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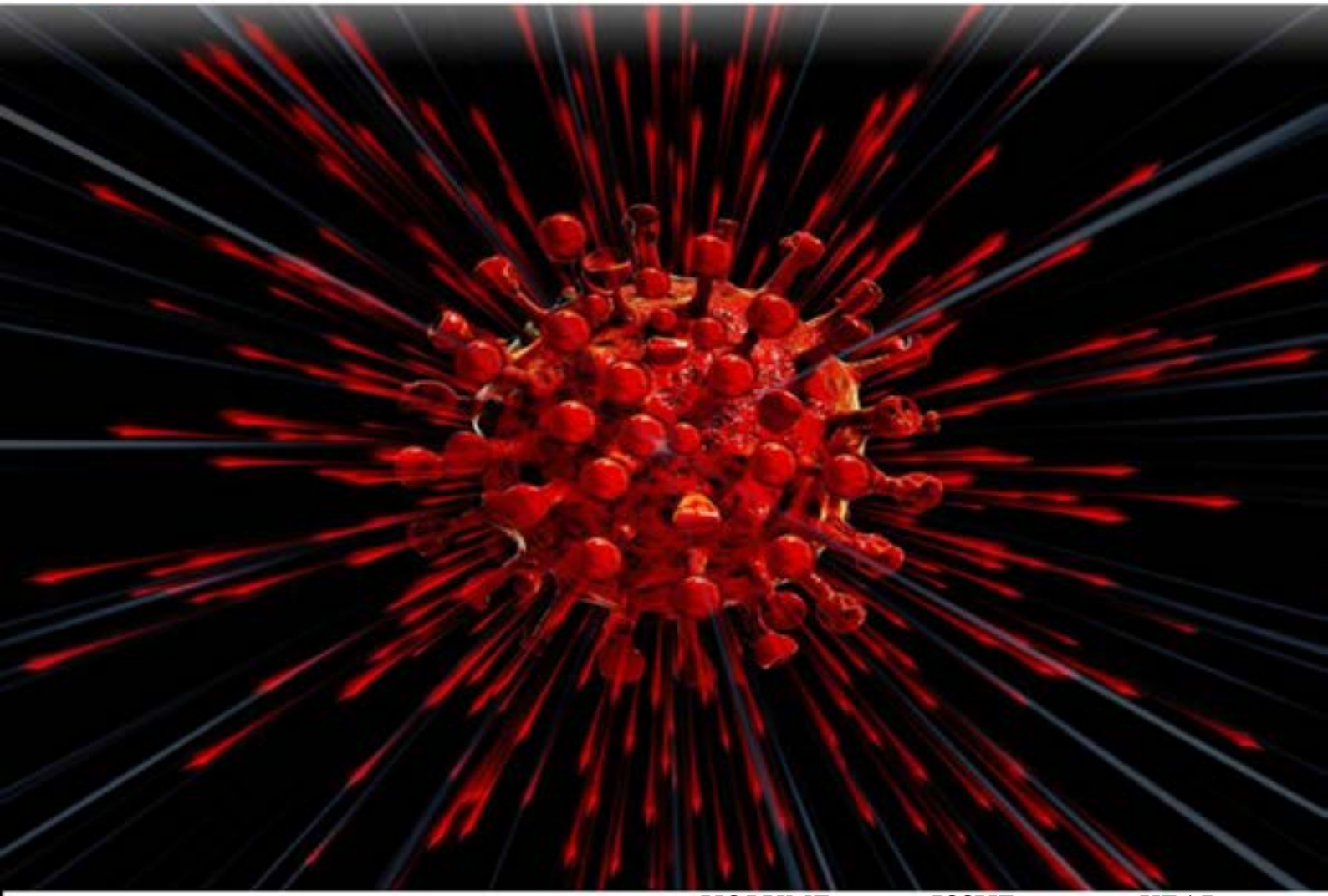

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Original Article

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Anatolian Curr Med J. 2024;6(5):293-298

Assessment of tumor location in adjuvant treatment decision for stage II colon cancer

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ABSTRACT

Aims: In stage II colon cancer, the aim is to evaluate the impact of tumor location and other clinicopathological factors on prognosis and survival.

Methods: The study included a total of 93 patients diagnosed with stage II colon cancer between January 2018 and December 2022, comprising 41 females and 52 males. Clinicopathological factors related to the patients were retrospectively investigated. Factors found to be significant in univariate analysis were further evaluated through multivariate analysis to identify independent factors.

Results: As a result of univariate analysis, variables such as tumor location (right-left colon), perineural invasion, surgical margin, intestinal obstruction, and lymph node dissection were found to be statistically significant for the risk of death ($p<0.05$). These variables, identified as significant in univariate analyses, were included in the multivariate cox regression model. According to the result of the multivariate cox regression model, individuals with intestinal obstruction were determined to have a 7.07 times higher risk of death (HR: 7.07; 95% CI: 2.42-20.62; $p<0.001$).

Conclusion: We observed an association between left colon tumors in stage II patients and poorer survival, and we noted that intestinal obstruction has an independent prognostic effect on survival.

Keywords: Adjuvant chemotherapy, colon cancer, prognosis, tumor localization

INTRODUCTION

Colorectal cancers (CRC) rank as the third most common cancer worldwide and represent the second leading cause of cancer-related deaths. Tumors located proximal to the splenic flexure are classified as right-sided, whereas those situated at or distal to the splenic flexure are termed left colon tumors.[1]

Right and left colon tumors originate from different embryological origins. The proximal two-thirds of the transverse colon derive from the midgut and are perfused by the superior mesenteric artery, while the distal one-third arises from the hindgut and is perfused by the inferior mesenteric artery.[2] These distinct embryological origins contribute to differences in the biology of these tumors.

The colon harbors a rich microbiota composed of intestinal bacteria. Notably, substantial differences exist in mucosal microbiota between patients with right-sided and left-sided colon cancer.[3] Additionally, the epithelia of the right and left colon exhibit distinct gene methylation and expression profiles.[4,5] Key oncogenes and tumor suppressors carry different mutations in right and left colon cancers. BRAFV600E and KRAS mutations are more prevalent in right colon tumors, whereas APC and TP53 mutations are frequently observed in left colon tumors.[6-8] The presence of mutations in APC, TP53, and KRAS may lead to diverse prognostic outcomes in CRC.[8] In addition to point mutations, amplifications of tyrosine kinases such as ERBB2 and epidermal growth factor receptor (EGFR), which are susceptible to targeted interventions, demonstrate higher prevalence in left-sided CRC.[9]

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Microsatellite instability (MSI) is observed up to 10 times more frequently in right colon tumors compared to left colon tumors.[10,11] MSI is a hypermutable condition resulting from the loss of DNA mismatch repair activity and is found in approximately 15% of all colorectal cancers. While 3% of these cases are associated with Lynch syndrome, the remaining 12% of sporadic MSI-high tumors are characterized by hypermethylation of the MLH1 gene, typically occurring in tumors with a CpG island methylator phenotype.[12] MSI has prognostic significance and contributes to clinical differences between right and left colon cancers, with MSI-high tumors exhibiting a better prognosis.[13]

There are distinct prognostic differences between right and left colon tumors based on the tumor stage. Metastatic colorectal cancer arising from the right colon typically exhibits a poorer prognosis when contrasted with metastatic colorectal cancer originating from the left colon.[14] In stage III disease, disease-free survival is shown to be lower in patients with right colorectal cancer.[15] For stage I and II diseases, conflicting prognosis results exist.

In early-stage colorectal cancers (stage I-III), surgical resection is the primary treatment method. For stage III disease, standard adjuvant therapy is advised for all patients, whereas for stage II disease, adjuvant chemotherapy is recommended specifically for those deemed at high risk.[1] Factors influencing the decision for adjuvant therapy in stage II disease include clinical and pathological risk factors such as lymphovascular invasion (LVI), perineural invasion (PNI), tumor perforation (TP), ileus, tumor budding (TB), and the number of removed lymph nodes being <12, as well as poorly differentiated histology.[2-4]

Notably, tumor localization is not among the factors influencing the adjuvant chemotherapy decision in stage II colon cancer. This study aims to evaluate right and left colon tumors, which differ embryologically, clinically, and prognostically, in stage II colon cancers concerning the decision for adjuvant treatment. The research also seeks to explore the relationship between clinicopathological factors and patients prognosis.

METHODS

The study initiated with approval of the Kayseri City Hospital Clinical Researches Ethics Committee (Date: 22.08.2023, Decision No: 895). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was conducted with patients aged 18 and above who underwent surgery and were diagnosed with stage II colon cancer between January 2018 and December 2022. A total of 93 patients under follow-up at Karadeniz Technical University and Kayseri City Hospital were included in the study. Epidemiological, pathological, and clinical characteristics of the patients were retrospectively recorded. Eight patients with insufficient data recorded in the hospital information system were excluded from the study. Patients with rectal cancer, as their treatments differ from colon cancer, were not included in the study. Tumors located in the cecum, ascending colon, and transverse colon were categorized as right colon cancer, while those situated in the splenic flexure, descending colon, sigmoid colon, and rectosigmoid were classified as left colon cancer. Data usage permission was obtained from relevant institutions, and ethics committee approval was obtained.

Statistical Analysis

Statistical analyses were performed using "IBM SPSS Statistics for Windows, Version 25.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA)." Descriptive statistics were presented as n and % for categorical variables, and mean±SD for continuous variables. The Kaplan-Meier method was employed to compare survival and Progression-Free Survival (PFS) times among various clinical parameter groups. Overall survival (OS) was calculated from the time of diagnosis to the last evaluation or death. PFS was evaluated as the time to recurrence or metastasis. Finally, multivariate cox Regression results for the risk of death associated with various clinical factors were provided, considering $p<0.05$ as statistically significant.

RESULTS

A total of 93 patients, including 41 females and 52 males, were included in the study. The mean age of the patients was determined to be 67.68±9.69. Right colon cancer was present in 32.3% of the patients, while left colon cancer was present in 67.7%. Demographic, pathological, and clinical characteristics of the patients are presented in Table 1.

As seen in Table 2, the overall median OS (months) could not be reached.

There was a statistically significant difference in median OS (months) among the right-left colon (p=0.048), grade (p=0.001), intestinal obstruction (p<0.001), and TB (p=0.049) groups (Figure 1,2,3,4).

As observed in Table 3, the overall median PFS (months) could not be reached.

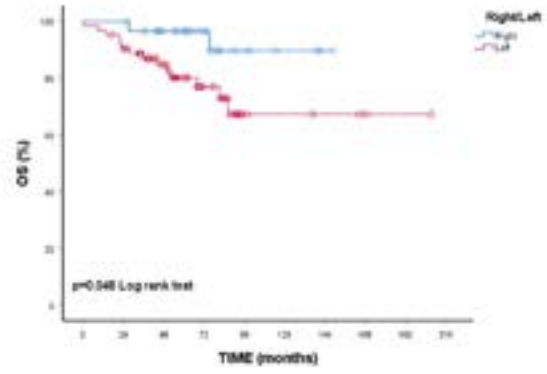

Figure 1. The relationship between right and left colon OS

OS: Overall survival

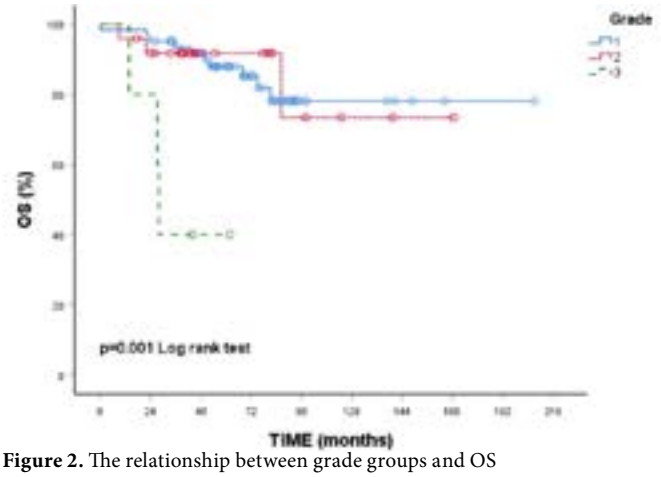

Figure 2. The relationship between grade groups and OS

OS: Overall survival

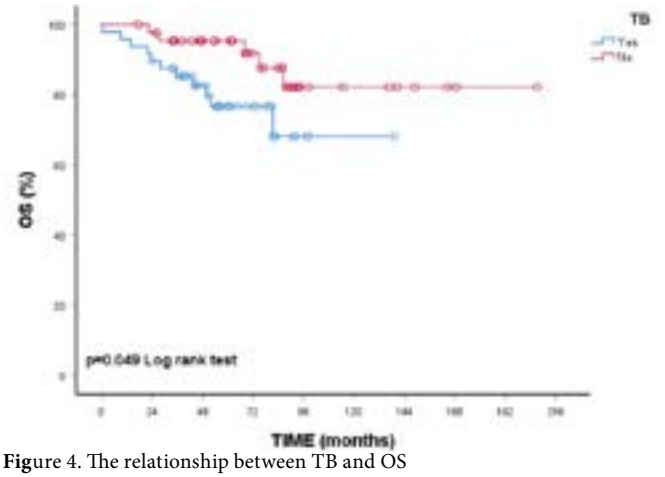

Figure 4. The relationship between TB and OS

TB: Tumor budding OS: Overall survival

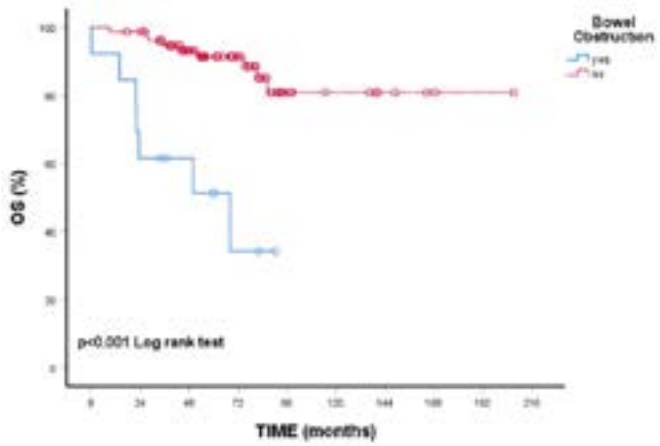

Figure 3. The relationship between bowel obstruction and OS

OS: Overall survival

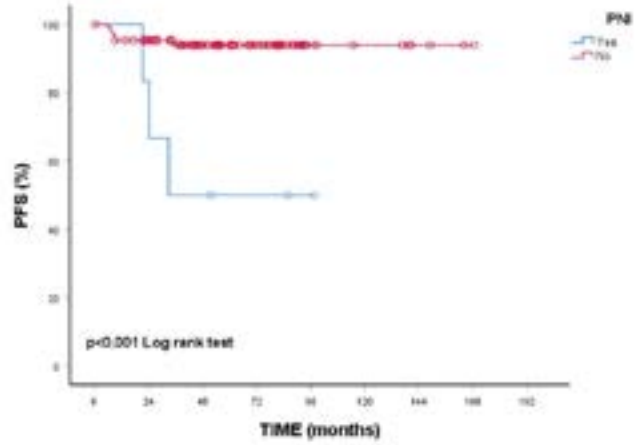

Figure 5. The relationship between PNI and PFS

PNI: Perineural invasion, PFS: Progression-Free Survival

There was a statistically significant difference in median PFS (months) among the PNI groups (p<0.001) (Figure 5).

As shown in Table 4, the variables right-left colon, PNI, CS, intestinal obstruction and removed lymph node were found to be statistically significant in terms of the risk of death (p<0.05) according to univariate (single-variable) analysis. These significant variables identified in univariate analysis were included in the multivariate cox regression model. According to the results of the multivariate cox regression model, individuals with intestinal obstruction were determined to have a 7.07 times higher risk of death (HR:7.07; 95% CI: 2.42-20.62; p<0.001) (p<0.001, -2 loglikelihood= 114.06).

DISCUSSION

According to the location of the tumor in the proximal and distal segments of the colon, the existence of two different categories of colorectal cancer has been suggested in many studies.[1,16,17] Despite having different biological and clinical characteristics, the role of tumor location in adjuvant therapy and the clinicopathological factors affecting adjuvant treatment decisions are often overlooked in studies related to colorectal cancer treatment. In our study, we investigated the role of tumor location in adjuvant therapy and the clinicopathological factors influencing adjuvant treatment decisions in stage II colon cancer. We observed that left colon tumors are associated with poorer survival and that intestinal obstruction has an independent prognostic effect on survival.

There are conflicting findings regarding the association between cancer location and mortality. It is known that right colon cancer has a worse prognosis than left colon cancer.[16] However, conflicting results have been reported in terms of prognosis according to stages. In one study, the mortality of right colon cancer was found to be higher in stage III colon cancer, whereas in our study, similar to our study, lower mortality was observed in patients with stage II colon cancer.[17,19] In another study, localized right colon cancer was found to have a better prognosis than left colon cancer in stage I-III.[18] Another study evaluated the effect of tumor location on prognosis in patients with stage II colon cancer and found that there was no statistically significant difference between tumor location and PFS and OS.[19]

There are studies reporting that right colon cancer has a higher risk of death than left colon cancer. [16,18,20,21] However, when classified by stage, studies have shown no difference in mortality between right and left colon in stage I colon cancer (HR, 1.003; P=93), and lower mortality similar to our study

Table 1. Examination of some demographic and clinical characteristics according to colon region

	Colon side		Statistic	p
	Right (n=30)	Left (n=63)		
Age	76 (45 - 86)	74 (40 - 96)	-0.530	0.596[m]
Gender				
Female	11 (36.7)	30 (47.6)	0.989	0.320[x]
Male	19 (63.3)	33 (52.4)		
Tumor Localization				
Rectosipmoid	---	6 (9.5)		
Sigmoid	---	41 (65.1)		
Descending colon	---	14 (22.2)		
Splenic flexure	---	1 (1.6)	---	
Transverse colon	3 (10)	1 (1.6)		
Ascending colon	19 (63.3)	---		
Cecum	8 (26.7)	---		
LVI				
Present	5 (16.7)	4 (6.3)	---	0.142[f]
Absent	25 (83.3)	59 (93.7)		
PNI				
Present	1 (3.3)	5 (7.9)	---	0.660[f]
Absent	29 (96.7)	58 (92.1)		
Grade				
1	18 (60)	45 (71.4)		
2	9 (30)	16 (25.4)	2.383	0.327[f]
3	3 (10)	2 (3.2)		
MSI IHK				
Not examined	4 (13.3)[a]	20 (31.7)[a]		
Stable	19 (63.3)[a]	42 (66.7)[a]	12.675	**0.002**[f]
High	7 (23.3)[a]	1 (1.6)[b]		
Localized perforation				
Present	0 (0)	2 (3.2)	---	1.000[f]
Absent	30 (100)	60 (96.8)		
Surgical margin				
Negative	28 (93.3)	57 (90.5)	---	1.000[f]
Positive	2 (6.7)	6 (9.5)		
Intestinal obstruction				
Present	2 (6.7)	11 (17.5)	---	0.211[f]
Absent	28 (93.3)	52 (82.5)		
Tumor budding				
Present	16 (55.2)	32 (50.8)	0.153	0.696[x]
Absent	13 (44.8)	31 (49.2)		
Removed lymph node				
≥12	28 (93.3)	47 (74.6)	---	0.050[f]
<12	2 (6.7)	16 (25.4)		
Mortality				
Alive	28 (93.3)	49 (77.8)	---	0.081[f]
Ex	2 (6.7)	14 (22.2)		
Adjuvant chemotherapy				
Present	13 (43.3)	17 (27)	2.486	0.115[x]
Absent	17 (56.7)	46 (73)		
Follow-up duration, Mean±SD	66.03±36.11			

m: Mann Whitney U testi, x: Pearson chi-square testi, f: Fisher's exact testi, a-b: No difference between groups with the same letter (Bonferroni corrected Z testi), median (min.-max.), n (%)

Table 2. Overall survival (OS) comparisons according to pathological features

OS (months)	2 years %	5 years %	Median (95% CI)	p
General	93.5	85.8	– (–)	
Right-left				
Right	100.0	96.6	– (–)	0.048
Left	90.4	80.1	– (–)	
LVI (Lymphovascular invasion)				
Present	88.9	88.9	– (–)	0.743
Absent	94.0	85.4	– (–)	
PNI (Perineural invasion)				
Present	–	66.7	– (–)	0.510
Absent	93.1	87.9	– (–)	
Grade				
1	95.2	88.0	– (–)	
2	91.8	91.8	– (–)	0.001
3	80.0	40.0	27.93 (26.28–29.57)	
MSI (Microsatellite instability)				
Not examined	83.3	79.2	– (–)	
Stable	96.7	88.0	– (–)	0.593
High	–	87.5	– (–)	
Surgical margin				
Negative	94.1	87.1	– (–)	0.246
Positive	87.5	70.0	– (–)	
Intestinal obstruction				
Present	61.5	51.3	68.00 (13.49–122.50)	<0.001
Absent	98.8	91.4	– (–)	
TB (Tumor budding)				
Present	89.6	76.6	– (–)	0.049
Absent	97.7	95.3	– (–)	
Removed lymph node				
≥12	96.0	89.5	– (–)	0.101
<12	83.3	71.4	– (–)	

The Kaplan–Meier curve and Log–rank test revealed statistically significant results with p<0.05.

Table 3. Progression-free survival (PFS) comparisons among patients

PFS (months)	2 years %	5 years %	Median (95% CI)	p
General	94.5	90.8	– (–)	
Right–left				
Right	–	96.7	– (–)	0.183
Left	91.8	87.9	– (–)	
PNI (Perineural invasion)				
Present	83.3	50.0	32.90 (–)	<0.001
Absent	95.3	93.9	– (–)	
SM (Surgical margin)				
Negative	95.2	92.6	– (–)	0.053
Positive	85.7	68.6	– (–)	
Intestinal obstrution				
Present	82.5	82.5	– (–)	0.186
Absent	96.3	92.2	– (–)	
TB (Tumor buding)			– (–)	
Present	95.6	90.7	– (–)	0.937
Absent	93.3	90.8	– (–)	
Removed lymph node				
≥12	96.0	93.0	– (–)	0.154
<12	87.8	81.1	– (–)	

The Kaplan-Meier curve and Log-rank test revealed statistically significant results with p < 0.05.

Table 4. Multivariate cox regression results for various clinical variables

OS (Overall survival)	Multivariate	
Variables	HR (95% CI)	p
Right-left (Ref: right)	2.87 (0.60-13.70)	0.185
PNI (Ref: absent)	1.39 (0.29-6.55)	0.672
CS (Ref: negative)	4.66 (0.90-23.95)	0.065
Intestinal obstruction (Ref: absent)	7.07 (2.42-20.62)	<0.001
Number of removed lymph nodes <12 (Ref: adequate)	1.27 (0.42-3.80)	0.669
p<0.001; -2 Log Likelihood=114.06		

has been reported in stage II right colon cancer (HR, 0.91; p<0.001).[18,20]

The inconsistent correlation between mortality and tumor location across different stages remains inadequately elucidated. However, this could be related to tumor biology. It is known that MSI tumors have a better overall prognosis.[21,22] MSI is more commonly observed in right colon tumors than in left colon tumors.[1] In a study, it was shown that MSI positivity is more common in stage II right colon cancers compared to stage III and IV[23] This may explain the better observed mortality in stage II disease in the right colon.

Intestinal obstruction stands as one of the high-risk factors impacting the consideration for adjuvant treatment in patients diagnosed with stage II colon cancer. However, data on the impact of obstruction on the prognosis of colorectal cancer are conflicting. Some studies have shown that intestinal obstruction has no prognostic effect on survival.[24,25] However, similar to our study, a multicenter analysis conducted by the gastrointestinal tumor study group showed that obstruction is an important prognostic indicator independent of stage.[26]

The distribution between right and left colon cancers of the patients in our study reflects the epidemiological trends observed in clinical practice. This strengthens the applicability of our findings to the clinical setting. However, the most important limitation of our study is that it was retrospective and the number of patients was limited. We believe that our findings can be improved and the prognostic significance of the distinction between right and left colon can be better examined in studies involving more patients and centers.

Limitations

Most important limitation of our study is that it was retrospective and the number of patients was limited. We believe that our findings can be improved and the prognostic significance of the distinction between right and left colon can be better examined in studies involving more patients and centers

CONCLUSION

Considering the significant differences in clinical, histological, microbiota, mutation, and genomic profiles between right and left colon tumors, it is plausible that they may exhibit different outcomes based on stages. While right colon tumors are generally considered to have a worse prognosis, we believe they may have a better prognosis in stage II patients. We think there is a need for more comprehensive studies that include a larger number of patients, where tumor location and clinicopathological factors are evaluated in the decision-making process for adjuvant treatment.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Kayseri City Hospital Clinical Researches Ethics Committee (Date: 22.08.2023, Decision No: 895).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

ANATOLIAN CURRENT MEDICAL

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Anatolian Curr Med J. 2024;6(5):299-305

Determining the effectiveness of basic first aid training provided to secondary school student

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ABSTRACT

Aims: The aim of this study is to evaluate the effectiveness of first aid training provided to middle school students from diverse socio-demographic backgrounds, and to examine how these differences influence the outcomes of the training.

Methods: The study was conducted in three middle schools located in the eastern part of Turkiye between April and July 2016. The population of the study consisted of 7th-grade students (n=391) attending these schools during the spring semester of the 2015-2016 academic year. All students were included in the sample without any selection, as participation was obtained through parental and student consent. Data were collected using the "Descriptive Information Form" and the "First Aid Education Knowledge Evaluation Form". First aid knowledge levels were assessed before the training, after the training, and two weeks post-training.

Results: The study found that the average first aid knowledge scores of students based on socioeconomic status were 58.61±6.26 for high, 60.86±5.86 for middle, and 56.44±6.26 for low socioeconomic status. Post-training, the average scores increased across all groups. These findings indicate that socioeconomic status affects first aid knowledge, but the training programs benefit all students and improve their knowledge levels.

Conclusion: The findings of this study indicate that while socioeconomic status exerts a significant influence on first aid knowledge, the training programmes implemented have resulted in notable improvements in the knowledge levels of all students.

Keywords: First aid training, school health, school health nursing

INTRODUCTION

Accidents occurring at home, in traffic, or in the workplace have been shown to have profound impacts on individuals and communities.[1-5] Over the past decade, the increase in natural disasters and human-made accidents has resulted in many incidents that pose devastating threats to children and adolescents in primary and secondary schools.[6] This situation has led to numerous studies emphasizing the critical importance of first aid in accident scenarios.[7-9]

First aid plays a crucial role in providing immediate assistance to individuals who are suddenly injured or fall ill until professional help arrives or the person recovers.[10] Correctly administered first aid is essential to minimize disability, enhance the safety of victims, and potentially save lives.[11] Therefore, first aid skills are vital for individuals of all ages.[12] First aid training is particularly effective for children aged 11-20, as they have developed the highest levels of physical, sensory, and psychomotor functions in this age group.[13] Short-term training programs have been shown to significantly improve first aid knowledge and practices among students aged 13-15, highlighting the suitability of this age group for such education.[14] Schools provide excellent opportunities to offer first aid and basic life support training, preparing students for emergencies, reducing the severity of injuries, and promoting a culture of safety.[15-18] Additionally, short-term first aid training programs have been found to

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significantly enhance students' knowledge, attitudes, and confidence in performing first aid.[19,20]

This study aims to evaluate the effectiveness of first aid training provided to middle school students across three different schools with varying socio-demographic backgrounds. By examining the impact on students from diverse socio-economic backgrounds, this research seeks to reveal how these differences influence the outcomes of first aid education. Additionally, the study addresses a significant gap in the literature by focusing on the effectiveness of training provided by pediatric nurses. The originality and significance of this study lie in its comprehensive approach to understanding how socio-demographic factors influence the outcomes of first aid education. The hypothesis of this study is that first aid training will enhance the first aid knowledge levels of students from different socio-demographic backgrounds.

METHODS

Ethics

The study was carried out with the permission of Ataturk University Faculty of Medicine Clinical Researches Ethics Committee (Date: 18.04.2016, Decision No: 04/10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Type of Study

The research was carried out using one of the Weak Experimental Designs, specifically a One-Group Pretest-Post-test Design, to determine the effectiveness of basic first aid training given to 7th-grade secondary school students.

Place and Time of the Study

The study was conducted in three secondary schools in a province in eastern Turkiye between April 2016 and July 2016.

Population and Sampling of the Research

The population of the study consisted of students studying at three secondary schools, which were determined according to the socioeconomic level classification in the city centre, in the spring semester of the 2015-2016 academic year. The study group included children aged 11 and over in the "Abstract Operations Period", in which rational solutions are produced against complex problems and ideas are developed in social events, according to Jean Piaget's theory of cognitive development.[21] In addition, considering previous studies, secondary school 7th-grade (12-14-year-old) students were included in the study to standardize the training program.[22,23] There are a total of 15 7th-grade classes in the three secondary schools where the study was conducted.

According to September 2015 data, there are 112 secondary schools in the city centre. These schools were divided into three groups (good, moderate, and poor) according to their socioeconomic levels in line with the information of the provincial directorate of national education. Each group was accepted as a layer, and one school from each layer was selected by drawing lots. All students (n=391) for whom parental and student permissions to participate in the study were obtained were included in the study without selecting a sample group. Private schools were not included in the study because permission for the study could not be obtained.

A power analysis was performed to determine whether the number of students included in the study was adequate. According to the power analysis, it was determined that the power of the research was 0.97 at a significance level of 0.05, an effect size of 0.5, and a confidence interval of 0.95.

Inclusion Criteria

Students who were studying in the 7th grade of secondary school, who were willing to participate in the study, and for whom written permission was obtained from the parents were included in the study.

Exclusion Criteria

Students who were not willing to participate in the study and for whom written permission could not be taken from the parents were not included in the study.

Research Variables

Independent variables: Basic first aid training provided to students

Dependent variables: First aid knowledge scores of students

Control variables: Sociodemographic characteristics of students

Data Collection Tools

"Identifying Information Form" and "First Aid Training Knowledge Evaluation Form (FATKEF)" prepared by the researcher based on the literature [22-24] review were used to collect the data.

Identifying Information Form: The "Identifying Information Form" was prepared to determine the socio-demographic characteristics of the students included in the study. In the form, there are questions that inquire about the class, gender, age, and first aid training status of the students to be included in the research.

First Aid Training Knowledge Evaluation Form (FATKEF): This form was developed and validated by Yalcin[22] in 2010 in line with the cognitive goals expected to be achieved in first aid training. This form, designed to measure the level of first aid knowledge in accordance with the basic first aid training content and the determined objectives, measures the level of basic first aid knowledge. The form consists of 34 multiple-choice questions, including general first aid information (8 questions), first aid provider characteristics (1 question), human body (1 question), evaluation of the patient/ injured and the scene (9 questions), first aid in bleeding (5 questions), first aid in case of burns and frostbite (3 questions), first aid in fractures (2 questions), first aid in poisonings (3 questions), and first aid in respiratory obstruction (2 questions). Each question is evaluated as no knowledge, knowledge present, and incorrect knowledge. If the response of the student to a question is correct, it is scored as 3 points; if it is "I don't know", it is scored as 2 points; if the response is incorrect, it is scored as 1 point. The Cronbach's alpha coefficient of the FATKEF was determined to be 0.743 by Yalcin[22], in this study, this value was found to be 0.60.

Data Collection

The data were collected by the researcher by face-to-face interview method. First of all, the "informed consent form" prepared by the researcher to obtain written permission from the parents of the students was given to the students in a sealed envelope and delivered to their parents. The consent forms signed by the parents were returned by the students. In addition, after the students were informed about the research and their verbal consent was obtained, they were allowed to participate in the study. Following the collection of consent forms, the school administrations were contacted, and a schedule was formed to apply the data collection forms and implement the training program.

First aid knowledge levels of the students were evaluated in the classroom environment to determine their first aid knowledge levels, to evaluate the results of the first aid training, and to measure the changes over time. The first application (pre-test) evaluating the students' levels of first aid knowledge was carried out before the training, and training on first aid was given following the pre-test. The second test (post-test) was administered one day after the training, and the third test (control test) was given two weeks after the training; all tests were evaluated with the same form (FATKEF).

The training sessions were held separately for 15 classes in the classroom environment, the duration of the training consisted of two lesson hours (90 minutes) for each class, and the training was held in two sessions. During the training, training materials such as first aid materials, training videos, video projectors, and training slides were used. Moreover, a training booklet containing the subjects taught in class was given to the students. In the training, direct instruction, question-answer, and demonstration techniques were used. Training sessions were given by the researcher, who also holds a trainer certificate approved by the red crescent. The students were given 40 minutes to respond to the questions on the data collection forms in each measurement.

Basic first aid training: Educational materials were created by using the presentations prepared by the Turkish red crescent for children aged 6-14. These materials are the slides to be used during the training and the "First aid training booklet" to be given to the students. Necessary permission to use these materials was taken from the Turkish red crescent. In addition, the materials to be used in the training were supplied by the Provincial Directorate of the Turkish red crescent taking the required permissions.

Statistical Analysis

The data were analysed in the computer environment using the SPSS (Statistical Package for Social Sciences) 21.0 package software. In the analysis of the data, percentage distributions, mean, and standard deviation, analysis of variance in repetitive measurements, independent groups t-test, analysis of variance, Kruskal-Wallis test, and Cronbach's alpha coefficient calculation were employed. The study findings were evaluated at a 95% confidence interval and $p<0.05$ significance level.

Methods

Written permission for the study was taken from the provincial directorate of national education. In addition, permission to use the first aid training knowledge form was taken from the corresponding author.

Families and their children who volunteered and were willing to participate in the study were included in the study, and it was explained that they were free to participate or not in the study. In addition, before collecting the data, an informed consent form containing information about the study was sent to the families, and their written consent was obtained. In addition, verbal permission was obtained from the children.

RESULTS

In the study, the effectiveness of basic first aid education provided to secondary school 7th-grade students was evaluated, and the findings obtained are presented in this section. Table 1 presents the distribution of the students included in the study by descriptive characteristics. It was determined that the mean age of the students included in the study was 13.18±0.54, 51.2% were male, and 48.8% were

Table 1. Distribution of students by descriptive characteristics

Characteristics	Number	%
Mean age of students*	13.18±0.54	
Age		
12 years old	27	6.9
13 years old	266	68.0
14 years old	98	25.1
Gender		
Female	191	48.8
Male	200	51.2
Socioeconomic status		
Good	129	33.0
Moderate	133	34.0
Poor	129	33.0
Total	391	100.0

*Mean ± Standard deviation

Table 2. Students' opinions regarding receiving training on first aid (n=391)

Characteristics	Number	%
Considering receiving training necessary		
Necessary	388	99.2
Unnecessary	3	0.8

Table 3. The distribution of the sources from which the students wanted to receive training on first aid (n=391)

Trainer	Number	%
Health professional	227	58.1
Teacher	85	21.7
Family	38	9.7
Internet	28	7.2
Coursebook	9	2.2
Television-radio	3	0.8
Newspaper-magazine	1	0.3

Table 4. Evaluation of the students' first aid knowledge levels through pretest, posttest, and control test (n=391)

	Pretest			Posttest			Control test		
Knowledge area	**Incorrect %**	**No knowledge %**	**Correct %**	**Incorrect %**	**No knowledge %**	**Correct %**	**Incorrect %**	**No knowledge %**	**Correct %**
1. The definition of first aid	16.4	5.1	78.5	1.5	1.0	97.4	2.8	1.0	96.2
2. Who will apply first aid	16.6	1.3	82.1	1.5	1.8	96.7	3.1	1.8	95.1
3. Priorities in first aid	63.4	4.9	31.7	2.3	0.5	97.2	1.8	0.3	98.0
4. What should be done first on the scene of injury	86.2	4.1	9.7	9.5	2.0	88.5	11.0	2.3	86.7
5. Basic practices in first aid	65.5	9.5	25.1	9.7	4.6	85.7	10.2	5.6	84.1
6. Emergency service telephone number	4.3	0.5	95.1	0.0	0.0	100.0	0.0	0.0	100.0
7. Information to be provided when the emergency service is called	88.2	3.3	8.4	11.5	10.5	78.0	12.5	11.3	76.2
8. Injured persons to whom priority intervention should be made on the scene of an accident	34.5	9.0	56.5	4.1	5.9	90.0	5.1	6.9	88.0
9. Chatacteristics of a first aid provider	69.8	11.5	18.7	4.1	6.6	89.3	4.6	7.7	87.7
10. What should be evaluated in terms of vital signs	37.9	7.2	55.0	15.6	2.3	82.1	16.4	3.3	80.3
11. Correct sequencing of the primary evaluations steps	60.6	15.1	24.3	17.1	0.8	82.1	18.9	0.8	80.3
12. What should be checked for CAB evaluation	42.7	16.9	40.4	6.9	10.0	83.1	9.0	9.7	81.3
13. How to ensure airway patency (A)	75.4	15.3	9.2	3.1	0.3	96.7	4.1	0.5	85.4
14. In what situation coma (recovery) position should be given	61.1	21.2	17.6	1.8	1.8	96.4	3.8	1.5	94.6
15. How to evaluate the presence of breathing in the primary evaluation	60.9	24.0	15.1	10.5	2.6	87.0	13.0	2.6	84.4
16. The purposes of evaluating the injured person	48.3	13.3	38.4	6.1	0.0	93.9	7.9	0.0	92.1
17. How to monitor the circulation (C) of the injured person	59.6	16.9	23.5	5.6	1.0	93.4	7.2	1.3	91.6
18. In what situation head-chin position should not be applied	69.1	16.6	14.3	16.1	0.8	83.1	17.1	0.8	82.1
19. What sequence should be followed while examining the injured person in the secondary evaluation	45.8	7.9	46.3	4.1	0.0	95.9	5.9	0.0	94.1
20. What should be done to an injured person with severe bleeding	55.8	2.0	42.2	5.1	0.5	94.4	7.4	0.5	92.1
21. What to do in case of nasal bleeding	62.1	6.1	31.7	1.3	0.3	98.5	2.3	0.3	97.4
22. What to do for internal bleeding while providing first aid	56.0	23.0	21.0	11.5	5.4	83.1	13.8	5.1	81.1
23. Shock symptoms	74.4	10.7	14.8	9.7	2.3	88.0	11.3	2.3	86.4
24. Internal bleeding symptoms	72.6	16.4	11.0	11.5	1.8	86.7	13.6	2.3	84.1
25. What to do to a person who froze due to exposure to cold in first aid	87.2	6.9	5.9	10.7	2.8	86.4	13.3	2.3	84.4
26. First aid to be provided to the injured person in case of an electric shock	37.3	4.9	57.8	1.0	0.0	99.0	1.8	0.0	98.2
27. What to do in case of burns while providing first aid	67.8	11.0	21.2	12.0	2.6	85.4	13.6	2.6	83.9
28. First aid practices when there is movement loss, swelling, and pain in the arm	50.4	13.3	36.3	6.1	2.3	91.6	8.4	2.3	89.3
29. The purpose of identifying fractures	56.3	12.0	31.7	9.2	3.1	87.7	11.3	2.8	85.9
30. What to do in case of poisoning through digestive system	72.9	11.5	15.6	10.2	4.1	85.7	13.3	3.6	83.1
31. What to do in case of respiratory tract poisoning while providing first aid	63.2	17.1	19.7	9.2	5.1	85.7	11.3	5.1	83.6
32. What to do in case of poisoning through the skin while providing first aid	64.7	14.3	21.0	9.2	5.6	85.2	11.5	5.1	83.4
33. What to do in case of partial blockage in the airway as a result of foreign material presence	77.0	11.5	11.5	1.0	0.8	98.2	1.5	0.8	97.7
34. What to do in case of total blockage in the airway as a result of foreign material presence	76.5	8.7	14.8	1.0	0.8	98.2	1.8	0.5	97.7

Table 5. Comparison of the students' first aid knowledge mean scores on the pretest, posttest, and control test (n=391)

Measurements	Mean±SD**	f	p
Pretest	58.66±6.57*		
Posttest	96.29±4.12	0.24	0.001
Control test	95.26±5.05		

f=Fisher, *The group causing signifciance as a result of advanced analysis **Mean ± SD, SD: Standard deviation

Table 6. Comparison of the students' first aid knowledge mean scores on the pretest, posttest, and control test according to their descriptive characteristics

Characteristics	Pretest Mean±SD**	Posttest Mean±SD	Control test Mean±SD
Age			
12 years old	59.22±4.96	96.96±3.56	95.67±5.06
13 years old	58.64±6.46	96.32±4.18	95.28±5.03
14 years old	58.55±6.53	96.06±4.14	95.10±5.15
Test and p	KW=0.631 p=0.729	KW=0.967 p=0.617	KW=0.440 p=0.803
Gender			
Female	58.92±6.25	96.24±4.47	95.30±5.19
Male	58.41±6.49	96.36±3.78	95.23±4.93
Test and p	t=0.801 p=0.424	t=0.298 p=0.766	t=0.144 p=0.886
Socioeconomic status			
Good	58.61±6.26*	97.21±3.55	96.12±4.68
Moderate	60.86±5.86*	96.46±4.32	95.41±5.35
Poor	56.44±6.26*	95.22±4.24*	94.24±4.99*
Test and p	f=17.079 p=0.000	f=7.889 p=0.000	f=4.663 p=0.010

f=Fisher, t=t-testi, KW= Kruskal-Wallis, * The group causing significance, **<mean ± SD, SD: Standard deviation

female. It was also found that 34.& of the students had a moderate level of socioeconomic status, 33.% had a good level, and 33. % had a poor level (Table 1). The students' opinions regarding the necessity of receiving training on first aid are presented in Table 2. 99.2% of the students stated that receiving training on first aid was necessary, while 0.8% saw it as unnecessary (Table 2). The distribution of the sources from which the students wanted to receive training is presented in Table 3. Accordingly, it was determined that the top three sources from which the students wanted to receive training on first aid were health professionals (58.1%), teachers (21.7%), and families (9.7%) (Table 3). After the training, a significant increase in students' first aid knowledge was observed. 100% of students correctly identified the emergency service number, and 99% knew the correct first aid for electric shock. However, knowledge levels were lower for more detailed practices like airway patency (96.7%) and CAB evaluation (83.1%). Table 5 shows statistically significant differences between the pre-test (58.66±6.57) and post-test (96.29±4.12) scores. These results indicate a substantial improvement in students' knowledge levels after the training. Socioeconomic status significantly impacted students' scores. The average scores for students from lower socioeconomic backgrounds increased from 56.44±6.26 in the pre-test to 95.22±4.24 in the post-test. The middle socioeconomic group had the highest scores (pre-test: 60.86±5.86, post-test: 96.46±4.32). No significant differences were observed across age and gender groups.

DISCUSSION

First aid training programs include making the first intervention in an emergency before professional medical help arrives, providing basic first aid while waiting for the ambulance, and taking measures supporting the injury or injured site.[7,19]

The present study was conducted to evaluate the effectiveness of the first aid training program provided to the 7th-grade students studying at three secondary schools in the east of Turkiye. Particularly, the effect of factors such as age, gender, and socioeconomic status on the students' first-aid knowledge levels as a result of the training program was examined.

The study revealed that the average age of the students was 13.18±0.54. Additionally, 99.2% of the students acknowledged the necessity of first aid training, indicating their readiness for such education. When studies conducted in this regard were reviewed, it was reported that first aid training for school-age children could be started at age 12 or earlier.[25-28] Health professionals were the most preferred source for receiving first aid training (58.1%). In various studies, it was stated that nurses and other health professionals were able to teach first aid to children with success at schools.[25,28-30] In the study they conducted with students, Banfai et al.[31] determined that students advocated that training on first aid should be received from a health professional rather than a teacher. In our study, consistent with the literature,[22] it was found that students are not only ready for education but also prefer to receive it from health professionals. This preference could enhance the quality of the training.

In this study, the students' first aid knowledge levels were assessed using a pretest, posttest, and control test. The pretest results indicated that most students knew the "telephone number of the emergency service." Similarly, Yalçın[22] (2010) found that the majority of students correctly identified the emergency service number.In the study by İbrahimoğlu et al.[7] (2024), nearly all students correctly answered the emergency service number following basic first aid training. Banfai et al.[31] (2017) also reported a high rate of correct responses in the pretest regarding the emergency service number The findings across these studies demonstrate similarities in students' knowledge of the emergency service number.

In the pretest, it was determined that the majority of students knew "who should perform first aid," "the definition of first aid," "the first aid provided to a person injured by electric shock," and "the injured person who should be prioritized in case of an accident." Similarly, in Yalçın's[22] study, it was found that the majority of students correctly identified "who should perform first aid," "the definition of first aid," "what to do first when seeing someone suffering from electric shock," and "the vital signs." Comparing the results of the two studies, it is evident that students in both studies have a high level of knowledge regarding first aid and yielded similar results. These findings suggest that students may have acquired first aid knowledge from their daily lives or previous experiences.

In the study, the pretest showed that the question "information to provide when calling emergency services" had the highest rate of incorrect answers. This can be attributed to students not having previously called an emergency number and lacking sufficient knowledge in first aid. During the training, students were shown practical examples of the necessary conversations when requesting emergency assistance. Consequently, the correct response rate for this question significantly increased in the post-test and was largely retained in the control test. Similarly, Çil Eyi et al.'s,[32] study reported a significant increase in correct responses to what should be communicated to 112 teams in the post-test.

First aid training given to children in schools is of great importance for them to respond effectively to emergencies and potentially save lives.[33] Training individuals, including children, in first aid can enhance their skills to provide immediate assistance in emergencies.[34] In our study, a significant increase was observed in the knowledge levels of students after basic first aid training. Students' knowledge in essential first aid topics such as "CAB assessment," "airway clearance," "breathing assessment," and "circulation monitoring" increased significantly. In the control tests, it was found that this knowledge was largely retained. Similarly, the literature indicates that children aged 11-15 can learn CAB applications and cardiopulmonary resuscitation.[25,26,35,36]

Although our short course was effective, the literature suggests that repeating first aid knowledge and extending the curriculum throughout the year enhances emergency performance and motivation.[25,26,28] This finding underscores the importance of the continuity and variety of training programs.

In our study, the percentage of students who correctly knew how to provide first aid to a patient with severe bleeding increased significantly from the pre-test to the post-test. Similarly, the percentage of those who knew the correct first aid for nosebleeds, common in school accidents, showed a marked increase. This aligns with the literature, where studies have shown that success rates in managing bleeding during first aid significantly increased between the pre-test and post-test, with substantial retention of knowledge several months later.[22,31,32] These findings demonstrate that first aid training effectively enhances students' knowledge and skills, particularly managing bleeding.

In our study, the percentage of correct responses for first aid topics such as shock position, first aid for burns, first aid for a person who is about to freeze, first aid for fractures, first aid for poisoning through ingestion, and first aid for partial or complete airway obstruction increased significantly from the pre-test to the post-test. In the control test, this knowledge was retained. These findings are consistent with previous studies.[19,22,32,35]

Yalçın[22] found that the first aid knowledge scores of 7th-grade students were significantly higher after training compared to before. Another study also reported that children's first aid knowledge and skills, which were initially low, improved significantly after training and remained high even four months later.[31] Comparing the pre-test, post-test, and control test scores, it is evident that there was a significant increase in first aid knowledge levels.

In the study, the average pre-test first aid knowledge scores based on students' socioeconomic status were found to be 58.61±6.26 for high socioeconomic status, 60.86±5.86 for middle socioeconomic status, and 56.44±6.26 for low socioeconomic status. Post-training, the average scores increased across all groups, supporting the hypothesis of the study.

The post-test and control test revealed some differences among students based on their socioeconomic status. Students from lower socioeconomic backgrounds had slightly lower average scores compared to other groups. However, the fact that students from the middle socioeconomic group had the highest average scores suggests that the impact of socioeconomic status on first aid knowledge is complex and cannot be explained by a single factor. Other factors, such as differences in educational environments, student participation, and motivation, may have also contributed to these findings. Therefore, it is important to consider the relationship between socioeconomic status and first aid knowledge from a broader perspective.

Limitations

One limitation of the study was that it was conducted only on 7th-grade students of three secondary schools located in the provincial center in the 2015-2016 academic year. Therefore, the study results can only be generalized to this group. Additionally, the data regarding the socioeconomic characteristics of the students were obtained from the provincial directorate of national education. The age group may also limit the generalizability of the study results to the broader population.

CONCLUSION

This study found statistically significant differences in first aid knowledge scores between pre-training, post-training, and control tests, with the differences attributed to pre-training scores. It was determined that age and gender had no effect, but socioeconomic status did.

These findings suggest that first aid education should be included in the curriculum at all educational levels, with an emphasis on increasing practical training in middle schools. Teachers should regularly receive first aid training, and these trainings should be conducted by nurses certified to teach first aid. Additionally, activating school health nursing and conducting similar studies with students at different grade levels is recommended.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ataturk University Faculty of Medicine Clinical Researches Ethics Committee (Date: 18.04.2016, Decision No: 04/10).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Investigation of the effect of psychological birth order on perceived parental attitudes and early maladaptive schemas in adults

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ABSTRACT

Aims: The aim of this study is to examine the effect of psychological birth order on perceived parental attitudes and early maladaptive schemas.

Methods: In this study, the psychological birth order inventory, perceived parental attitudes scale-child form, and young's schema scale were used. The sample consisted of 189 women and 102 men. Relational and predictive analyses were conducted regarding birth order, psychological birth order, perceived parental attitudes, and schema domains.

Results: There was a moderate positive relationship between the sibling rank of the women who participated in the study and the emotional deprivation schema area. For female participants, being the middle child was found to have a moderately positive relationship with emotional deprivation, dependence, pessimism, and defectiveness schemas. A weak positive relationship was found between being the middle child and emotional warmth maternal attitude, overprotective mother/father attitude, and rejecting father attitude scores.

Conclusion: The study concluded that there is a significant relationship between psychological birth.order and perceived parental attitudes as well as early maladaptive schemas.

Keywords: order of birth, psychological order of birth, perceived parental attitudes, maladaptive schemes, early maladaptive schemas

INTRODUCTION

As soon as a person is born, they are part of a physical and social framework that actively influences their personality development. Various factors, including physiology, inherited traits, social structure, and family dynamics, significantly shape people's personalities.[1] The evolving structure of one's personality governs their attitudes and behaviors.

Birth order significantly influences a person's personality and lifestyle. It refers to a person's position among siblings, which determines certain childhood responsibilities and experiences that impact their adult lives.[2] Alfred Adler, who introduced the concept of birth order, emphasized the importance of parents' attitudes and actions during a child's early years and the role of social relationships in shaping personality. He asserted that birth order influences personality but did not specify the exact attributes associated with each birth order.[3]

Adler highlighted the significance of an infant's birth position and how it is perceived during the psychological birth process.[4] He aimed to identify issues people face based on their birth order and sought solutions within his birth order concept. The fundamental birth situation involves the parents' attitudes and behaviors toward their children, which vary according to the children's birth order, sometimes consciously and sometimes unconsciously.[5,6]

Adler[7] underscored how birth order affects a child's place in the family. Despite the subjective nature of perceptions by parents and children, they live their individual lives independent of birth order. However, certain periods can significantly impact a child's personality.[8]

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Several definitions and theories about personality have been proposed. According to Cüceloğlu,[9] personality is the consistent way an individual relates to their inner and outer world, distinguishing them from others—a standard definition of personality.

From birth, a child is surrounded by a physical and social system, with parents as their first social environment. Parents play a crucial role in meeting the child's needs and profoundly impact their development.[10] The parent-child relationship is vital for healthy personality development. Parents act as role models, teaching behaviors by example. They must adopt an accepting mindset, respect themselves and others, communicate effectively, and raise self-assured children.[11]

Darling and Steing[12] highlighted the importance of family characteristics in children's psychosocial development.[13] The family significantly influences an individual's emotions, behaviors, perceptions, and habits developed in childhood and carried into adulthood. Different parental systems lead to diverse attitudes and actions, emphasizing the need to understand a person's upbringing and family background.[9]

Early life experiences are crucial in shaping emotions in adulthood.[14] Unmet developmental needs lead to maladaptive schemas.[15] Theorists define schemas as constructs related to early childhood experiences that manifest in adulthood.[16] Schemas can form in compatible, incompatible, positive, and negative ways. According to Young,[17] schemas start in childhood as cognitive and emotional constructs with lasting impacts, often leading to maladaptive behaviors.Young et al.[18] identified five schema areas from unmet needs and 18 early maladaptive schemas: impaired autonomy, disconnection, unrelenting standards, other-directedness, and impaired limits.[19]

This study aimed to show that psychological birth order has an effect on perceived parental attitudes and early maladaptive schemas. It is thought that individuals' early maladaptive schemas are related to their birth order and similarly, perceived parental attitudes are also shaped according to birth order. Considering that early life experiences and not providing of needs play a major role in the formation of early maladaptive schemas and perceived parental attitudes,[15] it is known that birth order is important in terms of affecting these experiences.[1]

METHODS

Ethics

The questionnaires we requested to use in our study were found appropriate with the decision of İstanbul Aydın University Ethics Committee (Date: 09.06.2021, Decision No: 2021/07). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study is derived from the master's thesis of Büşra Tüysüz (Examination of the Effects of Real and Psychological Birth Order in Adults on Perceived Structural Attitudes and Early Maladaptive Schemas) conducted under the supervision of Kahraman Güler.

Purpose of the Research

In this study, it was aimed to examine the effect of real and psychological birth order on perceived parental attitudes and early maladaptive schemas.

Model of the Research

The research was designed as a relational screening model.

Sample of the Research

The study's population consists of adults aged 18-45 living in İstanbul and Antalya, Turkiye. Using a convenience sampling method, the researcher selected 291 participants (189 women and 102 men) from these regions.

Data Collection Tools

Psychological Birth Order Inventory: This scale was developed by Campell, White and Stewart in 1991 and was adapted into Turkish by Melek Kalkan in 2005.[2] The PSDE consists of four subscales: single child, older child, middle child, and young child. There are 42 items in the scale.

Perceived Parental Attitudes Scale-Child Form 3: Developed by Arrindel et al. in 1999, with a reliability-validity study by Dirik[20] in Turkiye, this scale consists of 23 items. It includes three sub-dimensions: rejecting attitudes, overprotective attitudes, and emotional warmth attitudes, scored separately for mother and father.

Young Schema Scale: The scale was developed by Young. The validity-reliability study in Turkey was conducted by Soygüt, Karaosmanoğlu, and Çakır.[21] There are 18 dimensions covering the schema domains of impaired autonomy, disconnection, unrelenting standards, other-directedness, and impaired limits.

Data Collection

In this study, psychological birth order inventory, abbreviated perceived parental attitudes scale-child form and Young schema scale short form-3 were used as data collection tools. Before these data collection tools, there is an information form. Through the information form, information was given about the purpose of the research and that the participation was voluntary.

Statistical Analysis

After the data were transferred to the SPPS 25 program, the analyzes were started. Normality test, which is the first step of the analysis, was applied and when the skewness and kurtosis values of the variables were examined, it was seen that the relevant values were between -2 and +2.

RESULTS

In the study, 291 participants (189 women and 102 men) were analyzed. The average age of male participants was ($\bar{X}$=29, SD=7), the youngest age was 18 and the oldest age was 45. The average age of female participants was ($\bar{X}$=30, SD=8), the youngest age was 18 and the oldest age was 45 (Table 1).

Table 1. Descriptive statistics of participants' ages

	n	Min	Max	$\bar{X}$	SD
Erkek	102	18	45	29	7
Kadın	189	18	45	30	8

Min: Minimum, Max: Maximum, SD: Standard deviation

Table 2. Findings of the relationship between the perceived parental attitudes scale and the Young schema scale of female participants

	Emotional warmth/ mother	Overprotective/ mother	Rejection/ mother	Emotional warmth/father	Overprotective/ father	Rejection/father
Emotional deprivation	-.412**	.217**	.363**	-.280**	.276**	.294**
Social isolation/ mistrust	-.226**	.462**	.298**	-.149*	.345**	.222**
Defectiveness	-.484**	.175*	.443**	-.381**	.350**	.451**
Emotional inhibition	-.274**	.188**	.321**	-.226**	.220**	.301**
Enmeshment/ dependency	-.381**	.329**	.358**	-.261**	.329**	.239**
Abandonment	-.236**	.300**	.301**	-0.089	.282**	.200**
Vulnerability to harm	-.191**	.360**	.306**	-0.118	.374**	.254**
Failure	-.304**	0.093	.188**	-.279**	.168*	.175*
Pessimism	-.267**	.325**	.367**	-.194**	.323**	.264**
Entitlement/ insufficient self-control	0.014	.292**	.150*	0.080	.288**	.168*
Self-sacrifice	-0.031	.345**	.181*	0.041	.331**	0.035
Punitiveness	0.053	.365**	0.084	0.121	.312**	0.037
Unrelenting standards	-0.002	.230**	.146*	.150*	.209**	0.051
Approval-seeking	.184*	.322**	-0.027	.148*	0.128	-0.117

There is a positive relationship between unrelenting standards and overprotection/mother (r=.230, p<0.01), the rejection/mother (r=.146, p<0.01), the emotional warmth/ father (r=.150, p<0.01), and the overprotection/father (r=.209, p<0.01). there is a positive relationship between approval seeking and emotional warmth/mother (r=.184, p<0.01), the overprotective/mother (r=.322, p<0.01), and the emotional warmth/father (r=.148, p<0.01) (Table 2).

Table 3. When we examine the findings, the findings of the examination of the relationship between the psychological birth order scale and the Young schema scale of emotional female participants

	Eldest child	Middle child	Youngest child	Single child
Emotional deprivation	0.066	.318**	0.004	.263**
Social isolation/mistrust	.179*	.274**	0.025	.353**
Defectiveness	0.077	.376**	0.094	.248**
Emotional inhibition	0.011	.146*	0.032	.245**
Enmeshment/dependency	0.107	.327**	0.062	.235**
Abandonment	.196**	.240**	0.037	.277**
Vulnerability to harm	.223**	.236**	0.037	.269**
Failure	0.073	.228**	-0.007	.147*
Pessimism	.190**	.301**	-0.021	.237**
Entitlement/insufficient self-control	.234**	0.046	0.104	.158*
Self-sacrifice	.218**	.230**	0.059	.312**
Punitiveness	.363**	0.085	0.088	.232**
Unrelenting standards	.253**	.159*	.240**	.209**
Approval-seeking	0.127	0.110	0.047	.251**

**p<0.01, *p<0.05, Test used: Pearson Correlation Test

There is a positive relationship between vulnerability to harm and eldest child (r=.223, p<0.01), the middle child (r=.236, p<0.01), and the single child (r=.269, p<0.01). There is a positive relationship between self-sacrifice and eldest child (r=.218, p<0.01), the middle child (r=.230, p<0.01), and the single child (r=.312, p<0.01). There is a positive relationship between punitiveness and eldest child (r=.363, p<0.01), and the single child (r=.232, p<0.01). There is a positive relationship between unrelenting standards and eldest child (r=.253, p<0.01), the middle child (r=.159, p<0.01), the youngest child (r=.240, p<0.01), and the single child (r=.209, p<0.01). There is a positive correlation between approval-seeking and single child (r=.251, p<0.01) (Table 3).

There is a positive relationship between rejection/mother and middle child (r=.366, p<0.01), and the single child (r=.244, p<0.01). There is a negative relationship between emotional warmth/father and middle child (r=-.260, p<0.01), and the single child (r=-.173, p<0.01). There is a positive relationship between overprotection/father and eldest child (r=.178, p<0.01), the middle child (r=.237, p<0.01), and the single child (r=.310, p<0.01). There is a positive relationship between rejection/father and middle child (r=.340, p<0.01), and the single child (r=.171, p<0.01) (Table 4).

There is a negative relationship between emotional deprivation and the emotional warmth/mother (r=-.450, p<0.01), a positive relationship with the overprotection/ mother (r=.246, p<0.01) and the rejection/mother (r=.528, p<0.01). For fathers, there is a negative relationship between emotional deprivation and the emotional warmth (r=-.293, p<0.01), and positive relationships with the overprotection (r=.309, p<0.01) and the rejection (r=.492, p<0.01). There is a negative relationship between social isolation/mistrust and the emotional warmth/mother (r=-.246, p<0.01), a positive correlation with the overprotection/mother (r=.283, p<0.01) and the overprotection/father (r=.264, p<0.01). There is a negative relationship between defectiveness and the emotional warmth/mother (r=-.486, p<0.01) and a positive relationship with the rejection/mother (r=.511, p<0.01). There is a negative relationship between defectiveness and the emotional warmth/father (r=-.365, p<0.01), a positive relationship with the overprotection/father (r=.315, p<0.01)

Table 4. Findings of the relationship between the psychological birth order scale and the perceived parental attitudes scale of female participants

	Eldest child	Middle child	Youngest child	Single child
Emotional warmth/mother	0.058	-.326**	0.028	-.191**
Overprotective/mother	.202**	.254**	0.079	.433**
Rejection/mother	0.119	.366**	0.042	.244**
Emotional warmth/father	0.127	-.260**	0.020	-.173*
Overprotective/father	.178*	.237**	0.077	.310**
Rejection/father	0.002	.340**	0.016	.171*

**p<0.01, *p<0.05 Test used: Pearson Correlation Test

Table 5. Findings of the relationship between the perceived parental attitudes scale of male participants and the Young schema scale

	Emotional warmth/mother	Overprotective/ mother	Rejection/ mother	Emotional warmth/father	Overprotective/ father	Rejection/father
Emotional deprivation	-.450**	.246*	.528**	-.293**	.309**	.492**
Social isolation/ mistrust	-.246*	.283**	0.145	-0.160	.264**	0.041
Defectiveness	-.486**	0.170	.511**	-.365**	.315**	.511**
Emotional inhibition	-.351**	.360**	.423**	-.222*	.310**	.390**
Enmeshment/ dependency	-.485**	.239*	.420**	-.379**	.315**	.420**
Abandonment	-.290**	.327**	.408**	-.213*	.364**	.481**
Vulnerability to harm	-.203*	.305**	.349**	-0.104	.395**	.388**
Failure	-.475**	.296**	.455**	-.329**	.381**	.410**
Pessimism	-.236*	.374**	.358**	-.203*	.390**	.386**
Entitlement/ insufficient self-control	-0.054	.432**	.201*	-0.044	.299**	0.086
Self-sacrifice	-0.140	.423**	.313**	-0.062	.370**	.365**
Punitiveness	-0.142	.229*	.241*	0.014	.364**	.199*
Unrelenting standards	0.042	.211*	0.153	0.051	0.188	0.165
Approval-seeking	0.057	0.161	-0.039	0.061	0.187	0.021

**p<0.01, *p<0.05 Test used: Pearson correlation test

and the rejection/father (r=.511, p<0.01). There is a negative relationship between emotional inhibition and the emotional warmth/mother (r=-.351, p<0.01), a positive correlation with the overprotective/mother (r=.360, p<0.01), the rejection/mother (r=.423, p<0.01), a negative relationship between emotional inhibition and emotional warmth/father (r=-.222, p<0.01), a positive correlation with overprotective/father (r=.310, p<0.01) and the rejection/father (r=.390, p<0.01). There is a negative relationship between enmeshment/dependency and the emotional warmth/mother (r=-.485, p<0.01), a positive correlation with the overprotection/mother (r=.239, p<0.01) and the rejection/mother (r=.420, p<0.01). There is a negative relationship between enmeshment/dependency and the emotional warmth/father (r=-.379, p<0.01), a positive relationship with the overprotection/father (r=.315, p<0.01) and the rejection/father (r=.420, p<0.01). There is a negative relationship between abandonment and the emotional warmth/mother (r=-.290, p<0.01), and positive correlations with the overprotection/mother (r=.327, p<0.01) and the rejection/mother (r=.408, p<0.01). For fathers, there is a negative relationship between abandonment and the emotional warmth (r=-.213, p<0.01), and positive correlations with the overprotection (r=.364, p<0.01) and the rejection (r=.481, p<0.01). There is a negative relationship between vulnerability to the harm and emotional warmth/mother (r=-.203, p<0.01), a positive correlation with the overprotection/mother (r=.305, p<0.01), the rejection/mother (r=.349, p<0.01), the overprotection/father (r=.395, p<0.01), and the rejection/father (r=.388, p<0.01) (Table 5).

There is a negative relationship between failure and emotional warmth/mother (r=-.475, p<0.01), a positive correlation with the overprotection/mother (r=.296, p<0.01), and the rejection/mother (r=.455, p<0.01). For fathers, there is a negative relationship between the failure and the emotional warmth (r=-.329, p<0.01), and positive correlations with the overprotection (r=.381, p<0.01) and the rejection (r=.410, p<0.01). There is a negative relationship between pessimism and the emotional warmth/mother (r=-.236, p<0.01), and positive correlations with the overprotection/mother (r=.374, p<0.01) and the rejection/mother (r=.358, p<0.01). For fathers, there is a negative relationship with the emotional warmth (r=-.203, p<0.01), and positive correlations with the overprotection (r=.390, p<0.01) and the rejection (r=.386, p<0.01) (Table 5).

There is a positive correlation between entitlement/insufficient self-control and the overprotection/mother (r=.432, p<0.01), the rejection/mother (r=.201, p<0.01), and the overprotection/father (r=.299, p<0.01). There is a positive correlation between self-sacrifice and the overprotection/mother (r=.423, p<0.01), the rejection/mother (r=.313, p<0.01), the overprotection/father (r=.370, p<0.01), and the rejection/father (r=.365, p<0.01). There is a positive relationship between punitiveness and theoverprotection/mother (r=.229, p<0.01), the rejection/mother (r=.241, p<0.01), the overprotection/father (r=.364, p<0.01), and the rejection/father (r=.199, p<0.01) There is a positive correlation between unrelenting standards and the overprotective/mother (r=.211, p<0.01) (Table 5).

There is a positive relationship between emotional deprivation and eldest child (r=.225, p<0.01), the middle child (r=.337, p<0.01), the youngest child (r=.334, p<0.01), and the single child (r=.276, p<0.01). There is a positive relationship between social isolation/mistrust and the middle child (r=.213, p<0.01), and the youngest child (r=.198, p<0.01). There is a positive relationship between defectiveness and the middle child (r=.228, p<0.01), the youngest child (r=.318, p<0.01), and the single child (r=.205, p<0.01). There is a positive relationship between emotional inhibition and eldest child (r=.261, p<0.01), the middle child (r=.220, p<0.01), the youngest child (r=.368, p<0.01), and the single child (r=.208, p<0.01). There is a positive correlation between enmeshment/dependency and middle child (r=.256, p<0.01), the youngest child (r=.263, p<0.01), and the single child (r=.323, p<0.01). There is a positive relationship between abandonment and eldest child (r=.212, p<0.01), the middle child (r=.284, p<0.01). the youngest child (r=.380, p<0.01), and the single child (r=.351, p<0.01). There is a positive relationship between vulnerability to harm and eldest child (r=.205, p<0.01), the middle child (r=.314, p<0.01), the youngest child (r=.354, p<0.01), and the single child (r=.324, p<0.01). There is a positive relationship between failure and the eldest child (r=.221, p<0.01), the middle child (r=.248, p<0.01), the youngest child (r=.390, p<0.01), and the single child (r=.301, p<0.01). There is a positive relationship between pessimism and the middle child (r=.309, p<0.01), the youngest child (r=.331, p<0.01) and the single child (r=.397, p<0.01). There is

Table 6. Findings of the relationship between the psychological birth order scale and the Young schema scale in male participants

	Eldest child	Middle child	Youngest child	Single child
Emotional deprivation	.225*	.337**	.334**	.276**
Social isolation/mistrust	0.150	.213*	.198*	0.124
Defectiveness	0.149	.228*	.318**	.205*
Emotional inhibition	.261**	.220*	.368**	.208*
Enmeshment/dependency	0.128	.256**	.263**	.323**
Abandonment	.212*	.284**	.380**	.351**
Vulnerability to harm	.205*	.314**	.354**	.324**
Failure	.221*	.248*	.390**	.301**
Pessimism	0.131	.309**	.331**	.397**
Entitlement/insufficient self-control	.299**	0.190	.328**	.205*
Self-sacrifice	.314**	0.141	.409**	.367**
Punitiveness	.199*	0.194	0.189	.213*
Unrelenting standards	.374**	.209*	.273**	.235*
Approval-seeking	0.136	0.061	0.177	0.073

**p<0.01, *p<0.05 Test used: Pearson Correlation Test

Table 7. Findings of the relationship between the psychological birth order scale and the perceived parental attitudes scale of male participants

	Eldest child	Middle child	Youngest child	Single child
Emotional warmth/ mother	0.036	-.216*	-0.057	-0.130
Overprotective/mother	.340**	.296**	.306**	.456**
Rejection/mother	.331**	.356**	.311**	.322**
Emotional warmth/father	0.162	-0.146	0.065	-0.036
Overprotective/father	.306**	.282**	.239*	.422**
Rejection/father	.239*	.299**	.236*	.344**

**p<0.01, *p<0.05 Test used: Pearson Correlation Test

a positive relationship between entitlement/insufficient self-control and the eldest child (r=.299, p<0.01), the youngest child (r=.328, p<0.01), and the single child (r=.205, p<0.01). There is a positive relationship between self-sacrifice and the eldest child (r=.314, p<0.01), the youngest child (r=.409, p<0.01), and the single child (r=.367, p<0.01). There is a weak positive relationship between punitiveness and the older child (r=.199, p<0.01), and the one child (r=.213, p<0.01). there is a positive relationship between unrelenting standards and the eldest child (r=.374, p<0.01), the middle child (r=.209, p<0.01), the youngest child (r=.273, p<0.01), and the single child (r=.235, p<0.01) (Table 6).

There is a weak negative relationship between emotional warmth/mother and middle child (r=-.216, p<0.01). There is a positive relationship between overprotection/mother and the eldest child (r=.340, p<0.01), the middle child (r=.296, p<0.01), the youngest child (r=.306, p<0.01), and the single child (r=.456, p<0.01). There is a positive relationship between rejection/mother and eldest child (r=.331, p<0.01), the middle child (r=.356, p<0.01), the youngest child (r=.311, p<0.01), and the single child (r=.322, p<0.01). There is a positive relationship between overprotection/father and the eldest child (r=.306, p<0.01), the middle child (r=.282, p<0.01), the youngest child (r=.239, p<0.01), and the single child (r=.422, p<0.01). There is a positive relationship between rejection/father and the oldest child (r=.239, p<0.01), the middle child (r=.299, p<0.01), the youngest child (r=.236, p<0.01) and the only child (r=.344, p<0.01) (Table 7).

DISCUSSION

This study examined the effect of psychological birth order on perceived parental attitudes and early maladaptive schemas in adults. When considering the relationship between emotional deprivation schema sub-dimension and birth order, it was found that there was a moderate positive relationship in female participants and a moderate negative relationship in males. It was found that there was a positive relationship between being the median child of women and men who participated in the study and emotional deprivation, pessimism and tendency to harm schema areas. Literature studies found a weak relationship between early maladaptive schemas and birth order, with Nilüfer and Çınarbaş[22] indicating no antecedent effect.

The findings of our study revealed that rejecting parental attitudes showed significant relationships with various schema domains. In particular, moderate positive relationships were found with emotional deprivation, emotional frustration, pessimism, abandonment and entanglement/dependency schema domains. These results are in parallel with Yurtsever and Sütçü's[23] study, which found that negative maternal attitudes were significantly related to the schema domains of altruism, cruel standards and emotional deprivation. One of the most striking results of our study is related to cruel standards and self-sacrifice schemas. It was found that being the oldest child at the time of psychological birth was positively and moderately related to these two schema domains, whereas it was weakly related to the other schema domains. These findings suggest that parental attitudes and birth order may play an important role in children's schema development.

A moderately positive relationship was found between overprotective mothers and the schema domains of social isolation/mistrust, enmeshment/dependency, vulnerability to harm, punitiveness, approval seeking, and self-sacrifice. Overprotective father attitudes showed a moderate positive relationship with vulnerability to harm, pessimism, enmeshment/dependency, social isolation/mistrust, and punitiveness schemas. Macik's[24] study also concluded that overprotective parental attitudes are a risk factor for early maladaptive schemas.

In the study, a moderate positive relationship was found between psychological birth order and various domains of early maladaptive schemas such as defectiveness, pessimism, emotional deprivation and social isolation/insecurity in female participants. In particular, median children showed a higher level of association with early maladaptive schemas compared to other birth orders. This finding is consistent with Kalkan's[25] study on the link between psychological birth order and irrational relationship beliefs, as well as Shulman

and Mosak's[26] theoretical explanations suggesting that middle children may feel 'squeezed' and 'unimportant'. Together, these studies paint a consistent picture that emphasizes the impact of psychological birth order on individuals' thought structures and emotional schemas. The psychological birth order inventory used in the study also included items related to the middle child feeling less important and marginalized compared to other members of the family.

The feeling of being 'squeezed' and 'unimportant' that middle children experience may lead them to develop these maladaptive schemas. The study also found that punitiveness was moderately related to being the oldest child and early maladaptive schemas were weakly related to being the only or youngest child. Collectively, these findings underline the complex relationship between psychological birth order and the development of early maladaptive schemas.

Parental attitudes by gender revealed that fathers are crucial for emotional warmth in enmeshment/dependency and defectiveness schema domains for males. For females, mothers were essential in the failure schema sub-dimension. Positive parental attitudes of the same gender prevented the perception of failure. Aydoğdu and Dilekmen[27] found no differences between authoritarian, overprotective, and permissive parental attitudes by gender.[28]

Rejecting mother scores positively correlated with enmeshment/dependency, emotional inhibition, and emotional deprivation schemas. Insufficient self-control, emotional inhibition, and protective mother ratings were somewhat positively correlated. Anti-protective father scores marginally correlated with emotional deprivation schema. Overprotective and rejecting father views were somewhat positively correlated with enmeshment/dependency, self-sacrifice, emotional inhibition, pessimism, sensitivity to damage, and abandonment schema.

Failure and abandonment schema domains were moderately related to rejecting mother attitudes, while self-sacrifice, pessimism, and vulnerability to harm were moderately related to overprotective and rejecting mother attitudes. Middle children had a moderate positive relationship with rejecting mother attitudes and weak positive correlations with overprotective/mother, emotional warmth/mother, overprotective/father, and rejecting/father attitudes. Fathers in studies by İnci and Deniz[29] showed more positive attitudes toward their first and last children than middle children.

Negative parental attitudes affect early maladaptive schema areas. For instance, an overprotective attitude can lead to an enmeshment/dependency schema domain. Tim's[30] study similarly concluded that parental attitudes influence early maladaptive schema domains. The study found that being an only child had a positive relationship with self-sacrifice and pessimism. The single child factor most affected the pessimism schema area. Ardebili and Golshani[31] also found birth order differences in schema areas.

CONCLUSION

As a result of this study, it was found that there was a significant relationship between psychological birth order and perceived parental attitudes in early maladaptive schemas in adults. It was concluded that there is a moderate positive relationship between emotional deprivation, pessimism and vulnerability to harm schema domains and psychological birth order. It was determined that there was a positive relationship between being the middle child of women and men participating in this study and emotional deprivation, pessimism and vulnerability to harm schema domains. Another important finding of the study is that the median child feels less important and marginalized than the other members of the family. In the light of the findings obtained as a result of the study, it was determined that overprotective and rejecting parental attitudes contribute to early maladaptive schemas, while positive attitudes can prevent them, and it is thought that studies on parents will contribute to the future literature.

ETHICAL DECLARATIONS

Ethics Committe Approval

2021/07 dated 09.06.2021 It was approved with the decision of İstanbul Aydın University Ethics Committee (Date: 09.06.2021, Decision No: 2021/07).

Informed Consent

Informed consent was obtained from all subjects involved in the study.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Evaluation of the satisfaction of relatives of patients being treated in the intensive care unit

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ABSTRACT

Aims: There has been no previous study on the satisfaction of relatives of patients receiving treatment in the intensive care unit of our hospital. Our study was conducted to improve quality and service in our intensive care unit. A survey was conducted to evaluate the satisfaction of the relatives of patients receiving treatment.

Methods: The satisfaction of the relatives of the patients who were treated for at least 3 days in the 3rd Step general intensive care unit at Mardin Training and Research Hospital between 01, February 2023 and 01, June 2023 was evaluated in line with the surveys. A questionnaire was given to each patient's relative by the attending physician to be filled out.

Results: 114 patient relatives participated in the study. 12 patient relatives did not agree to fill out the survey. 102 patient relatives filled out the satisfaction survey.

Conclusion: Waiting room in intensive care unit conditions need to be improved. In our study. we think that patient relatives have confidence in the treatments applied to their patients and are satisfied with the skills and abilities of doctors and nurses.

Keywords: Intensive care units. questionnaire. outcome and process assessment

INTRODUCTION

Tertiary intensive care units are highly specialised environments. equipped with a plethora of sophisticated technologies. situated within the context of a hospital.[1] Such units are equipped to treat life-threatening diseases and to provide organ support through invasive monitoring. thus preventing multiple organ failure and reducing mortality.[2] Despite the similarities in the demographic characteristics of patients hospitalized in intensive care units. significant inter-hospital variability exists in intensive care unit occupancy rates. length of stay. number of patients per bed. number of patients per nurse. patient admission clinics. number of healthcare personnel working. and intensive care unit mortality rates.[3] Furthermore. the expectations and satisfaction of patients and their relatives with regard to ICUs also vary.[4,5]

Today's technology and successful developments in medicine have contributed to the prolongation of life expectancy with their contributions to diagnosis and treatment. Increasing life expectancy has led to an increase in the number of patients in need of intensive care. and the service quality of intensive care units has gained importance. Previously. the quality of intensive care units was evaluated based on the duration of hospitalization. mortality. and functionality of the patients in intensive care units. but later on. the satisfaction of the patients and their relatives receiving service from these units was evaluated.[6,4]

However. the majority of patients hospitalized in intensive care units have difficulty expressing themselves due to their poor general condition and changes in consciousness and are not in the decision-making stage. For this reason. satisfaction and quality assessment of the health service provided to the patient by their relatives have gained importance.[7,8-14]

There were no previous studies evaluating the satisfaction of patients and their relatives in intensive care units in our hospital. With the questionnaire form we prepared. we aimed to measure satisfaction with the quality of receiving information about their patients. the knowledge and approach of doctors and nurses who manage the treatment of the patient. the intensive care working order. the attitudes of intensive care unit staff towards patients and their relatives. and the process of decision-making about the treatment and care of their patients.

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METHODS

After the approval of Mardin Artuklu University Ethics Committee (Date: 14.12.2022. Decision No: 2022/14-18). the relatives of the patients who were followed and treated for at least 3 days in the 3rd step general intensive care unit of Mardin Training and Research Hospital between 01.02.2023-01.06.2023 were included in the satisfaction assessment survey. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Due to the density. functioning. and infection control in our hospital. the relatives of the patients were visited every day at 11.30 am under the supervision of the relevant specialist doctor. In order to reduce the contact of patient relatives in the intensive care unit. information was given by the relevant specialist doctor in the patient information room after the patient visit. During the face-to-face interview. the patient's relatives were informed about the survey. After obtaining consent from the patient's relatives who wanted to participate in the survey. they were included in the study. The survey questions were created by examining previous studies. Questions were added to the questionnaire due to the sociocultural situation of the province. It was asked about the idea of taking their patients to another hospital and whether there was a change in trust in hospital staff in this process.

The questionnaire was composed of nine sections. In the first section. the respondent's gender. degree of closeness. association with the patient. whether or not he or she had a relative who had been hospitalized in an intensive care unit before. educational level. and place of residence were asked. In the second section. the perspective on the knowledge and skills of hospital staff in the treatment applied to the patient was evaluated. In the third section. the frequency. accessibility. reliability. comprehensibility. and consistency of the information given to the patient's relatives were evaluated. In the fourth section. the level of knowledge of the patients' relatives about why their patients were admitted to the intensive care unit and the working order in the intensive care unit was evaluated. In the fifth section. transportation to the patient's relatives in case of an important change in the patient's clinic and the attitude towards them were evaluated. In the sixth section. the approach of the intensive care team to the emotions of the patient's relatives was evaluated. and in the seventh section. the physical conditions of the waiting room were evaluated. In the eighth section. the involvement of the patient's relatives in the decisions taken by the intensive care team in the treatment and care process related to their patients was evaluated. In the ninth section. the trust of patient relatives in hospital staff during the follow-up and treatment process of their patients was questioned.

Statistical Analysis

The data obtained in the study were analyzed using SPSS version 26 (IBM Corp.. Armonk. N.Y.. USA). Descriptive statistics were used in the analysis. Numbers and percentages of qualitative data were given. Mean. standard deviation. minimum. and maximum values were given for continuous variables.

RESULTS

Out of 114 relatives of patients. 12 refused to participate in the survey; 102 relatives of patients agreed to participate in the satisfaction assessment survey. answered the questionnaire. and returned it to us. The participation rate was 89.4%. The demographic data of patient relatives is shown in Table 1. In the first section. it was seen that there were more men among the relatives of the patients who answered the questionnaire (67.6%). It was seen that those who were close to the patient had more children. Of those who answered the questionnaire. 49% were university graduates.

Table 1. Distribution of demographic characteristics of patient relatives

		n	%
Q1. Your gender	Female	33	32.4
	Male	69	67.6
Q2. Your degree of closeness with the patient	Wife	14	13.7
	Parent	5	4.9
	Brother/sister	16	15.7
	Child	38	37.3
	Second degree relative	14	13.7
	Other	15	14.7
Q3. Do you live with the patient?	Yes	50	49.0
	No	52	51.0
Q4. If you do not live with the patient. how often do you see the patient?	Once a week	35	34.3
	Once a month	17	16.7
	Once a year	1	1.0
Q5. Have you ever had a relative hospitalized in intensive care unit?	Yes	62	60.8
	No	40	39.2
Q6. Level of education	No literacy	2	2.0
	Primary education	21	20.6
	High School	30	29.4
	University	49	48.0
Q7. Where do you live?	In the city where the Hospital is located	79	77.5
	Outside the city	23	22.5

The satisfaction ratings of patient relatives are shown in Table 2. According to the answers of the patients' relatives. their satisfaction was converted into scores between 0 and 100. The highest score in these sections was trust in the hospital and hospital staff. with 86.27±21.00. The care and treatment of the patient were 83.68±13.89. The lowest score was 63.15±10.52 for waiting area and logistic support.

Table 2. Distribution of satisfaction scores calculated from sections

	Min-Max	Mean±SD
S2-Patient care and treatment	40.00-100.00	83.68±13.89
S3 - Informing the patient's relatives	28.57-100.00	81.84±14.36
S4-Perception	41.67-100.00	80.07±15.16
S5- Attention to the patient's relatives	50-100	82.11±12.81
S6- Impact on the emotional state of the patient's relatives	30-100	78.58±17.52
S7- Waiting room and logistic support	33.33-100.00	63.15±10.52
S8- Decision making process	33.25-100.00	80.15±17.06
S9- Trust in hospital and hospital staff	25-100.00	86.27±21.00

SD: Standard deviation

Table 3. Patient relatives satisfaction

Care and treatment of the patient		n	%
Q1. Do you have confidence that the treatment provided to your patient is complete?	Very good	42	41.2
	Good	45	44.1
	Moderate	12	11.8
	Weak	3	2.9
Q2. How would you rate the skills and abilities of doctors?	Very good	53	52.0
	Good	44	43.1
	Moderate	5	4.9
	Weak	0	0
Q3. How do you evaluate the skills and abilities of nurses?	Very good	44	43.1
	Good	50	49.0
	Moderate	6	5.9
	Weak	2	2.0
Q4. Do you think that intensive care unit staff care about your patient?	Very good	40	39.2
	Good	53	52.0
	Moderate	5	4.9
	Weak	4	3.9
Q5. When you visited your patient. did you encounter any situation that disturbed you?	Never	49	48.0
	Sometimes	50	49.0
	Most of the time	1	1.0
	Always	2	2.0
Informing the patient relatives			
Q1. How would you rate the ease of getting information about your patient?	Very good	40	39.2
	Good	43	42.2
	Moderate	17	16.7
	Weak	2	2.0
Q2. How would you rate the frequency of information given to you about your patient's condition?	Very good	30	29.4
	Good	38	37.3
	Moderate	30	29.4
	Weak	4	3.9
Q3. How would you rate the understandability of the information about your patient?	Very good	46	45.1
	Good	48	47.1
	Moderate	6	5.9
	Weak	2	2.0
Q4. How would you rate the reliability of the information about your patient?	Very good	43	42.2
	Good	50	49.0
	Moderate	8	7.8
	Weak	1	1.0
Q5. Does the information about your patient cover everything you want to know?	Very good	47	46.1
	Good	40	39.2
	Moderate	11	10.8
	Weak	4	3.9
Q6. Is the information you received from the nurse and the doctor about your patient in the same direction?	Very good	42	41.2
	Good	50	49.9
	Moderate	8	7.8
	Weak	2	2.0
Q7. Are family members who receive information about your patient given the same information. or are they told different things in the explanations?	Very good	51	50.0
	Good	45	44.1
	Moderate	4	3.9
	Weak	2	2.0
Perception			
Q1. Do you understand why your patient's follow-up and treatment is carried out in the intensive care unit instead of the ward?	Very good	51	50.0
	Good	38	37.3
	Moderate	13	12.7
	Weak	0	0.0
Q2. Do you understand what happened to your patient and why things were done?	Very good	33	32.4
	Good	55	53.9
	Moderate	19	12.7
	Weak	1	1.0
Q3. Do you understand the conditions and working order of the intensive care unit?	Very good	27	26.5
	Good	55	53.9
	Moderate	19	18.6
	Weak	1	1.0
Q4. Do you understand why your patient's follow-up and treatment is carried out in the intensive care unit instead of the ward?	Very good	51	50.0
	Good	38	37.3
	Moderate	13	12.7
	Weak	0	0.0
Q5. Do you understand what happened to your patient and why things were done?	Very good	33	32.4
	Good	55	53.9
	Moderate	19	12.7
	Weak	1	1.0
Q6. Do you understand the conditions and working order of the intensive care unit?	Very good	27	26.5
	Good	55	53.9
	Moderate	19	18.6
	Weak	1	1.0
Attention to patient relatives			
Q1. Do you believe that someone will call you at home if there is any important change in your patient's condition?	Very good	52	51.0
	Good	41	40.2
	Moderate	8	7.8
	Weak	1	1.0
Q2. Are the employees polite and understanding towards you?	Very good	53	52.0
	Good	43	42.2
	Moderate	5	4.9
	Weak	1	1.0
Q3. Do you feel abandoned or lonely in the waiting area?	Absolutely not	22	21.6
	Sometimes	58	56.9
	Most of the time	21	20.6
	Always	1	1.0

In Table 2. informing the patient's relatives was scored to evaluate the satisfaction of the patient's relatives. and the score was 81.84±14.36. In this section. seven questions were asked of the relatives. and it was seen that they were generally satisfied (Table 3). In this section. 85.3% of the patients' relatives answered very well or well to the question. "Do you have confidence that the treatment applied to your patient is done completely?" In this section. 95.1% responded positively to the question. "How would you rate the skills and abilities of doctors?"

"How would you rate the ease of getting information about your patient?" The question was answered as very good or good by 81.4%. "Are family members who receive information about your patient given the same information. or are they told different things in the explanations?" was answered as very good or good by 94.1%. In this section. the lowest positive response rate was 66.7% with the question. "How would you rate the frequency of information given to you about your patient's condition?"

The mean score for the perception section in the patient satisfaction assessment was 80.07±15.16. In this section. six questions were asked of the patient's relatives (Table 3). Generally. positive answers were received. "Do you understand why your patient's follow-up and treatment are done in the intensive care unit instead of in the ward?" 87.3% answered very good or good. Very good or good answers to the question "Do you understand the conditions and working order of the intensive care unit?" were 80.4%.

In the "Table 2; Attention to patient relatives" section. the satisfaction score was 82.11±12.81. In this section. three questions were asked to the patients' relatives (Table 3). Their answers were generally positive.

Table 4 presents the questions utilized to assess the impact on the emotional state of the patient's relatives and the ensuing findings. Relative satisfaction in this section was found to be 78.58 ± 17.52 (Table 2). The question "Do you feel comfortable while visiting your patient?" was answered as very good or good by 81.3%. The question "Did one of the intensive care unit doctors take care of your current feelings?" was answered positively by 89.2%.

Table 5 presents a comprehensive overview of the inquiries and findings pertaining to the Waiting room and logistic support department. The department in question exhibits the lowest level of satisfaction. With a mean score of 63.15±10.52 (Table 2). The question "Do you have to personally take care of the work that needs to be done for your patient outside the intensive care unit?" was answered positively. with 39.2% saying that they had to take care of the patient and 60.8% saying that they did not have to take care of the patient. The question "Does the waiting room meet your needs?" was answered with 89.3% saying absolutely not or sometimes. To the question "Is the waiting room comfortable?" 84.3% answered moderately or poorly that they were not satisfied.

Patient relatives were evaluated in "Table 6 Decision Making Process" in the satisfaction assessment. The satisfaction score in this section was 80.15±17.06 (Table 2) and it was positive.

The questions asked about trust in the hospital and hospital staff in the satisfaction assessment of the patients' relatives and their answers are evaluated in Table 7. This department

Table 4.Impact on the emotional state of the patient relatives

		n	%
Q1. Do you feel comfortable visiting your patient?	Very good	34	33.3
	Good	49	48.0
	Moderate	12	11.8
	Weak	7	6.9
Q2. Did any of the intensive care unit doctors take an interest in your current feelings?	Very good	52	51.0
	Good	39	38.2
	Moderate	10	9.8
	Weak	1	1.0
Q3. Did any of the intensive care unit nurses care about your current feelings?	Very good	30	29.4
	Good	53	52.0
	Moderate	12	11.8
	Weak	7	6.9
Q4. Are you able to share issues that upset and distress you with intensive care physicians?	Very good	40	39.2
	Good	41	40.2
	Moderate	15	14.7
	Weak	6	5.9
Q5. Are you able to share the issues that upset and distress you with intensive care nurses?	Very good	38	37.3
	Good	40	39.2
	Moderate	18	17.6
	Weak	6	5.9

Table 5. Waiting room and logistic support

		n	%
Q1. Do you have to personally take care of the work that needs to be done for your patient outside the intensive care unit?	Absolutely not	17	16.7
	Sometimes	45	44.1
	Most of the time	22	21.6
	Always	18	17.6
Q2. Does the waiting room meet your needs?	Absolutely not	58	56.9
	Sometimes	33	32.4
	Most of the time	5	4.9
	Always	6	5.9
Q3. Is the waiting room comfortable?	Very good	6	5.9
	Good	10	9.8
	Moderate	21	20.6
	Weak	65	63.7

Table 6. Decision making process

		n	%
Q1. Did you feel that you were involved in decision-making about your patient's treatment and care?	I've always been included	32	31.4
	I am mostly included	63	61.8
	Mostly not included	7	6.9
Q2. Did you feel supported in your decision-making process?	I was highly encouraged	45	44.1
	I got some support	44	43.2
	Very little support	10	9.8
	I was never supported	3	2.9
Q3. Did you feel you had control over your patient's treatment and care?	I felt I had a good degree of control	36	35.3
	I felt I had some control	49	48.0
	I felt I had little control and that the health system was taking control	7	6.9
	I felt that I had no control and that the health system was in complete control	10	9.8
Q4. During the decision-making process about your patient's treatment and care. did you have enough time to have your concerns addressed and your problems answered?	I've had enough time	74	72.5
	I needed more time	28	27.5

Table 7. Trust in hospital and hospital staff

		n	%
Q1. Have you considered taking your patient to another hospital?	Yes	24	23.5
	No	78	76.5
Q2. If you are willing to take your patient to a different hospital	A better equipped hospital	15	14.7
	Environmental pressure	6	5.9
	Private hospitalization	2	2.0
	Other	1	1.0
Q3. your trust in hospital staff in terms of the treatment provided during your patient's hospitalization	Increased	76	74.5
	Unchanged	21	20.6
	Decreased	5	4.9

has the highest satisfaction rate with 86.27±21.00 (Table 2). Patient relatives were asked. " To the question "Have you thought of taking your patient to another hospital?" 76.5% answered no. To the question "Your trust in hospital staff in terms of treatment during the hospitalization of your patient?" 74.5% answered that they were satisfied (Table 7).

DISCUSSION

In our study. a satisfaction questionnaire was administered and evaluated by the relatives of patients under treatment in the intensive care unit to assess the quality of health care provided in the 3rd-level intensive care unit.

In our study. the response rate to the questionnaire was 89.4%. In other studies. the response rate was 80.2% in Aydın et al.[15] 52.60% in Erdal et al.[16] 69% in Hunziker et al.[7] and 75.4% in Stricker et al.[4] Compared to other studies. the participation rate in our survey was high. We think that the high participation rate in our study was due to the fact that the questionnaire form was given to the patient's relatives by the intensive care specialist who followed the patient.

The satisfaction evaluation of the patients was over 100 points. In the distribution of demographic characteristics of the relatives of the patients. 67.6% of the respondents to the patient satisfaction questionnaire were male. and 48% had a university education. In Erdal et al.[16] 56.9% were male and 36.5% were university graduates. and in Aydın et al.[15] 44% were male and 33.3% were university graduates. In our study. the high proportion of males among the respondents was related to cultural conditions and the fact that those with a higher level of education in the family were at the forefront when obtaining information from the physician.

In the evaluation of patient relatives' satisfaction. the scoring in the patient care and treatment section was found to be positively high. With the answers given by the relatives in the

questionnaire. it was evaluated as a positive result that they had confidence in the treatments applied to their patients. they were satisfied with the skills and abilities of doctors and nurses. their patients were cared for. and they encountered fewer negative situations during the visits of their patients. In other survey studies conducted in the section of patient care and treatment. the rates of Erdal et al.[16] Aydın et al.[15] and İncesu[17] were similar to our findings.

Satisfaction with the information given to the patient's relatives was answered positively in terms of the frequency of information given about their patients and the information given to family members that was understandable. reliable. and included every subject. Aydın et al.[15] İncesu.[17] Erdal et al.[16] found that when compared with previous studies on patient relatives' information in this section. it was similar to some and higher than others. Ali et al.[18] also emphasized in their study that effective communication with families reduces the stress on family members and patients. For patients who cannot participate in the decision-making process regarding their treatment. the aim should be to at least inform their relatives effectively during this process.[19] It should be kept in mind that multidisciplinary teams can also serve for this purpose.[20] We attribute the high level of patient relatives' satisfaction in our survey results to the fact that the specialist physician allocated sufficient time to the patient relatives and provided regular and understandable information about the patients in intensive care.

In the perception section. the relatives of the patients were asked to answer three questions. The relatives of the patients were asked why their patients were followed up and treated in intensive care instead of in ward conditions. what happened to their patients and why they were treated. and their perception of the conditions and working order of the intensive care unit. The answers were highly positive. In the studies of Erdal et al.[16] and Aydın et al.[15] it was also seen that patient satisfaction was high. We attribute the high rate in the perception section of our study to the establishment of understandable communication with the relatives of the patients.

In the section on caregiver care. "Do you believe that someone will call you at home if there is any significant change in your patient's condition? The question was answered as very good or good. With a rating of 91.2%. We think that the communication of the intensive care specialist physician with the patient's relatives is effective because of the high rate of positive responses of the patient's relatives to this question. The question "Do the staff behave politely and understandingly towards you?" was evaluated to determine whether the intensive care staff were sufficiently kind and polite when the patient's relatives and intensive care staff visited their patients in our intensive care unit and when it was necessary to communicate on any issue necessary for their patients. The question "Do you feel abandoned or lonely in the waiting area?" was answered as absolutely no or sometimes by 78.5%. According to the sociocultural values of the region of the patients hospitalized in intensive care. it was thought that more people coming for patient visits. communicating with other patient relatives during the waiting period. and sharing information about the hospital and their patients could be effective.

In the section where the effect on the emotional state of the patient's relatives was evaluated. the satisfaction score of the patient's relatives was 78.58±17.52. According to the answers given by the relatives of the patients in our study. it is seen that nurses and doctors are interested in their feelings. that they feel comfortable during the visit. and that they have a positive opinion about being able to share their problems with nurses and doctors.

Waiting room and logistic support received the lowest score in patient relatives' satisfaction. It is thought that the inadequate physical conditions of the waiting room and the lack of sufficient materials in the rest room reduce the satisfaction of the patient's relatives. In other studies[7,11,15-17,21] it was observed that patient satisfaction was low in the waiting room and logistic support section.

Decision-making process. most of the answers given by the patients' relatives in this section indicated that they were included in the decision-making process regarding the treatment and care of their patients. that they were supported in this process. that they felt that they had control over the treatment and care of their patients. and that they had enough time to address their concerns and answer their problems during the decision-making process regarding treatment and care. The patient satisfaction rate in our survey was found to be higher compared to other studies.[15-17] It is thought that the specialist physician who deals with the patient one-on-one in communication with the patient's relatives. sharing understandable information with the patient's relatives. and allocating sufficient time are effective.

Trust in the hospital and hospital staff received the highest score. The high rate of positive or unchanged responses to the questions "Have you considered taking your patients to another hospital?" and "Your trust in hospital staff in terms of the treatment provided during your patient's hospitalization" was considered to be the fact that the information sharing of intensive care staff and the relevant specialist physician with the patient's relatives was understandable and their concerns decreased with effective communication.

Limitations

Our study has some limitations; the opinions of the relatives of patients who did not participate in the survey are also valuable for evaluating the quality of intensive care services. The reason for not participating in the survey may be dissatisfaction. The fact that our study was single-centered is also one of the limitations of our study.

CONCLUSION

In our survey. the questions that were asked in order to evaluate the love of the relatives of the patients were; care and information of the patient. Informing the relatives of the patient. Perception. Interest in the relatives of the patient. Effect on the emotionality of the relatives of the patient. decision-making process. trust in the hospital and hospital staff. The resting time was quite high. but the lowest temperature level was in the waiting room and logistics support section.

As a result. we believe that the communication between the hospital staff and especially the relevant physician who are responsible for the follow-up and treatment of patients in intensive care and the relatives of the patients is not at

a level that can meet the comfort and needs of the waiting room for the relatives of the patients in the hospital and that improvements in this regard will increase the satisfaction of the relatives of the patients.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethical Committe of Faculty of Mardin Artuklu University (Date: 14.12.2022. Decision No: 2022/14-18).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design. execution. and analysis of the paper. and that they have approved the final version.

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Original Article

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Evaluating the quality and reliability of YouTube videos on Achilles tendinopathy: a comprehensive analysis

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ABSTRACT

Aims: This study evaluates the quality, reliability, and educational value of YouTube videos on Achilles tendinopathy.

Methods: A YouTube search using the keyword "Achilles tendinopathy" was conducted on June 20, 2024, using an incognito browser tab. The first 50 English-language videos were analyzed for upload date, duration, views, likes, dislikes, comments, and categorized by source and content. The DISCERN score, Global Quality Score (GQS), and Journal of the American Medical Association (JAMA) score were used to assess video quality and reliability. Statistical analyses included the Shapiro-Wilk test, Kruskal-Wallis test, Mann-Whitney U test, and Spearman test for correlations.

Results: Among 50 videos, the average DISCERN score was 42.5, GQS was 3.2, and JAMA score was 2.6, indicating moderate overall quality. Academic physician videos had higher scores. Exercise training videos scored significantly higher in quality assessments. The highest Video Power Index (VPI) was also found in videos by academic physicians.

Conclusion: YouTube videos on Achilles tendinopathy provide moderately sufficient information, with higher quality in videos produced by academic physicians and those focusing on exercise training. The study suggests a need for standardized, high-quality educational content on online platforms.

Keywords: Achilles tendon, tendinopathy, YouTube, quality, reliability

INTRODUCTION

In today's digital age, the accessibility and abundance of information through the Internet have dramatically transformed how individuals seek and consume health information. The Internet's role as a primary source for health-related data continues to expand exponentially.[1] Recent surveys indicate that over half of patients actively use the Internet for medical inquiries, with 60% of these individuals finding the information comparable to, or even superior to, that provided by healthcare professionals.[2] Moreover, recent studies have shown that approximately 80% of Internet users seek health-related information online, with a notable 30% of orthopedic patients researching their conditions on the web.[3] These trends highlight the growing reliance on digital platforms as essential tools for patient education and decision-making in healthcare.

Among chronic patients, 75% reportedly turn to online resources just before finalizing treatment decisions.[4] In this context, video-based materials have gained significant traction, as they are often perceived as more engaging and accessible than traditional text-based content. Consequently, platforms like YouTube have emerged as dominant sources of health-related information.[5] High-quality video content has been shown to improve patient outcomes by enhancing comprehension and understanding of medical conditions.[6] Since its launch in 2005, YouTube has evolved into a global platform, boasting 120 million daily active users and over 2.5 billion monthly active users, making it a critical resource for patient education.[7] However, despite its widespread use, YouTube's lack of peer-reviewed processes or standardized quality control for health-related videos presents significant risks. The absence of quality assurance mechanisms often

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results in the dissemination of poor-quality, inaccurate, or incomplete information, potentially misleading patients and impacting treatment outcomes.[8–11]

The Achilles tendon, the strongest and largest tendon in the human body, is particularly susceptible to both degenerative and traumatic injuries.[12] Achilles tendinopathy, a prevalent orthopedic condition resulting from overuse and microtrauma, is characterized by pain, swelling, and functional impairment. It disproportionately affects athletes as well as middle-aged, overweight, and sedentary individuals, with the Achilles tendon accounting for approximately 20% of all tendon injuries.[13,14] There are two main subtypes of Achilles tendinopathy-insertional and non-insertional-each with distinct pathophysiological mechanisms and treatment protocols, ranging from conservative management to surgical intervention. While most patients experience a favorable prognosis with appropriate care, effective management remains critical in preventing chronic disability.[15]

Considering the growing incidence of Achilles tendinopathy in younger, more internet-savvy populations, it is essential to evaluate the quality and reliability of online video content pertaining to this condition. Despite several studies analyzing the accuracy of YouTube videos across various medical topics, no previous research has systematically assessed the quality and educational value of videos specifically related to Achilles tendinopathy. This study, therefore, seeks to fill this gap by evaluating the reliability, educational content, and overall quality of YouTube videos on Achilles tendinopathy. We hypothesize that, similar to findings from studies on other orthopedic conditions, the quality and reliability of YouTube videos on Achilles tendinopathy are likely to be inadequate or incomplete.

METHODS

This study was exempt from ethical approval due to its observational design, utilizing only publicly available videos. All procedures were carried out in accordance with the ethical rules and the principles.

A search using the keywords 'Achilles tendinopathy' was conducted on YouTube (http://www.youtube.com) on June 20th, 2024, in Ankara, Turkiye. After logging out of all Google and YouTube accounts, Google Chrome (Google LLC, Mountain View, CA) incognito tab was used to eliminate confounding factors, conducting the search in a browser with no history or cookies, and without altering YouTube search options or applying any filters. Studies of user behavior in internet search engines have shown that over 90% of users focus on the results within the first three pages.[16] Therefore, the videos were sorted by the default 'relevance' filter, and only the first 50 videos were recorded for evaluation. Only videos in English were included in the study. Excluded were videos unrelated to Achilles tendinopathy, those in non-English languages, advertisements, silent content, videos shorter than 30 seconds, and duplicates. If these criteria were met, the next acceptable video was recorded and evaluated. This descriptive study examined publicly available videos on the internet and did not involve any human participants or animals. Therefore, it was exempted from institutional review by our ethics committee as it only involved the use of public access data, consistent with similar studies in the literature.[17,18] No patient information was used, so patient consent was not obtained.

Video Characteristics

For each video, the following characteristics were extracted: upload date, video duration, number of views, number of comments, number of likes, and number of dislikes. From these values, the days since upload, view ratio (number of views/days) and like ratio (like × 100 / [like + dislike]) were calculated. The video power index (VPI) was calculated as the like ratio × view ratio / 100, a method developed by Erdem and Karaca in their examination of the quality of YouTube videos on kyphosis.[19] The VPI, validated in multiple orthopedic studies, serves as a quantitative index to gauge video popularity, as YouTube does not provide such a metric.[9,20] Videos were categorized based on their creators into four groups: (1) academic physician (linked to research institutions, universities, or colleges); (2) nonacademic physician (independent or associated with physician groups without university or research affiliations); (3) nonphysician/trainer (health professionals like physical therapists and athletic trainers); and (4) other (patient-generated content, medical information, or animations from educational or health websites). Videos were also classified based on their content into the following categories: (1) disease-specific information; (2) surgical techniques or approaches; (3) nonsurgical management; (4) exercise training; and (5) patient experience.

Video Quality, Reliability, and Accuracy of Content

The DISCERN score, global quality score (GQS), and Journal of the American Medical Association (JAMA) score were utilized to assess the quality, reliability, and accuracy of the videos.[9,21,22] Two senior orthopedic and traumatology surgeons independently evaluated the videos using these scoring systems. Their scores were then summed and averaged to determine the final DISCERN, GQS, and JAMA scores. The DISCERN score evaluates information quality through 16 questions, each rated from 1 to 5, totaling 16 to 80 points. Scores are categorized as: 63-80 (excellent), 51-62 (good), 39-50 (medium), 27-38 (poor), and 16-26 (very poor) (**Table 1**). The JAMA scoring system assesses video accuracy and reliability using four criteria-authority, quality, clarity, and currency-each rated from 1 to 4 points, with 1 indicating low level, 2 and 3 indicating medium level, and 4 indicating high accuracy (**Table 2**). The GQS scoring system assesses the educational value of videos with five questions, each rated from 1 (low quality) to 5 (excellent quality) (**Table 3**).

Table 1. DISCERN Scoring System

Criteria	Description
Authorship	Authors and contributors, their affiliations, and relevant credentials should be provided
Attribution	References and sources for all content should be listed clearly, and all relevant copyright information noted
Currency	Dates that content was posted and updated should be indicated
Disclosure	Web site "ownership" should be prominently and fully disclosed, as should any sponsorship, advertising, underwriting, commercial funding

Score: 0-4, JAMA: Journal of the American Medical Association

Table 2. Global Quality Score	
	Question
Section 1	**Is the publication reliable?**
1	Are the aims clear?
2	Does it achieve its aims?
3	Is it relevant?
4	Is it clear what sources of information were used to compile the publication (other than the author or producer)?
5	Is it clear when the information used or reported in the publication was produced?
6	Is it balanced and unbiased?
7	Does it provide details of additional sources of support and information?
8	Does it refer to areas of uncertainty?
Section 2	**How good is the quality of information regarding treatment choices?**
9	Does it describe how each treatment works?
10	Does it describe the benefits of each treatment?
11	Does it describe the risks of each treatment?
12	Does it describe what would happen if no treatment is used?
13	Does it describe how the treatment choices affect overall quality of life?
14	Is it clear that there may be more than 1 possible treatment choice?
15	Does it provide support for shared decision-making?
Section 3	**Overall rating of the publication**
16	Based on the answers to all of the above questions, rate the overall quality of the publication as a source of information about treatment choices
Each item is scored from 1 to 5 and then summed	

Table 3. JAMA scoring system	
Score	Description of quality
1	Poor quality, poor flow, most information missing, not useful for patients.
2	Generally poor, some information given but of limited use to patients.
3	Moderate quality, some important information is adequately discussed.
4	Good quality, good flow, most relevant information is covered, useful for patients.
5	Excellent quality and excellent flow, very useful for patients.
Score: 1-5	

Statistical Analysis

Descriptive statistics for video characteristics such as duration, days since upload, likes/dislikes, and comments, as well as views by video source and content categories, were reported as mean, standard deviation (SD), minimum, and maximum. The Shapiro-Wilk test was used to assess normal distribution of the variables. As the parameters did not show a normal distribution, the Kruskal-Wallis test was employed for group comparisons, and the Mann-Whitney U test identified the group causing the difference. Spearman test was used to assess correlations between groups. All scoring systems were independently assessed twice, by two orthopaedic surgeon. Intraobserver and interobserver agreements were determined using intraclass correlation coefficients (ICCs). Statistical significance was considered at $p<0.05$.

RESULTS

In the current study, 50 videos were evaluated, with descriptive statistics provided in Table 4. According to the DISCERN scoring, 8 (16%) videos were of excellent quality, 7 (14%) were of good quality, 23 (46%) were of medium quality, 11 (22%) were of poor quality, and 1 (2%) was of very poor quality. The JAMA score was determined to be low (one point) in 5 (10%) videos, moderate (two or three points) in 22 (44%) videos, and high (four points) in 23 (46%) videos. The GQS score indicated that 1 (2%) video was of poor quality with one point, while 20 (40%) videos were of excellent quality with five points. The mean video duration was 422.4±27.2 seconds (range, 65-1342 seconds). The mean views was 292342.43±745.12. The videos received a mean number of 1931.2±49.5 likes and 82.3±19.6 dislikes, with a mean view ratio of 111.72±24.4. The mean like ratio was 95.8±7.21, and the mean number of days since upload was 1623.5±368.2. The mean VPI was 105.15±23.5. In our assessment of video reliability, quality, and content for all 50 videos reviewed, the overall mean DISCERN score was 42.5±12.3, whereas the mean GQS and JAMA scores were 3.2±1.05 and 2.6±1.1, respectively.

Table 4. Video characteristics				
Characteristic	**Mean**	**SD**	**Min**	**Max**
Video duration (seconds)	422.4	27.2	65	1342
Days since upload	1623.5	368.2	78	4213
Views	292342.43	745.12	1345	2417422
Likes	1931.2	49.5	5	31125
Dislikes	82.3	19.6	0	1853
Comments	92.1	21.3	0	1542
View ratio	111.72	24.4	564	142377
Like ratio	95.8	7.21	3233	7834
VPI	105.15	23.5	292	137124
DISCERN	42.5	8.3	16	75
GQS	3.2	0.8	1	5
JAMA	2.6	0.8	1	5
SD: Standard deviation, Min: Minimum, Max: Maximum, VPI: Video Power Index, GQS: Global Quality Score, JAMA: Journal of American Medical Association				

Table 5 presents the mean and standard deviation values for the DISCERN, GQS, and JAMA scores, as well as the VPI. There was no significant correlation between the video source and VPI, DISCERN, GQS, and JAMA scores ($p>0.05$). However, it was observed that these scores tended to be higher in videos created by academic physicians. Analysis of the relationship between video content and the VPI, DISCERN, JAMA, and GQS scores revealed that exercise training videos had significantly higher scores ($p=0.032$). Analysis of the relationship between VPI and DISCERN, GQS, and JAMA scores found a statistically insignificant and weak correlation ($p>0.05$, Coefficient = -0.10, 0.15, and -0.12, respectively). JAMA results showed a moderate correlation with DISCERN and GQS results ($p<0.05$, Coefficient = 0.650 and 0.620, respectively), while a very strong correlation was observed between DISCERN and GQS results ($p<0.05$, Coefficient=0.975) (Table 6). The intraobserver and interobserver reliability of the two raters was good for the

DISCERN, GQS and JAMA scores (ICC 0.892, 95% CI 0.804 to 0.929).

Table 5. DISCERN, GQS, JAMA and VPI scores according to video source and content

	DISCERN mean±SD	GQS mean±SD	JAMA mean±SD	VPI mean±SD
Video source				
Academic physician	48.5±6.2	3.4±0.6	3.7±0.5	125.5 ±24.2
Non-academic physician	40.2±8.1	3.0±0.7	2.5±0.7	90.4±22.3
Non-physician/trainer	38.5±7.2	2.8±0.9	2.2±0.8	75.3±19.4
Others	35.8±8.0	2.5±0.8	2.0±0.7	60.7±18.5
Video content				
Disease-specific information	43.2±7.3	3.5±0.8	3.2±0.9	105.7±19.5
Surgical techniques	40.1±8.1	2.9±0.7	2.7±0.8	95.3±18.3
Non-surgical management	42.8±7.0	3.2±0.5	2.5±0.6	110.4±22.1
Exercise training	48.6±6.0	3.3±0.5	3.4±0.6	135.6±25.4
Patient experience	37.5±6.5	2.8±0.6	2.4±0.7	85.2±17.6

GQS: Global Quality Score, JAMA: Journal of American Medical Association, VPI: Video Power Index

Table 6. Correlation between scores and VPI

Correlation	Coefficient	p value
DISCERN-GQS	0.975	0.043
DISCERN-JAMA	0.650	0.039
GQS- JAMA	0.620	0.041
VPI-DISCERN	-0.10	0.125
VPI-GQS	0.15	0.212
VPI-JAMA	-0.12	0.174

VPI: Video Power Index, GQS: Global Quality Score, JAMA: Journal of American Medical Association

DISCUSSION

The key finding of this study is that YouTube videos on Achilles tendinopathy generally provide information of moderate quality. While there was no significant correlation between the source of the videos and their DISCERN, GQS, or JAMA scores, it is noteworthy that exercise training videos consistently received higher scores compared to other types of content. This suggests that exercise-focused videos tend to offer more reliable and accurate information. In summary, the study highlights that although the overall reliability, accuracy, and educational value of YouTube videos on Achilles tendinopathy are moderate, exercise training videos stand out for their superior quality.

Nowadays, patients are increasingly relying on online resources for informed decision-making. YouTube's popularity is growing due to its visual appeal and the ease of accessing health information.[5] However, the quality of online information is variable and inconsistent, which can destabilize the clinician-patient relationship due to the lack of a filtering process.[23] Goyal et al.[24] found that 78% of YouTube videos about carpal tunnel syndrome contained at least one misleading statement.[2] Numerous studies have assessed the quality of health-related videos on YouTube. The first study by Keelan et al. [25] evaluated vaccine-related videos and found low-quality scores for various medical conditions. Similarly, studies on hip arthritis, lumbar surgery, anterior cruciate ligament tears, and rotator cuff tears have reported poor quality results.[26,27] In the current study, the mean DISCERN score of 42.5 out of 80 indicates incomplete specific educational content, the mean GQS score of 3.2 out of 5.0 suggests moderate general educational quality with suboptimal to adequate videos, and the mean JAMA score of 2.6 out of 4.0 shows moderate to low reliability and accuracy. It was found that YouTube videos about Achilles tendinopathy contained moderate-quality information, consistent with existing literature, suggesting that standardizing these videos could improve their quality.

Examining existing studies on video sources reveals that the most important factor in obtaining sufficient information is the video source itself, with physician-prepared videos generally having better information quality.[28] However, Dincel et al.[11] found that even though videos about Achilles tendon rupture uploaded by doctors had higher quality scores than those from other groups, they still did not contain sufficient quality information. In our study, the highest VPI scores were for videos by academic physicians, indicating that patients are more interested in these videos.

The findings of this study have important implications for patient care and the use of online health information. As patients increasingly turn to platforms like YouTube, the discovery that Achilles tendinopathy videos generally provide moderately accurate information raises concerns about informed decision-making. While exercise training videos demonstrated higher reliability and educational value, the overall moderate quality of content may lead patients to make treatment decisions based on incomplete or inaccurate information, potentially impacting clinical outcomes. The lack of a peer-review system on YouTube exacerbates the risk of patients accessing misleading content, complicating the clinician-patient relationship when patients come with preconceived, and often inaccurate, notions. Inadequate or partial online information can lead to delays in seeking appropriate care or misinterpretations of treatment options. Therefore, clinicians must engage in discussions with patients about the limitations of online health videos, steering them toward more reliable sources. YouTube could enhance its algorithms to prioritize evidence-based, peer-reviewed content from reputable sources in health-related searches. Furthermore, implementing a verification system that labels high-quality, fact-checked videos with a "trusted content" badge could assist patients in easily identifying reliable resources.

Limitations

There are possible limitations to this study. Firstly, YouTube's dynamic nature means search results can vary. The top results analyzed represent information available on a single day, but these can be influenced by YouTube's search algorithm, which considers user location, search history, and previously viewed videos. Efforts were made to address this by examining the top 50 results, which is more than an average user

would typically search. Secondly, while the evaluation was performed by two orthopedic surgeons, the intraobserver and interobserver reliability of their scores was consistently good. Another limitation of the study is the terminology, as Achilles tendinopathy is also known as Achilles tendinitis and Achilles tendinosis. The term "Achilles tendinopathy" was used because it encompasses both tendinitis and tendinosis. Future studies should incorporate a broader range of search terms including "Achilles tendon pain" and "heel pain". Lastly, a readability analysis of the video transcripts was not conducted. Patient education materials should be at or below a sixth-grade reading level, as recommended by the American Medical Association and the National Institutes of Health. Videos from physician or academic sources likely exceeded this level. Future studies should evaluate the readability of video transcripts to better understand the accessibility of online health information and address gaps in patient comprehension. Moving forward, research should focus on strategies to improve the quality of online health content. One potential direction is the development of standardized guidelines for creating health-related videos, ensuring that they are accurate, reliable, and easily understandable for the general population. Collaboration between healthcare professionals and content creators could help improve the quality and trustworthiness of online resources.

CONCLUSION

This study highlights that YouTube videos on Achilles tendinopathy generally provide moderate-quality information, with academic physician-produced and exercise training videos showing relatively higher standards. However, there remains a need for improvement in the accuracy, reliability, and educational value of online health content. To address this, standardized guidelines should be developed to ensure videos are based on reliable evidence and are peer-reviewed. Promoting greater involvement from physicians in content creation and incorporating readability assessments are also essential strategies for making these videos more accessible and effective for a wider patient audience. These improvements will help enhance patient education, foster better decision-making, and strengthen the clinician-patient relationship.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was exempt from ethical approval due to its observational design, utilizing only publicly available videos.

Informed Consent

This article did not require informed consent as it did not involve human subjects.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Is essential tremor a risk factor for carpal tunnel syndrome? A prospective study excluding the most common comorbid conditions

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ABSTRACT

Aims: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremity, resulting from compression of the median nerve. Tremor, a rhythmic and involuntary movement of any part of the body, is the most common movement disorder, affecting millions of people worldwide. There is limited research on the coexistence of CTS and ET (essential tremor).

Methods: This prospective study included patients aged 18-65 who presented to the neurology outpatient clinic and were diagnosed with ET. Participants supplied informed consent, a sociodemographic form, and the Fahn-Tolosa-Marin Clinical Tremor Rating Scale (FTM TRS). Patients were evaluated for the presence and severity of CTS with electromyography (EMG). The EMG data were categorized as normal, mild, moderate, and severe CTS.

Results: In the study, the average age of the 50 ET patients was 56.0 (35.0-64.0) years. The gender distribution comprised 22 (44.0%) males and 28 (56.0%) females. The following tremor locations were reported: 41 (82.0%) in both upper extremities, 3 (6.0%) in the right upper extremity, 2 (4.0%) in the left upper extremity, 1 (2.0%) in both upper extremities, head tremor, and voice, and 3 (6.0%) in both upper extremities and head tremor. A high prevalence of CTS was detected in ET patients (46%). Additionally, a positive correlation was found between CTS in ET patients, long disease duration, and female gender. No significant relationship was found between FTM TRS Part A, Part B, Part C, total scores, and median sensory and motor nerve amplitude and velocity values in ETS patients.

Conclusion: CTS is more common in patients with ET. This suggests that ET may be a risk factor for CTS, independent of other factors. Early diagnosis and treatment of CTS in patients with ET is important to improve their quality of life.

Keywords: Essential tremor, carpal tunnel syndrome, Fahn-Tolosa-Marin clinical tremor rating scale.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremity, resulting from compression of the median nerve.[1] The prevalence in the general population is between 4-5%.[2] It is known that individuals aged 40-60 years and women are at a higher risk for developing CTS.[2] Symptoms such as numbness, tingling, burning, and pain in the hand can lead to significant functional impairment of the affected hand.[3,4] Diagnosis of CTS is made through clinical and physical examination findings, in addition to electrodiagnostic tests.[2,3]

While CTS is an idiopathic condition, it has been associated with various other diseases.[5] It is known that prolonged wrist extension and flexion, as well as exposure to vibration, are risk factors for CTS.[2,5] Mechanical, traumatic hand movements are one of the risk factors for CTS.[2,4] The prevalence of CTS is 15 times higher in jobs involving high-force, high-repetitive, and low-force, low-repetitive tasks, supporting vibration, and repetitive movements as risk factors.[6]

Tremor, defined as a rhythmic and involuntary movement of any part of the body, is the most common movement disorder, affecting millions of people worldwide.[7] Essential tremor (ET) and Parkinson's disease (PD) are the two most common tremor disorders in adults.[8] While ET is characterized by the presence of action tremor, PD is defined by resting tremor,

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though it is well known that both disorders can include both types of tremor and share other overlapping clinical features.[9]

The association between tremors in PD and CTS has been studied, and differing opinions among experts have been held on whether tremors are a risk factor for CTS.[4,6,10,11] In contrast, there is limited literature on the coexistence of CTS with the more common ET.[8] Furthermore, the existing studies on ET and CTS often do not adequately represent ET in terms of age and the severity of the tremor.[12,13]

Considering the negative impacts of ET and CTS on quality of life and daily activities, even when occurring independently, determining the influence of ET on the commonly encountered CTS should be regarded as a research priority in clinical studies.[14,15]

METHODS

This prospective study included patients aged 18-65 who presented to the neurology outpatient clinic and were diagnosed with ET between August 1, 2023, and August 1, 2024. Ethical approval for this study was obtained from the Kastamonu University Clinical Researches Ethics Committee (Date: 05.07.2023, Decision No: 2023-KAEK-52). The study was conducted according to the Declaration of Helsinki.

The study population was defined as individuals aged 18 to 65 because elderly patients may have electromyography (EMG) anomalies and extremely old patients are likely to have concomitant disorders. The exclusion criteria are patients with systemic diseases known to cause CTS, such as diabetes mellitus (DM), hypothyroidism, rheumatoid arthritis (RA), or chronic renal failure. Patients with conditions that could mimic CTS or interfere with its evaluation, such as cervical radiculopathy, proximal median neuropathy, significant polyneuropathy, or notable orthopedic abnormalities, as well as those diagnosed with multiple sclerosis, myasthenia gravis, PD, or other movement disorders. Additionally, patients who were pregnant, undergoing hormone or corticosteroid therapy, or had a history of trauma or surgery to the hand or wrist were excluded from the study.[16]

Participants who agreed to take part in the study provided informed consent, and a sociodemographic form specifically designed for patients with ET was administered, which included details on age, sex, dominant hand, and disease duration. All patients underwent detailed neurological examination by a neurologist. Additionally, the Fahn-Tolosa-Marin Clinical Tremor Rating Scale (FTM TRS) was applied.[17]

The FTM TRS rating scale is divided into three parts (A, B, and C), and the subtotal score from each part can be summed to produce a total score or used separately in independent analyses. Part A primarily measures the severity of resting tremor. Part B focuses on action tremors of the hands or arms. Part C assesses functional disability, evaluating the severity of tremors during daily activities such as speaking, eating, personal hygiene, dressing, and working. On this scale, higher scores indicate more severe symptoms.[18]

Participants underwent a neurological motor and sensory examination of both hands. Ulnar and radial entrapment neuropathies were excluded from the study. Patients were evaluated for the presence and severity of CTS through EMG. The EMGs were conducted and interpreted by a neurologist with at least five years of experience in electrophysiology. The median, radial, and ulnar motor nerve response amplitudes and latencies were measured by the same neurologist. EMG results were interpreted according to the nerve conduction study criteria outlined in the American Association of Electrodiagnostic Medicine (AAEM) guidelines.[19]

Mild CTS was defined as the prolongation of median distal sensory conduction in the orthodromic, antidromic, or palmar pathways + a reduction in sensory action potential amplitudes below normal levels. Moderate CTS included these findings along with the prolongation of median nerve distal motor latency. Severe CTS was characterized by the absence of median nerve sensory action potentials, a significant reduction in the amplitude of the thenar M-response, delayed distal latencies, and partial denervation findings in the thenar EMG.

RESULTS

In the study, the mean age of the 50 patients with ET was 56.0 (35.0-64.0) years. The gender distribution comprised 22 (44.0%) males and 28 (56.0%) females. Regarding handedness, 38 (76.0%) were right-handed, 5 (10.0%) left-handed, and 7 (14.0%) ambidextrous.

Occupational distribution was as follows: 13 (26.0%) retired, 14 (28.0%) homemakers, 11 (22.0%) workers, 6 (12.0%) civil servants, and 6 (12.0%) students. Among the participants, 18 (36.0%) had chronic diseases. Tremor locations were reported as follows: 41 (82.0%) in both upper extremities, 3 (6.0%) in the right upper extremity, 2 (4.0%) in the left upper extremity, 1 (2.0%) in both upper extremities, head tremor, and voice, and 3 (6.0%) in both upper extremities and head tremor. The disease duration was 4.0 (2.0-10.0) years. All patients had upper extremity involvement, while none had lower extremity involvement. Head tremor was observed in 9 (18.0%) patients, voice tremor in 5 (10.0%), and a family history of tremor in 22 (44.0%). Table 1 provides descriptive statistics for the individuals included in the study.

Table 2 compares age, sex, disease duration, Part A, Part B, Part C, and total score variables based on EMG status. As a result of these comparisons, there were no statistically significant differences found between age, handedness, Part A, Part B, Part C, and total score variables across the EMG groups ($p>0.05$). However, there was a statistically significant difference between sex and disease duration in the EMG groups ($p<0.05$). This difference is attributed to the higher representation of males in the normal group and females in the moderate group. For disease duration, this significance arises from the observation that those with mild disease had a longer duration compared to those in the normal group.

Table 1. Descriptive statistics of participants included in the study

Characteristics	Patients (n=50)
Age	56.0 (35.0-64.0)
Gender	
Male	22 (44.0)
Female	28 (56.0)
Dominant hand	
Right	38 (76.0)
Left	5 (10.0)
Bilateral	7 (14.0)
Occupation	
Retiring	13 (26.0)
Homemaker	14 (28.0)
Worker	11 (22.0)
Civil servent	6 (12.0)
Student	6 (12.0)
Chronic disease	
Yes	18 (36.0)
No	32 (64.0)
Tremor location	
Both upper extremities	41 (82.0)
Right upper extremity	3 (6.0)
Left upper extremity	2 (4.0)
Both upper extremities, head and voice tremor	1 (2.0)
Both upper extremities and head tremor	3 (6.0)
Disease duration	4.0 (2.0-10.0)

Data are expressed as mean ± standard deviation, n (%) and median (25th percentile-75th percentile).

Table 2. Comparison of A, B, C, and total scores according to EMG levels

Characteristics	EMG			p
	Mild CTS (n=40)	Moderate CTS (n=5)	Normal EMG (n=55)	
Age	58.5 (32.0-64.0)	63.0 (36.0-64.0)	54.0 (38.0-65.0)	0.891
Gender				
Male	15 (37.5)[ab]	0 (0.0)[a]	29 (52.7)[b]	0.040
Female	25 (62.5)[ab]	5 (100.0)[a]	26 (47.3)[b]	
Dominant hand				
Right	31 (77.5)	4 (80)	41 (74.5)	
Left	4 (10.0)	0 (0.0)	6 (10.9)	0.985
Bilateral	5 (12.5)	1 (20.0)	8 (14.5)	
Disease duration	8.0 (3.0-10.0)[a]	4.0 (1.0-7.5)[ab]	3.0 (2.0-9.0)[b]	0.032
Part A	3.0 (2.0-4.0)	3.0 (2.0-3.5)	3.0 (2.0-4.0)	0.860
Part B	2.0 (1.0-8.0)	6.0 (2.0-8.5)	8.0 (1.0-10.0)	0.476
Part C	2.0 (1.3-4.0)	2.0 (0.0-3.5)	2.0 (0.0-5.0)	0.388
Total score	8.0 (5.3-15.0)	8.0 (8.0-13.0)	11.0 (6.0-19.0)	0.664

Data are expressed as median (25th percentile-75th percentile) and n (%), Similar characters on the same line indicate group similarity, whereas dissimilar characters indicate group differences.

Table 3. Relationship between EMG status and occupation in women

Characteristics	EMG			p
	Mild CTS (n=25)	Moderate CTS (n=5)	Normal EMG (n=26)	
Occupation				
Housewife	10 (40.0)	2 (40.0)	16 (61.5)	0.282
Others	15 (60.0)	3 (60.0)	10 (38.5)	

Data are expressed as n (%), EMG: Electromyography, CTS: Carpal tunnel syndrome

Figure 1. Relationship between median sensory and motor nerve amplitude and velocity measurements and Parts A, B, C, and total score.

Table 4. EMG distribution of participants for right and left sides in the study

Characteristics	Patients (*n*=50)
EMG (Right hands)	
Mild CTS	20(40.0)
Moderate CTS	2(4.0)
Normal	28(56.0)
EMG (Left)	
Mild CTS	20(40.0)
Moderate CTS	3(6.0)
Normal	27(54.0)

Data are expressed as n (%), EMG: Electromyography, CTS: Carpal tunnel syndrome

Table 3 evaluates the relationship between EMG status and occupation among women, revealing no statistically significant difference (p>0.05).

Table 4 presents the EMG results of the patients in the study, indicating that among the 22 patients (44%) diagnosed with CTS, 22 had bilateral involvement, while 1 patient (2%) had CTS in the left hand. According to the EMG results, 27 patients (54%) were assessed as normal. The distribution of EMG results for the right hand was as follows: mild in 20 (40.0%), moderate in 2 (4.0%), and normal in 28 (56.0%). The distribution for the left hand was mild in 20 (40.0%), moderate in 3 (6.0%), and normal in 27 (54.0%).

Figure 1 examines the relationship between FTM TRS Part A, Part B, Part C, and total score with the measurement levels of sensory conduction velocity and amplitude for the right and left hands, revealing no statistically significant relationship (p>0.05).

Statistical Analysis

The normality of the data distribution was assessed using histograms, Q-Q plots, and the Shapiro-Wilk test. Chi-square analysis was used for comparisons between categorical variables. For comparisons of continuous variables across groups, the Kruskal-Wallis test was applied. The Bonferroni test was utilized for multiple comparisons. The relationships between continuous variables were determined using Pearson correlation analysis. Data analysis was performed using IBM SPSS Statistics version 22. A significance level of p<0.05 was considered statistically significant.

DISCUSSION

One of the most impressive findings of our study was that CTS was present at a high rate of 46% in ET patients, even after the most frequent comorbidities were eliminated. Other notable findings were that female gender and extended disease duration were substantially linked with CTS in ET patients.

CTS is multifactorial, with obesity, DM, hypothyroidism, and RA commonly associated with CTS.[5,20] Although 37% of patients in our study reported chronic diseases, these conditions are not significant risk factors for CTS. To determine the specific impact of ET, all associated diseases that could potentially act as risk factors were excluded from the study.

The global prevalence of CTS has been reported to range from 2.7% to 5.8%.[5,21,22] Among the most commonly associated conditions that increase the risk of CTS, a history of previous wrist fracture is identified as the most significant risk factor, demonstrating a 2.29-fold increase in risk. Other associated conditions that increase the risk include RA (2.23-fold), obesity (2.06-fold), osteoarthritis of the wrist and carpus (1.89-fold), insulin use (1.52-fold), and diabetes (1.51-fold). Smoking, hormone replacement therapy, the combined oral contraceptive pill, and oral corticosteroids were not found to be associated with CTS.[5]

CTS has been reported to occur in up to 15% of diabetic patients.[22] Similarly, a relationship has been noted between CTS and hypothyroidism, with evidence suggesting that nearly 29% of hypothyroid patients might have signs of CTS on nerve conduction studies.[23] Another study reported this prevalence as 32.5%.[24] In our study, however, CTS was observed in 46% of patients with ET, indicating that this rate is higher than that reported for the associated conditions of DM and hypothyroidism.

The incidence of CTS is shown to increase after the age of 55.[25] In another study, it was found that CTS increases with age, reaching 22.2% in individuals over 55 years, compared to 6 % among participants aged 25 to 34.[26] The higher prevalence in older patients is thought to reflect different pathophysiological conditions.[27] Contrary to these studies, our research did not identify an age-related increase between ET and CTS. It is known that the prevalence of ET increases with age, particularly in older individuals, and it appears that a similar trend may occur with CTS.[25,28] The estimated prevalence of ET is 0.9%, which rises to 4.6% in individuals aged ≥65 years.[8] In contrast, our study did not find an age-related increase in CTS among patients with ET. Among the limited studies in the literature examining the relationship between ET and CTS, Eliacik et al.[12] a CTS prevalence of 16% in patients with ET, noting that the study included participants under the age of 45 and a healthy control group, which may not reflect the typical age of occurrence for both ET and CTS, representing a limitation of the study. In our study, however, CTS was observed in 46% of patients. The average age of 54 in our patient population may explain the difference in prevalence compared to Eliacik's study.[12]

Moreover, female sex and age have been associated with CTS.[20] The female-to-male ratio has been reported to vary between 2 and 7 in different studies.[20,25,29] In a study examining housewives who underwent surgery for CTS, a 3.6-fold higher incidence of CTS was reported.[30] Another study found that, when considering other risk factors, 47.5% of housewives were affected by CTS.[20] The higher prevalence among women and housewives has been attributed to their involvement in high-risk occupations for CTS, including household chores.[20,29] In our study, no significant difference was found between housewives and other professions regarding the incidence of CTS in patients with ET, suggesting that the increase in CTS observed in women may be related to essential tremor.

Lam et al.[25] found that patients with CTS are twice as likely to be overweight (BMI>25) compared to the general population, and that female patients are twice as likely to be obese (BMI>30) compared to their counterparts in the general population. In another study, individuals classified as obese (BMI>29) were found to be 2.5 times more likely to develop CTS than slender individuals (BMI<20).[20] In our study, the average BMI was found to be 27.95. The high prevalence of CTS in our study may be particularly vulnerable to confounding factors such as BMI. However, it is clear that the 46% prevalence of CTS in patients with ET cannot be solely attributed to elevated BMI.

ET is a deceptively simple clinical syndrome associated with a complex network of clinical, pathological, and genetic phenomena.[31] Classic ET is a clinical syndrome characterized by action tremor, occurring in the upper extremities in the absence of other neurological signs in 95% of cases. The tremor usually begins in the upper extremities and is symmetric in approximately 80% of patients.[31] In our study, 100% of patients with ET exhibited tremor in the upper extremities, with only 66% presenting bilateral upper extremity tremor. No association was found between the severity of tremor and CTS.

PD, a common movement disorder, is characterized by bradykinesia, rigidity, postural instability, and tremor. The characteristic tremor in PD is unilateral and at rest, disappearing with voluntary movement.[32] Due to the presence of unilateral tremor, many researchers have investigated the association between PD and CTS.[4,6] Han et al.[4] demonstrated in their study that CTS developed in the hand without tremor, indicating that tremor in the dominant hand is not associated with the development of CTS. They suggested that tremors in PD involve the fingers more than the wrist.

Sonographic studies have shown median nerve enlargement in both ET and PD.[10,11,13] It has been reported that repetitive movements in patients with ET lead to median nerve enlargement, which may contribute to the development of CTS.[13] Although this study demonstrated a relationship between the severity of tremor and median nerve enlargement as assessed by the Fahn-Tolosa-Marin Tremor Rating Scale (FTM-TRS), our study did not find an association between tremor severity and CTS when evaluated by EMG.

The cause of the relationship between ET and CTS has not yet been established. It is known that ET is associated with structural changes in the cerebellum, and cerebellar plasticity is observed in its pathophysiology.[12,33] Interestingly, changes in cerebellar activity have been demonstrated in CTS.[34] Yu et al.[35] showed that more than 70% of patients with median and radial nerve involvement benefited therapeutically for at least 60 minutes after the cessation of transcutaneous afferent patterned stimulation.

CONCLUSION

A high prevalence of CTS has been observed in patients with ET, suggesting that ET itself may be a risk factor for CTS, independent of other associated diseases and conditions previously identified. Additionally, a positive correlation was found between CTS in ET patients, long disease duration, and female gender. Considering the significant impact of both ET and CTS on individuals quality of life, early diagnosis and treatment should be prioritized to improve the long-term management of CTS in patients with ET.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval for this study was obtained from the Kastamonu University Clinical Researches Ethics Committee (Date: 05.07.2023, Decision No: 2023-KAEK-52).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Meningomyelocele defect repair: surgical technique selection

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ABSTRACT

Aims: Surgical repair of meningomyelocele is important in terms of infection, cerebrospinal fluid (CSF) leakage, and preservation of neural structures. While there are numerous techniques available for repair, there are few guidelines on when flap repair should be performed. In this study, we employed a method to select the surgical technique.

Methods: Thirty-two patients with meningomyelocele who underwent surgery were included in the study. The decision to use or not to use a flap was based on the ratio of defect height to width and the ratio of the axillary line to defect width.

Results: Fasciocutaneous transposition flap (FTF) repair was performed in 17 patients, whereas primary repair was performed in 15 patients. There was no statistically significant difference between the groups in terms of preoperative characteristics of the patients. In the FTF group, one patient experienced necrosis at the wound site, and one patient developed a cerebrospinal fluid fistula. In the primary repair group, necrosis was observed in one patient, CSF fistula developed in two patients, and central nervous system infection developed in one patient. No statistically significant difference was found between the groups in terms of complications.

Conclusion: The results obtained in the present study suggest that the shape of the defect and the ratio of intact tissue to defect size are more important than the size of the defect itself in achieving appropriate tension during repair. By employing the patient selection guidelines we achieved successful outcomes using a different flap technique.

Keywords: Meningomyelocele, spinal dysraphism, postoperative complications

INTRODUCTION

Meningomyelocele is the most common congenital anomaly of the central nervous system (CNS) compatible with life. During embryonic development, it presents as a defect in the closure of the neural tube. Genetic, nutritional, and ethnic factors play a role in its manifestation. The incidence varies between 0.17 and 6.39 per 1000 births.[1] In patients with meningomyelocele, neural tissues, along with meningeal structures, externally herniate to varying degrees. The repair of this defect is important for preserving neural tissues, avoiding CSF leakage, and preventing infections.[2]

Various techniques for defect repair have been described in the literature. There are techniques applied in musculocutaneous and cutaneous styles, as well as rotational, transpositional, single-pedicle, and multi-pedicle techniques. The aim of all techniques is to close the defect as early as possible and with the lowest rate of complications. Different approaches have been followed in determining when flap repair should be performed in patients; however, there are few guiding studies on this.[3-6]

The aim of the present study was to present the approach used in selecting the surgical technique and compare surgical results and early postoperative outcomes in patients with meningomyelocele operated on by a single surgeon.

METHODS

The entire study was conducted in accordance with the Helsinki Declaration of 1975 (as revised in 2004 and 2008) This retrospective cohort study was approved by the Ethics Committee of Harran University (HRU/23.24.03). Since this was a retrospective study, consent was not obtained from the patients or their relatives.

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The study included 32 patients with meningomyelocele operated on by a single surgeon at our Hospital between March and September 2023. Data on the preoperative and postoperative conditions of meningomyelocele patients were accessed through the hospital information management system. Preoperative, intraoperative, and postoperative characteristics were examined, and patients for whom sufficient data regarding these characteristics could not be obtained were not included in the study. The patients were followed up in the neonatal intensive care units, and follow-up notes were recorded daily in the system.

The surgical procedure was performed in the same way in all patients until skin closure. All patients were operated under general anesthesia in the prone position. In all patients, the neural placode was identified under neuromonitoring, and it was sutured with 4-0 vicryl suture. The dura was then freed from the surrounding tissue and closed watertight with a 4-0 silk suture. No artificial dura was used in the patients. If necessary, duraplasty with fascia was performed, and all patients underwent watertight primary suturing to repair dural defects. After closing the dura in all possible cases, the skin defect was closed with primary suturing using 2-0 prolene suture (Figure 1). In patients in whom primary suturing was not possible, the skin defect was closed using a unilateral FTF, and the defect was sutured with 2-0 prolene suture (Figures 2, 3). Patient selection was made according to the guidelines reported by Kemaloğlu et al.[7] when deciding on the repair technique. Kemaloğlu et al. stated in their guidelines that; if the defect height/width ratio was ≥1.5, two parameters were evaluated: if the ratio of the length between the posterior axillary lines to the defect width was ≥3, primary repair was performed; if the ratio was <3, FTF repair was performed. If the defect height/width ratio was <1.5, FTF repair was performed. The longest diameter of the defect was considered when calculating the flap size during repair. A fasciocutaneous flap of appropriate size, 1 or 1.5 times the length of the defect diameter, was used to repair the defective area from a region parallel to the defect. No drain was placed under the skin or tissue adhesive was applied.

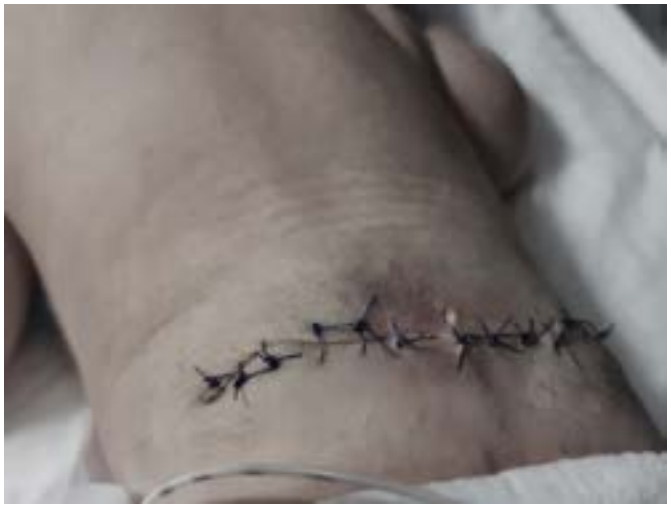

Figure 1. Patient with cerebrospinal fluid (CSF) fistula after primary repai

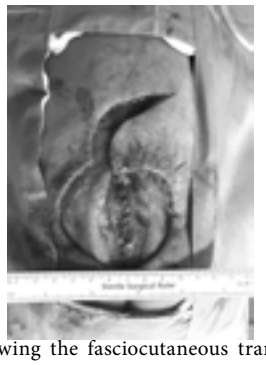

Figure 2. Images showing the fasciocutaneous transposition flap before suturig

Figure 3. Images showing the fasciocutaneous transposition flap after suturing

The preoperative characteristics of patients were compared based on the surgical technique applied, and statistically significant differences were evaluated. Birth week, maternal age, birth weight, Apgar scores, additional anomalies (such as ventricular septal defect, atrial septal defect, patent ductus arteriosus, necrotizing enterocolitis, herniation), presence of motor deficit, surgical intervention time interval, defect localization (classified as cervical-thoracolumbar), and defect size (classified as <5 cm, 5–8 cm, and >8 cm) were reported for all patients, and statistical differences among the patients based on the type of surgery were assessed. All motor deficits observed below the level of the lesion in patients were grouped together under a single category without distinction.

The examination of postoperative characteristics included analyzing patients for wound necrosis, CSF fistula, ventriculoperitoneal (VP) shunt requirement, CNS infection, length of hospital stay, and mortality. Postoperative head circumference was monitored daily. In patients with symptomatic hydrocephalus diagnosed by Transfontanellar Ultrasonography (TFUS) or other cranial imaging methods showing a significant increase in head circumference, a VP shunt was placed. The diagnosis of CNS infection was based on the CSF culture results.

Statistical Analysis

Statistical analysis were conducted using SPSS 29.0 software package. A p value of <0.05 was considered statistically significant in all analyses. Chi-square and Fisher's exact tests were used to compare independent categorical variables, and variables are presented as numbers and percentages. The conformity of independent continuous variables to normal distribution was evaluated using Shapiro–Wilk test. Since none of the variables followed a normal distribution, the Mann–Whitney U test was used to compare continuous

Table 1. Relationship between surgical technique and the preoperative characteristics of the patients included in the study

Preoperative characteristics	Total	Surgical Technique		p	OR (95% GA)
		1(FTF) n (%)	2(Primary) n (%)		
Gender					
Female*	26 (81.2)	16 (94.1)	10 (66.7)	0.076[1]	0.125 (0.013-1.232)
Male	6 (18.8)	1 (5.9)	5 (33.3)		
Age of mother				0.766[2]	1.009 (0.909-1.120)
Median (25p-75p)	24.5 (21.0–29.7)	24.0 (21.0–30.0)	25.0 (21.0–29.0)		
Birth weight				0.682[2]	1.000 (0.998-1.002)
Median (25p-75p)	3100 (2900–3300)	3000 (2930–3225)	3100 (2700–3400)		
Birth week					
<37 weeks*	6 (18.8)	4 (23.5)	2 (13.3)	0.659[1]	0.500 (0.078-3.223)
37–42 weeks	26 (81.3)	13 (76.5)	13 (86.7)		
APGAR (minute 1)				0.502[2]	0.912 (0.585-1.421)
Median (25p-75p)	8.0 (7.0–8.0)	8.0 (7.0-8.0)	8.0 (7.0–8.0)		
APGAR (minute 5)				0.941[2]	0.968 (0.567-1.652)
Median (25p-75p)	9.0 (8.0–9.0)	9.0 (8.0–9.0)	9.0 (8.0–9.0)		
Additional anomaly					
No*	27 (87.1)	15 (88.2)	12 (85.7)	1.000[1]	0.198 (0.044-0.904)
Yes	4 (12.9)	2 (11.8)	2 (14.3)		
Motor deficit					
No*	14 (43.8)	8 (47.1)	6 (40.0)	0.688[3]	0.750 (0.184-3.057)
Yes	18 (56.3)	9 (52.9)	9 (60.0)		
Defect localization					
Cervical*	1 (3.1)	0 (0.0)	1 (6.7)	0.469[1]	-
Thoracolumbar	31 (96.9)	17 (100.0)	14 (93.3)		
Defect size					
<5cm	3 (9.4)	3 (17.6)	0 (0.0)	-	-
5-8cm	27 (84.4)	13 (76.5)	14 (93.3)		
>8cm	2 (6.3)	1 (5.9)	1 (6.7)		
Surgery time				0.313[2]	1.000 (0.979-1.022)
Median (25p-75p)	24.0 (24.0–48.0)	24.0 (24.0–36.0)	24.0 (24.0–48.0)		

[1] Fisher's exact test was used, [2] Mann–Whitney U test was used, [3] Chi-square test was used, * reference group for odds ratio

variables, and the findings were presented as median and 25th-75th percentile values.

RESULTS

The study included 32 patients, which included 81.2% (n = 26) women and 18.8% (n = 6) men. No significant difference was found in the preoperative characteristics of the patients with respect to the surgical technique. FTF repair was performed in 17 patients, whereas 15 patients underwent primary repair. All patients in the FTF repair group had defects in the thoracolumbar region, whereas one patient in the primary repair group had a defect in the cervical region. In the FTF group, the defect diameter was <5 cm in 3 patients, 5–8 cm in 13 patients, and >8 cm in 1 patient. In the primary repair group, the defect diameter was 5–8 cm in 13 patients and >8 cm in 1 patient (Table 1).

When postoperative characteristics were compared with respect to the surgical technique, necrosis at the wound site was observed in 1 patient in each group (p=1.000). CSF fistula was observed in 1 patient in the FTF group and in 2 patients in the primary repair group (p=0.589). There was no significant difference between the surgical techniques in terms of hospital stay, postoperative VP shunt placement, and CNS infection. One patient who developed a central nervous system infection was operated on the 72nd hour and presented with CSF leakage. Mortality occurred in four patients, two patients in the FTF group and two patients in the primary repair group (Table 2). Patients who developed necrosis at the wound site were followed up for wound care and monitored. Of the 3 patients who developed CSF fistula, wound revision was performed in 1 patient who underwent primary repair.

DISCUSSION

This study was conducted in Şanlıurfa province, which has the highest birth rate and consanguineous marriage rate in Turkiye (TurkStat data). Therefore, it is reasonable that 32 patients were operated in a short time compared to other studies in the literature. In patients with meningomyelocele, the goal of surgical repair can be summarized as closure of the neural placode, prevention of CSF leakage, prevention of systemic and CNS infections, and preservation of neural function.

In the literature, it has been reported that primary repair is possible in 75% of patients, whereas various procedures are used to close the skin defect in 25% of patients.[3,4] Studies have been conducted on various repair methods including primary repair, skin grafts, muscle flaps, and fasciocutaneous

Table 2. Relationship between surgical technique and postoperative characteristics of patients included in the study

Postoperative characteristics	Total	Surgical Technique		p	OR (95% GA)
		1 n (%)	2 n (%)		
Necrosis at the wound site					
No*	30 (93.8)	16 (94.1)	14 (93.8)	1.000[1]	0.875 (0.050-15.326)
Yes	2 (6.3)	1 (5.9)	1 (6.7)		
CSF fistula					
No*	29 (90.6)	16 (94.1)	13 (90.6)	0.589[1]	0.406 (0.033-4.997)
Yes	3 (9.4)	1 (5.9)	2 (13.3)		
Postoperative hydrocephalus VP shunt					
No*	21 (65.6)	9 (52.9)	12 (80.0)	0.108[2]	3.556 (0.730-17.323)
Yes	11 (34.4)	8 (47.1)	3 (20.0)		
Length of hospitalization					
Median (25p-75p)	18.0 (10.0–38.0)	18.0 (10.0–38.3)	18.0 (7.0–31.0)	0.395[3]	1.018 (0.949-1.092)
CNS infection					
No*	31 (96.9)	17 (100.0)	14 (93.3)	0.469[1]	-
Yes	1 (3.1)	0 (0.0)	1 (6.7)		
Mortality					
Alive	28 (87.5)	15 (88.2)	13 (86.7)	1.000[1]	1.154 (0.142-9.385)
Dead	4 (12.5)	2 (11.8)	2 (13.3)		

[1] Fisher's exact test was used, [2] Chi-square test was used, [3] Mann-Whitney U test was used

flaps.[3,5] Regardless of the method used, tension should be minimized, CSF fistula should be prevented, and a soft support for the neural tube should be established. In their study, Haktanir et al.[5] used bilateral fasciocutaneous flaps for defect repair in patients with meningomyelocele and did not encounter any complications such as necrosis, wound dehiscence, or CSF fistula. Atik et al.[6] performed repair with a bilobulated fasciocutaneous flap in 20 patients and encountered a CSF fistula in 2 patients and flap failure in 1 patient.In their study, Mutaf et al.[8] developed a new technique called the triangle repair technique and encountered only minimal hematoma complications in one out of five patients. Kankaya et al. used a V-Y rotation flap in 17 patients and compared the dorsal skin and defect areas of the patients. They selected the flap technique for repair according to this ratio and applied bilateral flaps in 6 patients and quadrilateral flaps in 11 patients. Among the patients who underwent quadrilateral flap application, wound dehiscence occurred in one patient, whereas necrosis developed in another. No complications were observed in the other patients.[9] In a study conducted by Jabaiti et al.[10] complications developed in 7 of 48 patients. They reported necrosis in 3 patients, seroma in 2 patients, meningitis in 2 patients, and CSF fistula in 1 patient. High complication rates were reported in repairs made with large musculocutaneous flaps.[11] Anitha et al.[12] reported a total complication rate of 24% in their study involving 27 patients who underwent various surgical procedures using different techniques. They noted that the incidence of wound dehiscence was higher in patients who underwent primary closure.Sharma et al.[13] applied various techniques to achieve tension-free closure in 22 patients with meningomyelocele, reporting complications in three patients. In one patient who underwent a triple rotational flap procedure, necrosis at the wound site was observed, while in two patients who underwent Limberg flap and local transposition flap procedures, wound dehiscence was reported. Shim et al.[14] conducted a study involving 14 patients with meningomyelocele. Primary repair was performed in 12 patients, while repair using the Limberg flap technique was carried out in 2 patients, 2 patients experienced complications. When compared with musculocutaneous flaps, local cutaneous flaps are easier to apply because of reasons such as shorter dissection time and less bleeding. Therefore, many surgeons use cutaneous flaps in different techniques such as advancement flaps, transposition flaps, bilobed flaps, V-Z plasty, and Limberg flap. Limberg flap is a frequently used method where the flap is lifted from the defect periphery and does not cause damage in muscles. The fundamental element in reducing wound complications is tension-free closure. To achieve this, an understanding of flap principles is essential. Relying on a single defect width value is insufficient to determine the appropriate reconstruction method. If such an approach is employed, complication rates are likely to be higher, similar to those reported in the literature. Patients present with tissues of varying quality and availability. We believe that surgical planning is significantly more related to the success of a reconstruction. In the present study, we performed repair using fasciocutaneous transposition flaps in 17 out of 32 patients, where the flap was raised from the defect periphery similar to the Limberg flap and V-plasty. Primary repair was performed in 15 patients. The guidelines reported by Kemaloğlu et al.[7] were used to decide on the repair method for the patients.The ratio of the defect area to the dorsal skin area is more important than the defect area in flap usage. Therefore, repair with a fasciocutaneous flap in all patients where we anticipated high tension during repair, even if the defect diameter was <5 cm was preferred. In addition, if we anticipated that a tension-free closure could be achieved, we preferred primary repair even if the defect diameter was larger than 5 cm. Among the 17 patients who underwent flap repair, one patient necrosis at the wound site and one developed CSF fistula. In the primary repair group, necrosis developed in one patient and CSF fistula developed in two patients. One patient with CSF fistula was re-operated. Other

patients recovered following wound care and monitoring. In a study investigating postoperative infections in patients with myelomeningocele, the infection incidence was found to be 30%.[1] In another study, the rates of CNS infections were reported as 16%, and the rate of sepsis was 29%. The incidence of CNS infections was found to be higher in patients with larger defects and those whose surgeries were delayed.[15] It is hypothesized that delays in the surgical repair of myelomeningocele are associated with an increased rate of infections due to bacterial colonization, which may lead to wound infections or meningitis/ventriculitis post-repair.[16] In our study, a CNS infection was observed in a patient who underwent primary repair. This patient was operated on the 72nd hour post-delivery and presented with postoperative CSF leakage. Our overall rate of CNS infections is lower compared to the literature. When comparing surgical techniques regarding CNS infection rates, we did not find any significant differences. In the literature, complication rates vary between 7% and 33%.[17-19] In this study, the complication rate was 11% in the FTF group and 26% in the primary repair group. When we examined the defect diameter of patients who developed complications after primary repair, we observed that all patients had a defect diameter of >8cm and underwent VP shunt placement. This finding is consistent with the literature; the relatively high complication rate compared to flap repair may be related to these factors. Compared to the literature, the complication rates in the FTF group were considerably lower. When compared in terms of necrosis at the wound site, CSF fistula, CNS infection, mortality, and length of hospitalization, no statistically significant difference was found between the two surgical techniques. Upon examination of the preoperative characteristics of patients subjected to different surgical techniques, we discerned no statistically significant differences, thereby indicating the absence of any confounding factor impeding the comparison of surgical outcomes.

Limitations

The retrospective design was a limitation of this study. However, considering that the preoperative characteristics were examined in detail and no statistically significant preoperative differences that could influence the postoperative outcomes of surgical techniques were identified, our results seem to be consistent. Furthermore, the fact that all surgeries were performed by a single surgeon minimizes variations in surgical procedures.

CONCLUSION

Meningomyelocele is an important condition that requires close monitoring and early intervention from birth because it can lead to various complications if not promptly addressed. Implementing timely and appropriate surgical procedures after birth helps prevent potential complications that may arise later. Although various repair techniques have been described, we emphasized that proper patient selection is more crucial for the choice of repair technique. By utilizing the intact tissue-defect ratio, we found that the postoperative complication rates of the surgical techniques we applied were lower compared to the literature. The method of selecting surgical techniques in our study indicates that the ratio of the defect to healthy tissue is more important for repair under appropriate tension than the size of the defect itself.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethics Committee of Faculty of Harran University (Date: 25.12.2023, Decision No: HRÜ/23-24-03).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Investigation of Babesia species using molecular methods

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ABSTRACT

Aims: To determine the presence of *Babesia* species in ticks in the Ankara region and neighboring provinces; the aim of this study was to detect and distribute *Babesia* species using molecular methods in ticks collected from nature and hosts.

Methods: *Babesia* was detected at the species level by conventional PCR method by DNA extraction of 191 tick samples collected from Ankara and neighboring provinces, which applied to the Parasitology National Reference Laboratory of the Ministry of Health, General Directorate of Public Health, between 2020-2021.

Results: A total of 191 tick samples were examined in the study, and as a result of the conventional PCR study, 4 *Babesia* agents were found positive, 1 of them was *Babesia* bigemina (*B. bigemina*), 2 were *Babesia* ovis, 1 was *Babesia* spp. were determined.

Conclusion: In tick-borne diseases such as Babesiosis; it should not be forgotten that ticks continue to focus some infections in nature and serve as reservoirs for disease agents in nature, and the necessary strategies for tick control should be followed.

Keywords: *Babesia* spp, tick, parasite

INTRODUCTION

Babesiosis is one of the important diseases that is seen worldwide and is transmitted by ticks and causes medical, veterinary and economic problems. Ticks are ectoparasites that can attach to many living creatures including amphibians, birds, mammals and reptiles with blood-sucking habits and cause the spread of diseases.[1,2] In addition, due to the suitability of climate, surface shape and vegetation, ticks and tick-borne diseases are frequently seen. Ticks and tick-borne diseases are seen at different rates in countries due to reasons such as climate, surface features and suitability of vegetation. Tick-borne diseases are frequently encountered, especially in countries where animal husbandry is high, such as Turkiye.[3]

Tick-borne diseases such as Babesiosis cause a decrease in meat and milk yield, deterioration in wool quality and, most importantly, death, especially in cultured animals. In addition to yield losses, treatment costs also increase the economic dimension of these diseases.[4,5]

Diagnosis of acute Babesiosis is traditionally made by clinical and microscopic methods.[6] Microscopy is insufficient in species identification and low parasitemia. Serological tests such as enzyme-linked immunosorbent assay (ELISA), indirect immunofluorescence assay (IFA), indirect hemagglutination test (IHA), complement fixation (CF) and latex agglutination test (LAT) have been used for a long time in determining subclinical infections and infected animals.[7] Serological tests used in herd screening have disadvantages such as cross-reactivity and false seropositivity due to the presence of antibodies in treated animals. Interest in molecular methods such as polymerase chain reaction (PCR) and reverse line blotting (RLB) has increased since species identification is provided and their sensitivity and reliability are higher.[8,9] Today, molecular methods are widely used in the diagnosis of tick-borne diseases.[10]

In this study, we aimed to diagnose the Babesiosis agent carried by ticks using the PCR method, since microscopic techniques were insufficient to identify the species and the possibility of making a definitive diagnosis was low.

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METHODS

This study was conducted with the decision of Çankırı Karatekin University Science, Maths and Social Sciences Ethics Committee (Date: 09.11.2021, Decision No: 09.11.2021/23). The study was also conducted. In addition, permission was obtained from the head of the Microbiology Reference Laboratories and Biological Products Department for the study. This article based on the master's thesis of Sinem Tunçer (814206/2023).

Sample Collection

Of the 191 ticks collected, 152 were collected from various animals (Sheep, Goat, Marten, Dog, Cat, Rodent, Crocidura), 32 from humans and 5 from nature. Within the scope of the study, ticks were collected considering their seasonal activities. Ticks were collected from suitable habitats in Ankara and its districts (Center, Bala, Beypazarı, Çubuk, Kahramankazan) and Kastamonu, Tokat, Yozgat, Eskişehir, Bartın, Sakarya and Çankırı between March 2020 and October 2021. Those taken from the field were collected by the tick flagging method and from farm animals and dogs. Ticks were identified at the genus and species level microscopically according to their morphological characters.[11] Samples for PCR were stored at -20°C until the study before the experiment.

For PCR, homogenization of ticks is required. In this study, magnetic bead-based extraction method was used and samples were extracted one by one. This method is simple, fast and convenient, effective in removing inhibitors, was preferred in order to produce pure high molecular weight genomic DNA and to obtain more purified products.

DNA extraction from homogenized ticks was performed according to the manufacturer's instructions (Qıagen, Hilden, Germany). Samples were homogenized by adding 500 µl PBS to 1.5 ml Eppendorf tubes, placing them in a pestle-disintegrated state, and vortexing. For tissue lysis, 200 µl ATL buffer and 20 µl proteinase K were added and left at +50°C overnight. For cell lysis, 200 µl AL buffer was added to the lysed sample and slowly withdrawn. Cells were lysed by waiting at 56°C for 10 minutes. 250 µl binding solution and 50 µml magnetic beads were added and incubated at room temperature for 5 minutes. The tubes were placed on a magnetic rack and the liquid in the tube was discarded without touching the magnetic beads. For washing, 600 µl of AW1 buffer was added and mixed on the mixer for 3 minutes, centrifuged and placed on a magnetic rack, and the liquid in the tube was discarded without touching the beads. 700 µl of AW2 buffer was added and mixed on the mixer for 3 minutes, centrifuged and placed on a magnetic rack after centrifugation, and the liquid in the tube was discarded without touching the beads. A second wash was performed with 500 µl of AW2 buffer. After centrifugation, it was placed on a magnetic rack and the liquid in it was discarded again. To get rid of the ethanol in the tube, 700 ml of distilled water was added to the samples in the magnetic rack and immediately withdrawn. 200 µl of AE buffer was added and incubated on the mixer at room temperature. The centrifuged samples were placed on the magnetic rack and the liquid remaining on the side was transferred to clean tubes as DNA extract. DNA extracts were kept at -20 °C until use. Positive control samples were obtained from the Turkiye Republic Health Ministry of Health General Directorate, Microbiology Reference Laboratories and Biological Products Department. In addition, distilled water was used as a negative control. DNA size markers, 100 bp ladder, have been loaded on each side.

In order to identify the presence of *Babesia* species, conventional PCR was performed for the separation of the 18S rRNA protozoa-specific gene region before DNA sequence analysis. For PCR, forward and reverse primers recommended for the 18S rRNA gene region (BJ1- GTCTTGTAATTGGAATGATGG and BN2-TAGTTTATGGTTAGGACTACG primers) were used.[12] Primers were commercially produced (Sentabiolab-Ankara).

After amplification, 1.5% agarose gel (Biomax-EEC European Economic Community) was prepared for the evaluation of amplified products. TBE buffer (Sigma Aldrich Merck Darmstadt/Germany) was used as the running buffer during agarose gel electrophoresis. After the agarose was melted in this buffer, it was cooled to 60^0C, nucleic acid stain (Gelred nucleid acid stain) was added to the agarose gel at a ratio of 1:10000 and poured onto the prepared horizontal gel table. An electrophoresis comb was placed on the agarose poured in a thickness of 5 mm and 30 minutes was waited for the gel to solidify completely. At the end of this period, the comb was removed without damaging the gel. 100 bp DNA ladder (Biomatik Delaware/USA) was loaded into the first well of the gel. 5 µl of amplification products were mixed with 1 µl of loading buffer (Sigma Aldrich Merck Darmstadt/Germany) and loaded onto the gel. The tank lid was closed, a power supply providing direct current to the electrodes was connected, and it was checked whether the movement was towards the anode. The amplified DNA samples were subjected to electrophoresis at 90 volts for 50 minutes. They were visualized under UV light with a gel imaging system (Biostep UST-20M-8X Transilluminator-Germany).

Statistical Analysis

Four samples that were found to be positive for *Babesia* spp. were sent for DNA sequence analysis. Nucleotide analysis was performed using ABI 3730XL sanger sequencer and BigDay Terminator v3.1 cycle sequencing kit to obtain DNA sequence. The obtained data were subjected to NCBI (national center for biotechnology information) blast algorithm and database.

Mega software (version 6.0) was used for phylogenetic analysis.[13] Phylogenetic tree was constructed using the neighbor-joining method based on Kimura.[14] The software used a 2-parameter model.[15] Bootstrap resampling was calculated from 1000 pseudo-replicates with random seeds.[16]

RESULTS

Of the 191 tick samples collected, 95 were male, 85 were female and 11 were nymphs. A total of 4 samples were identified as *Babesia* positive. 81 were identified as *Rhipicephalus sanguineus* (*R. sanguineus* (54♂; 27♀), 6 as *R. bursa* (6♀), 4 as *R. turanicus* (1♂; 3♀), 59 as *Hyalomma marginatum (H. marginatum)* (25♂; 29♀), 5 as nymphs of *Hyalomma* spp., 4 as *H. aegyptium* (3♂; 1♀), 4 as *Haemaphysalis parva* (1♂; 3♀), 8 as *Hae. erinacei* (7♂; 1♀), 1 as *Dermacentor marginatus* (1♂)

Table 1. Samples found positive by molecular analysis (PCR) (n=4)

County	Collected from	Ticks	İnfection Rates					PCR (+)		
			Larva		Nymph	Adult		*Babesia bigemina*	*Babesia ovis*	*Babesia* spp.
			F	M		F	M			
Ankara/Çubuk	Human	*Hyalomama aegyptium*	-	-	-	-	1	+(118)		
Ankara	Human	*Rhipicephalus sanguineus*	-	-	-	-	1		+ (62)	
Eskişehir	Goat	*Rhipicephalus sanguineus*	-	-	-	-	1		+(116)	
Tokat	Crocidura	*Ixodes spp.*	-	-	1	-	-			+(130)

Note: F: Female M: Male. A total of 119 ticks were examined

and 24 as *Ixodes ricinus* (3♂; 15♀), 6 as nymphs of *Ixodes spp.* When the distribution of the collected ticks by province was examined, 37 *R. sanguineus*, 6 *R. bursa*, 2 *R. turanicus*, 33 *H. marginatum*, 2 *H. aegyptium*, 3 *Hae. parva,* 1 *D. marginatus* were found in Ankara. While 14 *I. ricinus* species were found in Sakarya, 8 *Hae. erinacei* and 2 *R. turanicus* were detected in Tokat.

The 18S rRNA gene sequence results obtained with primers determined that samples 62, 116, 118 and 130 were positive for *Babesia* species. One of the positive samples (sample 118) was *Babesia bigemina* (*B. bigemina)*, two (samples 62, 116) were *B. ovis*, and one (sample 130) was *Babesia* spp. One *B. bigemina* was found in a male *H. aegyptium* tick taken from a human in Çubuk district of Ankara, one of the two *B. ovis* was found in a male *R. sanguineus* tick taken from a human in Ankara province, the other was found in a male *R. sanguineus* tick taken from a goat in Eskişehir province, 1 *Babesia* spp, and *Ixodes* spp. was found in a nymph taken from crocidura in Tokat province. Table 1 shows samples that were positive by conventional PCR.

A phylogenetic tree was drawn by comparing the obtained results with the data recorded in NCBI. The phylogenetic tree includes data on the strain, *Babesia* species, the country from which it was obtained, and the species of organism. The sample identified as *Babesi*a spp. (130) is in the same clade as *B. rossi* and *Babesia* spp. The two samples identified as *B. ovis* (62, 116) are in the same clade as the other *B. ovis* cases. *B. bigemina* (118) is in the same clade as the other *B. bigemina*'s.

DISCUSSION

Babesiosis, caused by parasites of the genus *Babesia*, is a worldwide tick-borne zoonotic disease. Ixodes ticks are the primary vectors for the transmission of *Babesia* to vertebrates, including humans. *Babesia* parasites are found in various vertebrate reservoirs, while humans are accidental and terminal hosts. Many different species of *Babesia* parasites have been found in animals, but only a few have been found in humans. *B. microti, B. divergens*, and *B. bovis* are the most common causes of human babesiosis.[17]

In the northeastern and upper Midwestern United States, the main species seen in humans is *B. microti*, with the primary reservoir being the white-footed mouse. *B. microti* is endemic in the United States and sporadic in the rest of the world. In Europe, the bovine parasites *B. bovis* and *B. divergens* have been isolated from human patients, and *B. divergens*

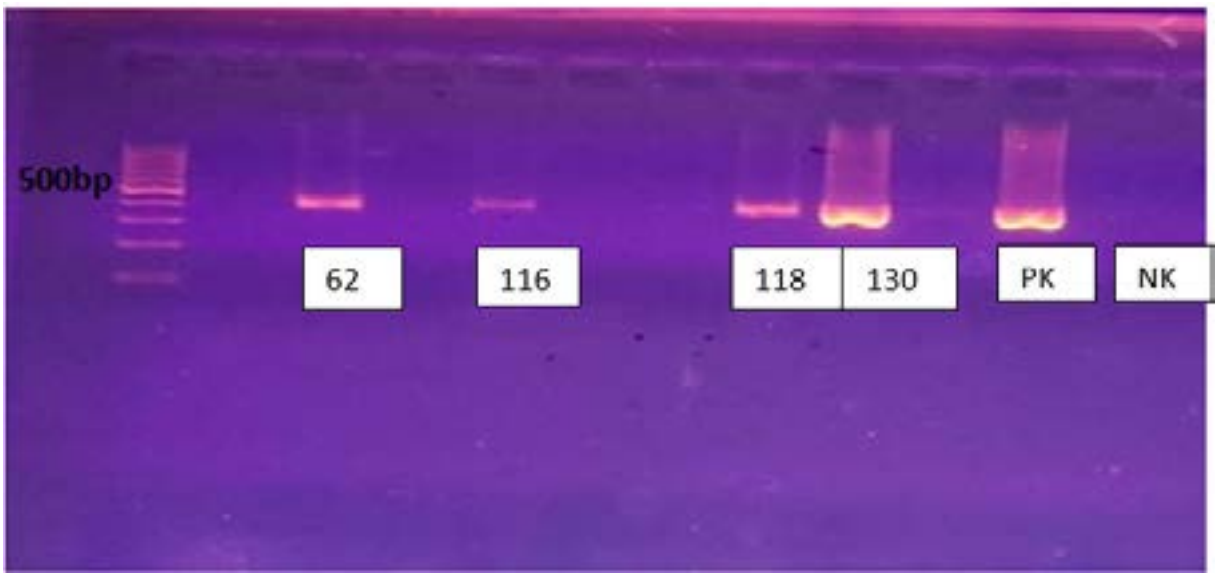

Figure 1. Gel electrophoresis image including samples 62, 116, 118 and 130 after amplification and positive and negative controls. M: marker, PK: positive control, NK: negative control, PO: positive samples (Original)

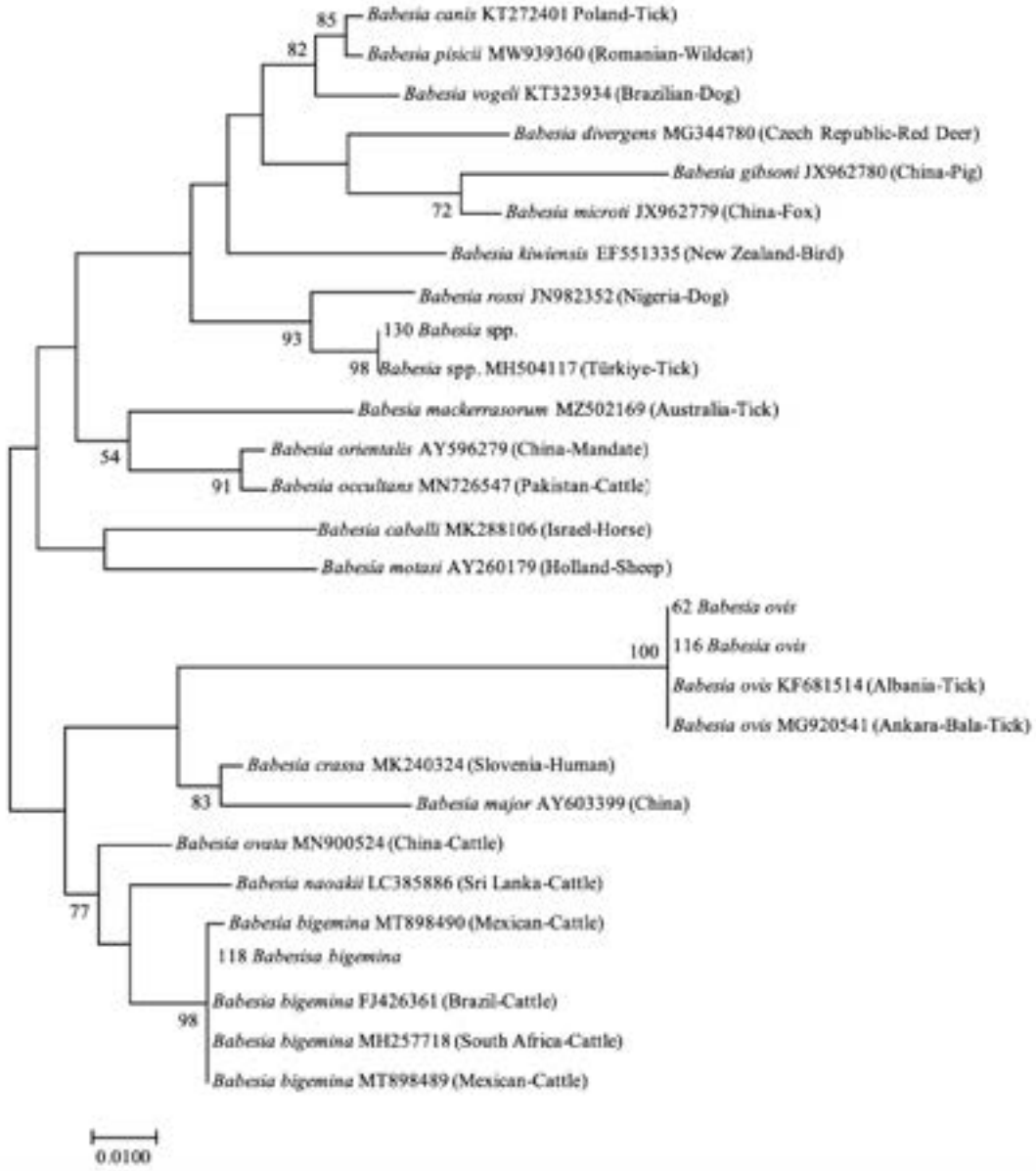

Figure 2. Molecular phylogenetic analysis of Babesia spp. drawn with the maximum likelihood method

infection has generally been detected in individuals who have undergone splenectomy.[18]

The disease occurs especially in the summer months when vector ticks become active. High fever, respiratory distress, pulmonary edema, disseminated intravascular coagulation, renal failure, hemoglobinuria, coma, and splenic rupture are observed in babesiosis. The disease may present itself as a long-term course despite antibiotic treatment. It may progress severely and result in death in patients with a history of travel to endemic areas, in patients who have been exposed to ticks, in older ages, and in patients who have undergone splenectomy. Human babesiosis is most commonly caused by tick bite, but it may also occur through blood transfusion, transplacental, or perinatal transmission.[18,19]

In studies conducted on ticks that infect humans in the Central Anatolian region of Turkiye, *B. bovis, B. ocultans, B. microti*, and *B. ovis* were found.[17,20-22] In our study, *B. microti*, *B. bovis,* and *B. divergens*, which were reported as zoonotic species, could not be determined. *Babesia* parasites have been defined as blood parasites that cause significant economic losses for farm animals, and many studies have reported the presence of *Babesia* species in domestic animals using microscopic and molecular methods. In studies conducted on farm animals in the Central Anatolia, Black Sea, Southeastern Anatolia and Marmara Regions between 2005 and 2020, *B. ovis, B. bigemina* and *Babesia* spp. positivity was detected using PCR and Reverse Line Blotting (RLB) methods.[22-27]

In a study conducted in Izmir, Konya and Gaziantep in 2021 with 152 racehorses, positivity was detected using standard and nested PCR tests. *B. ovis* was found with the sequencing study. This result is the first detection of *B. ovis* DNA in racehorses in Turkiye to date. It should be noted that *B. ovis*, a parasite generally thought to occur in sheep, should also be taken into account in future epidemiological studies on horses.[28]

In studies conducted in Turkiye, ticks are known as the main vectors for *Babesia* species and play an important role in their transmission between animals. In studies conducted in various parts of Turkiye, *B. crassa, B. rossi, B. occultans* and *B. bigemina* were detected in ticks belonging to the genera *Hyalomma* spp., *Haemaphysalis* spp., *Rhipicephalus* spp., *Dermacentor* spp. and *Ixodes* spp using PCR and RLB techniques. *Babesia* spp. and *B. caballi* were found for the first time in horses and *B. vulpes* in foxes. Three of the *Babesia* spp found in our country, suspected to be a new species, were named *Babesia* sp. Rabbit 1, *Babesia* sp. Rabbit 2 and *Babesia* sp. novel (*B. sp ucbas*).[29-33]

Onyiche et al.[34] (2021), found that 3069 *Babesia* species were detected positive in 137.364 ticks in 104 eligible studies from 1985 to 2020. The study shows that global estimates are 2.10%. In total, 19 different *Babesia* species of both human and veterinary importance were detected in 23 tick species. Of the molecular techniques, nested polymerase chain reaction (PCR) was the study with the highest rate at 2.80%. Similarly, in our study, the positivity rate was found to be 2.1% with conventional PCR.[34]

Microscopic examination is widely used in laboratory diagnosis of pathogens in blood smears. However, there are serious problems such as similar morphologies of different parasites, carrier animals with low parasite counts, inability to identify parasites in acute conditions at the beginning of the disease, low sensitivity, need for an expert, and inability to identify species. There are also situations such as cross-reactivity and inability to distinguish active from past infection in serological tests used to detect parasite-specific antibodies. However, antigen-based serological tests can overcome certain limitations. However, there may be difficulties in identifying antigens.[35]

With the advancement of molecular biology, PCR-based diagnostics offer researchers the opportunity to detect and identify a large number of parasites in clinical samples and their natural hosts down to the subspecies or strain level. This innovative method has proven to be the most sensitive and specific method for detecting agents and new strains, eliminating the disadvantages of both microscopy and serology, and is a basic tool for evaluating therapeutic efficacy.[35] Considering all these, conventional PCR was preferred among molecular methods in our study.

CONCLUSION

Four *Babesia* agents were found to be positive (4/191) 2.1%. 1 of these was reported *as B. bigemina*, 2 as *B. ovis* and 1 as *Babesia* spp. Today, the majority of disease agents are of animal origin. The majority of these are zoonotic agents. The limitations of this study may be the inability to collect more ticks. The use of 191 ticks in this study may be due to regional or seasonal collection limitations. Although *Ixodes* ticks are known as summer/pasture ticks, their incidence is high except for a few months of the year. The prevalence of Babesiosis in ticks was found to be lower than in mammals. As in this study, it is thought that keeping regional Babesiosis agent screenings in ticks as up-to-date as possible and following them will provide significant advantages in the control and fight against the disease and agent. It should not be forgotten that ticks act as reservoirs in nature for tick-borne diseases such as Babesiosis and tick control strategies should be followed.

ETHICAL DECLARATIONS

Ethical Approval

This study was conducted with the decision of Çankırı Karatekin University Science, Maths and Social Sciences Ethics Committee (Date: 09.11.2021, Decision No: 09.11.2021/23). The study was also conducted. In addition, permission was obtained from the head of the Microbiology Reference Laboratories and Biological Products Department for the study.

Informed Consent

Informed consent is not required in this bacterial strain study.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Review

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Sexual dysfunctions (SD) and selective serotonin reuptake inhibitors (SSRIs): from preclinical studies to intervention strategies

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ABSTRACT

In the light of existing literature, we reviewed the causes, management and potential therapeutic benefits of SSRI (Selective serotonin reuptake inhibitor) agents regarding sexual functions. (SSRIs) are the most commonly used medications for the treatment of depression, based on their effectiveness and safety profile. Sexual dysfunctions (SD) caused by SSRIs are one of the most important reasons for discontinuation of treatment in both genders. Knowing the intervention strategies in patients who develop SD is pivotal for the proper management of sexual side effects and the treatment adherence of patients. The effects of SSRIs on sexual functions can also be used to treat certain disorders. SSRIs have a high success rate in the treatment of premature ejaculation and their off-label use for this purpose is widely recognized.

Keywords: Selective serotonin reuptake inhibitors, sexual dysfunctions, ejaculation disorders

INTRODUCTION

Selective serotonin reuptake inhibitor (SSRI) drugs have been the most commonly used drugs in the world for the last 30 years for major depression treatment. SSRIs are recommended as first-line therapy for the treatment of moderate to severe depressive disorders.[1] Six widely used SSRI molecules currently available on the market are, fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram. Five of these SSRI molecules -other than fluvoxamine- also are indicated for panic disorder, social anxiety disorder, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), and premenstrual dysphoric syndrome treatments. Besides their indicated use, above mentioned molecules can also be treatment alternatives for fibromyalgia and premature ejaculation as off-label medication choices.[2]

SSRI group drugs are considered to be relatively safe, due to their low incidences of anticholinergic side effects (excluding paroxetine), particularly when compared to tricyclic antidepressants in terms of cardiac adverse effects, and they have a wide therapeutic index. Due to mentioned advantages, these molecules became increasingly used drugs all over the world. The prevalence of SSRI use in general population has been reported to be 3.5%.[3]

Based on multiple comparative studies, SSRIs and other antidepressants have not been found to be superior to each other in terms of treatment effectiveness. However, SSRIs tuned out to have higher patient compliance because they have more tolerable side effects.[2] Randomized controlled clinical trials showed that, SSRIs have more or less equivalent antidepressant efficacy. On the other hand, there may be individual differences in pharmacokinetics and pharmacodynamic aspects, which may affect clinical responses among patients, therefore some patients may respond better to a particular SSRI than to another.[4]

All SSRIs are ligands of serotonin transporter (SERT) and they basically inhibit serotonin transportation, thereby increase the synaptic availability of serotonin that remains in the synaptic cleft and bind to postsynaptic receptors. This enhanced persistence of serotonin and accordingly increased serotonergic activity in the central nervous system (CNS) however, also lead to a decrease in the number and sensitivity of postsynaptic serotonin receptors (5-HT receptors). Each member of the SSRI family can affect SERT to a different degree. Escitalopram for instance, has the highest known SERT selectivity. SSRIs also differ in terms of different parameters such as elimination half-life and their ability to inhibit cytochrome P450 (CYP) enzymes.[2]

One of the most common clinical side effects associated with SSRI use is sexual dysfunction (SD). The prevalence of

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sexual side effects in patients receiving SSRI therapy is found as high as 50-70% in various studies. Common symptoms include decreased libido, difficulty in raising the arousal, and delayed or failure of orgasm.[5-7] In fact, the incidence of SD seems to be higher than the number of SDs being reported. In a study, only 14% of patients who experienced SD due to antidepressant use spontaneously reported this side effect to their physician.[8] The development of SD is an important issue since it leads to the discontinuation of the treatment[9] and has been shown to lead to poor adherence patterns in patients who choose to continue SSRI therapy.[10]

Serotonin is a neurotransmitter that is effective in all three phases of sexuality: desire, arousal and orgasm. The increase in serotonin levels that develops with SSRI use seems to play a role in the development of SD by inhibiting libido, ejaculation and orgasm. Main SD associated with SSRI use are lack of desire, loss of arousal as erectile dysfunction, delayed orgasm or anorgasmia, and delayed ejaculation. Although the underlying mechanisms regarding the causes of SDs due to SSRI use remain partially understood, the distribution and the interaction of serotonin with various other neurotransmitters, may help explain some features of the adverse actions of these agents. The effect on lack of desire may be related to serotonin induced reduction in dopamine levels in the CNS. Additionally, SSRIs may inhibit nitric oxide synthase, leading to impaired erectile function.[11]

This review focuses on SD due to SSRI use, especially ejaculation problems, which are amongst the most common SD types seen in male patients. Clinical and preclinical studies investigating the ejaculation problems due to SSRI use were reviewed in the light of current literature and therapeutic approaches were summarized.

SD DUE TO SSRIS

Treatment response to SSRIs may differ between men and women. Various studies have shown that women may respond better to SSRIs than men.[12] SD and other side effects associated with SSRIs may also differ based on gender. These differences may be due to gender-related variations in the pharmacokinetic profile.[12-13] Genetic differences in liver cytochrome enzyme systems may cause individual differences in side effects of SSRIs. Genetically poor metabolizers are expected to have higher blood SSRI concentrations and therefore potentially have a greater risk of side effects compared to ultra-rapid metabolizers.[14]

SSRIs can cause SD both in men and women. SDs can occur either in a single phase of sexuality -lack of desire, loss of arousal, orgasmic dysfunctions- or can be seen in multiple phases. The main sexual side effects observed in women using SSRIs are decreased sexual desire, decreased vaginal lubrication, and anorgasmia. The main sexual side effects observed in men using SSRIs are decreased sexual desire, delayed ejaculation or anorgasmia, and erectile dysfunction.[15]

Although SD appears to be a side effect of all antidepressants at different rates (such as tricyclic antidepressants, MAO enzyme inhibitors, venlafaxine, duloxetine, etc.), the highest prevalence has been reported for SSRI drugs. In a meta-analysis, the incidence of SD after SSRI use was found to be 27.4% with sertraline, 20% with citalopram, 16.6% with paroxetine, and 15.5% with fluoxetine.[16] According to post-hoc analyzes of data from the multicenter STAR-D (Sequenced Treatment Alternatives to Relieve Depression) study, in which over 4000 patients with depression were followed-up, SD incidence was found 21% in patients whose depressions were in remission with citalopram treatment.[17]

Despite SD is a very common adverse effect of SSRI use, it is a subject that patients may have difficulty in expressing their problem, unless specifically questioned by a physician or a therapist, thus the frequency of SD developing with SSRI use cannot be determined exactly. It has been found that female patients using antidepressants are less likely to report developing SD to their physicians than male patients.[18]

Various studies were aimed to find out which phases of sexuality are most affected by SSRI use in men and women. In a study evaluating the sexual side effects of SSRIs, paroxetine was found to be associated with a greater incidence of sexual side effects than other SSRIs. Analysis of phase-specific sexual function showed that anorgasmia, erectile dysfunction, and decreased vaginal lubrication were more associated with paroxetine.[8]

In a study comparing SD developing in 1022 patients using SSRIs, the highest rate of development of SD was found to be associated with citalopram (72.7%) and paroxetine (70.7%). The development of SD due to sertraline, fluvoxamine and fluoxetine was found to be 62.9%, 62.3% and 57.7%, respectively.[17] Another study of patients taking fluoxetine, paroxetine, and sertraline found that all three drugs reduced libido (55%), arousal (50%), duration of orgasm (36%), and intensity of orgasm (42%) equally during treatment.[19] Ekselius et al.[5] compared the effects of sertraline and escitalopram on SD, where no significant difference was found in the prevalence rates of phase-specific SD. Clayton et al.[20] reported that men are more likely to experience dysfunction in the desire and orgasm phase and less likely to experience dysfunction in the arousal phase compared to women.

Since SD due to SSRI use is one of the most important reasons for discontinuation of anti-depressant therapy[17]; clinicians should be careful about this adverse effect and monitor their patients. In some of the patients SD improves over time, whereas some patients with SD complaints, do not exhibit an improvement during the treatment course, and in some patients complaints may even worsen over time.[21] The signs of SD development during depression therapy are important for the clinician to recognize, as it not only causes the patient to discontinue the treatment, but also causes decreased self-esteem problems in relationship with their partners and a reduction in their quality of life.[21]

Although SD due to SSRI use is an important therapy problem, this effect can be used for the treatment of particular diseases. In the treatment of conditions such as paraphilia, the libido-reducing side-effects of SSRIs are utilized.[22] One of the important occasions where SSRIs are used off-label in clinical practice, is premature ejaculation (PE). SSRIs

delaying effect on ejaculation time is used for the treatment of patients diagnosed with PE.

PREMATURE EJACULATION AND USE OF SSRIS IN PE TREATMENT

Ejaculation consists of two major physiological phases, emission and expulsion. Ejaculation is completed with the expulsion of semen from the urethra. In the emission phase, rhythmic contractions occur in the epididymis and vas deferens, under the stimulation of sympathetic fibers originating from the medulla spinalis. This rhythmic movement forces seminal fluid to pass into the urethra. Later, in the ejection phase, which is mainly controlled by sacral parasympathetic fibers, semen is expelled from the urethra by the relaxation of external urethral sphincter and rhythmic contractions of the bulbospongiosus and bulbocavernosus muscles.[23] Any problem occurring in one of these two phases may cause dysfunctions such as premature ejaculation, late ejaculation, retrograde ejaculation, and failure to ejaculate.

The most common disorder among male SD is premature ejaculation (PE). There are study results reporting the frequency of PE as 20-30%.[24,25] The diagnosis of PE is a self-reported diagnosis, and different authorities have established different diagnostic criteria for PE. One of the most commonly used diagnostic criteria was determined by the International Society of Sexual Medicine (ISSM). To diagnose PE according to ISSM criteria, from the first sexual intercourse onwards, ejaculation must always and almost always occur before or within approximately one minute after vaginal penetration.[26]

In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), published in 2013, PE was defined as a man's ejaculation within 1 minute and a feeling of lack of control during ejaculation. The symptoms must last longer than six months and are not due to another mental disorder (DSM-5).[27]

With the introduction of SSRI drugs in the treatment of PE, significant success has been achieved.[28] Numerous previous clinical studies have shown that the use of SSRIs prolongs the ejaculation time.[29]

The effects of a SSRI during acute and chronic use differ significantly at the molecular level. After acute administration of an SSRI, existing SERTs are blocked, which increases the level of serotonin in the synaptic cleft. Increased serotonin levels activate 5-HT1A and 5-HT1B auto-receptors, and as a result, less serotonin is released into the synaptic cleft within minutes. Under physiological conditions, the net effect of acute SSRI administration is only a slight or no increase in 5-HT neurotransmission. With extended use of SSRIs, a progressively increasing level of serotonin is seen in the synaptic cleft due to long-term blockade of SERT. Over time, desensitized 5HT1A receptors become unable to suppress serotonin release from the presynaptic cell. Thus, with chronic use of SSRIs, the level of serotonin in the synapse increases significantly. The duration of chronic administration (average 2-3 weeks) is the time during which the clinical antidepressant effect of SSRIs begins. The inhibitory effect of SSRIs on ejaculatory behavior is more pronounced when administered chronically than when administered acutely.[30]

Despite the late onset of their antidepressant effects, SSRIs appear to be effective in preventing premature ejaculation after both acute and chronic administrations.[31] The mechanism by which their effects on premature ejaculation occur within hours, is not fully understood. It is thought that acute administration delays ejaculation through a direct inhibitory action of increased serotonin on ejaculation.[31]

Previous preclinical and clinical studies have consistently shown that decreased serotonin neurotransmission, 5-HT2C receptor hyposensitivity, and 5-HT1A receptor hypersensitivity may play a role in the physiology of premature ejaculation.[32]

Off-label use of SSRIs, particularly paroxetine, sertraline fluoxetine, and citalopram, is a first-line pharmacotherapy intervention in the treatment of premature ejaculation.[33] Paroxetine appears to be the most studied SSRI in the literature, and reviews examining the use of paroxetine in the treatment of premature ejaculation have shown its effectiveness in premature ejaculation management.[31]

A meta-analysis of 19 randomized controlled trials examining the effectiveness of SSRIs in the treatment of premature ejaculation found fluoxetine, escitalopram, and paroxetine to be effective in treatment, with paroxetine having a higher treatment success than other agents.[34] On the other hand, there are also study results that show no significant difference between SSRIs.[35]

Dapoxetine, a specific SSRI manufactured solely for the treatment of premature ejaculation, is also used in the treatment. Dapoxetine is an SSRI with a short half-life of 19 hours that is approved for the treatment of PE in many countries. Dapoxetine is administered in doses of 30 mg and 60 mg, 1 to 3 hours prior to the intercourse and has been shown to significantly prolong the time to ejaculation.[36,37]

There are currently various options for PE treatment other than SSRIs and Dapoxetine. Treatment can be provided with special sexual therapy techniques using developed behavioral techniques.[33] Phosphodiesterase type 5 inhibitors (i.e. sildenafil) are used in the treatment of PE cases accompanied by erectile dysfunction.[38] Although topical local anesthetics such as lidocaine were widely used in the past to reduce the sensitivity of the glans penis and delay ejaculation, they are no longer preferred. Tramadol, a centrally acting opioid analgesic, prolongs the ejaculation period by inhibiting the reuptake of serotonin and norepinephrine. However, it is not a frequently used agent due to the development of tolerance to tramadol, its potential for dependence, and the risk of respiratory depression at high doses.[39]

Clinical studies alone are insufficient to explain the mechanism by which SSRIs prolong ejaculation time. The effects of SSRIs on ejaculation physiology have also been studied in many preclinical studies.

EFFECTS OF SSRIS ON EJACULATION PHYSIOLOGY: DATA FROM PRECLINICAL STUDIES

The control of ejaculation in the CNS, medulla spinalis and genital tract is regulated in a complex manner by many neurotransmitters and neuromodulators, including

serotonin, dopamine, noradrenaline, oxytocin, nitric oxide (NO) and ATP.[28] Serotonin and the serotonergic system are important in the regulation of ejaculation, both in the central and peripheral nervous systems. The available evidence to date suggests that the general effect of serotonin on ejaculation is inhibitory.[40]

In the nervous system, serotonergic activity is controlled by presynaptically located 5HT1A and 5HT1B auto-receptors and the SERT. When serotonin is released from axonal terminals, it binds to serotonin receptors and causes a wide range of effects. Under normal conditions, serotonin is transported from the extracellular space back to the presynaptic neuron via SERT, thereby terminating its effect. SSRI group drugs block the reuptake of serotonin from the synaptic cleft by inhibiting SERT, thus increasing the serotonin concentration.[41] The function of 5HT1A and 5HT1B auto-receptors is to prevent serotonergic hyperstimulation, by suppressing the release of serotonin.[41]

Systemic administration of SSRIs has been shown to increase serotonin levels in the rat brain by 2 to 4-fold within one hour.[42] Microinjection of serotonin into the serotonergic projection area in the forebrain has been reported to prolong ejaculation latency in rats.[43]

Sympathetic nerves originating from the thoracolumbar region of the spinal cord and parasympathetic nerves originating from the sacral region integrate peripheral and central signals, ensuring that ejaculation occurs normally. There is an intense serotonergic transmission from the CNS to the spinal cord. 5-HT1A, 5-HT1B and 5-HT2C receptors are intensely expressed in the sacral parasympathetic nucleus of the spinal cord.[43]

Ejaculation latency was shortened in rats after systemic administration of 8-OH-DPAT, a selective agonist of 5-HT1A receptors. Consistent with the effect of serotonin to inhibit ejaculation, 8-OH-DPAT blocks this inhibitory effect by reducing the release of serotonin into the synaptic cleft.[44] Subcutaneous administration of 5-HT1B receptor agonists (anpyrtoline, TFMPP), whose expression is shown in the hypothalamus and at the lumbosacral level of the spinal cord, has been shown to impair ejaculation in rats.[45] Systemic acute administration of 5-HT2C agonist DOI has been shown to suppress ejaculation in rats, and ejaculation is restored by the administration of 5-HT2C antagonists.[46]

Preclinical findings support clinical study results. It has been found that activation of 5-HT1A receptor accelerates ejaculation, while activation of 5-HT1B and 5-HT2C receptors plays an inhibitory role in ejaculation.[47] Recent studies have repeatedly demonstrated the important role of serotonin 5-HT2C receptors in the regulation of ejaculation. 5-HT2C antagonist drugs, such as lorcaserin, have been shown to shorten the time to ejaculation.[48]

Current preclinical data demonstrate that 5-HT1A receptors play an important role in ejaculation control. Based on these study results, researchers have sought to develop selective antagonists that directly target 5-HT1A auto-receptors, suggesting that this could provide specific treatment for PE. Some researchers found that specific 5-HT1A receptor blockade did not affect ejaculation time.[47] However, administration of a 5-HT1A antagonist with an SSRI resulted in a significant prolongation of ejaculation latency.[49] This finding also supports that 5-HT1A receptors are activated only when serotonin levels are elevated (auto-receptor activity).

Although some studies have shown acute inhibition of ejaculation by administration of molecules such as paroxetine and fluoxetine,[28,50] it has been shown that long-term treatment with paroxetine and fluoxetine is more successful in delaying ejaculation.[51] The delayed onset of ejaculation due to SSRI agents is similar to the late onset of antidepressant activity of SSRIs and suggests that desensitization of 5-HT1a auto-receptors is required for delayed ejaculation.[41] 5-HT1a receptors may co-localize with 5-HT7 receptors in the cell membrane,[52] and it has been hypothesized that hetero-dimerization of these receptors may facilitate the desensitization of 5-HT1A auto-receptors induced by SSRIs.[53]

Ejaculation delaying effects of SSRIs seems to be determined not only at the level of serotonin and serotonin receptors but also by some genetic variations. Some research results with SERT knockout rats provide important evidence in this context. Male SERT knockout rats (SERT– / –) exhibit a strong genotype with lower basal ejaculation performance compared to carrier (SERT+/+) or heterozygous serotonin carrier rats (SERT+ / –).[54] Results from another study found that, (SERT–/–) rats had up to a nine-fold increase in extracellular serotonin levels,[55] a decrease in the number of ejaculations, and an increase in ejaculation latency compared to (SERT+/+) rats.[56] It has been shown that differences in SERT genetic variants may be responsible not only for the sexual side effects but also for other adverse effects of SSRI drugs (nonspecific adverse effects such as nausea, vomiting, dizziness, etc.).[57]

INTERVENTION STRATEGIES FOR SSRI-RELATED SD

While nonspecific side effects such as gastrointestinal intolerance (nausea, loss of appetite, vomiting, diarrhea) that frequently develop due to SSRIs often improve with continued use of the drug,[58] sexual side effects have been reported to persist in up to 80% of cases.[59]

In a meta-analysis of 62 randomized controlled trials involving over 6000 patients examining the development of sexual side effects related to antidepressant use, it was shown that sexual side effects related to SSRI and tricyclic antidepressants were one of the most important reasons for discontinuation of treatment. It has been understood that 14% of patients using SSRIs discontinued their treatment due to sexual side effects related to SSRIs.[60]

Researchers have found that, if left untreated, SD can have even more negative effects on the quality of life that is already poor due to depression, can affect interpersonal relationships, and can negatively impact the patient's self-esteem.[61]

In a patient who develops SD due to SSRI, the recommended options to control the undesirable side effects are as follows: waiting for SD to resolve spontaneously, reducing the dose of

SSRI used, changing the medication, trying to reduce the side effects with a drug holiday or add-on treatment.[62]

Figure 1 summarizes the intervention strategies that clinicians can use in the management of SD due to SSRI use.

Figure 1. Management of sexual dysfunctions due to selective serotonin reuptake inhibitor use

WAITING FOR SPONTANEOUS IMPROVEMENT

In two studies on waiting for spontaneous improvement without changing the drug in SSRI-induced SD, partial recovery rates are reported in the range of 14% to 20% and complete recovery rates between 6% and 10% at a 6 month time period.[17,63] The rate of spontaneous improvement of side effects by this approach seems to be quite low. In fact, this situation may be preferred because it does not require additional medication or intervention; however, patient selection is very important. For patients whose treatment is likely to end within a few months at the latest, it may be preferable to wait for spontaneous improvement. In addition, in patients with mild to moderate sexual side effects who do not experience any significant distress from these side effects, waiting may be preferred. The decision to wait should be made together with the patient.

REDUCING THE DOSE OF SSRI

If the patient is being treated with high doses of SSRIs, reducing the dose of SSRIs may be considered as an option to reduce sexual side effects. Current data suggest that SSRI-associated side effects are related to the SSRI dose. Therefore, reducing the SSRI dose may be helpful in relieving side effects.[64] One study found that reducing the current medication dose by 50% -in patients with SD due to SSRI treatment- provided significant improvement in sexual functions.

However, this strategy cannot be used in every patient, as some patients may experience sexual side effects even at starting doses.

When reducing the dose to improve side effects, care should be taken not to get below lower than minimally required dosage, which will provide the minimum effective concentration. It should be noted that sub-therapeutic doses of medication will reduce the severity of sexual side effects but may also cause relapse of depression. Reducing the dose of medication is a method that can be preferred during maintenance therapy, but only when the acute phase of the disease has regressed and the symptoms are under control. Reducing the dose is not preferred in patients whose depressive symptoms are not yet under control, as it may increase the risk of relapse. When reducing the dose of an SSRI, rapid reduction is not preferred. The dose should be reduced gradually and carefully. If the patient adapts to gradual dose reduction, then this approach should be preferred.

Drug Holiday

Drug holidays can be defined as temporarily reducing the dose of a drug or pausing for a short period of time (a few days, in general). Drug holiday is a method that can only be used if sexual activity is scheduled.

For an SSRI with a short half-life, such as paroxetine, a drug holiday may involve postponing the time of taking the drug until after sexual intercourse. To date, only one clinical trial has been conducted to evaluate the effect of drug holidays on SSRI-induced SD. This study reported that drug holidays improved sexual function in sertraline and paroxetine users. However, there was no improvement in sexual side effects in those taking fluoxetine. The authors speculated that this may be due to the long half-life of fluoxetine.[65] In a recently published randomized controlled trial, patients who developed SD due to SSRI use were given a drug holiday twice a week, and at the end of 8 weeks, a significant difference was observed between the control group and the intervention group in terms of side effects. It has been determined that sexual side effects that developed in patients who took a drug holiday improved and that there was no worsening of existing mental illness with the drug holiday.[66]

A long drug holiday carries the risk of causing symptoms to relapse. Alternative approaches include using a lower dose (approximately half) of the drug during periods of expected or planned sexual activity. It is not appropriate to use the drug holiday method in patients using SSRIs with long half-lives such as fluoxetine.

Switching Medication

It may involve changing the current SSRI molecule to a drug from a different group known to have fewer sexual side effects, such as selective serotonin noradrenaline reuptake inhibitors (SNRIs), vortioxetine, agomelatine, and monoamine oxidase inhibitors.[67] If sexual side effects are severe, and cause great distress to the patient, or if there are other side effects of the drug other than sexual side effects, and if the expected treatment response is not achieved with the current drug, a change in antidepressant medication is recommended.[67] If the patient is not benefiting from the SSRI treatment he or she is using, changing the antidepressant would be a logical attempt. Current literature suggest that SSRIs and SNRIs cause more SD compared to placebo, however agomelatine, bupropion, moclobemide, nefazodone and mirtazapine have been found to have very low SD side effects.[68] As explained in the previous section; since SSRIs do not differ significantly from each other in terms of the risk of developing sexual side effects, switching from one SSRI to another is not recommended.

Several randomized controlled trials have found that, exchanging SSRI therapy with bupropion, improves sexual side effects.[15] There are also study results showing that there is a significant improvement in sexual side effects when SSRI treatment is replaced with mirtazapine.[69] Another study, changing from an SSRI to nefazodone, reported an improvement in sexual function.[70]

There are also study results showing significant improvement in sexual side effects with switching from SSRI to vortioxetine[71] and agomelatine.[72]

Switching Medication

Another intervention strategy in patients with drug-induced SD is to add a molecule that has been shown to reduce sexual side effects to the SSRI treatment. Add-on therapy is generally applied to patients who have seen significant benefits from their current SSRI treatment and who do not want to change their medication. Add-on treatment is most commonly done by adding an antidepressant from a different group (i.e. bupropion, mirtazapine, trazodone), adding a phosphodiesterase-5 inhibitor (sildenafil, tadalafil), or adding a 5-HT1A partial agonist (buspirone) to the existing SSRI regimen.

Patients who have benefited from their SSRI treatment, who do not plan to change their treatment, and who are expected to continue antidepressant treatment for a longer period of time are suitable patients for add-on treatment.[68]

Among add-on strategies, bupropion might have the most strong evidence for efficacy and tolerability.[73] A cochrane meta-analysis reported that adding 300 mg of bupropion to SSRI therapy significantly reduced sexual side effects.[74] Results of another randomized controlled trial in which 150 mg/day bupropion was added to SSRI treatment showed that adding bupropion to the treatment produced a similar enhancement.[75,76]

The addition of phosphodiesterase-5 inhibitors to SSRI treatment has been tried most frequently in male patients who developed erectile dysfunction due to SSRIs. Randomized controlled trials have shown that adding 50 mg sildenafil to SSRI treatment reduces drug-induced erectile dysfunction.[77,78]

In one study, sildenafil was added to men and women using SSRIs, and it was shown that SD symptoms such as decreased libido and decreased arousal were reduced in both men and women.[79]

Addition of 30 mg/day mirtazapine to SSRI treatment has also been shown to reduce sexual side effects.[80]

In two randomized controlled trials evaluating the addition of the 5-HT1A partial agonist buspirone to SSRI treatment, was found to reduce the incidences of SDs,[81,82] whereas the addition of cyproheptadine, a 5HT2C receptor antagonist, and ginkgo biloba to the treatment did not significantly improve sexual side effects.[68]

In summary, the decision on which of the five suggested intervention strategies presented above to choose should be made on a completely patient-specific basis. The appropriate strategy should be selected by taking into consideration many factors, such as the degree of distress caused by sexual side effects, the presence of drug-related other side effects, the duration of treatment, and the patient's comorbid diseases. The patient should be informed about possible intervention strategies and included in the decision-making process. This aims to increase the patient's compliance with treatment. In questioning and monitoring SD due to SSRI use in patients, it is recommended to use scales that evaluate sexual function in detail such as international erectile dysfunction index and sexual function questionnaire.[68]

CONCLUSION

In conclusion, due to their effectiveness, safety and cost-effectiveness, SSRI drugs are among the most important and first choice drugs in the treatment of many psychiatric diseases, especially depression. As summarized above, current literature indicates that SSRI-induced SD is quite often. Since waiting for a recovery without amending drug regimen can negatively impact treatment compliance, it is crucial to address SD side effects proactively. The recommended options to control the undesirable side effects are waiting for SD to resolve spontaneously, reducing the dose of SSRI used, changing the medication, trying to reduce the side effects with a drug holiday or add-on treatment. Each intervention strategy should be tailored individually to the patient, considering the benefit they derive from their current treatment, the degree of remission, and any coexisting medical conditions.

Finally, current information in the literatue highlight the importance of actively inquiring about possible sexual side effects in order to detect probablre SDs. Understanding the molecular basis of sexual side effects caused by SSRIs is also highly important for the development of new drugs and treatment strategies in this area.

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All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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