is highly essential for talent identification, choice of favorable sport, and to maximize the talent of athletes (6). Numerous studies have been conducted on genetic polymorphisms that have an impact on athletic performance and inter-individual variation (4,7). In this context, genes such as angiotensin I-converting enzyme (*ACE),* and α-actinin-3 (*ACTN3*) have been largely studied (47). However, the importance of the *PPARα* gene has only recently been paid attention to (8-10).

PPARα, a transcriptional factor that belongs to the nuclear receptor family located on chromosome 22 has been one of the genes studied on health and athletic performance in recent years (11,12). *PPARα* controls the expression of genes implicated in left ventricular growth, control of body weight, glucose, and fatty acid metabolism, including fatty acid transport, uptake by the cells, intracellular binding, activation, catabolism (especially mitochondrial fatty acid oxidation), or storage (13,14). The expression level of *PPARα* is moderate, primarily within the kidney, brown fat, and large intestine (11), but higher in tissues implicated in fatty acids utilization such as liver, skeletal and cardiac muscle (15,16).

In the early 2000s, *PPARα* intron 7 G/C polymorphism (rs4253778) was associated with left ventricular growth and the risk of coronary artery disease (17,18). The highly comprehensive study also found out that athletes with combined power/endurance activity (wrestling, boxing, ice hockey, court tennis) had a higher frequency of the *PPARα* intron 7 CC genotype compared to controls (19). On the contrary, Cieszczyk et al found more prevalent frequency of G allele and GG genotype in elite combat athletes (wrestling, boxing) than controls (20). It was demonstrated that *PPARα* CC homozygous carriers of males and females had a higher jumping performance (reactive strength index) than GG and GC genotypes (21). Also, Gineviciene et al indicated that male athletes with *PPARα* CC and *PPARα* GC genotypes had significantly increased muscle mass and single muscular contraction power than GG homozygotes (8). Similarly, middle-school students with *PPARα* C allele outperformed of handgrip strength testing than GG homozygotes (22). However, Broos et al observed that the *PPARα* intron 7 G/C polymorphism does not affect strength traits in the sedentary population (23). Studies showed that GG homozygotes and G allele were more dominant with the types of endurance athletes (18,24,25). The meta-analysis has revealed that being the C allele carrier may provide an advantage to be an elite level soccer player, whereas the G allele may be beneficial to be an elite level endurance athlete (26). Furthermore, the C allele of *PPARα* was significantly more frequent in football players compared to controls (27). On the contrary, the G allele frequency was found to be higher in soccer players than in combat sports athletes and motorcycle riders (28).

Though it is hypothesized that the intron 7 C allele affects power and mixed power/endurance and G allele affects endurance performance, previously published studies on the effect of *PPARα* intron 7 G/C polymorphism on power and endurance performance are not consistent. There is no general agreement about the effect of *PPARα* intron 7 G/C polymorphism on power, mixed power/endurance, and endurance performance. Therefore, the present study aimed to examine allele frequencies and genotype distribution of *PPARα* intron 7 G/C in elite Turkish football players, wrestlers, long-distance runners, and compare endurance-oriented athletes with power/endurance-oriented athletes.

MATERIAL AND METHODS

Subjects

The elite Turkish wrestlers (n=53), football players (n=71), long-distance runners (n=34), and non-athletic individuals (n=56) were selected from individuals residing and born in Turkey (n=214). Detailed information about the study protocol before

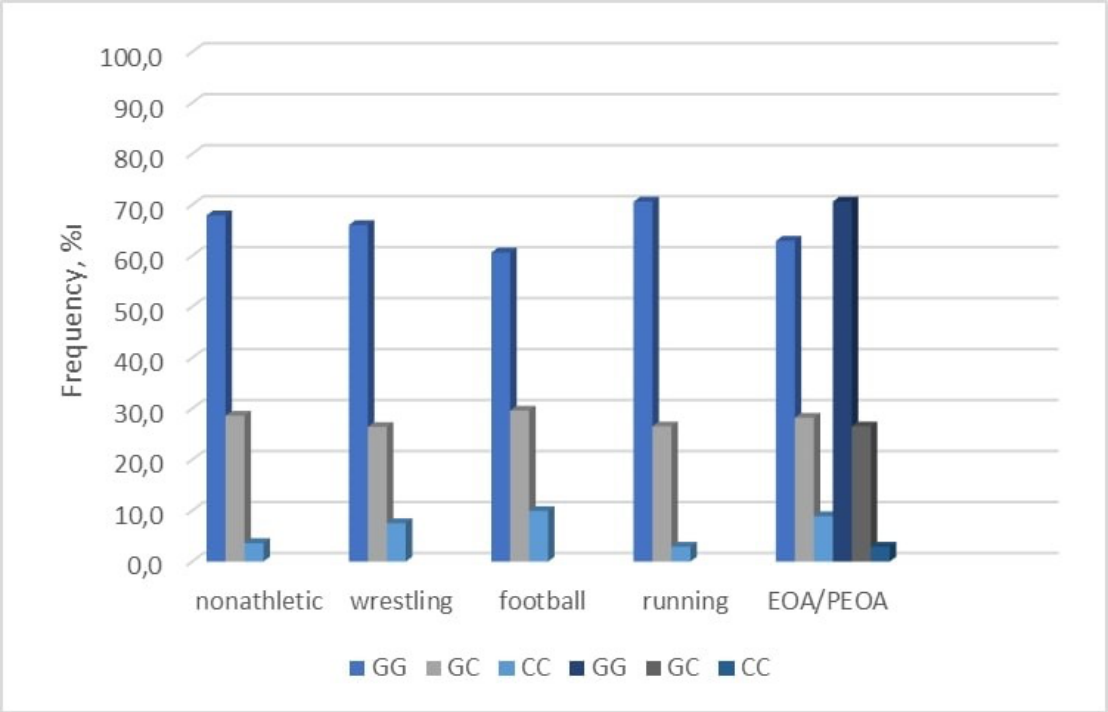

Figure 1. Distribution of PPARα 7 intron genotypes among Turkish athletes and non-athletic individuals EOA: endurance-oriented athletes, PEOA: power/endurance-oriented athletes (p> 0.05)

the study were given to the players, runners and wrestlers and signed informed agreement forms were obtained from them. This study was conducted in accordance with the principles of the Declaration of Helsinki II. Turkish athletes were chosen from men who participated in both national- and international-level competitions. The characteristics of 214 men were aged 22-26; height 170.1 ± 178.8 cm, weight 62.4 ±77.5 kg. The footballers were from 3 professional teams: Kayserispor, Kayseri Erciyespor, Tavşanlı Linyitspor. The wrestlers training at the camp for free style juniors and seniors national wrestling team were included. The track and field athletes were elite long distance runners. The athletes were classified into two groups according to their sport disciplines included endurance-oriented athletes (5000, 10,000 meters or marathon runners) and power/endurance-oriented athletes (wrestlers and football players). The study was approved by Gazi University, (Non-Invasive) Clinical Research Ethical Committee with the number of 217 and the date 23/05/2012.

Genotyping

Blood samples were obtained from 158 elite Turkish athletes, and 56 non-athletic individuals randomly selected (control group). Genomic DNA was extracted by the phenol/chloroform method (29). *PPARα* intron 7 G/C polymorphism was carried out by polymerase chain reaction-restriction fragment length polymorphism method with *Taq1* enzyme (PCR-RFLP). Forward-ACAATCACTCCTTAAATATGGTGG and reverse-AAGTAGGGACAGACAGGACCAGTA primers were used for *PPARα* intron 7 G/C polymorphism, generating a fragment of 266 bp. PCR amplification was performed for 35 cycles, each of which consisted of 94°C for 30 s, 56°C for 30 s, and 72°C for 1 min. *Taq1* digestion of the PCR products was carried out by adding 6 U of *TaqI*, and 1x restriction enzyme buffer in a volume of 20 µl, and incubation for 4 hours at 65°C (30). The fragment of 266 bp digested by *TaqI* generated 216 bp and 50 bp in the presence of the CC genotype, and 266 bp in the presence of the GG genotype. PCR and restriction products were separated by 2% and 3% agarose gel electrophoresis, respectively, and visualized in UV light.

Statistical Analysis

The genotype distribution of *PPARα* intron polymorphism was assessed and compared within each athlete group and between each of the five groups of athletes (wrestling, football, running,

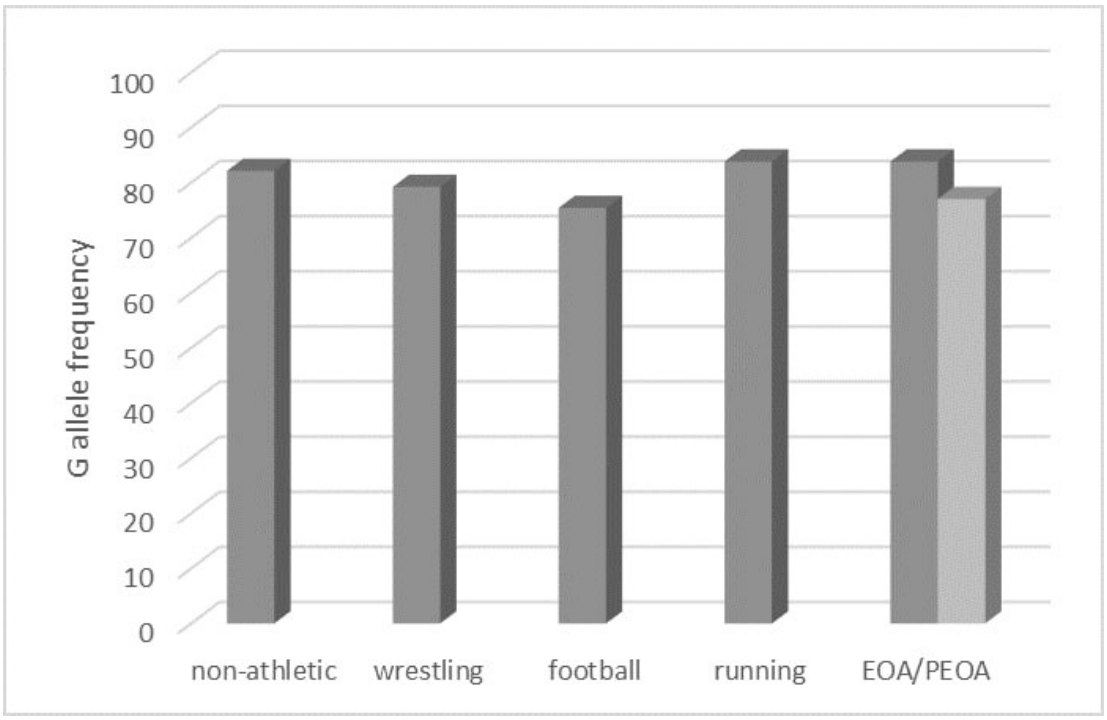

Figure 2. Distribution of PPARα intron 7 G allele among Turkish athletes and non-athletic individuals EOA: endurance-oriented athletes, PEOA: power/endurance-oriented athletes (p> 0.05)

endurance-oriented athletes, power/endurance-oriented athletes) and non-athletic individuals by chi-square test or Fisher exact test. Allele frequencies were determined by the gene-counting method. The allele frequencies were compared within each athlete group and between each of the five groups of athletes and non-athletic individuals by Z-test (31). P values <0.05 were considered statistically significant.

RESULTS

The study was performed on 158 elite Turkish athletes and 56 non-athletic individuals. Athletes were classified into two groups by their sport disciplines, as endurance-oriented (long-distance runners) and power/endurance-oriented (wrestlers, and football players). The genotype distribution and allele frequencies of the *PPARα* intron 7 G/C were determined in the three-sport disciplines (wrestling, football, and running) and non-athletic individuals

PPARα genotype distributions in all athletic groups were in agreement with Hardy–Weinberg equilibrium. *PPARα* genotype distributions were determined and compared within each athlete group and between each of the five groups of athletes (wrestling, football, runners, endurance-oriented athletes, power/endurance-oriented athletes) and non-athletic individuals by chi-square test or Fisher exact test (p> 0.05) (Figure. 1).

Furthermore, the frequencies of the *PPARα* G allele in all athlete groups and non-athletic individuals were calculated and compared between each of the five groups of athletes and non-athletic individuals using the Z-test (Figure. 2).

G allele frequencies in endurance-oriented and power/endurance-oriented athletes were 84% and 77%, respectively. There were no significant differences in genotype distribution and allele frequencies of *PPARα* among different groups of athletes (p>0.05).

The frequencies of *PPARα* 7 GG genotype in athletes and non-athletic individuals were higher than those of *PPARα* CC genotypes. The *PPARα* GG genotype was more common among endurance-oriented athletes (70.6%) than those of power/endurance-oriented athletes (62.9%). However, the frequency of *PPARα* CC genotype was low level in endurance-oriented athletes (2.9%) in comparison with power/endurance athletes (8.9%).

DISCUSSION

Athletic performance is a complex trait and it is affected by genetic and environmental factors. Numerous polymorphisms are more common in elite

athletes than in the general population. A variety of genetic factors associated with metabolic pathways are known to affect athletic performance. *PPARα* regulates the expression of multiple genes implicated in the metabolism of energy, fats, and glucose in the skeletal muscle as well as other tissues (32).

In this study, the allele and genotype frequencies of *PPARα* intron 7 G/C polymorphism were investigated in elite Turkish football players, wrestlers and long-distance runners by PCR and RFLP methods and compared allele and genotype frequencies of this polymorphic region within each athlete group and between athlete groups and non-athletics. The three-sport disciplines (wrestling, football, and running) were categorized according to sports disciplines, as endurance-oriented (long-distance runners) and power/endurance-oriented (wrestlers, and football players). There was no considered statistically significant difference among groups for allele and genotype comparisons. ($P<0.05$). GG genotype frequency 66%, 60.6%, 70.6 and 67.9; GC genotype frequency was 26.4%, 29.6%, 26.5% and 28.6 and CC genotype was 7.5%, 9.9%, 2.9% and 3.6% for wrestlers, footballers, runners and controls respectively. G allele frequency 79.2%, 75.4%, 83.8 and 82.1 and C allele frequency was 20.8%, 24.6%, 16.2% and 17.9 for wrestlers, footballers, runners and controls respectively.

Studies on *PPARα* and other polymorphisms in elite Turkish wrestlers are limited (33). This is the first study on the association of *PPARα* intron 7 G/C polymorphisms with elite Turkish wrestlers. *PPARα* gene G/C polymorphism was not found significantly different between elite Turkish wrestlers, long-distance runners, footballers, and non-athletic individuals. The frequency of the GG genotype is less likely in mixed power/endurance sports such as wrestling, football, and boxing (8). Ahmetov et al found no significant difference in C allele frequencies between Russian wrestlers and controls (9). However, in the whole cohort, these authors found that the C allele is associated with anaerobic components of physical performance. They suggested that the C allele may be advantageous for power-related sports disciplines (19,34). Contrarily, Cieszczyk et al found significantly higher frequencies of the GG genotype and the G allele in elite Polish combat athletes such as judo, wrestling, and boxing (20). The acyclic nature of combat sports, uncertainty in effort performed during combat sports and the dissimilarity of participants may affect the results.

While aerobic metabolism is dominant for the energy supply during a football match, power and strength play a more critical role in the determination of success in football. A 90-minute match is played at an intensity near to anaerobic threshold and it requires various explosive activities involving jumping, kicking, tackling, turning, sprinting, changing speed, and powerful contractions to maintain balance and control of the ball against the defensive press (35).

There are controversial studies investigating *PPARα* intron 7 G/C polymorphism on footballers, pointing out a significant or no significant relationship between football players and controls. The association of the G allele and GG genotype with endurance athletes was repeated in several studies (18,24,25), whereas the association of the C allele on mixed power-endurance and power/strength is not clear. The G allele and GG genotype were found to be higher in professional and young Turkish football players (36,37. In this study, GG genotype distribution and G allele frequency of elite football players were similar to those of non-athletic individuals. Similar to the current study, Gineviciene et al obtained no significant difference in *PPARα* (G/C) polymorphisms of professional Lithuanian football players compared to controls (38).

One study investigating *PPARα* gene G/C polymorphism on Russian team sports athletes found that footballers had a significantly higher frequency of C allele among 14 team sports athletes. The finding suggested that anaerobic metabolism may be vital for game performance in footballers. The C allele may facilitate glucose utilization rather than fatty acid oxidation in response to anaerobic exercise (27). Similarly, Egorova et al showed that elite Russian football players had a higher frequency of the *PPARα* C allele (39). In contrast, Cocci et al found that the G allele frequency was meaningfully higher in soccer players than in combat sports athletes and motorcycle riders (28). Proia et al found a higher frequency of G allele and GG genotype in professional Italian soccer players (40). The present study detected higher the frequencies of GG genotype and G allele than those of the frequency of the *PPARα* C allele among groups.

It is hypothesized that *PPARα* is activated during endurance exercise**.** Several studies have supported that the G allele and GG genotype is associated with endurance athletes (26). Ahmetov et al found a higher frequency of GG genotypes in a group of Russian endurance-oriented athletes (swimmers, cross-

country skiers, skaters, and triathletes) compared to controls (19). Mavlyanov et al reported a higher frequency of G allele and G/G genotype of cyclists and runners than in rowers (45). One possible explanation of this result is the similarity of physical fitness components between runners and cyclists. Eynon et al observed a higher frequency of GG genotypes in elite Israeli endurance athletes compared to sprinters (25). Endurance athletes (rowing, marathon, biathlon, triathlon, cross-country skiing, swimming, skating (3,000-5,000), and road cycling) demonstrated a higher frequency of GG genotype and G allele compared to controls (17,18). Ginevičienė et al found that the frequency of *PPARα* GG genotype was higher in Lithuanian elite endurance athletes compared to in speed/power and mix sports (8). Maciejewska et al revealed that elite Polish endurance athletes had a higher prevalence of *PPARα* intron 7 G allele, and GG genotype compared to controls (24). It was found a higher frequency of GG genotype and G allele between power/endurance-oriented (wrestlers, and football players) (63%) and endurance-oriented (long-distance runners) (70.6%) sports disciplines in this study.

There are also studies reported no association between the *PPARα* intron 7 G/C polymorphism and athletes. *PPARα* intron 7 G/C polymorphism was not significantly different in endurance-oriented athletes (long-distance runners) compared to the control group. Similarly, it was shown that there was no significant difference among Ukrainian athletes such as endurance-oriented: cross-country skiers, and rowers; and power-oriented: short-distance runners, short-distance swimmers, jumpers, and throwers (41). The PPARα gene rs4253778 G/C polymorphism has no major effect on physical performance in endurance athletes (42,43). Tsianos et al found no association between *PPARα* rs4253778 G/C polymorphism and marathon performance of runners (44). Tural et al found a significant association between the *PPARα* GG genotype, G allele and aerobic performance in elite Turkish endurance athletes (46). The findings in the present study indicate no strong association between *PPARα* intron 7 G/C polymorphism and mixed power/endurance and endurance athletes. In the study, while the *PPARα* gene GG genotype and G allele were not statistically different in athlete groups, a tendency to have increased GG genotype (70.6%) and G allele (84%) was observed in endurance-oriented athletes. There may be possible explanations for these results. Each gene polymorphism may have a limited contribution to endurance performance (18). This study included 34 elite endurance athletes. Firstly, it is thought that it would be appropriate to increase the number of athletes to interpret a definite association with endurance performance. A proper number of participants are needed for a genetic study. There is a good deal of studies on endurance athletes from different sport disciplines (swimmers, cross-country skiers, skaters, and triathletes, rowing, etc.) but, studies specifically on long-distance runners are rare. The athletic status and ethnicity of athletes may affect the results of the study.

CONCLUSION

The findings in the present study indicate no strong association between *PPARα* intron 7 G/C polymorphism and mixed power/endurance and endurance athletes. Elite Turkish endurance athletes tend to have a higher frequency of GG genotype and G allele. While *PPARα* intron 7 G/C polymorphism is a novice candidate for athletic performance, it may be a favorable gene for endurance performance. Further study with larger sample size and homogeneous groups is needed to clarify the association between PPARα polymorphism and endurance athletes. Also, *PPARα* polymorphism needs to be investigated on sport disciplines (as sprints, jumps, throws) requiring high force output for a short period of time.

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Author contribution: Methodology: MK, KG; Writing-Original draft: MK, KK, MG; Investgation; MK, KK; Writing and Editing: KK, MG; Supervision: MG, KG; Statistical Analysis: TK.

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

Ethical approval: The study was approved by Gazi University, (Non-Invasive) Clinical Research Ethical Committee with the number of 217 and the date 23/05/2012.

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RESEARCH ARTICLE

THE MODERATOR ROLE OF PAIN DURATION IN RELATION BETWEEN PAIN CATASTROPHIZING AND PAIN INTENSITY

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ABSTRACT

Purpose: Pain catastrophizing is one of the most important factors contributing to pain experience and duration of action. This study aimed to explore the moderator role of pain duration in the hypothetical relation between pain catastrophizing and pain intensity in patients with chronic musculoskeletal pain syndrome (CMPS).
Material and Methods: Seven hundred and eight patients with CMPS (mean age: 28.52 ± 7.75 years) participated in this cross-sectional and descriptive study. The pain intensity and catastrophizing of the patients was assessed with the Visual Analog Scale (VAS) and Pain Catastrophizing Scale (PCS), respectively. The time elapsed since the participants' first experience of pain (number of days) was recorded as pain duration.
Results: There was a positive correlation between pain duration ($r=0.181$, $p<0.001$), pain intensity ($r=0.432$, $p<0.001$) and total score of pain catastrophizing. According to univariate and multivariate regression analysis, pain duration adjusting for pain catastrophizing maintained its predictor effect on pain intensity ($p<0.001$). According to hierarchical model, the effect of pain catastrophizing on pain intensity was 44.7%, its effect increases to 48.5% adding pain duration.
Conclusion: The results of this study supports that pain duration has no critical effect on the relation between pain catastrophization to pain intensity in patients with CMPS.

Keywords: Pain catastrophizing, musculoskeletal pain, pain duration, moderator

INTRODUCTION

One of the common symptoms of musculoskeletal disorders is pain. Chronic musculoskeletal pain syndrome (CMPS) which has a quite high lifetime prevalance, is an indicator for the intensity of the underlying musculoskeletal disorders (1). Although the presence and duration of CMPS are associated with biopsychosocial, physical, and environmental factors, the factors contributing to the high prevalence and duration of action of CMPS remain unclear (2,3).

Pain catastrophizing, defined as an emotional response to anticipated or actual pain, has attracted much more attention in the last two decades (4-6). Pain catastrophizing has a multidimensional structure that consists of three aspects (magnification, rumination, and helplessness) (7). Magnification is defined as exaggeration of pain

intensity and threat, rumination is the cognitive process that focuses on pain and its effects, and helplessness is the belief that people with pain cannot cope with itAccording to many chronic pain models, pain catastrophizing has an essential role in the initiation and chronification of pain (8). The contribution of pain catastrophizing on pain intensity are conflicting (9-12). It has been reported that the higher the catastrophication of pain, the lower the pain threshold and the higher the pain intensity, but the mechanism of action is not clear (13,14).

Catastrophizing was found to be associated with pain behavior, health care use, hospital stay, and analgesic drug use. Several studies have reported that females experience more catastrophizing than males (15). Catastrophizing is correlated with increased pain experience and increases pain intensity up to 7% to 31% (16). In contrast, catastrophizing has been shown to be highly associated with disability and better predicts disability than disease-related variables or pain.13 The wide range of variance in pain ratings and the fact that catastrophizing was not predicts pain as good as disability suggested that there may be moderator variable between pain catastrophizing and pain (17). Chronic pain sufferers often have both high pain intensity and pain duration. In addition, it has been reported that high pain frequency can alter pain modulation (18). Therefore, we thought that the moderator variable might be the duration of pain. In the light of our hypothesis, the aim of current study was to examine the moderator role of pain duration in the hypothetical relationship between catastrophizing pain (with its sub-dimensions) and pain intensity in female patients with CMPS.

MATERIAL AND METHODS

Study Design

In this cross-sectional study, data were collected with an online survey database (Google Forms). The survey access link was shared at regular weekly intervals from the social media (facebook Denizli female's group). Access time to the survey database was 6 weeks. Personal informations such as name and e-mail address were not collected.

The research has been approved by Pamukkale University Non-Interventional Clinical Research Ethics Committee (Date: 13.04.2021, Number: 08) and performed in accordance with the Helsinki Declaration. Online informed consent was obtained from all participants prior to access study assessment form.

Participants

The study inclusion criteria were as follows: being a female, living in Denizli, being age between 18 and 45 years, being literate and have social media access, having musculoskeletal pain for at least 3 months, not receiving psychotherapy and not using heavy psychiatric drugs, not having undergone a surgical operation in the past year, not having a diagnosis of serious metabolic, orthopedic and neurological disease. A total of 900 patients assessed for eligibility. Ninety patients excluded because of not meeting the inclussion criteria (n=192). Finally, 708 patients were included into this study.

Data Collection

Demographic information of participants were recorded. The time elapsed since the participants' first experience of pain was recorded as days. This data was used to determine the pain duration. Pain intensity was assessed by the Visual Analog Scale (VAS), and the catastrophic behavior was assessed by the Pain Catastrophic Scale (PCS). This scale was developed by Sullivan et al (4) to investigate the effective catastrophic factors in the mechanism of pain. There are 13 questions in this scale and can be filled by patients in less than five minutes. Patients score the items between 0 and 4, considering their previous pain experiences and other factors associated with pain. Of these items, 8th, 9th, 10th, 11th items were rumination; 6th, 7th, 13th items magnification; 1st, 2nd, 3rd, 4th, 5th and 12th items were about the helplessness dimension (19).

Statistical Analysis

Data were analyzed by Statistical Package for the Social Sciences. Continuous variables were presented as mean ± standard deviation and median (maximum and minimum). The conformity of continuous variables to normal distribution was tested with the Shapiro-Wilk test. Spearman Correlation Coefficient was used to determine the relation between pain catastrophizing and pain intensity and duration. Hierarchical regression analysis was used to examine the moderator role of pain duration. Hierarchical multiple regression analyses were performed with the processing steps.

Table 1. Descriptive data of participants

Variables	Mean ± SD	Median (Min-Max)
Age (year)	28.52 ± 7.75	18-45 (25)
BMI	23.4 ± 4.31	14,84-51,07 (22,09)
Years of education	13.66 ± 3.15	5-21 (15)
Pain Intensity (VAS)	4.87 ± 1.8	0.62-10 (4.8)
Pain Duration (days)	457.19 ± 677.13	2-4680 (180)
PCS	21.89 ± 10.71	0-52 (20)
Rumination	6.65 ± 4.61	0-29 (6)
Magnification	5.92 ± 2.65	0-12 (6)
Helplessness	10.19 ± 5.2	0-24 (10)

SD: Standart Deviation; PCS: Pain Catastrophizing Scale; VAS: Visual Analog Scale; BMI: Body Mass Index

In the first step univariate regression analyses was done. Second step is the multivariate regression analyses of all variables. The third step is the analysis of adding pain catastrophizing to the relation between pain duration and pain intensity, or adding pain catastrophizing to the relation between pain intensity and pain duration. A p value was set at ≤ 0.05 level.

RESULTS

Seven hundred and eight female patients (the mean age of 28.52 ± 7.75) were included into this study. Descriptive data of patients were shown in Table 1.

The correlation between pain catastrophizing, pain intensity and pain duration was shown in Table 2. Pain duration showed weak and significant association with the total score of pain catastrophizing ($r=0.181$, $p<0.001$) and sub-dimensions of rumination ($r=0.149$, $p<0.01$) and helplessness ($r=0.262$, $p<0.001$). VAS score showed a moderate and significant association with the total score of pain catastrophizing ($r=0.432$, $p<0.001$), and helplessness ($r=0.44$, $p<0.001$). VAS score showed a weak and significant association with the sub-dimensions of rumination ($r=0.351$, $p<0.001$) and magnification ($r=0.273$, $p<0.001$). Pain duration ($b=0.261$, $p<0.001$) and pain catastrophizing ($b=0.451$, $p<0.001$) made significant contributions to the prediction of pain intensity. Once pain catastrophizing was controlled, pain duration significantly contribute to the prediction of pain intensity ($b=0.192$, $p<0.001$) (Table 3).

According to hierarchical model 1, the effect of pain duration on pain intensity was 26.1%. When pain catastrophizing was added to the the second step, this effect increased up to 48.5%. According to hierarchical model 2, the effect of pain catastrophizing on pain intensity was 44.7%. When pain duration was added to the second step, this effect increased up to 48.5% (Table 4). As a result, pain duration did not moderate the association between pain catastrophizing and pain intensity.

DISCUSSION

This study aimed to identify the moderator role of pain duration in the hypothetical relation between pain catastrophizing and pain intensity in patients with CMPS. Both pain duration and pain catastrophizing predicts pain intensity. Once pain catastrophizing was controlled, pain duration

Table 2. Correlation analysis chart

Variables		Pain Duration	Pain Intensity
PCS	**r**	0.181	0.432
	p	**<0.001**	**<0.001**
Rumination	**r**	0.149	0.351
	p	**0.037**	**<0.001**
Magnification	**r**	0.100	0.273
	p	0.165	**<0.001**
Helplessness	**r**	0.262	0.44
	p	**<0.001**	**<0.001**

PCS: Pain Catastrophizing Scale

Table 3. Univariate and multivariate regression analysis results

	Univariate Regression					Multivariate Regression				
DV: Pain Intensity	**β**	**t**	**p**	**95% C.I. Lower**	**95% C.I. Upper**	**β**	**t**	**p**	**95% C.I. Lower**	**95% C.I. Upper**
Pain Duration	0.192	50.176	**<0.001**	0.000	0.001	0.261	6.451	**<0.001**	0.000	0.001
PCS	0.415	110.166	**<0.001**	0.058	0.082	0.451	12.06	**<0.001**	0.064	0.088

DV: Dependent Variable; Std Beta: Standart Beta; C.I.: Confidence Interval; Pain Catastrophizing Scale

Table 4. Results of hierarchical regression analysis

DV: Pain Intensity		**Independent**	**β**	**t**	**p**	**%95 C.I. Lower**	**%95 C.I. Upper**	**R^2**
Hierarchical model 1	**Step 1**	**Pain Duration**	0.261	6.451	**<0.001**	0.000	0.001	0.261
	Step 2	**Pain Duration**	0.192	5.176	**<0.001**	0.000	0.001	0.485
		Pain Catatstrophizing	0.415	11.166	**<0.001**	0.058	0.082	
Hierarchical model 2	**Step 1**	**Pain Catatstrophizing**	0.447	11.921	**<0.001**	0.063	0.088	0.447
	Step 2	**Pain Catatstrophizing**	0.415	11.166	**<0.001**	0.058	0.082	0.485
		Pain Duration	0.192	5.176	**<0.001**	0.000	0.001	

DV: Dependent Variable; Std Beta: Standart Beta; C.I.: Confidence Interval

maintained a predictor effect on pain intensity. According to hierarchical analyses, pain duration did not moderate the association between pain catastrophizing and pain intensity in patients with CMPS.

The duration of past pain experience indicates how long participants have lived with pain. We hypothesized that the time that the participants have lived with pain may explain the contribution of pain catastrophizing to reported pain levels. Consistent with the study hypotheses, both pain duration and pain catastrophizing predicted pain intensity in our sample. The relationship between catastrophizing and pain was examined by considering many different control variables (20,21). According to the results, catastrophic thinking and depression were statistically significant predictors of pain intensity. Other control variables such as age, culture, ethnicity, literacy level, socio-economic status and pain frequency are pivotal to understanding the multifactorial structure of the pain. The other mentioned before should be evaluated to conclude the variables that contribute this association.

The association between pain intensity and pain catastrophizing was found weak at the current study and concluded that pain duration does not moderate the mentioned association. Increased activity in the anterior cingulate cortex and insula and decreased activity in the prefrontal areas are related to pain catatstrophizing (22). This is called central sensitization of pain. Due to central sensitization, pain is no longer dependent on the presence or duration of harmful environmental stimuli. (23). According to this mechanism, it is possible that the pain duration did not play a moderator role in the association between pain intensity and catastrophizing. And also, based on cross-sectional studies, it is not possible to prove whether the pain duration leads to catastrophizing pain, but once activated, this cycle may reinforce each other. Such activation integrates all aspects of pain and facilitates cingulate cortex (24). Since there is no validated scale assessing the duration of pain, the authors of current study prefered to question with the time elapsed since participants' first experience of pain. Considering that it is difficult for the participants to remember their past pain experiences, more objective data could be obtained if the number of painful days in the last 1 year were questioned. Cano et al evaluated pain duration as the time elapsed from the first experience of pain and concluded that the interaction between pain duration and catastrophizing was important for perceived willing partner responses, but not for pain intensity (25). Kjøgx et al revealed that the pain frequency is the moderator in the relationship between pain and catastrophizing (26). In this study, not only the duration of the pain, but also the frequency of the pain, how many days the pain lasted on average, and how many days they felt pain in the last one month were questioned. Considering that pain should be evaluated in multiple ways, it may be a more accurate approach to evaluate the frequency of pain with these parameters.

Other contributing factors related to this association such as pain type, pain localization, psychosocial status, age, etc were not analyzed in this study. The limitation of this study is that other contributing factors could be analyzed to eliminate the confounding factors for this association between pain and catastrophizing. Also collected data with an online survey database and we could not prevent the same person from filling out the form twice. This issue was a handicap for the authors to distinguish between data duplication.

CONCLUSION

In conclusion, this study supports that the duration of pain is a predictor, but not a moderator, in the relation between pain catastrophizing and pain intensity in patients with CMPS. Control variables other than pain duration that contribute to this relation should be clarified in future studies.

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RESEARCH ARTICLE

VISUAL EVOKED RESPONSES IN ADOLESCENT IDIOPATHIC SCOLIOSIS

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ABSTRACT

Purpose: In electrophysiological studies conducted with adolescent idiopathic scoliosis (AIS) patients, no prior studies examining the visual evoked potentials of AIS patients were found in conjunction with objective vertical perception. The aim of this study was to examine the visual evoked potentials of individuals with AIS and healthy individuals in terms of their brain responses.
Material and Methods: Twelve AIS patients (12.75±0.86 years) and 10 healthy subjects (13.80±1.68 years) participated. A 64-channel electroencephalography (EEG) recording system, Embedded Microcontroller Unit (EMISU), visual stimulation unit, EEG cap, and video recording system were used to examine brain responses after applying visual stimulus.
Results: In AIS and control groups (CG), three positive and two negative peaks were observed after applying the stimulus. In the AIS, the first and second negative, and second positive peaks, and in the CG, the second positive and negative peaks appeared significantly earlier in the frontal region. The amplitude of the third positive peak in all regions was found to be higher in the AIS. In AIS and CG, the second positive peak was found to be significantly higher in the parieto-occipital region.
Conclusion: It can be judged that AIS patients use more sources for processing the vertical visual stimuli than procedures compared to healthy individuals. In light of the findings obtained, the effect of treatments applied to AIS patients with the method used in this study can be evaluated in terms of brain responsiveness. In addition to the subjective visual perception of individuals with AIS, this method can also evaluate objective vertical perception.

Keywords: Adolescent Idiopathic Scoliosis, vertical perceptions, electroencephalography

INTRODUCTION

Scoliosis is a three-dimensional spine deformity with multiple epidemiological causes (eg congenital, neuromuscular, etc). Adolescent idiopathic scoliosis (AIS) is the most common (80-90%) type of scoliosis (1, 2). Etiopathogenetic factors of AIS are genetic, neurological, bone growth abnormalities, metabolic, hormonal dysfunction etc. (3, 4). Studies investigating neurological changes in AIS have mainly focused on explaining the etiopathogenesis, brain structures, and functions (5, 6). EEG is a non-invasive and easily applicable method, has an important place in clinical

observations as well as being of great importance in brain research. The brain responses to stimuli (i.e. visual) given from outside during the spontaneous activity of the brain are called the (visual) evoked potentials (7).

The number of studies investigating brain responses in AIS is very limited. These EEG studies differ in terms of the number of electrodes used and the analysis approach, whereas the methodology of comparing AIS with the control group (CG) was utilized in a similar fashion like other neurological studies. In this context, Robb et al. indicated that there was no difference in EEG results similar between AIS and CG (8). In contrast, It was suggested that pathological changes may have occurred in subcortical structures due to increased low-frequency brain activities and observation of paroxysmal activity in AIS and that cerebellar dysfunction may be related to its etiology (9, 10). Besides differences in brain responses, hemispheric changes associated with the type of curvature has drawn attention. Pathological EEG results were found in contralateral hemisphere in AIS with lumbar curvature, in ipsilateral hemisphere in those with thoraco-lumbar curvature, and in the bilateral hemisphere in those with thoracic curvature (10). In contrast, Petersen et al. (11) did not find a systematic relationship as Dretakis et al. stated (10). Pinchuk et al. reported increased bioelectrical activity in the left hemisphere, especially left thalamus (12). Although there are differences of opinion among these studies, the cause of functional impairment in the puberty process may be related to the overloading of the adaptation-compensation mechanism of the central nervous system. In addition, EEG could not provide a method to predict the prognosis of scoliosis and to determine the relationship between the convex side and the hemisphere with changes (12).

The aim of this study was to examine the VEPs of individuals with AIS and CG. In former literature, there are no EEG records while the participants were in balance standing. Besides, no studies examining VEPs of scoliosis patients were found in the literature. In this respect, the current study targets a specific focus of research in the cognitive related brain responses of this neurospinal disorder..

MATERIAL AND METHODS

The study was approved by Dokuz Eylul University, Non-Interventional Research Ethics Committee, (Date: 21.11.2013, Number 2013/42-07) while the children and their parents were informed about the study, and written consent were obtained. Twelve patients with AIS (11 female, 1 male) and 10 healthy subjects (8 female, 2 male) participated in the study. The average age of the AIS group was 12.75 ± 0.86 years, and 13.80 ± 1.68 years for controls. The inclusion criteria were as follows; having a diagnosis of AIS, being between 10-16 years old, having a Cobb angle of 20° to 50°, a Risser sign determined to be 0-

Table 1. Demographic characteristics of individuals according to AIS and control groups.

	AIS Group (n:12) X±SD	**Control Group (n:10) X±SD**	**z**	***P***
Age (years)	12.75 ± 0.86	13.80 ± 1.68	-1.591	*0.112*
Height (cm)	160.58 ± 6.00	173.00 ± 7.94	-1.587	*0.113*
Weight (kg)	50.50 ± 9.03	54.00 ± 10.24	-0.265	*0.791*
BMI (kg/m^2)	19.50 ± 2.80	19.82 ± 2.89	-0.363	*0.717*

X: Average, SD: Standard deviation, BMI: Body mass index, z: Mann-Whitney U value

3. The exclusion criteria were selected as; former spinal operation, accompanying mental problems, other neurologic, muscular, or rheumatic diseases.
The Lenke classification was used to classify AIS patients' curvature types and the Cobb method to determine the curvature size.
EEG was recorded in an isolated and dark room that blocks electromagnetic waves, electrical and acoustical noise. The isolated room was monitored with a video camera with the knowledge of the individuals, and communication was provided by a sound system.
A 64-channel EEG recording system (Jasper 10-20 system), Embedded Microcontroller Unit (EMISU) (13), visual stimulation unit, EEG cap, and video recording system were used.
An electro gel (ECI Electro-Gel, ElectroCap International, Inc. ABD) was used to ensure the conductivity between the electrodes on the EEG caps and the scalp. The electrical potential of the earlobes was assumed to be zero and was referenced accordingly. The impedances of the electrodes were kept at 5 kOhm during recording. Electrooculography (EOG) records were taken with electrodes placed around the right and left eye area of the participants.

Line-alignment Visual Setup

The stimuli prepared in the MATLAB software environment for visual stimuli were applied to the participants through the EMISU device. To process vertical line perception, a set of pseudorandomized preset vertical lines have been prepared. In order to estimate the individual behavioral responses, the midline deviation values were obtained. The individual reference values were then taken as reference for each session. All the visual stimuli were created with red lines with angle values determined by the system, randomly within ± 15 degrees of this vertical reference value. These visual stimuli were applied to the participants through a 19-inch LCD screen in the form of red lines on a black background (Figure 1). In the records, 120 stimuli were sent and the inter stimulus interval (ISI) was around 3 to 3.5 seconds.
EEG analysis has been conducted offline via Scan 4.5 software (Neuroscan, USA). The epochs of 1000

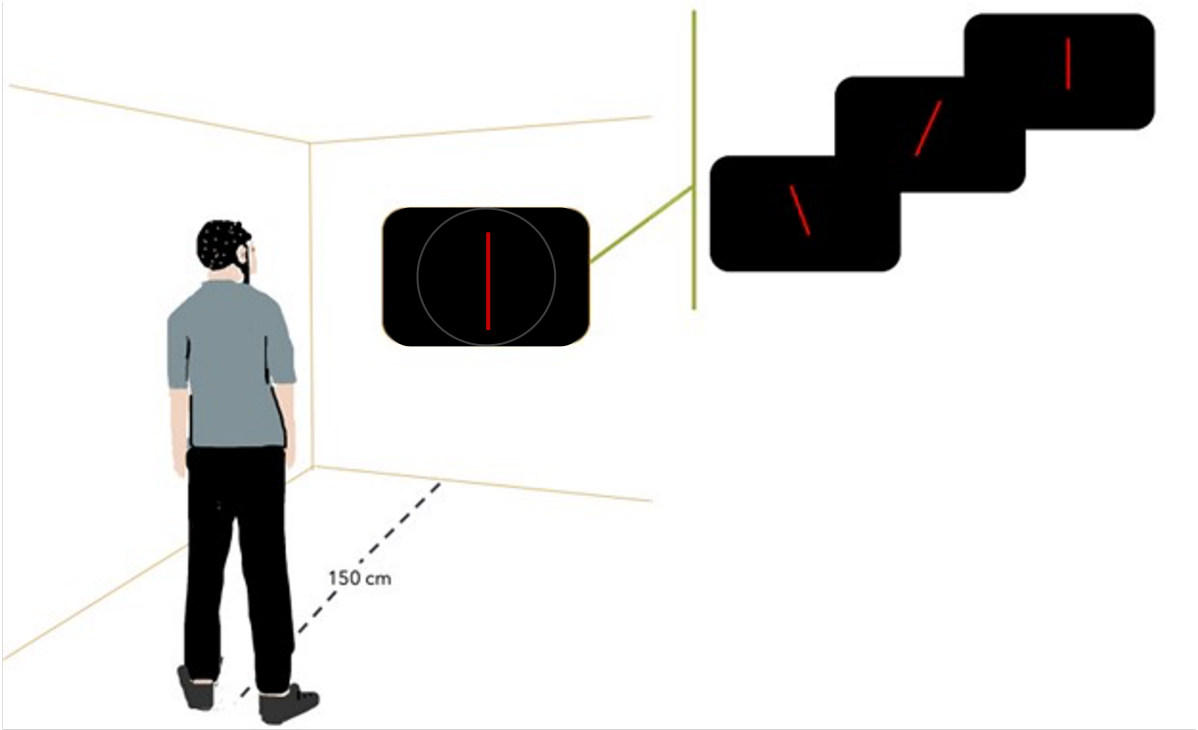

Figure 1. Subjective visual vertical perception tests environment: There should be a distance of 150 cm between the screen on which the experimental pattern is projected and the participant. A black camouflage with a circle-shaped gap in the middle of the screen is used in order not to refer to the verticality of the screen's edges. The participant can only see alerts through the circle-shaped space. In addition, the whole experiment was carried out in a dark environment in order to prevent reference to the quality of the wall lines, ceiling or various objects in the room.

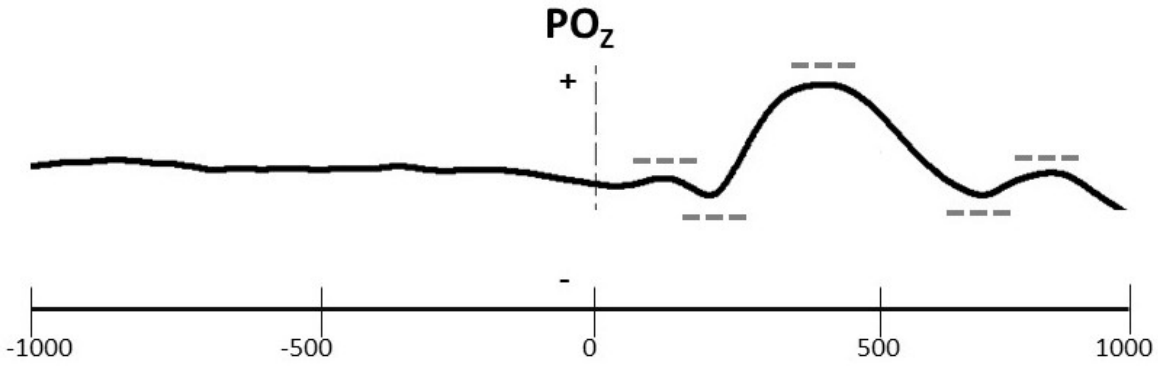

Figure 2. The average (N=12) brain response that occurs after the visual stimulus. The sample brain responses at the POZ electrode of the central parieto-occipital region are shown. The gray dashed lines show the brain response components examined. The moment of stimulation is indicated by the dashed line at "0.0". The horizontal axis is the time axis, 1000 msec before the stimulus and 1000 msec after the stimulus. The bottom side shows the negative direction, and the top side shows the positive direction to show the vertical axis amplitude (μV) values.

ms before and 1000 ms after the stimulus were created and were examined. In these epochs, those with an amplitude greater than ± 50 μV in the EOG electrode channels and those containing noise were eliminated.

The files obtained for each participant were baseline corrected based on the time axis and filtered with a digital bandpass filter with 0.5 - 3.5 Hz limit values (12 dB / oct and zero phase shift, Neuroscan 4.5). After the filtering process, the mean file was created for each individual. In measuring the amplitude of electrophysiological responses, the responses with the greatest amplitude between 0-1000 ms were measured and evaluated in μV. EEG recordings were taken from 64 channels. However, primarily the F3, FZ and F4 electrodes in the frontal region, which is the primary area for cognitive processing and PO3, POZ and PO4 electrodes in the parieto-occipital region, which is the primary area for visual stimuli, were examined. For the comparison between regions, F3-PO3, FZ-POZ and F4-PO4 electrodes were used. Excitation potentials comprise a series of electrical changes in the peripheral and central nervous system and are usually associated with sensory pathways and cognitive processing.

The processing of any external stimulus in our brain is completed within an average of 1000 ms after the stimulus is applied during wakefulness. After the stimulus is applied, different positive and negative peaks appear in the signals recorded by electroencephalography. Accordingly, a negative amplitude represents a decrease, and as a contrary a positive amplitude represents an increase in signal direction after stimulus application in conjunction with electrode recording site (Figure 2). The timing and the polarity of the signals are thus recorded and labeled, which enables further identification of these peaks and relates them to certain sensory and cognitive functions.

Statistical analysis of the data was made with the SPSS 22.0. Since the data did not show normal distribution, nonparametric tests were used. Differences between the two groups were analyzed using the Mann Whitney U test and in-group evaluations with the Wilcoxon test. In all statistical analysis, p values of less than 0.05 (≤ 0.05) were considered significant.

RESULTS

The distribution of demographic characteristics of the participants by groups is shown in Table 1. There was no difference between the groups in terms of age, height, weight, body mass index (BMI) ($p > 0.05$). The Cobb angle of patients with AIS was 32.33° ± 6.70. According to curvature types, the distribution of AIS patients was Lenke 1 in 41.7%, Lenke 3 in 33.3%, and Lenke 5 in 25%. In both AIS and CG, three positive and two negative peaks were observed after applying the stimulus. The peak that appeared in the positive direction 30 to 209 ms after the stimulus was

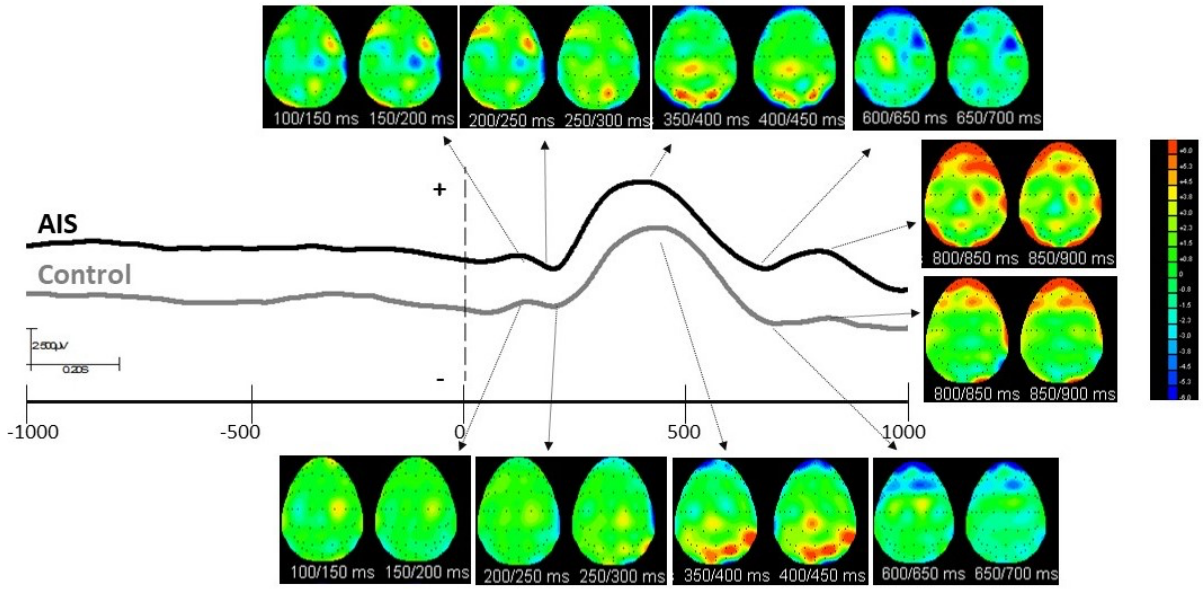

Figure 3. The brain response that occurs after the visual stimulus and topological distributions. Brain responses at the POZ electrode of the parieto-occipital region are shown. Black line indicates patient group (N=12), gray line indicates healthy control group (N=10). The horizontal axis is the time axis, 1000 msec before the stimulus and 1000 msec after the stimulus. The moment of stimulation is indicated by the dashed line at "0.0". The bottom side shows the negative direction, and the top side shows the positive direction to show the vertical axis amplitude (μV) values. The topological distributions are provided in respective time windows as a colormap (red to blue color codes are provided on the right side).

evaluated as the first positive peak, the negative peak at 60 to 313 ms as the first negative, the positive peak at 183 to 500 ms as the second positive, the negative peak at 299 to 799 ms as the second negative, the positive peak at 687 to 948 ms after the stimulus was evaluated as the third positive peak respectively.

In the AIS group, the first positive peak occurs 30 msec to 160 msec after the stimulus, the following peaks were as first negative at 101 to 239 msec, the second positive at 187 to 500 msec, the second negative at 440 to 694 msec, and third positive at 748 to 914 msec (Figure 3).

In the CG, the first positive peak 41 to 209 msec after the stimulus, followed by first negative at 119 to 291 msec, second positive at 190 to 489 msec, second negative at 299 to 799 msec, third positive at 734 to 948 msec (Figure 3).

When the latencies of the brain responses were examined in the frontal region, the first positive peak in the F4 electrode AIS appeared significantly earlier in the CG (p=0.016). The second negative and third positive peaks in POZ and PO4 electrodes in the parieto-occipital region were significantly earlier in the AIS than CG (p=0.011, p=0.025, respectively).

When the amplitude of the brain responses was examined, the amplitude of the third positive peak in all measurement regions was found to be higher in the AIS than in CG (p=0.021 at F3 electrode, p=0.036 at FZ electrode, p=0.030 at F4 electrode, p=0.001 at PO3 electrode, p=0.014 at POZ electrode, p=0.017 at PO4 electrode) (Figure 4).

Topological distribution

In three comparisons (F3-PO3, FZ-POZ, F4-PO4) in the AIS, the first negative peak, second positive and second negative peaks appeared significantly earlier in frontal region than parieto-occipital region (p=0.002 in first negative peak, p=0.002 in second positive peak, p=0.002 in second negative peak in the F3-PO3

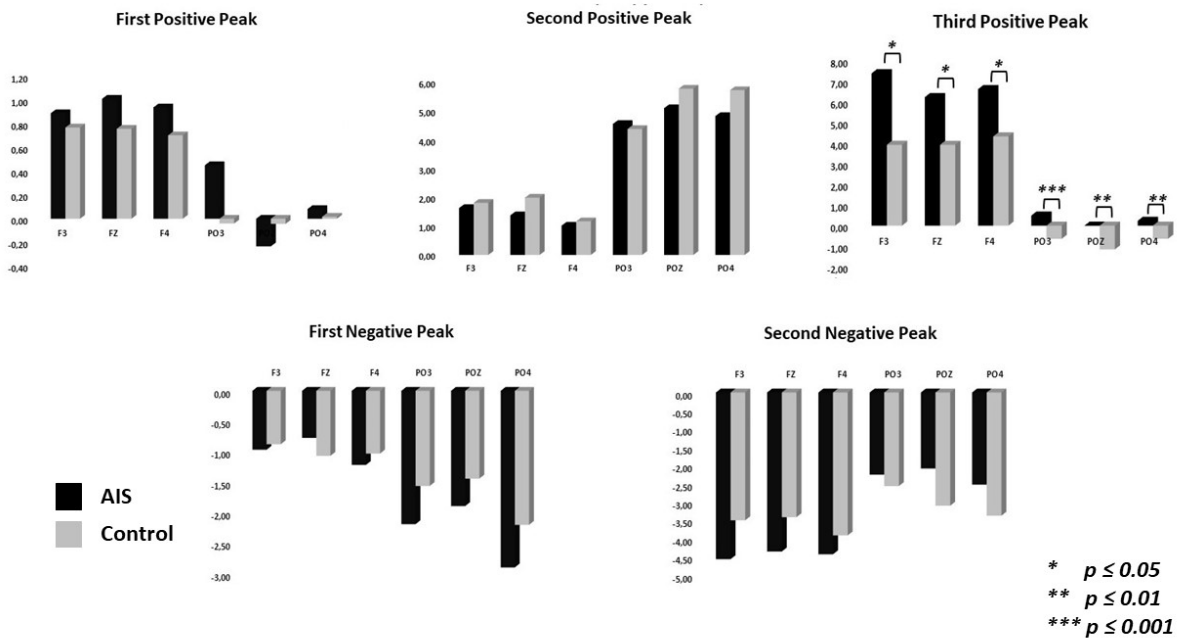

Figure 4. Average values of response peaks after stimulation. y-axis shows the amplitude of the peaks in μV. Gray bars represent control group, black bars represent AIS group The panels are categorized in regard to peaks in consecutive order.

comparison; p=0.002 in first negative peak, p=0.002 in second positive peak, p=0.005 in second negative peak in the FZ-POZ comparison; p=0.041 in first negative peak, p=0.003 in second positive peak, p=0.002 in the second negative peak in F4-PO4 comparison).

In the comparison between the F3-PO3 and FZ-POZ electrodes in the CG, the first positive peak, the second positive peak, and the second negative peak appeared significantly earlier in the frontal region than the parieto-occipital region, whereas in the F4-PO4 comparison, only the second positive peak and the second negative peak appeared significantly earlier than the parieto-occipital region in the frontal region (p=0.008 in the first positive peak, p=0.028 in the second positive peak, p=0.005 in the negative peak in the F3-PO3 comparison; p=0.012 in the first positive peak, p=0.017 in the first negative peak, p=0.009 in the second positive peak, p=0.005 in the second negative peak in the FZ-POZ comparison; p= 0.009 in the second positive peak, p=0.005 in the second negative peak in the F4-PO4 comparison).

In the AIS group, the amplitude of the second positive peak was found to be significantly higher in the parieto-occipital region than the frontal region in the comparison between the F3-PO3, FZ-POZ, and F4-PO4 electrode regions (p=0.002), the amplitudes of the second negative and third positive peaks were found to be significantly higher the frontal region than parieto-occipital regions (p=0.010, p=0.050, p=0.023 in the second negative peaks, p=0.002 in the third positive peaks respectively) (Figure 4).

In the comparison between the F3-PO3, FZ-POZ, and F4-PO4 electrode regions in the healthy CG, the amplitude of the second positive peak in the parieto-occipital regions was significantly higher than the frontal region as in the AIS group (p=0.022, p=0.007, p=0.005, respectively). The amplitude of third positive peaks were significantly higher in the frontal region than parieto-occipital regions (p=0.005) (Figure 4).

DISCUSSION

This study aims to examine the VEPS in AIS in terms of brain responses. For the first time, the experimental design has been utilized in this study to evaluate the alignment related visual evoked potentials of patients with AIS. As the study results showed, the component of late positive brain responses appeared earlier and its amplitudes were

higher in the AIS than in the CG, in all measurement regions.

In the literature, EEG studies on patients with AIS are very limited, except for one they were conducted between 1970-1980s. Besides, EEG records were obtained with a limited number of electrodes (such as 12, 16 electrodes). On the contrary, 64 channels were used in the current study. When the results of the studies were examined, a consensus could not be reached in terms of changes in brain responsiveness in patients with AIS.

Robby et al. and Petersen et al. stated no difference in brain responses between AIS and CG (8, 11). Also, Enslein et al., evaluated the change in beta and theta waves during sleep in their research in AIS. The study stated that they encountered abnormal EEG findings in 2 of 28 subjects and possible abnormalities in 7. However, there was a significant difference in brain responses between patients with AIS and CG in this study like other studies (15). Lukeschitsch et al., Deratakis et al., and Sahlstrand et al. reported that the idiopathic scoliosis group differed significantly from EEG results in a healthy population (9, 10, 16). Also, in previous studies, EEG signals were taken in a sitting or lying position. In current study, EEG signals were received while standing as a first in this respect. The standing posture is more appropriate, especially for the evaluation of visual vertical perception. Accordingly, vertical alignment related real-world experience and body position for perception (e.g. not in supine position) were achieved.

When the studies in the literature were reviewed, no studies evaluated the VEPs in AIS. Hence, they are examined for the first time in this study.

In the literature, there are studies investigating differences between the curvature type and hemispheres as well as examining the EEG signals in scoliosis patients. Pathological EEG results were found in the contralateral hemisphere in AIS with lumbar curvature, in the ipsilateral hemisphere in patients with thoraco-lumbar curvature, and in the bilateral hemisphere in patients with thoracic curvature (10). Pinchuk et al. reported increased bioelectrical activity in the left hemisphere, especially left thalamus (12). In this study the difference between the hemispheres was not examined because the curvature types of the subjects were various, only the anterior and posterior regions of the head were compared.

Surely, there are many general theories in the literature about the way the brain works. In one of these, Basar suggested oscillating neural populations (17, 18, 19, 20). This theory states that the brain exhibits oscillatory activity in different frequency bands, which are respectively called delta, theta, alpha, beta, and gamma. In present study, the delta was investigated by filtering the signals in 0.5-3.5 Hz frequency band.

It is stated in the literature that the delta response after the stimulus is related to a conscious and cognitive function, to be obtained during the decision-making phase, and is the result of target stimulus recognition process (21, 22, 23, 24). In addition, if the task given involves decision making the potential responses related to visual and auditory events are more pronounced. In this study, the second positive component, occurring 187-500 msec after the stimulus in AIS, and 190 to 489 msec after the stimulus in CG, is the higher peak after the stimulus. The reason that there was no difference in latencies and amplitudes between CG and AIS may be because the visual lines were applied at different angles, and the processes of recognizing and comparing stimuli were similar in both groups. The reason that the second positive peak appears earlier in the frontal region and its amplitude is higher can be explained that the frontal region is responsible for higher-level cognitive processes.

In AIS, third positive peak occurs 748-914 msec after the stimulus, while in CG at 734-948 msec. The late-positive brain responses component appeared earlier in AIS group in the parieto-occipital region compared to CG, and its amplitudes were higher in all measurement regions (F3, FZ, F4, PO3, POZ, and PO4 electrodes) than in CG.

In studies conducted with electroencephalography in sleep and wakefulness processes, it is known that there are late components in the brain (25, 26). It has been shown that these late components, which occur after the stimulus is applied, are related to complex cognitive processes such as conflict monitoring in wakefulness (26, 27). In this study, the amplitudes of the third positive peak, which is the late response component, were found to be different in AIS and CG. In the study, the stimuli were randomized to the participants in the range of ± 15°in the experimental design. Since the vertical perceptions of the group with AIS are different compared to the healthy CG, the group with AIS may have attributed more resources in the posterior frontal axis when

processing stimuli in their brains. Hence there has been a different degree of frontal and occipital potentials as can be found in the color maps and the statistical data above. These showed that Parieto-Occipital areas as well as Frontal lobes were more involved in AIS to enable a similar task, therefore the patient groups' performance have been apparently less effective than of normal subjects. Furthering from our initial results, this sensory-cognitive domain needs further studies to paint a full picture of complex cortical dynamics in AIS.

This study also had a number of limitations. Firstly, the study was not designed according to curve types of patients with AIS. Secondly, the values of the subject visual vertical perception of patients with AIS were not determined and the experimental design was not based on the perceptions of the participants. On the positive side, our study constitutes a first as the experimental design, the position where the EEG is applied, and the method used during EEG analysis. These are the first use of 64 EEG channels encompassing the standing posture as a dynamic process, and the use of visual evoked potentials during EEG analysis for the first time in patients with AIS.

One of the major problems in scoliosis is false body perception, which may differ due to the type of curve. Due to the comparatively small number of our sample group, the distribution between groups as a result of classification was not possible for further statistical analysis. However, this remains an important issue that should be investigated in our future studies.

CONCLUSION

In the light of these results, the AIS denotes a series of complex phenomena where the brain dynamics remark a rather disturbed cognitive sensory resource management. The experimental design used in this study can be suggested as an objective measurement method in evaluating the vertical visual perception of patients with AIS. In addition to the subjective visual perceptions of patients with AIS, objective vertical perceptions can also be evaluated with these methods. In addition, with the method used in this study, the effect of treatments applied to patients with AIS in terms of brain responsiveness can be evaluated. With the measurement methods used in this study, a new perspective has been gained for the clinical evaluation of patients with AIS.

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Conflict of interests: None.

Ethical approval: Ethics committee approval for the research was obtained from the Non-Interventional Research Ethics Committee of Dokuz Eylul University with the decision number 2013/42-07, dated 21.11.2013 and protocol number 1217-GOA. For the changes made in the method and consent forms, it was taken again with the decision number 2015/16-29, dated 18.06.2015 and protocol number 1217-GOA.

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RESEARCH ARTICLE

INVESTIGATION OF ORAL MUCOSITIS INCIDENCE AND RISK FACTORS IN PATIENTS RECEIVING CHEMOTHERAPY

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ABSTRACT

Purpose: Oral mucositis is a common complication of cancer treatment that may negatively impact the patient's cancer treatment outcome. This study was done to determine the incidence of oral mucositis development and risk factors in patients receiving chemotherapy.
Material and Methods: This cross-sectional study included 150 participants undergoing outpatient cancer chemotherapy. To determine the development of oral mucositis, the participants were evaluated for the first course of chemotherapy (day 0) and the next course of chemotherapy treatment (day 14). 'Patient Information Form' and the World Health Organization' Mucositis Grading Scale' were used to collect data for the study. Descriptive statistics, and logistic regression were used to analyze the results.
Results: According to oral mucosal assessment, incidence of oral mucositis was 27.3%. The mean onset and the mean recovery of oral mucositis were 4.16 ± 2.13 days and 8.72 ± 2.32 days. The most common oral problems were mouth dryness (53.3%), dental caries (44%), and decreased sense of taste (32%). In the oral mucosal assessment performed on the 14th day, 9 patients were found to be grade 1. Patients with a history of mucositis (OR = 5.76, CI = 2.33–14.24, p = 0.00) showed a significantly higher incidence of oral mucositis.
Conclusion: In this study, the incidence of oral mucositis and risk factors that may affect the development of oral mucositis in patients receiving chemotherapy were investigated. Mucositis history was found as a risk factor in oral mucositis development. Early recovery of oral mucositis after chemotherapy was observed. Therefore, patients should be followed up in the early period after chemotherapy.

Keywords: Chemotherapy, oral mucositis, mucositis, risk factors.

INTRODUCTION

One of the common complications of cancer treatment is oral mucositis that negatively impacts the patient's cancer treatment outcome. Oral mucositis affects the entire mucous membrane-covered surface from the mouth to the rectum and usually begins as early as 3 to 4 days after the administration of chemotherapy and generally peaks in severity 7 to 14 days later (1,2). Many drugs used in cancer treatment are known to increase the risk of mucositis. Due to the lack of standardized scoring criteria, tumor location, and different treatment regimens the prevalence and incidence data of oral mucositis vary (1,3).

A study conducted on chemotherapy protocols showed that the incidence of oral mucositis ranged between 6.1% and 90% (4). The results of the study showed the effects of chemotherapy regimens on the

development of mucositis. According to the study, the incidence of ulcerative mucositis is up to 70%. (5). Although the diagnosis and treatment are similar, patients are not equally at risk in oral mucositis development. In addition to the chemotherapy and radiotherapy treatments given, some individual characteristics of the patient facilitates the development of mucositis. Risk factors associated with the patient are more complex and less defined (2,6-8). Although the impact of patient-related factors on the development of oral mucositis in adults is obvious, findings are inconsistent and very few appear to be evidence based (6,9-11).

There is no proven gold standard for the prevention and/or treatment of oral mucositis. Although mucositis is a common complication of cancer treatment, the quality of life of the patient can be improved by providing comfort. Thus, oral diagnosis and effective oral care can improve the quality of life (12,13). As it is very important to assess the associated risk factors of mucositis for its prevention and management; therefore, additional research is needed to identify these risk factors (14,15). This prospective cohort study is carried out to determine the incidence and risk factors for oral mucositis in patients receiving chemotherapy.

Research Questions:

- Do the sociodemographic characteristics and features related to oral hygiene affect the development of oral mucositis?
- Do the disease and treatment-related characteristics affect the development of oral mucositis?

MATERIAL AND METHODS

Study Design and Sample

Outpatients receiving chemotherapy from the daily chemotherapy unit of a training and research hospital in the west of Turkey from April to August 2016 were selected for this a cross-sectional study. All the patients enrolled for the study were over 18 years of age, agreed to participate in the study, and underwent the first course of chemotherapy. Patients who had impaired oral mucous membrane integrity were excluded from the study. Power analysis on the G-Power statistical program based on Type 1 error of 0.05 and Type 2 error of 0.20 (80%) was used to determine the sample size of the study, which was 139. Logistic regression analysis results from the study conducted by Salvador (2005) were used (16). A total of 166 patients were reached, but 16 refused to participate in the study. A total of 150 patients were included in the study.

Data Collection and Research Tools

The Patient Information Form

This form was prepared by the researchers, which consisted of both personal characteristics (age, gender, diagnosis, education level, income status, presence of chronic illness, body mass index) and illness/oral health characteristics (smoking status, dental caries, dental brushing, oral care frequency, sense of taste, dryness and cracking on the lips, chemotherapeutic agent, number of chemotherapy courses, chemotherapy history and history of oral mucositis development).

The World Health Organization Mucositis Grading Scale

Based on the anatomical variation of the oral mucous membrane and rating at the scale of “0” to “4” according to the mucositis formation, classification was made. Grade “0” indicates no change; Grade “1” shows soreness or erythema; Grade “2” shows erythema, ulcers, patient can swallow solid diet; Grade “3” shows ulcers, extensive erythema, and Grade “4” denotes mucositis to the extent that alimentation is not possible (7,17).

The applicability of the questionnaires was evaluated by conducting a pilot study. Patients in the pilot study were not included in the study data. Data were collected by the first researcher through face-to-face interviews. The patient provided the demographic and oral care information, and the hospital database provided the data regarding the clinical condition (diagnosis, chemotherapeutic agent, number of chemotherapy courses, chemotherapy history). Potential participants who met the inclusion criteria were informed about the study when they came to receive the first chemotherapy course (day 0). On receiving their consent, their mouth was evaluated using the ‘World Health Organization Mucositis Grading Scale’. Intraoral examination was conducted using the ‘World Health Organization Mucositis Grading Scale’ when patients came to receive their next course of chemotherapy (day 14), and ‘Patient Information Form’ was used to collect all information. Then, the inner parts of the mouth were examined using a light source. Filling out the forms for the first and second follow-up and do the intraoral examination took about 30–40 min. All intraoral assessments were performed by the first researcher to eliminate interobserver variability. As per the

Table 1. Sociodemographic and Treatment Characteristics of the Patients (n: 150).

Characteristic	n	%
Gender		
Female	96	64.0
Male	54	36.0
Income Situation		
Low	79	52.7
Middle	71	47.3
Education Level		
Illiterate/Primary education	129	86.0
High school/University	21	14.0
BMI		
Thin/Normal	47	31.3
Overweight/obese	103	68.7
Chronic Diseases		
Yes	74	49.3
No	76	50.7
Smoking		
Yes	16	10.7
No	134	89.3
Alcohol use		
Yes	2	1.3
No	148	98.7
Diagnosis		
GIT cancer*	65	43.4
Gynecologic cancer**	41	27.3
Breast cancer	26	17.3
Other diagnoses***	18	12.0
Chemotherapeutic agent**		
5-FU	57	38.0
Paclitaxel	44	29.3
Carboplatin	34	22.7
Other drugs*****	146	97.3
Chemotherapy History		
Yes	124	82.7
No	26	17.3
Mucositis History (n:124)		
Yes	57	46.0
No	67	54.0

***: Stomach, colon, rectum, and pancreas cancer. **: Cervical, ovarian, fallopian tube and endometrial cancer**
*****: Renal, prostate, lung, bladder, head and neck cancer. ****: Each drug has been used by more than one patient.**
*******: Cisplatin, cyclophosphamide, doxorubicin, oxaliplatin, gemcitabine, and irinotecan**

chemotherapy protocols, patients came to the unit for treatment every 14 days. Therefore, intraoral assessments of the patients were carried out twice, during the first (day 0) and the second course of chemotherapy (day 14).

Data analysis

SPSS 22.0 program was used to analyze data. The descriptive characteristics of patients were evaluated using the percentage test. The risk factors affecting oral mucositis development were examined using logistic regression analysis. The variables related to demographic characteristics, treatment, and oral care in the model were chosen by considering univariate analysis and were in line with the literature (9,15,18-20). For all analyses, $p < 0.05$ was accepted as the level of significance.

Ethical Considerations

The non-interventional ethics committee of the university and a training and research hospital in İzmir where the study was conducted approved the study (Dokuz Eylül University Non-Interventional Researches Ethics Committe, Date: 07.04.2016,

Decision no: 2016/09–33). The verbal and written informed consent were provided from patients. Research and publication ethics were complied with in the article.

RESULTS

This study examined a total of 150 patients. The mean age of the participants in the study was 57.05 ± 10.96. Of the patients, 64% were female, 52.7% had less income than their expenses, 64.6% were primary school graduates, 34.7% were overweight, 49.3% had chronic diseases, 89.3% did not smoke, 98.7% did not use alcohol. The patients had gastrointestinal cancer (42.7%), gynecologic cancer (26%), and breast cancer (17.3%). When the most used chemotherapeutic agents by patients were taken into account, 38% of the patients were treated with 5-FU, 29.3% with paclitaxel, 22.7% with carboplatin (Table 1). Of the patients, 44% had dental caries, 32% had a decreased sense of taste, 53.3% had mouth dryness, 25.3% had decreased appetite, and 18.7% had dry and cracked lips. Of the patients, the rate of those who brushed their teeth once a day and those who never did were found to be the same (32%). Of the individuals, 30% did oral care once or twice a day while 22% did not practice oral care at all. It was found that 82.7% of the patients had received chemotherapy previously and among these (n = 124), 46% had a history of mucositis. According to oral mucosal assessment, 94% of the patients were found

Table 2. Oral Care Characteristics of the Patients (n: 150)

Characteristic	**n**	**%**
Dental caries		
Yes	66	44.0
No	84	56.0
Decrease in the sense of taste		
Yes	48	32.0
No	102	68.0
Dryness in mouth		
Yes	80	53.3
No	70	46.7
Decrease in appetite		
Yes	40	26.7
No	110	73.3
Dry and cracked lips		
Yes	28	18.7
No	122	81.3
Dental brushing frequency		
Never	48	32.0
Once a day	48	32.0
Twice a day	39	26.0
Three times a day	15	10.0
Frequency of oral care		
Never	33	22.0
Once a day	45	30.0
Twice a day	45	30.0
Three times a day and more	27	18.0
14th day Oral Mucositis Grading Score		
Grade 0	141	94.0
Grade 1	9	6
Development of Oral Mucositis within the 14-day period		
Yes	41	27.3
No	109	72.7
Variable	**$\overline{X}$ ±SS**	
Start after chemotherapy (days)	4.16 ±2.13	
Ending after chemotherapy (days)	8.72 ±2.32	

to be grade 0 on day 14. However, oral mucositis developed and recovered in some patients within a period of 14 days. Thus, 27.3% of oral mucositis incidence is presented in Table 2.

The development of mucositis within the 14-day period was examined, and the mean starting day and the mean ending day of oral mucositis were found to be 4.16 ± 2.13 days and 8.72 ± 2.32 days. The risk factors affecting the oral mucositis development were determined using logistic regression analysis. According to the logistic regression analysis, age, gender, chronic disease, smoking status, chemotherapy history, dental caries, dental brushing frequency, oral care frequency and body mass index were not found to be risk factors for the development of oral mucositis. However, mucositis history was found to be a risk factor in the development of oral mucositis (OR = 5.766, CI = 2.33–14.24, p = .000) (Table 3).

DISCUSSION

Oral mucositis is a common problem seen in patients receiving chemotherapy. The examination of studies on its incidence show that the related literature has spread over a wide range (4). The study by Wilberg et al., (2014) reported that 12% of patients had grade 1–2 (21). The incidence of oral mucositis was found to be 27.3% in our study, whereas 51.7% was reported in the study by Çakmak and Nural (2019) (22). In another meta-analysis, the incidence of oral mucositis ranged from 20% to 80.4% (23). The results of our study are consistent with the literature and it has been revealed that mucositis is an important problem in patients receiving chemotherapy.

After chemotherapy, oral mucositis begins on days 3–4th and peaks on days 7–14th (1). The study by Vokurka et al., (2011) showed that the mean onset of oral mucositis was 4 days, and the end was 11 days while the study by Cheng Fong et al., (2011) showed that the onset of oral mucositis as 4.7 ± 2.7days and the duration of mucositis was 6.3 ± 4 days (9,11). This study showed that the onset of oral mucositis was 4.16 ± 2.13 days, and the end was 8.72 ± 2.32 days. The results showed that the day oral mucositis ended was earlier compared to the literature.

Some studies found a significant relationship between age and oral mucositis, while others did not. The risk of oral mucositis was high in patients □ 60 years of aged, as per the study by Yang et al., (2013) (10). Another study showed that the risk of oral mucositis increases with age (22). However, few studies did not show any relationship between age and oral mucositis (11,16,24,25). Similarly, there was no significant correlation between age and oral mucositis in this study. The fact that our result was not related to age is thought to be due to the characteristics of the study group.

This study showed gender was not a risk factor for oral mucositis development. Similarly, other studies did not show any correlation between gender and oral mucositis (11,16,24,26,27). However, according to the studies the incidence of oral mucositis developed by women is higher (10,19,28,29). Similarly, another study also reported a higher risk of oral mucositis in females than that in males and interpreted that the metabolism of 5-FU might differ according to gender (30).

In this study, no relationship was found between cancer types and the risk of oral mucositis. Similarly, the study by Çakmak and Nural (2019) showed that cancer types did not affect the incidence of oral mucositis (22). The study by Nishimura et al., (2012)

Table 3. Distribution of Risk Factors Affecting Oral Mucositis Development in Patients

Risk Factor	OR	CI		p
Age	1.012	0.98	1.04	.526
Gender	2.104	0.93	4.71	.073
Diagnosis	0.974	0.88	1.06	.562
Mucositis history	5.766	2.33	14.2	**.000**
Chronic disease	0.741	0.36	1.53	.415
Smoking	1.700	0.58	5.01	.338
Chemotherapy history	0.816	0.32	2.05	.666
Dental caries	0.491	0.23	1.04	.065
Dental brushing frequency	1.036	0.71	1.50	.850
Oral care frequency	1.188	0.83	1.70	.347
Body mass index	0.975	0.91	1.03	.418

OR = Odds ratio, CI = confidence interval

showed that the risk of oral mucositis was higher in breast cancer patients (31). Different results may have been obtained due to the diagnosis in different stages, changes in treatment protocols, and individual differences (22).

Shouval et al., (2019) found that low body mass index was a risk for oral mucositis (18) while Robien et al., (2004) reported a body mass index of ≥ 25 as a risk factor for oral mucositis (26). However, some studies did not find body mass index as a risk factor for oral mucositis (11,16). In this study, the regression analysis showed that body mass index was not a risk factor for oral mucositis development.

The risk of mucositis is triggered by factors such as poor oral hygiene, dental problems, high levels of microorganisms in the mouth flora, and a decrease in salivary secretion (15,32). Ramirez-Amador et al., (2010) found no significant relationship between oral hygiene and mucositis (24). As for this study, dental caries, oral care, and tooth brushing were not found to be risk factors for oral mucositis. The results showed that the most common oral problems were mouth dryness (53.3%), dental caries (44%), and decreased sense of taste (32%). Like our study results, the most common oral complications reported in other studies were mouth dryness and changed sense of taste (21,22). It is thought that the risk factors found should be taken into account by nurses in oral care planning.

Individuals with a history of chemotherapy and mucositis are at higher risk of developing oral mucositis as they are more susceptible to oral mucosal cell damage (6). In our study, no correlation was found between the history of chemotherapy and the development of oral mucositis. Similarly, studies by Nishimura et al., (2012) and Çakmak & Nural (2019) did not find any relationship between chemotherapy history and the development of oral mucositis (22,31). However, regression analysis in this study showed that a history of oral mucositis and previous chemotherapies increased the risk of oral mucositis to 5.76-fold. Cheng Fong et al., (2011) and Vokurka et al., (2011) reported that the development of oral mucositis in previous chemotherapies was a risk factor for oral mucositis (9,11). Considering all these results, it is thought that it may be important to know the chemotherapeutic agents that patients are exposed to in oral care planning.

Smoking has an adverse impact on tissue healing as it affects microcirculation (6). The risk of oral mucositis was increased due to smoking (22), whereas other studies had different conclusions. Vatca et al., (2014) found that the incidence of oral mucositis was lower in smokers since the activity and percentage of keratinized cells in the buccal mucosa of smokers increased (27). Smoking was not found to be a risk factor in this study. In addition, many studies do not correlate smoking with the development of oral mucositis (10,24,26). Findings may be related to characteristics such as the patient's smoking frequency, cigarette content, and oral care after smoking.

Many of chemotherapy agents used for cancer treatment increase the risk of mucositis (6). Studies conducted on this topic also demonstrate differences. A meta-analysis study (n = 2448) showed about 14% of the incidence of severe mucositis (grade 3–4) was related to 5-FU (25). The study by Shouval et al., (2019) found correlation between oral mucositis and methotrexate (18). Cheng Fong et al., (2011) reported that patients who received methotrexate or adriamycin-based therapy developed oral mucositis frequently (9). The study by Vokurka et al., (2009) found that high-dose melphalan-containing regimens increased oral mucositis development (33). This study showed no correlation between the chemotherapy agents and the development of oral mucositis. It is thought that the risk of oral mucositis development depends not only on the chemotherapy agent but also on the duration and the dose of chemotherapy.

CONCLUSION

This study examined the incidence of oral mucositis and risk factors that may influence oral mucositis development in patients receiving chemotherapy. Mucositis history was found as a risk factor in oral mucositis development. The incidence of oral mucositis was 27.3%. Most of the patients were grade 0 on day 14 after chemotherapy, but oral mucositis ended before day 14 in the patients. Therefore, it is important to do early follow-up of patients after chemotherapy and manage oral mucositis. Health professionals should give importance to patient training and follow-up in consistent with clinical guidelines.

Limitations

This study has a few limitations. First, the patients were treated on an outpatient basis, so they visited on day 14 in line with their chemotherapy protocols. Therefore, intraoral assessments could not be

conducted before day 14. Patients were asked regarding the beginning and end of oral mucositis. Second, each patient was in a different stage, different treatment procedures were being applied, and the oral care practices of the patients differed. Finally, the risk of oral mucositis may increase with increasing duration and number of chemotherapy courses. In this study, patients were not followed up after the 14th day. Therefore, longer patient follow-up is recommended in future studies. Our results may not be generalisable and need to be further investigated in a larger cohort.

Implication for Nursing Practice

Mucositis is an important complication that negatively affects the quality of life because it causes many psychological, social and economic problems in the patient. There is no standard treatment or care practice to prevent mucositis. Effective management of oral mucositis can be sustained by continuing nursing care during cancer treatment. It should not be forgotten that patients with a history of mucositis are in the risk group, oral health of these patients should be evaluated regularly during chemotherapy and changes in the mouth should be noticed in the early period. The mouth area should be brought to a full healthy level before chemotherapy. Identification of patients with a high risk of mucositis is very important in order to prevent complications that may occur in the patient. It will also alleviate the clinical, psychosocial and economic burdens that may occur during the chemotherapy process. The important role of mucositis risk estimation in providing individualized cancer care should not be forgotten. It is expected that the importance given to oral care by patients who have knowledge about oral care needs will increase.

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RESEARCH ARTICLE

THE EFFECT OF KINESIO TAPING TENSION ON THE PRESSURE-PAIN THRESHOLD AND PAIN TOLERANCE: A RANDOMIZED, CONTROLLED, DOUBLED-BLINDED TRIAL

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ABSTRACT

Purpose: To our knowledge, no study has demonstrated the effects of Kinesio Taping (KT) tension on pressure-pain threshold and tolerance. The aim of the study was to investigate the effect of KT tension tensions on pressure pain threshold and tolerance.
Material and Methods: A double-blind, randomized controlled study was conducted with 90 healthy male subjects with an average age of 21.04 ± 2.0 years. The subjects were randomized into four groups: 0% tension (n=23), 50% tension (n= 24), 75% tension (n=22) and 100% tension groups (n=21). The KT was applied from distal to proximal, exposing the lateral epicondyle region on the dominant side. Pressure pain threshold and pain tolerance were measured using digital algometer over the lateral epicondyle. Measurements were carried out, before, immediate after and 30 minutes after KT.
Results: There was no statistically significant difference between the groups in terms of PP threshold, pain tolerance and intensity ($p>0.05$). There was a significant in-group difference only in the 100% Tension Group in terms of PP threshold ($p<0.05$). On the other hand, a significant difference was observed in the 0% tension and 50% tension groups on the pain severity measurements ($p<0.05$).
Conclusion: The results demonstrated that the KT at different tensions did not affect the pressure pain threshold or tolerance. The outcomes also considered the efficacy of low- and high-tension KT on pain tolerance and severity, respectively. A further study should investigate the pain threshold and tolerance in clinical cases with a long-term follow-up.

Keywords: Algometer; kinesio taping, pressure pain threshold, pain tolerance

INTRODUCTION

Kinesio Taping (KT) is a unique taping approach based on the natural healing physiology of the human body, providing support and stability to muscles and joints without affecting joint motion (1). In recent years, KT has become increasingly popular in treating musculoskeletal injuries and neuromuscular rehabilitation (2). KT has been reported to provide

recovery of the elastic fibres. Pain and spasm have been notified to decrease with KT application (3, 4).

KT provides traction to elevate the epidermis. This mechanical effect reduces the pressure on the receptors under the dermis, reducing nociceptive stimuli (5). Different mechanisms explain the role of KT on pain (e.g., reducing oedema and inflammation, gate control theory, stimulation of descending inhibitory pathways, and regulation of superficial and deep fascia functions) (6, 7).

KT can stretch up to 30-40% of its resting size in the longitudinal direction and has approximately the same weight/thickness as the skin. KT also can be applied with two different techniques as basic and correction. Furthermore, different tension techniques are used in clinical conditions. The amount of tension generally applied in the clinic as follows; 100% (full tension), 75% (high tension), 50% (medium tension), 15-25% (light tension), 0-15% (very light tension) and no tension (3).

The effect of KT applications involved at different tensions on pain has been demonstrated. However, there is insufficient data on pain threshold and tolerance. Pain threshold is defined as the intensity of the slightest stimulus that causes pain in the person. The pressure-pain (PP) threshold is the minimal pressure (force) that causes pain (8). PP threshold measurement reflects nociceptive sensitivity in superficial and deep tissues (9). Pain threshold assessment is more complex than assessing other sensory thresholds due to the concept of pain and human physiology. For the pain threshold, the individual should distinguish between painful and painless sensations instead of two types of sensation (10).

Pain tolerance is often more particular and inter-individual than pain threshold. Pain tolerance is commonly influenced by prejudice and experience. Evaluation of pain-related comprehensive parameters (pain threshold and tolerance) with objective methods is critical in clinical situations requiring physiotherapy and rehabilitation, both in determining the effectiveness of the treatments applied and in giving personalized pain treatment (11, 12).

Although the positive effect of KT on reducing pain is widely comprehended in clinical practice, the correct tension of KT on pain threshold and tolerance are not well-studied (13-15). To our knowledge, no study has demonstrated the effects of KT tension on pressure-pain threshold and tolerance. The aim of the study was to investigate the effect of KT tension tensions on pressure pain threshold and tolerance.

MATERIAL AND METHODS

Study Characteristics and Sample

A double-blind, randomized controlled study included 147 healthy male volunteers. The study was carried out in accordance with the ethical principles and the Helsinki Declaration. The study protocol was approved by the ethics committee of Muğla Sıtkı Koçman University Human Research Ethics Committee (Date: 06.10.2018, Decision no: 152). The study protocol was submitted to clinicaltrials.gov ((NCT04263077). The research was supported by Muğla Sıtkı Koçman University Scientific Research Projects Coordination Unit (Project No: 19/079/01/3/4).

Exclusion criteria of the study were; (1) having a diagnosis and treatment of lateral epicondylitis, (2) any neurological or systemic disease that impairs sensation/pain perception, (3) having a disease (e.g., diabetes, rheumatoid arthritis, peripheral vascular disease), (4) elastic taping skin sensitivity, (5) open wound, ulcer, fungal infection in the area to be taped, (6) exposure to the upper extremity and/or cervical region injury in the last six months

Sample Size

The sample size was calculated using the effect size (ES) and standard deviation (SD) values of a similar study (16). The following formula was used;

(1) Alpha (Bidirectional)=0.05, Beta=1-0.80 = 0.20
(2) Standardized ES = ES / SD = (10.7-8.9) / 2=0.9
(3) Sample Size = 16 / (Standardized ES) * 2= 20

Consequently, 20 cases were required in each group. A minimum of 22 cases were included in the groups considering the possibility of loss (10% drop-out rate) in the number of cases.

Recruitment, Randomization and Blinding

The study was carried out with healthy volunteer male students studying at Muğla Sıtkı Koçman University Faculty of Health Sciences. Participants were informed before the study, and their consent was obtained. First, 147 healthy volunteer individuals were informed about the study. Forty-seven individuals (33 did not meet the eligibility criteria, 14 did not want to participate in the study) were excluded due to various reasons (Figure 1). One hundred male

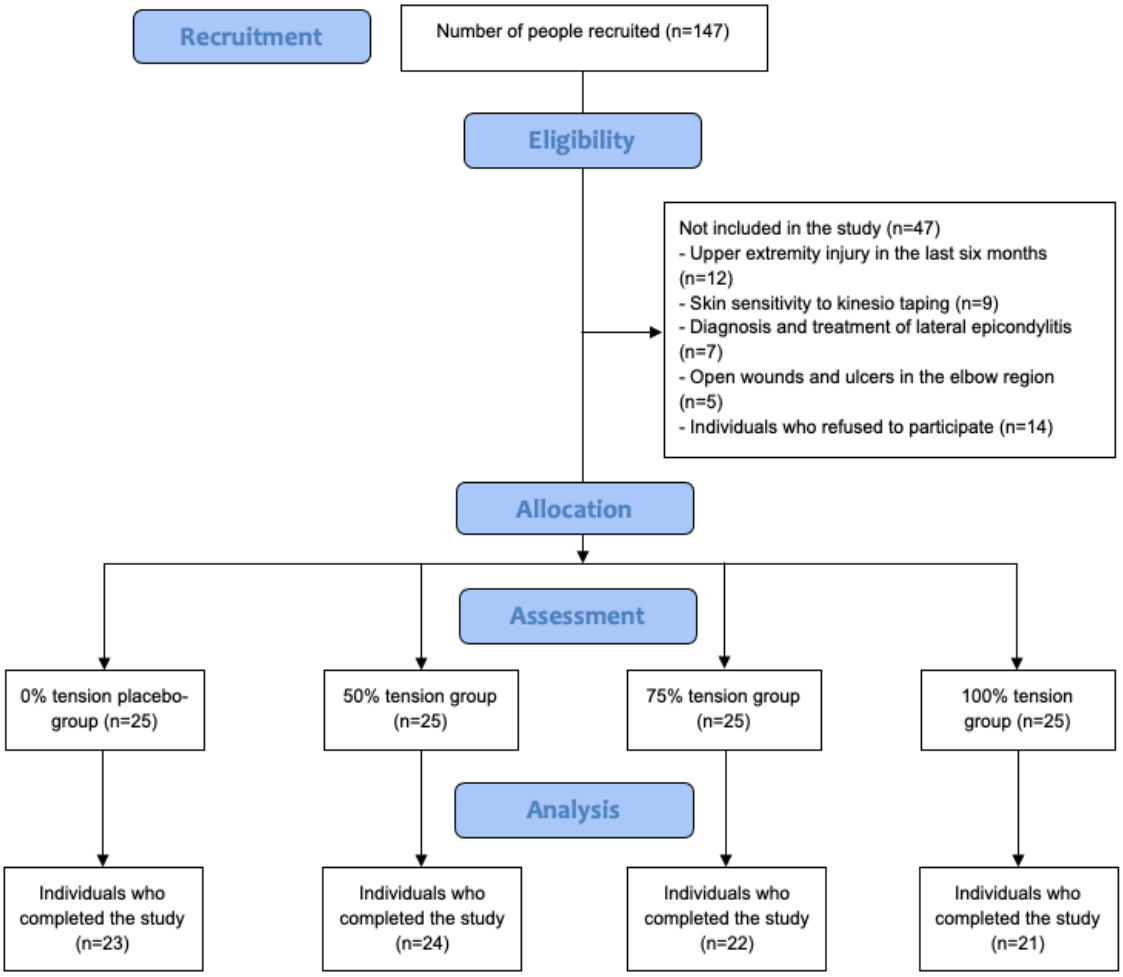

Figure 1. CONSORT flow diagram of the study

individuals were randomized using the Microsoft Excel Office (v16, Microsoft Corporation, Washington) program with a simple randomization method. Twenty-five people in each group were assigned to the intervention arms: (1) 0% tension group, (2) 50% tension group, (3) 75% tension group, (4) 100% tension group. Due to the pandemic, 2 cases in the 0% tension group, 1 case in the 50% tension group, 3 cases in the 75% tension group and 4 cases in the 100% tension group could not continue in the study. The cases and evaluator of the study were blind.

Data Collection

The individual characteristics of the participants were recorded. In order to test the presence of allergic reaction/sensitivity, KT adhered to the inner surface of the forearm without tension. Cases showing sensitivity or allergic reactions resulting from the initial test were excluded. PP threshold, pain tolerance and intensity assessments were conducted before, immediately after, and 30 minutes after KT. All measurements were applied to the lateral epicondyle region three times and averaged. A 60-second rest period was set between each measurement to avoid temporal sensitization (17). Measurements were performed by a physiotherapist who was blind to KT tensions and had no previous clinical experience in the taping technique.

Pressure-Pain Threshold Assessment

The "J Tech Commander Digital Algometer" (J Tech Medical Industries, Utah, USA) was used for PP threshold measurement. Before using the algometer, the patients were informed about the device and measurements. Pressure and pain sensations were tested on individuals' other body areas. The subjects were placed in a sitting position with their elbows

slightly flexed and their backs supported. The tip of the rubber-coated 1 cm2 probe of the algometer was placed perpendicular to the lateral epicondyle region, and pressure was applied. For the PP threshold value, the subjects were asked to say "stop" at the first moment when the pressure sensation turned into pain, and the probe was immediately withdrawn. At this point, the value read from the algometer was recorded as the pressure pain threshold value (18). It was ensured that the subjects did not see the screen of the algometer device while measuring (Figure 2).

Pain Tolerance Assessment

The same device was used for pain tolerance assessment. The tip of the rubber-covered 1 cm2 probe of the algometer was placed perpendicular to the lateral epicondyle region. The pressure was applied to assess maximum pain tolerance. The probe was withdrawn when the patients could not tolerate pressure. The highest value was recorded as pain tolerance (19) (Figure 2).

Pain Severity Assessment

The pain intensity felt at the PP threshold level was evaluated with the Visual Analogue Scale (VAS) (20). the participants marked the severity of their pain on a 100 mm line. VAS assessment was conducted immediately after PP threshold measurement. The average of three repetitive measurements was recorded.

Intervention

Kinesio Taping

5cm x 5m beige-coloured KinesioTex Gold (NM – GKT15024, Kinesio Holding Corporation, Albuquerque) was used for KT. The diamond shape taping technique on the lateral epicondyle of the subject (18, 21) regarding the groups as follows: (1) 0% tension group, (2) 50% tension group, (3) 75% tension group, (4) 100% tension group. The physiotherapist who conducted the interventions had a KT performer certificate from The Kinesio Taping Association International (KTAI).

The diamond shape technique used four "I tape" (2.5 cm x 12 cm). The middle points of the bands were stretched according to the tension groups' amount of tension. The ends of the tapes overlapped without tension. KT was applied from distal to proximal, exposing the lateral epicondyle area. In 50% Tension Application Group, 12 cm. One centimeter holding margin was measured from the ends of the long "I band". The 10 cm section in the middle was extended by 20% of its length and brought to 12 cm. The ten cm section in the middle was extended 30% of its length and brought to 13 cm in the 75% tension group. In the 100% tension group, the remaining 10 cm was extended to 40% of its length and brought to 14 cm, and then it was taped according to the diamond shape technique. The 0% tension group received the

Figure 2. Pressure-pain threshold and pain tolerance assessment

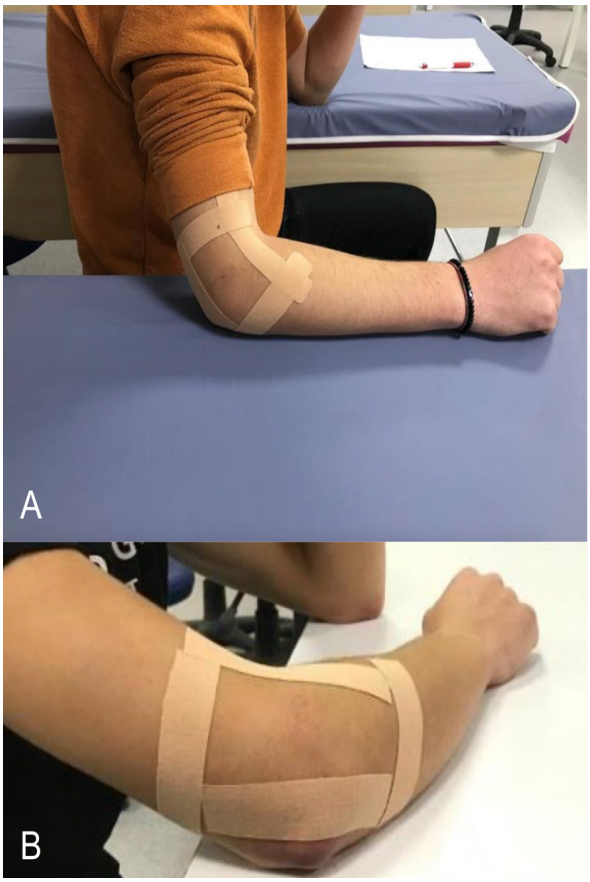

Figure 3. Taping techniques (a: 0% tension, b: intervention group)

Table 1. The comparative baseline characteristics of the groups

	0% tension (n=23)	50% tension (n=24)	75% tension (n=24)	100% tension (n=24)	p
Age (years, mean±SD)	20.78±1.76	20.79±1.79	21.45±2.20	21.19±2.29	0.62
Boy (meter, mean±SD)	1.78±0.07	1.76±0.07	1.78±0.06	1.77±0.06	0.66
Kilo (kg, mean±SD)	72.70±10.60	72.70±10.60	67.68±7.88	73.57±10.48	0.16
BMI (kg/m^2, mean±SD)	23.01±2.75	23.93±3.52	21.24±2.08	23.35±2.74	0.01

SD: standard deviation, n: number of patients, BMI: Body Mass Index

same KT application without tension (3, 18) (Figure 3).

All KT applications in study groups were performed in the sitting position with the elbow slightly flexed and the accessories that could prevent the taping removed. In the required case, the elbow area was cleaned of hair, and KT was applied to the skin. The KT was applied for 30 minutes (3, 5). The subjects remained at rest during this time.

Statistical Analysis

Statistical analysis was performed using the SPSS (v22, IBM, USA) program. Continuous variables were presented as mean and standard deviation. Categorical variables were given as numbers and percentages. Kolmogorov Smirnov and Shapiro Wilk tests determined the conformity of the data to the normal distribution (by checking the "Skewness and Kurtosis"). In order to apply the analysis of variance in repeated measurements, whether the sphericity assumption could be met was examined with the Mauchly Sphericity test. The same analysis was evaluated with the Friedman test was preferred on the contrary condition. A one-way analysis of variance evaluated the differences in the tension between the groups. Statistical significance level was used as $p<0.05$. Statistical analyzes were performed by a statistician blinded to the groups.

RESULTS

A total of 90 individuals were enrolled in the study. The mean age of the participants was 21.04±2.0 years (ranged 18 to 28 years). A comparative baseline characteristic of the groups is presented in Table 1. There was a statistically significant difference only in BMI ($p<0.05$) (Table 1).

There was no statistically significant difference between the groups in terms of PP threshold, pain tolerance and intensity ($p>0.05$) (Table 2) (Figure 4). There was a significant in-group difference only in the 100% Tension Group in terms of PP threshold ($p<0.05$) (Table 2) (Figure 4). Pain threshold of the 100% tension group was gradually decreased in three measurements before, immediately after and 30 minutes after the KT application. In-group pain tolerance measurements showed no statistically significant difference ($p>0.05$) (Table 2). There was a significant difference in the 0% tension and 50% tension groups on the pain severity measurements ($p<0.05$). Both groups' pain tolerance was decreased. On the other hand, no significant difference was observed in the other tension groups ($p>0.05$) (Table 2).

DISCUSSION

The present study aimed to investigate the effect of KT tension tensions on pressure pain threshold and tolerance. The study's results demonstrated that the KT technique applied at different tensions did not affect the pressure pain threshold or tolerance. The 100% tension was found to be effective on the PP threshold. On the other hand, 0% tension and 50% tension groups' pain severity were decreased. The outcomes considered the efficacy of low- and high-tension KT on pain tolerance and severity, respectively.

There are two unique aspects of the present study. To our knowledge, this is the first randomized

controlled study investigating the effects of KT at different tensions on pressure pain threshold and pain tolerance. Existing studies primarily aim to evaluate the pain intensity of the KT technique (22, 23). Another notable characteristic of the study is to ensure the pain assessment with a sensitive device, "algometer". Healthy female individuals were observed to have a lower PP threshold than male subjects (24). Based on the presumption that hormonal differences may affect the results of the study, only male subjects were included in the study. There are many studies investigating the effect of KT on pain. A current randomized controlled trial focused on the perception threshold of KT, pressure pain threshold, and soft tissue stiffness in thirty healthy female subjects. The study's results indicated that fan strips of KT intervention applied to the waist provided higher pressure pain threshold values, lower soft tissue stiffness and higher perception threshold results compared to placebo and Y-type KT. In addition, the authors stated that different taping techniques did not demonstrate significant differences in terms of perceived pain during the acute period. It should be noted that Liu et al. enrolled female individuals in their study (25). Contrarily, our study only included male individuals. This methodological difference in sample choice constructed our results more generalizable. In addition, similar results were obtained with fan strip KT, unlike the diamond shape technique in our study, which showed the KTs' particulate results from pain perception in more specific application techniques. Koçak et al. evaluated the effect of KT on pain in lateral epicondylitis patients. The ring technique on the forearm extensor muscle group was positively affected for 3 and 12 weeks for both rest and activity VAS (26). Shakeri et al. used a diamond shape technique on pain intensity in 30 women diagnosed with lateral epicondylitis. The results proved the favorable effect of 75% tension KT application on pain (18). Ay et al. evaluated the pain intensity of 61 patients diagnosed with cervical myofascial pain

Table 2. Between and in group comparison of the measurements

		0% tension (n=23)	50% tension (n=24)	75% tension (n=24)	100% tension (n=24)	p
PP threshold	Baseline	12.7±13.06	12.83±2.58	11.82±2.48	13.72±3.12	0.19
	Immediate	12.70±2.84	12.92± 3.44	12.41±2.62)	13.78±2.75	0.47
	30 min	11.76±2.68	12.86±3.59	11.71±2.45	11.75±2.78	0.46
	p (in-group)	0.07	0.58	0.29	**0.00**	
Pain tolerance	Baseline	22.28±3.13	22.57±3.11	20.90±3.98	22.19±3.23	0.36
	Immediate	22.67±2.28	22.75±3.57	21.93±4.34	21.91±3.39	0.76
	30 min	21.59±4.24	22.52±3.62	21.57±3.70	21.37±4.20	0.76
	p (in-group)	0.70	0.83	0.36	0.81	
Pain severity	Baseline	3.93±1.66	3.79±1.63	3.73±1.63	4.36±1.32	0.56
	Immediate	3.64±1.97	3.04±1.37	3.16±1.78	3.89±1.69	0.31
	30 min	3.33±1.61	3.40±1.46	3.37±1.64	4.05±1.96	0.44
	p (in-group)	**0.03**	**0.03**	0.17	0.24	

SD: standard deviation, n: number of patients, PP: pain-pressure

syndrome after KT application. "I tape" was found to be effective on pain intensity (27). In our study, statistically significant results were obtained in the 0% tension and 50% tension groups in the change of pain severity assessment over the acute period. Namely, pain intensity decreased more in the lowest stretch (50%) and non-stretch KT groups. This outcome suggested that choosing low tensions to improve pain-related symptoms in subsequent studies may provide more clinically effective results.

As stated above, no study has investigated the effects of KT on PP threshold and pain tolerance in healthy individuals. A few studies investigated this hypothesis on rigid taping. Chen et al. applied intermittent, non-tension and 100% rigid tension tape in one session to healthy cases. The PP threshold values in the 100% tension group were higher. However, no significant difference was found between the groups (28). Similar to this study, we evaluated the effectiveness of KT in healthy subjects in terms of pressure pain threshold. Our results also supported these outcomes in terms of statistical significance. Therefore, the PP threshold is presumed not to be affected by the tension of KT. However, a subjective aspect of the pain assessment should also be evaluated by patient-reported outcome measures to reveal the psychological aspects of pain evaluation in terms of pressure sensation (29, 30).

Koçak et al. and Ay et al. conducted a PP threshold assessment with an algometer. The results proved an increment in pressure threshold after KT in medium to long term (26, 27). Our study proved an increase in PP threshold in 0 to 30 min (immediate and acute effect). However, long-term studies proved the contrary effect of KT. Therefore, the following studies might focus on both acute and long-term effects of KT to provide a comparative effect in various periods of monitorization.

Regarding the pain tolerance results in our study, there were no significant differences between and in group assessment. According to these results, the tension-type and the also KT application have no acute positive effect on pain tolerance. However, considering the relationship between pain tolerance and subjective pain experiences, it has ascertained the essence of including subjective measurement parameters such as kinesiophobia and pain catastrophizing in a comprehensive evaluation (29, 30).

Evaluating pain is critical for clinicians. PP threshold measurements are still based on a subjective evaluation, even if measured with an objective measurement method, an algometer device (31). Pain threshold can be affected by the gender, past experiences and sociocultural level of the person (32). Increased mechanical pain sensitivity is a consequence of various pain conditions that challenge medical diagnosis and may be essential for developing chronic pain. Accurate evaluation of the pain level is vital to determine the effectiveness of the treatments applied and to give personalized pain treatment (33). Therefore, controversial results are obtained from several studies, as noticed above. Further studies should yield similar methodologies to provide research integrity on this topic.

Clinicians need to provide maximum benefit in treatment. Kinesio taping has recently become a frequently used method in treating painful conditions in different areas of physiotherapy and rehabilitation (14, 15). We believe that our results would provide an

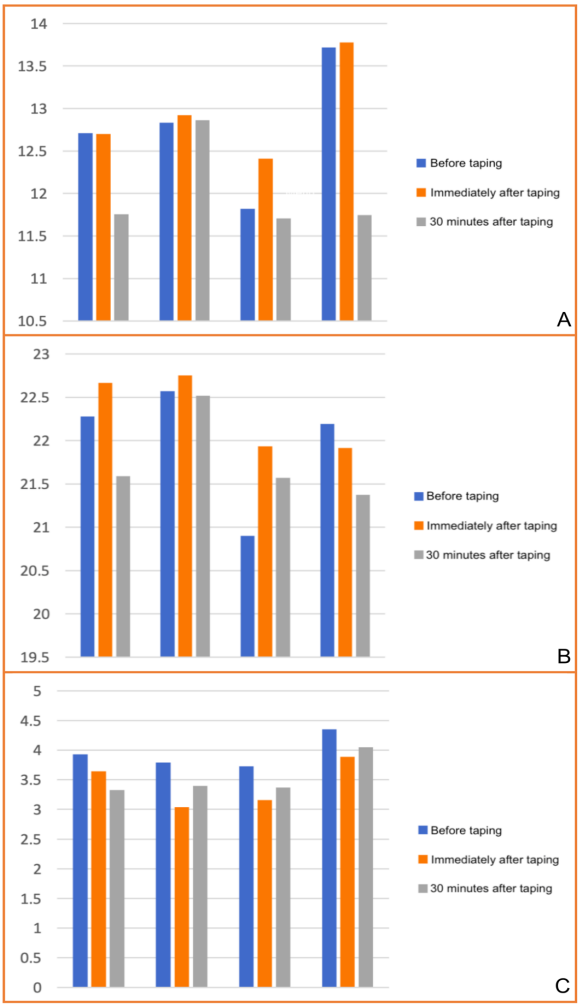

Figure 4. Score changes (a: pressure-pain threshold, b: pain tolerance, c: pain severity)

essential contribution in terms of the effectiveness of KT-tension on pressure pain threshold and tolerance.

Limitations

The limitations of the present study should be acknowledged. First, the cases were healthy volunteers. Therefore, the pain sensation might not clearly represent the clinical cases, including severe chronic pain conditions. Second, enrolled cases are monitored for the acute effect of pain. However, long-term pain evaluation results are more valuable in terms of clinical practice. Third, post-hoc analysis was not given for the Friedman test. Lastly, subjective pain assessment tools with a psychosocial dimension might add holistic insights and perspectives (30).

CONCLUSION

The study's results demonstrated that the KT technique applied at different tensions did not affect the pressure pain threshold or tolerance. The 100% tension was found to be effective on the PP threshold. On the other hand, 0% tension and 50% tension groups' pain severity were decreased. The outcomes considered the efficacy of low- and high-tension KT on pain tolerance and severity, respectively. A further study should investigate the pain threshold and tolerance in clinical cases with a long-term follow-up.

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Conflict of interests: The authors report no conflicts of interest and certify that no funding has been received for this study and/or preparation of this manuscript.

Ethical approval: The study was carried out in accordance with the ethical principles and the Helsinki Declaration. Informed consent of the patients was obtained. The study protocol was approved by the ethics committee of Muğla Sıtkı Koçman University Human Research Ethics Committee (Date: 06.10.2018, Decision No: 152). The study protocol was submitted to the clinicaltrials.gov (NCT04263077).

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RESEARCH ARTICLE

EFFECTS OF AGEING AND VITAMIN D LEVEL ON PLANTAR FASCIA STIFFNESS

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ABSTRACT

Purpose: The study aimed to examine plantar fascia stiffness in individuals over and under 65 years of age, and to question the predicted effect of age and vitamin D level on the dominant side plantar fascia stiffness.
Material and Methods: Forty adults were included to the study. The participants were divided into two groups as equal or above 65 years and below 65 years. Plantar fascia stiffness was evaluated using a digital hand-held myotonometer. Data on vitamin D levels were extracted from medical records.
Results: Plantar fascia stiffness was higher in the right (∆= 141.80±39.86 N/m, p=.001), and left foot (∆=116.85±38.45 N/m, p=.004), and in the dominant side (∆= 153.6±38.2 N/m, p<.001) in participants over 65 years of age. Age had a significant positive predicted effect on plantar fascia stiffness (β=.595, R2= 0.35, p<.001). Vitamin D level had a significant negative effect on plantar fascia stiffness (β=-.328, R2 =.108, p=.03).
Conclusion: The results of the research showed that plantar fascia stiffness was higher in individuals over 65 years of age. The stiffness of PF is slightly decreased as the vitamin D level improved.

Keywords: Soft tissue, biomechanics, ageing, vitamin D

INTRODUCTION

The plantar soft tissue is a multilayered structure consisting of skin, fat cells, and fascia (1). The plantar fascia begins at the anteromedial edge of the calcaneal tuberosity and ends at the base of the proximal phalanges (2). It provides mobility by transferring the tension produced from the foot muscles to the other structures and directs joint movements. Fascia is tightly attached to the underlying muscle tissue along its peripheral length (3). Changes in the mechanical structure of the fascia (e.g., stiffness) may limit muscular flexibility and joint movement (4). According to sonographic images, increased stiffness of the heel pad as a result of ageing is accompanied by increased plantar fascia thickness and decreased echogenicity (2, 5). Ultrasound elastography results confirmed that the plantar fascia thickened in the presence of pathology (6). The thickness of plantar fascia has been reported as higher in individuals above 45 years according to sonographic findings (2). Contrary to these reports, results of the sonoelastography study in healthy people above and below 50 years of age revealed that the plantar fascia softens with age (7). To sum up, there is no consensus on which diagnostic method should be used to examine the plantar fascia changes. Quantitative demonstration of the stiffness of the PF in addition to the thickening with ageing may

help to understand the change in the biomechanics of the foot more clearly. While plantar fascia thickness gives us information as an anatomical section, it may be valuable to examine the biomechanical property of stiffness responses. Due to being inexpensive, simple, and quick, myotonometer evaluation is considered appropriate to assess the stiffness of the plantar fascia. When the studies have done so far were examined, it was seen that the plantar fascia assessment with a myotonometer was performed in only seven studies (6, 8-13). No study examined the differentiation in plantar fascia stiffness with ageing using a myotonometer.

Vitamin D takes part in many biological processes including immune system modulation, and its relationship with connective tissue is not yet clear (14). The importance of vitamin D in the musculoskeletal system is due to its role in calcium and bone metabolism (15). It increases the absorption of calcium, and positively affects bone mineralization and muscle function (16). In addition, vitamin D is a steroid hormone whose importance is known especially for the structure and functions of the musculoskeletal system (17). In adults aged 65 and over, the endogenous synthesis of vitamin D is reduced by 25% compared to young adults (18). Decreases in vitamin D levels trigger secondary hyperparathyroidism, leading to loss of bone mass and muscle strength (16). There is also evidence that low vitamin D levels are associated with sarcopenia (19). In the literature, the relationship between vitamin D deficiency and muscle dysfunction is thought to be based on the loss of vitamin D receptor functions, increased oxidative stress, and impaired mitochondrial function (20). The number of studies on the efficacy of vitamins directly in soft tissue is limited. While it is well known that vitamin C deficiency causes a decrease in the tensile strength of abnormal collagen fibers and fibrous tissues in connective tissue (21) however, no research has been conducted on vitamin D effect on plantar fascia stiffness yet.

Ageing is the most common cause of vitamin D deficiency (18), biomechanical dysfunction of the foot (22), and thickened plantar fascia. However, to date, only limited information has been reported on the effects of vitamin D status on fascial tissue structure. Moreover, it is unclear whether ageing and vitamin D levels are associated with plantar fascia stiffness. On this basis, this research aimed to examine the effects of ageing and vitamin D levels on plantar fascia stiffness.

MATERIAL AND METHODS

This descriptive, cross-sectional study was carried out with 40 adults who were invited to the research laboratory by e-mail or telephone. This study was in agreement with the standards set by the Declaration of Helsinki and approved by Acıbadem Mehmet Ali Aydınlar University, Medical Research Review Board (ATADEK) (Date: 30.09.2022, Decision No: 2022/15/15). All participants signed informed consent. The participants were divided into two groups as equal or above 65 years and below 65 years. A comparison of plantar fascia stiffness by age was performed by dividing the participants into two groups, over age ≥ 65 years and underage < 65 years. The dominant extremity was questioned and recorded with the individual feedback of the participants. Estimated effect analysis of age and vitamin D levels on the dominant side plantar fascia stiffness were performed with all participant data.

Participants

Individuals with a medical history other than hypertension were not invited to the study. The exclusion criteria were; i) history of peripheral vascular disease, ii) history of active plantar fasciitis, iii) existence of plantar fascial ulceration, low or high longitudinal arch, retrocalcaneal bursitis, Achilles tendinopathy, and skin lesions around the heel, iv) history of surgery or trauma around the heel, v) history of neuropathic or radicular pain, vi) existence of diabetes, vii) history of rheumatologic, neurological disease and neuroarthropathy, viii) existence of malignancy. Individuals who were 18 years or older, had more than 10° ankle dorsiflexion and normal medial longitudinal arch height, had no pain around the heel, and had a vitamin D evaluation record within the last week were included in the study. Demographic and anthropometric information [height (cm), weight (kg), body mass index (kg/m2)], and the dominant side of the participants were recorded. Data on vitamin D levels were extracted from medical records of the blood tests performed a month before the assessments, of participants.

Evaluation of Plantar Fascia Stiffness

Plantar fascia stiffness was evaluated using a myotonometer (MyotonPRO, Myoton AS, Tallinn, Estonia). An external force is sent from the probe of the myotonometer to the tissue to be examined (muscle body, muscle-tendon junction, fascia, tendon, skin, etc.). This mechanical impulse creates

an elastic deformation in the tissue. Pressure changes occurring between the inner probe and the outer plexiglass frame during measurement are detected by computer-connected customized transducers (12). The oscillations are recorded with the frictionless and sensitive accelerometer sensors located at the other end of the probe. Tissue stiffness can be determined in this way. Stiffness [N/m], is a biomechanical property and is defined as the resistance to external forces that will cause the examined tissue to change its shape. Stiffness is stated to be the opposite of compliance. Detailed information can be found in the user guide of the device (23) and the video at the link (https://www.youtube.com/watch?v=PwAB84JLVwg) The use of a myotonometer is reliable in the evaluation of plantar fascia stiffness (8). However, measurements can be affected by different ankle positions (9). A study showed that physical activity causes an increase in the thickness of the distal part of the plantar fascia and that the proximal part is not affected by the level of physical activity (24). As a result of this information, positioning was standardized before measurements. The participants were asked to lie prone, the hip and ankle joints were positioned in neutral (0^o) and the knee was in extension. A prior to the evaluation, the information related to the participants and the pattern were entered. All measurements were performed bilaterally and three times in the resting position and the data were recorded in the MyotonPRO software. The device was programmed to take 5 pressure-displacement measurements (every 5 beats, the duration of 1 pulse is 15 ms and the interval between beats was 8 ms) per recording prior to administration. Three measurements were taken from the reference point (25) where the calcaneal distal anterior corner and the inner corner of the medial longitudinal arch meet for the borderline between the first and second metatarsal bones (9) and the proximal beginning of the plantar fascia (8), and the average of the measurements was recorded. When the red light on the plexiglass frame of the device probe turned green, the practitioner stopped the pressure application perpendicular to the relevant tissue and waited until 5 strokes were performed. After each application, the acceleration graph was examined and the measurements were repeated if there were any deviations from the normal. Recordings were reloaded into the software and reported for each participant. Care was taken not to move the device during the application and to maintain its correct position. All the evaluations were performed at neutral room temperature and at the same time of day.

Statistical Analysis

Data analysis was performed with the Statistical Package for Social Science (SPSS) program, version 25 (IBM Inc., Chicago, IL, USA). In descriptive data, the continuous numerical variables were presented as mean±SD and categorical variables were presented as frequency. To determine whether the parameters were normally distributed skewness and kurtosis (-1.5 and +1.5) were used (26). The Chi-square test was used to analyze differences in nominal and categorical data by groups. The Independent Sample t-Test was used in the analysis of the differences between the groups since the parameters were normally distributed (27). Linear Regression Model was used to examine the effect of age and vitamin D levels on dominant side plantar fascia stiffness. Before the regression analyses, linear relationship, cook's distance, normal distribution, homoscedasticity checks, and correlation level analyzes were performed (27). The two hypotheses were developed to examine the relationship between age, D vitamin levels, and plantar fascia stiffness. First, the study claims that there will be a positive relationship between age, and plantar fascia stiffness (H1: Age affects the plantar fascia stiffness level). Second, a lower level of D vitamin will increase the plantar fascia stiffness (H2: The vitamin D levels affect the plantar fascia stiffness level). Statistical significance was deemed to be a p-value of $<.05$.

In power analysis with the G*Power software (version 3.1.9.2), the t-test confirmed that our sample size was sufficient in the model of differences (effect size=.95, p=.05, n1/n2=1, and n=20) between two independent means (greater than $1-\beta= 0.95$) (28).

RESULTS

The baseline characteristics of the participants are shown in Table 1. Forty individuals with a mean age of 55.4±12.4 years were included in the present study. While the mean age was 66.3±1.6 years in Group 1, which included participants aged 65 and over, in Group 2, which included participants aged 65 and under, the mean age was 44.5±8.0 years. 75% (n=30) of the participants were female and the gender distribution in both groups was equal. Each group included 5 men and 15 women. 35 of the participants

(87.5%) had right-side dominance. Of 5 people with left dominance (12.5%), two were in Group 1 (10%) and three were in Group 2 (15%). The mean BMI of all participants was 28.2±5.4 kg/m^2, the mean of Group 1 was 29.7±3.5 kg/m^2, and the mean of Group 2 was 26.7±6.5 kg/m^2 (p = .08). The mean level of vitamin D was found to be 38.6±25.7 ng/mL in all participants. In Group 1 this means was 31.2±18.9 ng/mL and 46.0±29.7 ng/mL (p = .07) in Group 2.

The plantar fascia stiffness differences according to the age groups of the participants are shown in Table 1. The right (mean difference = 141.8±39.9 N/m, p = .001) and left foot (mean difference = 116.9±38.5 N/m, p = .004) plantar fascia stiffness was higher in the group over 65 years of age. While the mean plantar fascia stiffness of the dominant side was 577.3±142.6 N/m in all participants, it was 654.2±113.7 N/m in Group 1 and 500.5±128.1 N/m in Group 2 (mean difference = 153.6±38.2 N/m,

Table 1. Characteristics and clinical features of participants

		Total	**Group 1 age ≥ 65 years**	**Group 2 age < 65 years**
Female Gender n (%)		30 (75%)	15 (75%)	15 (75%)
Left Side Dominance n (%)		5 (12.5%)	2 (10%)	3 (15%)
Age (year)	mean±SD (min-max)	55.4±12.4 (31-70)	66.3±1.6 (65-70)	44.5±8.0 (31-58)
Vitamin D (ng/mL)	mean±SD (min-max)	38.6±25.7 (4.70 – 108.1)	31.2±18.9 (14.0 – 88.4)	46.0±29.7 (4.7-108.1)
Presence of Hypertension n (%)		17 (42.5%)	14 (70%)	3 (15%)

Plantar Fascia Stiffness (N/m)	**Groups**	**Mean±SD**	***p***	**95 CI%**
Right Plantar Fascia Stifness	Age ≥ 65 Years	654.5±114.9		
	Age < 65 Years	512.7±136.3		
	Mean Difference	141.8±39.9	.001	61.1 to 222.5
Left Plantar Fascia Stifness	Age ≥ 65 Years	636.5±103.2		
	Age < 65 Years	519.7±137.5		
	Mean Difference	116.8±38.4	.004	39.0 to 194.7
Dominant Side Plantar Fascia Stifness	Age ≥ 65 Years	654.2±113.7		
	Age < 65 Years	500.5±128.1		
	Mean Difference	153.6±38.2	<.001	76.1 to 231.1
Dominant Side Plantar Fascia Stifness	Male	583.8±151.42		
	Female	557.9±117.1		
	Mean Difference	25.90±52.5	.625	-80.5 to 132.3

p<.05 significance level. p repesents significance level of T-test. SD: Standard Deviation. N/m: Newton/meter. ng/mL refers to nanograms/millilitre.

p<.001). No statistically significant difference was observed in dominant side plantar fascia stiffness in all participants (583.8±151.42 N/m vs 557.9±117.1 N/m) and groups (661.2±125.2 N/m vs 633.0±75.9 N/m in Group 1 and 506.4±137.7 N/m vs 482.8±104.8 N/m in Group 2) according to gender (p>.05).

The hypothesis results are represented in Table 2. In a significant regression model (F(1, 38)=20.85, p <.001), 35% of the variance (R2= .35) in dominant side plantar fascia stiffness was explained by the age variable. Accordingly, the age variable predicts the dominant side plantar fascia stiffness positively and significantly (β=.595, t(38)= 4.56). The model for vitamin D level (F(1, 38)=4.58, p = .03) was also significant. 10.8% of the variance (R2= .108) in dominant side plantar fascia stiffness was explained by the vitamin D variable. Accordingly, the vitamin D variable predicted dominant side plantar fascia stiffness negatively and significantly (β=-.328, t(38)= - 2.14).

DISCUSSION

This study aimed to investigate the effects of age and the level of vitamin D on plantar fascia stiffness. Both hypotheses were confirmed by the findings of the present study. One of our hypotheses was that increasing age would have resulted in higher stiffness of the plantar fascia. In line with our hypotheses, individuals above 65 years had a higher level of stiffness compared to middle-aged individuals and age had an interaction with plantar fascia stiffness. Our second hypothesis was related to vitamin D concentration which was confirmed by showing the association between improved vitamin D concentration and decreased plantar fascia stiffness. Studies using myotonometer have reported that plantar fascia stiffness as average of 446.4 N/m (mean age: 27.8±5.1 years) (13), 476.0 N/m (mean age: 28.95±2.8) (10), 511.7 N/m and 533.2 N/m (mean age: 35.53±15.0 years) (11) in healthy individuals. In this research, plantar fascia stiffness ranged from 500.5 N/m to 519.7 N/m in the group under 65 years of age (mean age: 44.5±8.0 years), and between 654.5 N/m and 636.5 N/m in the group 65 years and older (mean age: 66.3±1.6 years). The number of studies examining plantar fascia stiffness with different evaluation methods under the effect of age variable is limited (2, 5, 7, 22). It can be said that, unlike the sonoelastography results (7) the linear increase of the plantar fascia stiffness, which was previously shown in sonographic images (2, 5) was demonstrated once again in our research results with the myotonometer evaluation of the linear increase with age. In this direction, our findings may support the hypothesis that plantar fascia stiffness increases with ageing. Advancing age also results in altered plantar pressure distribution by increasing pressure and force variables (29). Differentiated pressure distribution of the plantar surface, such as increased contact area and the maximum force causes higher stiffness of the plantar fascia (30). Also, age itself leads to an alteration in muscle stiffness (31), our results are in line with the above-mentioned literature and older adults had higher stiffness values than middle-aged individuals. Advancing age predicts a 35% increase in plantar fascia stiffness. Therefore,

Table 2. Age and vitamin D predicted effect on the dominant side plantar fascia stiffness

H1: Ageing affects the dominant side plantar fascia stiffness level

	Dominant Side Plantar Fascia Stiffness							
	B	Std. Error	*Beta coefficient*	*t*	R^2	*df*	*F*	*p*¶
Age (year)	6.85	1.5	.595	4.56	.354	1, 38	20.85	<.001

H2: Vitamin D levels affect the dominant side plantar fascia stiffness level

	Dominant Side Plantar Fascia Stiffness							
	B	*Std. Error*	*Beta coefficient*	*t*	R^2	*df*	*F*	*p*¶
Vitamin D (ng/mL)	-1.82	.85	-.328	-2.14	.108	1, 38	4.58	.039

p¶: Linear Regression Model. Std. Error: Standard Error. N/m: Newton/meter. ng/mL refers to nanograms/millilitre.

we can propose that ageing has an undeniable effect on the stiffness of plantar fascia.

Cheng et al. showed that PF thickness was higher in males than females by sonographic examination in 28 healthy individuals (14 females, aged: 20-79 years) (5). Similarly, Taş et al., reported that the thickness of the plantar fascia was higher in males than females by ultrasonography in 60 healthy sedentary individuals (30 females, aged: 19-50 years) (32). However, in our research results, no difference was observed in myotonometer results at the plantar fascia stiffness level by gender. The reason for these results may be related to the fact that the differentiation by gender cannot be evaluated with myotonometer as much as sonography and ultrasound, or due to the majority (75%) of male participants in this study. The effect of gender in the plantar fascia stiffness evaluation with a myotonometer should be examined in research setting that includes equal numbers of male and female participants.

Low vitamin D level was observed in individuals with calcaneal spurs (33). In our study, the stiffness of PF was negatively predicted by the vitamin D level of 10.8%. A striking finding of our study is that vitamin D influences the mechanical structures of PF. Moreover, a study reported that an increase in transforming growth factor-beta (TGF-β) because of vitamin D deficiency, leads to myofibroblast differentiation by enhancing mitochondrial reactive oxygen species production in patients with Dupuytren's contracture (34). TGF-β is also involved in palmar and plantar fibromatosis (35) and Vitamin D deficiency leads to up-regulation of TGF-β in serum (34). This information suggests that with the indirect TGF-B effect, vitamin D may play an important role in maintaining a well-balanced facial tissue microenvironment. Based on these findings, the effects of vitamin D concentration on plantar fascia tissue should be investigated with a longitudinal design. We can say that the strengths of this study are (i) examining the interaction of vitamin D and PF alone for the first time and (ii) investigating the effect of both age and vitamin D on plantar fascia at the same time.

The main limitation of this study is that we did not examine the plantar pressure distribution. Further studies may include an assessment of plantar pressure distribution and question its possible association with the stiffness of plantar fascia. Also, more research is needed including the examination of the effects of calcium metabolism, lipid levels, and hormonal alterations on plantar fascia stiffness. In addition, given the limitation of myotonometer use in the evaluation of tissues located below other tissue layers, it is likely to record better results in further studies using a combination of sonoelastrography, ultrasound, sonography, and myotonometer for changes in plantar fascia stiffness. Another limitation is that we do not have the opportunity to evaluate the subcutaneous fat thickness on the sole of the foot. Further studies could perform subcutaneous fat thickness for plantar fascia evaluations.

CONCLUSION

In conclusion, the results of this study suggest that plantar fascia stiffness increases with ageing and is also slightly affected by vitamin D levels. Interventions to reduce plantar fascia stiffness can be included in primary prevention to prevent the adverse effects of ageing on foot health. The effect of vitamin D supplements on plantar fascia stiffness should be examined in further studies.

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RESEARCH ARTICLE

THE RISK FACTORS FOR PARASTOMAL HERNIA DEVELOPMENT: A 8-YEAR RETROSPECTIVE STUDY IN COLORECTAL SURGERY

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ABSTRACT

Purpose: Although parastomal hernia is a common complication of ostomy surgery, the exact risk factors for its development remain unclear. The aim of this study was to determine the incidence and risk factors of parastomal hernia in ostomy patients.
Material and Methods: A retrospective study was conducted. The data from a cohort of 952 ostomy patients' hospital records between 2013 and 2020 were extracted and analyzed. Patients' ostomy-related characteristics, complication notes, and the occurrence of parastomal hernia were retrieved.
Results: The patients' mean age was 59.6 years (±14.4 years), and 524 (55%) of them were male. Colorectal cancer (476 patients,50%) was the most common etiology for surgery. Parastomal hernia developed in 100 (10.5%) of patients. Age >65 (OR=1.753; 95%CI=1.071-2.869), BMI >24.9 (OR=2.009; 95%CI=1.201-3.362), co-morbidity (OR=1.773; 95%CI=1.021-3.080), laparoscopic surgery (OR=5.643; 95%CI=3.113-10.230), height of ostomy (OR=1.906; 95%CI=1.122-3.236), left lower quadrant ostomy location (OR=2.252; 95%CI=1.319-3.845), prolapse (OR=7.876; 95%CI=3.571-17.372), and other ostomy-related complications (OR=2.888; 95%CI=1.179-7.074) were risk factors based on logistic regression analysis.
Conclusion: The incidence of parastomal hernia was nearly one in ten patients after colorectal surgery with an ostomy. Advanced age, co-morbidity, laparoscopic surgery, the height of the ostomy, the left lower quadrant ostomy location, prolapse, and other ostomy-related complications were independent risk factors.
Keywords: Parastomal hernia, ostomy, stoma, colorectal surgery

INTRODUCTION

Parastomal hernia (PSH), defined as an incisional hernia at the site of an intestinal ostomy, is a common complication that occurs in 4–48% of ostomy surgeries (1-3). Even though PSHs can be asymptomatic, a substantial proportion of patients with PSHs report a low quality of life (4). Peristomal dermatitis, pain, and problems with ostomy

appliances that result in leakage are common symptoms associated with PSH. Additionally, it can result in life-threatening consequences such as obstruction, perforation, and strangulation (1, 5, 6). These surgical emergencies are associated with higher morbidity and mortality as well as a decline in quality of life (4, 7).

The repair methods for PSH include a primary suture of the defect, stoma relocation, and mesh repair (1). The risk of recurrence of PSH is approximately 70% after a primary suture repair and 20% after a mesh repair (8-10). Unfortunately, stoma relocation is also associated with the risk of PSH in the new location and the risk of incisional hernia in the area of the closed ostomy, with reported recurrence rates between 24 and 86% (11). PSH repair is technically challenging and is associated with increased morbidity. Some authors have suggested that placing a “preventive” parastomal mesh during ostomy formation reduces the risk of PSH occurrence (12-14). However, mesh insertion can lead to severe complications such as wound infection, dense adhesions, difficult-to-treat fistulas, and obstruction. Besides, a multicenter randomised trial did not support the use of a reinforcing mesh for preventive or prophylactic purposes because it had no impact on the incidence of PSH (15). Since preventing PSHs is preferable to treating them, it is crucial to identify their risk factors.

Age, female gender, obesity, diabetes, wound infection, aperture size, laparoscopic procedure, and transperitoneal route have been considered to increase the risk of PSH, but their precise roles remain controversial (1, 16-19). Verifying the risk factors for the development of PSH can help avoid hernia/mesh repair-related complications, enhance the quality of life, and reduce medical costs. The aim of this study was to determine the incidence and risk factors of PSHs in colorectal surgery..

MATERIAL AND METHODS

The Study Design and Patients

This was a retrospective cohort study examining the hospital archival records of ostomy patients followed in the stoma therapy unit of Dokuz Eylul University between January 2013 and December 2020. This research was reported using the STROBE checklist (20). All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committees and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study was approved by the Dokuz Eylul University, Non-Invasive Research Ethics Committee (Approval Date: 10.11.2021, Number: 2021/32-12). All patients gave their written consent both for the surgery and to participate in the study.

A chart review was created to include hospital records in the study. The eligibility of consecutive patient hospital records (n=1714) was initially evaluated using the sample inclusion criteria. The inclusion criteria were to be older than 18 years of age, to have an ostomy after colorectal surgery, and to be followed up in the outpatient clinic at least three times after discharge. The forms of patients who did not follow up after ostomy creation and had missing information were excluded from the study. The final study sample consisted of 952 patient records after the exclusion of 61 forms with missing information and patients lost to follow-up.

Sample Size

From a preliminary analysis of the patient records, it was estimated that there were approximately 200 patient records per year. All patient files were reviewed in order to determine the incidence more accurately and to reach the maximum number of patients who were diagnosed with PSH. Therefore, a prior power analysis was not performed. G-Power version 3.0.10 was used to determine the post-power analysis of this study. The power of the study was revealed to be 99% based on the results of the regression analysis with an alpha of 0.05 and a two-tailed test.

Surgical Technique for Ostomy Creation

All ostomies were created in the middle of the rectus abdominis muscle via a transperitoneal route. Initially, a circular incision was made in the area of skin defined for the ostomy. The anterior rectal sheath was cut in a cruciform manner. The rectus abdominis muscle was split in the middle to reveal the posterior rectal sheath. This structure, along with the peritoneum, was longitudinally cut. The intestine stump was then grasped with Babcock forceps and pulled through the skin incision. The ostomies were then fixed with Vicryl 3-0 (Ethicon, Inc., Somerville, NJ) sutures after being matured by mucocutaneous eversion.

Outcome Measures and Data Acquisition

After the creation of ostomy surgery, patients were trained in ostomy care and scheduled for outpatient follow-up by three wound, ostomy, and continence (WOC) nurses and physicians. WOC nurses evaluated patients in terms of the condition of the ostomy and complications during follow-up outpatient visits, and they recorded physical examination findings and ostomy complications on hospital record forms.

Hospital records, including patients' characteristics, outpatient follow-up, and complication notes, were extracted, anonymized, and recorded in a secure database. The primary outcome variable was PSH's presence or absence. PSH was defined as a defect in the abdominal fascia that allowed the intestine to bulge or herniate into the parastomal area. PSH was initially evaluated by physical examination (while supine or erect and performing the Valsalva manoeuvre) and confirmed by a computed tomography (CT) scan. Factors such as gender, body mass index, co-morbidities, smoking status, preoperative neo-adjuvant chemo-radiotherapy, type of ostomy (end/loop colostomy, end/loop ileostomy), the reason for ostomy creation, marking of the stoma site in the preoperative period, type of surgery (emergency or elective), approach type (laparoscopy or open), the height of ostomy, the aperture size of ostomy, other ostomy-related complications, and stomal prolapse were examined to determine the factors causing PSH. The height of the ostomy, the aperture size of the ostomy, and complications were assessed by WOC nurses. The height of the ostomy was determined by measuring its maximum height from the surface of the skin. Using a special instrument frequently used by WOC nurses, the aperture size of all ostomies was measured in millimetres. The instrument consists of a ring with a central hole. The aperture size of the ostomy was determined by placing the instrument on the mucocutaneous line and reading the measurement in millimetres on the device. The height and aperture size of the ostomy were assessed and recorded on the first postoperative day during the initial patient encounter. Valid and reliable definitions were used to identify complications (21). Prolapse was defined as the term for the intestine telescoping through the stoma. Peristomal skin complications were defined as disruptions of skin integrity such as redness, epidermis loss, warmth, itchiness, or pain. Other ostomy-related complications were classified as stenosis, fistula, and retraction.

Validity and Reliability

The PSH diagnosis in the patient records should have been accurate. Thus, PSH was determined both on paper (physical examination notes) and digitally (CT scan). In addition, a protocol for data extraction using graph review was developed prior to data collection based on previous research (16, 19, 21, 22). Two researchers (CA and DC) meticulously checked and reviewed all the data to ensure its validity and dependability. The analysis did not include missing data. Confounding factors were also taken into account using advanced statistical analysis. The assumptions of observations being dependent and independent variables being linearly related to logic were verified and met before analyzing logistic regression.

Statistical Analysis

The data were analyzed using the SPSS 22.0 program. Absolute values and percentages were used to represent categorical data. Chi-squared and t-tests were utilized to determine the relationship between each independent variable and PSH. The variables' ability to predict the development of PSH was evaluated using a logistic regression model. According to the literature and taking univariate analyses into consideration, the predictor variables for the logistic regression model were chosen.

RESULTS

Among the 1714 potential ostomy patient records screened for eligibility, 952 (55.5%) were recruited. The mean age of the patients was 59.6 years (± 14.4 years), and 524 (55%) of them were male. The mean BMI was 26.50 ±10.4 kg/m². Colorectal cancer (476 patients, 50%) was the most common etiology for surgery. Six hundred twenty-two (65.3%) patients underwent elective surgery. The most common type of ostomy was an end colostomy, which was performed on 415 (43.6%) patients. The right lower quadrant was the most frequently used location for ostomies in 483 patients (50.7%), followed by the left lower quadrant in 435 patients (45.7%).

PSHs were identified in 100 (10.5%) of the patients. Age (p=0.002), BMI > 24.9 kg/m² (p=0.003), laparoscopic surgery (p<0.001), the aperture size of the ostomy (p=003, p=0.002), end colostomy (p<0.001), ostomy location in the left lower quadrant

Table 1. Patient characteristics and risk factors for parastomal hernia formation (univariate analysis)

	Parastomal Hernia -	Parastomal Hernia+	Total	*P value*
Age (yr)				
<65	529 (92.0)	46 (46.0)	575 (60.4)	***.002***
>65	323 (85.7)	54 (54.0)	377 (39.6)	
Gender				
Female	390 (45.8)	38 (38.0)	428 (45.0)	*.139*
Male	462 (54.2)	62 (62.0)	524 (55)	
BMI				
<24.9 kg/m²	371 (43.5)	28 (28.0)	399 (41.9)	***.003***
>24.9 kg/m²	481 (56.5)	72 (72.0)	553 (58.1)	
Comorbidity				
No	321 (37.7)	28 (28.0)	349 (36.7)	*.057*
Yes	531 (62.3)	72 (72.0)	603 (63.3)	
Smoking				
No	400 (46.9)	51 (51.0)	451 (47.4)	*.443*
Yes	452 (53.1)	49 (49.0)	501 (52.6)	
Preoperative CT&RT				
No	426 (50.0)	52 (52.0)	478 (50.2)	*.705*
Yes	426 (50.0)	48 (48.0)	474 (49.8)	
Preoperative stoma site marking				
No	535 (62.8)	62 (62.0)	597 (62.7)	*.877*
Yes	317 (37.2)	38 (38.0)	355 (37.3)	
Aetiology of disease				
Benign	330 (38.7)	42 (42.0)	372 (39.1)	*.526*
Malign	522 (61.3)	58 (58.0)	580 (60.9)	
Indication of surgery				
Colorectal cancer	431 (50.6)	45 (45.0)	476 (50.0)	*.290*
Other	421 (49.4)	55 (55.0)	476 (50.0)	
Type of the surgery				
Elective	560 (65.7)	62 (62.0)	622 (65.3)	*.459*
Emergency	292 (34.3)	38 (38.0)	330 (34.7)	
Type of approach				
Laparoscopic	59 (6.9)	29 (29.0)	88 (9.2)	***< .001***
Open	793 (93.1)	71 (71.0)	864 (90.8)	
Type of the ostomy				
End colostomy	349 (41)	66 (66)	415 (43.6)	***< .001***
Loop colostomy	50 (5.9)	5 (5)	55 (5.8)	
End ileostomy	241 (28.3)	13 (13)	254 (26.7)	
Loop ileostomy	212 (24.9)	16 (16)	228 (23.9)	
Ostomy location				
Left lower	368 (43.2)	67 (67)	435 (45.7)	***< .001***
Right lower	453 (53.2)	30 (30)	483 (50.7)	
Left upper	15 (1.8)	3 (3)	18 (1.9)	
Right upper	16 (1.9)	0 (0)	16 (1.7)	
Aperture size of ostomy (mm)				
Horizontal (mm)	37.01 ± 6.89	39.23 ± 7.75	37.24 ± 7.02	***.003***
Vertical (mm)	42.65 ± 7.62	45.23 ± 8.02	42.92 ± 7.70	***.002***
Height of ostomy				
< 10 mm	344 (40.4)	56 (56.0)	400 (42.0)	***.003***
> 10 mm	508 (59.6)	44 (44.0)	552 (58.0)	
Peristomal skin complications				
No	632 (74.2)	67 (67.0)	699 (73.4)	.124
Yes	220 (25.8)	33 (33.0)	253 (26.6)	
Stomal prolapse				
No	829 (97.3)	83 (83.0)	912 (95.8)	***< .001***
Yes	23 (2.7)	17 (17.0)	40 (4.2)	
Other ostomy-related complications*				
No	818 (96.0)	90 (90.0)	908 (95.4)	***.019***
Yes	34 (4.0)	10 (10.0)	44 (4.6)	
Total	852 (100)	100 (100)	952 (100)	

BMI: Body Mass Index, CT Chemotherapy, RT: Radiotherapy) *Fisher exact test was used.

Table 2. The complications associated with ostomy.

	Total	
	(n)	%
Participants evaluated (n)	**952**	**100**
No complication	**573**	**60.2**
Peristomal skin complications	**253**	**26.6**
Parastomal hernia	**100**	**10.5**
Prolapse	**40**	**4.2**
Other complications	**44**	**4.6**

ostomy-related complications (p=0.019), and prolapse (p<0.001) were associated with PSH based on univariate analysis. Table 1 presents the demographic and ostomy characteristics of patients according to the development of PSH.

In the late period, 39.2% of patients experienced one or more complications. Among the participants, 4.2% had a prolapse, 10.5% had PSH, and 4.6% had other complications. The complications associated with an ostomy are listed in Table 2.

Logistic regression analysis was conducted to assess whether the seventeen index variables significantly predicted the development of PSH. When seventeen predictor variables are considered together, they significantly predict whether or not PSH is developed (X2 = 125.188, df=17, p<0.001). Table 3 presents the odd ratios, which suggest that the odds of PSH were increasingly greater as age > 65 (OR=1.753; 95%CI=1.071-2.869), BMI>24.9 (OR=2.009; 95%CI=1.201-3.362), co-morbidity (OR=1.773; 95%CI=1.021-3.080), laparoscopic surgery (OR=5.643; 95%CI=3.113-10.230), the height of ostomy (OR=1.906; 95%CI=1.122-3.236), left lower quadrant ostomy location (OR=2.252; 95%CI=1.319-3.845), prolapse (OR=7.876; 95%CI=3.571-17.372), and other ostomy-related complications (OR=2.888; 95%CI=1.179-7.074).

DISCUSSION

This study determined the incidence of parastomal hernia and identified risk factors associated with its development. Understanding the risk factors for PSH is crucial because the surgical team can potentially reduce the incidence of related complications, improve quality of life, and reduce medical costs. In this study, the incidence of PSH was 10.5%; however, the actual incidence may have been higher, as only symptomatic patients were included. We demonstrated that age > 65 years old, BMI > 24.9, co-morbidity, laparoscopic approach, the height of ostomy < 10 mm, ostomy location in the left lower quadrant, stomal prolapse, and other ostomy-related complications were all significantly associated with PSH formation.

PSH formation may be influenced by both patient-related and technical factors. In numerous studies, a correlation between PSH and patient-related factors such as age (3, 14, 17, 18, 23, 24), obesity (16–18, 25–27, 28), and female gender (17, 18) has been well documented. However, a recent meta-analysis demonstrated that smoking, end colostomies, emergency surgery, no preoperative stoma site marking, diabetes, hypertension, peristomal infection, severe cough, operation time, and surgical techniques were risk factors for PSH in individual studies. It also suggested that more research is required to approve these risk factors (17). Therefore, it is thought that the results of this study will shed light on the literature.

A recent meta-analysis showed that older age is a risk factor for PSH (17). The authors suggested that this may be due to the thinning of the abdominal muscles, weakening of muscle strength, and increased thickness of subcutaneous fat with the increasing age of the patient. However, only three studies (7,14,18) identified the age threshold as a risk factor for PSH (≥ 60 years, ≥ 65 years, or ≥ 75 years). We reported that the risk of developing PSH increases with age over 65. Considering the lack of evidence that age stratification is a risk factor for PSH, our study may contribute to the literature.

Obesity has been proven to influence PSH formation. This may be because obese patients have thicker abdominal subcutaneous fat, thinner abdominal wall muscles, and higher intra-abdominal pressure (17, 30). Consistent with previous research, this study defined obesity as having a BMI ≥ 25 kg/m², which is considered a significant risk factor for the development of PSH (7, 31). Co-morbidities such as diabetes (18) and chronic obstructive pulmonary disease (1, 29) have been shown to be factors in the development of PSH. This study did not examine co-morbidities under subheadings, which may be considered one of its limitations. Despite this fact, the results of this study demonstrated that the presence of any co-morbid disease significantly increased the risk of developing PSH.

Some studies had reported an increased risk of PSH following laparoscopic surgery (16, 19, 23, 32, 33),

Table 3. Independent significant factors predicting parastomal hernia formation (multivariate analysis)

	Peristomal Hernia		
Variable	**Odds ratio**	**Confidence Interval**	***P value***
Age >65	1.753	1.071-2.869	***.025***
Gender	1.530	.943-2.482	*.085*
BMI >24.9 kg/m²	2.009	1.201-3.362	***.008***
Comorbidity	1.773	1.021-3.080	***.042***
Smoking	1.182	.735-1.901	*.490*
Benign/malign	1.089	.629-1.886	*.761*
Stoma site marking	1.157	.663-2.017	*.608*
Elective/emergency	.793	.435-1.443	*.447*
Laparoscopic approach	5.643	3.113-10.230	***< .001***
Height of ostomy < 10mm	1.906	1.122-3.236	***.017***
Left lower ostomy location	2.252	1.319-3.845	***.003***
Type of ostomy (end/loop)	.782	.417-1.465	*.443*
Aperture size of ostomy-horizontal (mm)	1.025	.980-1.072	*.276*
Aperture size of ostomy-vertical (mm)	1.029	.979-1.081	*.263*
Prolapse	7.876	3.571-17.372	***< .001***
Peristomal skin complications	1.251	.735-2.127	*.409*
Other ostomy-related complications	2.888	1.179-7.074	***.020***
Constant	.004		***< .001***
	Hosmer and Lemeshow Test: .747 Nagelkerke R Square: .252 p: ***< .001*** X^2= 125.1888 df= 17		

(BMI: Body Mass Index)

whereas others had found no association (5). This study revealed a statistically significant association between PSH and the laparoscopic approach. Shiraishi et al. reported in a retrospective study that the laparoscopic approach was associated with the formation of ostomies that did not pass through the middle of the rectus abdominis muscle (19). In the laparoscopic approach, in creating an ostomy, the operating table is usually not flat, but in an upside-down and right-lateral position, pneumoperitoneum may persist. Dislocation of the stoma site and difficulty passing the ostomy through the middle of the rectus abdominis muscle may occur due to the position of the muscle and the pneumoperitoneum. Before creating an ostomy during laparoscopic surgery at our institution, the patient was not routinely replaced. Regardless of the required time, before creating the site for the passage of the ostomy, it is essential to lay the patient flat and release the pneumoperitoneum. This is the direction in which we intend to modify our routine procedures.

There are many surgical factors that increase the risk of PSH. We found a significant correlation between an ostomy height of less than 10 mm or an ostomy location in the lower left quadrant and the development of PSH. A recent meta-analysis revealed that aperture size was a risk factor for PSH (17). In a different study, the authors hypothesized that an aperture greater than 43 mm was a risk factor for PSH (29). However, current recommendations

state that there is no ideal data on aperture size and recommend minimizing aperture size to ensure adequate blood flow to the intestine (3). Our study revealed that aperture size was not associated with PSH development. Kozan et al. reported that not marking the stoma site preoperatively was a risk factor for PSH. This may be due to the fact that preoperative stoma marking ensures that the ostomy is correctly positioned within the abdominal rectus muscle (27). In addition, the relationship between peristomal skin complications and PSH has been demonstrated in other studies (19, 34). This could be due to frequent pouch leakage caused by PSH, which can cause peristomal skin damage. However, we found no association between preoperative stoma site marking or peristomal skin complications and the development of PSH. Moreover, this study found a significant association between PSH and ostomy-related complications, including stenosis, fistula, and retraction. These complications are often related to improper ostomy placement or construction, which may account for the increased incidence of PSH. The association between PSH and stomal prolapse has been previously demonstrated (19, 35), and the incidence of stomal prolapse was found to be significantly higher in patients with PSH than in patients without PSH in this study.

Our study has some limitations that need to be acknowledged. This study was designed to be a single-institution retrospective trial. Secondly, it only disclosed the results of a specific period. Due to the fact that not every patient was visited after surgery, the PSH rate may be lower than the actual rate. Our findings, on the other hand, demonstrated a clear review of PSH in a relatively large consecutive series.

CONCLUSION

In conclusion, PSH is a common and problematic complication of gastrointestinal surgery, and prevention is preferable to treatment. The prevalence of PSH increases with advancing age, obesity, and the presence of co-morbid conditions. Stomal prolapse and other ostomy-related complications were also significantly associated with PSH. During laparoscopic surgery, the creation of an ostomy requires special consideration. Positioning the operating table flat and releasing the pneumoperitoneum may decrease the incidence of PSH following laparoscopic surgery. Creating an ostomy with proper surgical technique can reduce stoma-related complications and PSH development.

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